

THE WOMEN'S INTERAGENCY HIV STUDY

SECTION 42: FRAILTY PROTOCOL

A. STUDY PURPOSE

With the advent of successful antiretroviral therapy (ART), HIV-infected women are surviving into old age. In women without HIV infection, aging and aging-related events such as menopause, are marked by an increasing inflammatory state, changes in hormone levels, accelerated loss of muscle mass, and relative and/or absolute increases in fat mass. These changes ultimately lead to clinical features of musculoskeletal senescence – often called frailty. In the Women's Interagency HIV Study (WIHS) we found a high prevalence of frailty, a form of physical vulnerability, even in mid-life, at average age 39 years (17% HIV+, 10% HIV-). **We therefore hypothesize that 10 years later, frailty will have increased with age.** Alternatively, prevalence could have dropped due to better control of HIV infection and adherence to medications. As select physical function measures are now part of WIHS Core measures, we can track potential changes in frailty prevalence, frailty onset, and fluctuations in the frailty phenotype (e.g., severity).

B. SPECIFIC AIMS

Specific Aim 1: To implement select physical function assessments as part of the core WIHS visit once per year to assess prevalence, incidence and fluctuation of frailty according to the Fried criteria.

C. HYPOTHESES

Hypothesis 1: Women with HIV infection will experience a higher prevalence of frailty (Fried frailty score, 3-5), compared to women without infection.

Hypothesis 2: The cross-sectional prevalence of frailty will increase as women age.

D. RESEARCH DESIGN AND METHODS

1. STUDY DESIGN

The proposed is an addition to the WIHS Core protocol, and is a longitudinal study of all WIHS women, aged 40 years and older at Visit 43.

Approximately 2/3 of participants from each site should be HIV-positive and 1/3 HIV-negative, which would provide us with approximately 1700 WIHS participants for analysis at Visit 43.

2. INCLUSION CRITERIA

All WIHS participants age 40 years and older at Visit 43 at each site are eligible. Inclusion criteria include:

- Enrollment and participation in the WIHS core study at all WIHS sites
- Age 40 years or older at visit 43

3. EXCLUSION CRITERIA

There are no specific exclusion criteria for this component of the Core protocol. However, if women are not able to perform some or all of the physical function assessments, the reason/s for this should be noted on the *Functional Performance Tests (PBM)* data collection form. Each participant should complete as many of the frailty assessments as possible.

4. SCHEDULING THE FRAILTY ASSESSMENT

Women will complete the frailty assessments as part of their core WIHS visit. The frailty measures should take up to 10 minutes.

E. FUNCTIONAL PERFORMANCE TESTS

1. OVERVIEW

WIHS participants will be compared by HIV-status on their Fried Frailty Index (FFI) score. Strength will be assessed in both the lower extremities (Repeated Chair Stands) and upper extremities (Grip Strength). Lastly, walking speed will be assessed with a 4-meter walk test. The battery of tests that tap into the risk dimensions described above was selected based on the 2005 Fried frailty protocol (Terzian 2005) and updated (chair stands) with the assistance of Dr. Michael Yin based on his experience in the Musculoskeletal (MSK) substudy in the WIHS. Operationalization of the FFI, for calculation of a score, is done in agreement with the Male AIDS Cohort Study (MACS). The approximate time for completion of the physical components of the FFI components is approximately 10 minutes. The following battery of tests may be performed in any order at any point during the Core WIHS visit:

1. Repeated Chair Stands
2. Grip Strength
3. 4-meter walk

a. Rationale of performance based assessments

Direct assessment of physical performance has become standard practice in epidemiologic observational studies of health and disease processes. The most commonly used assessments were initially designed to differentiate function in older adults,^{1,2} but modifications in administration and scoring³ can improve the utility of these assessments to discriminate meaningful differences and change in functional capacity in most middle-age persons. Although the measurement ceiling of these tests may be low for young and some middle-age adults (i.e., they can easily achieve the maximum possible performance on all tests), repeat assessment following standardized procedures over subsequent visits can aid in identifying the approximate point at which meaningful loss of functional capacity begins to emerge.

The physical function assessments that are included in the Fried Frailty Index were originally implemented in the WIHS in 2005. The test battery is commonly administered and has demonstrated reliability and predictive validity in older adults.²⁻⁶ The number of repeated chair stands is increased from 5 to 10, as has been done in a few other studies^{7,8} and is currently being done as part of Dr. Michael Yin's MSK Study at 3 WIHS sites. By taking a split time after 5 completed chair stands, comparability with previous batteries will be maintained.

b. Safety Issues

The vast majority of participants should be able to attempt each performance test. Walking aids may not be used for the chair stand test. Exclusion from any performance test shall be based on examiner assessment or participant concerns that the test would be unsafe. In the latter case, the examiner should describe the test and discuss with the participant his/her specific concerns about attempting the test including physical problems and known disabilities. Refusal, reason for not attempting a test, or inability to perform a test should be recorded on the *PBM* data collection form (see instructions below).

The detailed protocols describe how to administer the tests safely, including instructions on how to support the participant, if required. The examiner should be ready to place both hands on the participant to stabilize her if necessary. If the participant loses balance, the examiner should grab/catch the participant with both hands at the trunk to stabilize her.

If the participant begins to fall, the examiner should reach under the participant's shoulders from behind and slowly ease her down to the floor, rather than try to catch the participant while standing still. This strategy should protect both the participant and examiner from injury. If the participant falls and is not injured, the examiner should have the participant get on her knees or on all fours, place a chair next to the participant, and have the participant support herself on the chair as he/she helps lift the participant under the shoulders. The examiner should not try to lift the participant from the floor by him/herself.

c. Participant and Exam Space Preparation

- Footwear: To reduce effects of different footwear on test performance, the participant should wear tennis shoes or comfortable walking shoes with minimal or no heels. The participant may perform the tests in stocking or bare feet if appropriate footwear is not available.
- The standard chair should be placed on a non-skid surface (e.g., low pile carpeting) with the back of the chair against a wall for stability. There should be adequate room in front and on the sides of the chair for the examiner and participant to move freely. The chair selected for this aspect of the frailty assessment can support 1000 pounds.

d. General Instructions

Since motivation and level of understanding can have a significant impact on performance, each component of the exam should be administered strictly according to the protocol and in the following sequence:

- Explain the procedure to the study participant making sure to convey key points from the suggested script.
- Demonstrate the procedure using the suggested script.
- Ask the participant if she has any questions.
- Re-explain the procedure briefly using the suggested script.
- Ask the participant to perform the procedure.
- Begin all timed procedures with the words, ***“Ready? Go!”***

Use the script provided to assure that all key points are covered when you describe each test and how to perform it properly. Do not provide additional description or encouragement beyond the key points provided by the standard scripts.

Demonstrate each maneuver correctly. Experience has shown that participants follow more closely what the examiner does rather than what he/she says. If the participant indicates she does not understand the test maneuver, demonstrate it again rather than solely relying on repeating the verbal instructions.

Limit practice trials for each test to those described in the individual measurement procedures.

Allow the participant to rest between tests if out of breath or fatigued during the assessments. If a test is not attempted because the participant refuses or cannot understand the instructions, record "participant refused." If you or the participant considers the test unsafe, record "Not attempted/unable" on the data form. If a test is attempted, but cannot be completed or scored, record reason under "Other" on the form.

e. Equipment and Supplies

- 1) Digital stopwatch (repeated chair stands, walk test)
- 2) Tape (walk test)
- 3) Flash Furniture Elegance Stacking Chiavari Chair in Black (approx. \$50)
Material: Resin
Seat Size: 15.5"W X 16"D. Back Size: 13.5"W X 19"H. Seat Height: 17.75"H.
Overall Dimension: 15.75"W x 18.5"D x 36.5"H. Shipping Weight: 10 Lbs.
<http://www.amazon.com/dp/product/B00D9E00T0/?tag=fbhp-20>
- 4) Jamar dynamometer Model 5030J1 (grip strength)
- 5) Measuring tape (walk test)

f. Recording Results and Scoring

Results for all functional performance tests should be captured on Form *PBM*, and scoring of results will be calculated centrally.

2. PERFORMANCE TESTS

a. Repeated Chair Stands (note: the required chair has no arms and is not cushioned)

This is a test of lower extremity strength in which the participant stands up from a seated position ten times as quickly as possible. The time it takes to stand five times and ten times is recorded.

If the participant can arise from the chair without having to help oneself using arms, attempt ten stands.

- a) Explain the test.

Script: "In this test, I want you to stand up ten times as quickly as you can, keeping your arms folded across your chest." "When you stand up, come to a full standing position each time, and when you sit down, sit all the way down each time. I'll demonstrate two chair stands to show you how it is done."

- b) Demonstrate the test.

Cross your arms over your chest and then rise two times as quickly as you can, counting as you stand up each time.

- c) Begin the test

Script: "When I say 'Go' stand ten times in a row, as quickly as you can, without stopping. Stand up all the way, and sit all the way down each time.

Ready? Go!"

Start timing as soon as you say "Go." Count: "1, 2, 3, 4, 5, 6, 7, 8, 9, 10" as the participant stands up each time. After the participant stands up for the fifth time,

glance at the time and depress the split button on the stopwatch (see instructions on stopwatch in **Appendix B**).

- d) If the participant is unable to complete the chair stands correctly (e.g., is not coming to a full stand), stop the procedure, repeat the demonstration, wait 1 minute, and begin the procedure again.
- e) If the participant stops before completing five stands, confirm that she cannot continue by asking:

Optional script: ***“Can you continue?”***

If she says yes, continue timing. Otherwise, stop the stopwatch.

- f) If the participant stops before completing ten stands, confirm she cannot continue by asking:

Optional script: ***“Can you continue?”***

If she says yes, continue timing. Otherwise, stop the stopwatch.

- g) Scoring:

If the participant refuses to do the test or cannot understand the instructions, score “participant refused.”

If the procedure was not attempted because the participant was unable to perform the test, score “Not attempted/unable.”

If participant attempted but was unable to complete five stands without using her arms, score as “Attempted, unable to complete five stands without using arms” and record the number completed without using arms (Question C4).

If five chair stands were completed, record the number of seconds, to a hundredth of a second, required to complete five stands (Question C2).

If participant completed five stands but was unable to complete ten stands without using her arms, score as “Attempted, unable to complete ten stands without using arms” and record the number completed without using arms (Question C5).

If ten chair stands were completed, record the number of seconds, to a hundredth of a second, required to complete ten stands (Question C3).

b. Grip Strength



The grip strength examination is used to test how strong the participant's hands are. We will be using the same Jamar Dynamometer and the same protocol utilized at each WIHS site in 2005.

a) Tester Instructions: The key points.

- The participant should be seated in an armless chair (e.g., the one used for chair stands)
- Her elbow should be bent at a 90 degree angle
- The dynamometer should be set at "2" strength for testing of all participants.
- Do not allow the participant to squeeze the dynamometer before testing.
- The tester must coach the participant by saying "**squeeze, squeeze, squeeze**" while the participant is squeezing.
- Tell the participant to stop when you see the arrow starting to go down.
- Record the results of each trial before the next attempt.
- Repeat the examination three times in the dominant hand.

b) Preparation

Participants with one or more of the following conditions that affect their DOMINANT HAND should not be tested: Do NOT switch to the other hand:

- Acute flare-up of wrist/hand; for example, arthritis, tendonitis or carpal tunnel syndrome.
- Less than 13 weeks after surgery for fusion, arthroplasty, tendon repair or synovectomy of the upper extremity.
- If the technician has concerns that this test may exacerbate symptoms of heart disease (e.g., angina), the situation should be investigated. Ask the participant if she is currently having symptoms from heart problems. This does NOT exclude the participant from the grip strength test. Local procedures may be developed in this situation to assure safety for the participant.

Use the following questions to assess whether the participant can complete the Grip Strength Test.

Script: *“In this exercise, I am going to use this instrument to measure the strength in your dominant hand. I will ask you a few questions first”*

1. *“Have you had recent worsening of pain in your wrist or any acute flare-up in your dominant?”*
2. *“Do you think you could safely squeeze this as hard as you can with your dominant hand?”*
3. *“Have you had any surgery on your hands or arms during the last 13 weeks?”*

In subsequent tests, perform the hand grip test only on the dominant hand that was established at her first test.

c) Testing

Script: *“I’d like you to take your dominant arm, bend your elbow at a 90-degree angle, press your arm against your side and grab the two pieces of metal together like this.”*

Examiner should demonstrate at this point.

Script: *“When I say ‘squeeze,’ squeeze as hard as you can. The two pieces of metal will not move but I will be able to read the force of your grip on the dial. I will ask you to do this three times. If you feel any pain or discomfort, tell me and we will stop.”*

Examiner should demonstrate at this point.

d) Performance and Scoring

Face the participant and squeeze the dynamometer so that the participant can see the dial rotate.

Script: *“Now you should bend your elbow at a 90-degree angle, press your arm against your side and grip the two pieces of metal with your dominant hand. Your wrist should be straight. Ready? Go! Squeeze, squeeze, squeeze!”* (Tell the participant to “**stop**” when the arrow starts going down.)

Record whether or not the grip strength test was completed. If unable, indicate why she was unable to complete the grip strength test and STOP TESTING. If attempted, but unable physically, STOP TESTING.

Record the strength for the **first** attempt in kilograms (Question D6). The Dynamometer should be read at eye level. Round down to the nearest line on the dynamometer (will always be an even number). Be sure to set the dynamometer dial to zero prior to each attempt. A minimum of three attempts with the dominant hand must be made. Record the strength for the **second** attempt in kilograms (Question D7). Record the strength for the **third** attempt in kilograms (Question D8).

c. 4-meter walk test

a) Preparation

The walking course for the 4-meter walk test should be marked out in advance of the participant’s test in an unobstructed corridor long enough (ideally 7-8 meters

in length) such that the participant won't inadvertently slow her pace because of a wall close to the end of the walk. Using the measuring tape, place pieces of tape 4 meters apart. Participants needing to use a walking aid, or with prosthetics, are excluded from participating in the 4-meter walk. Participants should be asked to wear comfortable footwear (sneakers, comfortable walking shoes) and not footwear that impedes their walking (high heels).

b) Explain the test

Script: ***"In this test, I would like you to walk at your usual pace from this line (or cone) to the line at the end of the hall. Do you think you could do that? Good. Can you see the tape? Good. To do this test, place your feet with your toes behind, but not touching, the line (cone) where we start. I will time you. We will do this two times. Let me demonstrate what I want you to do."*** (Demonstrate for the participant.)

Script: ***"When I say 'Ready, go!' walk at your usual pace to the line. I will walk with you."***

c) Performing the Test

When the participant is properly at the starting tape, say **"Ready, go!"** and start the stopwatch as the participant begins walking; keep the stopwatch behind the participant so she can't see it. Your arm can provide support if the participant loses balance. Stop the stopwatch when the participant's first foot is completely across the finish line.

The participant will then be asked to perform the measured walk a second time.

Script: ***"Now, I'd like you to try this test a second time. When I say **'Ready, go!'** walk at your usual pace to the line. I will walk with you."***

When the participant is properly at the line, say **"Ready, go!"** and start the stopwatch as the participant begins walking; keep the stopwatch behind the participant so she can't see it. Your arm can provide support if the participant loses balance. Stop the stopwatch when the participant's first foot is completely across the finish line.

The participant will be allowed only two attempts at completing the measured walk unless there is external influence that interrupted her during the walk. For example, if the participant trips on her own during the first attempt, it will be recorded as such on the data form and she will then go on to perform her second attempt. However, if during either of her attempts, she trips due to interference from another person, she may repeat that attempt.

Record the time in seconds (rounded to the first decimal point) of the two trials on the data form. Please see **Appendix B** for instructions on how to use the Stopwatch for this test. If the participant did not attempt or complete the trial, record the reason.

3. QUALITY ASSURANCE

The examiner requires no special qualifications or experience to perform this assessment. Training should include:

1. Read and study Manual of Operations.
2. View training video (available on WIHS Administrative website).

3. Attend WIHS training session on performance test administration techniques (or receive training by experienced examiner).
4. Practice on at least two other staff or volunteers.
5. Discuss problems and questions with local expert.
6. The primary examiner/trainer for each WIHS site will be certified by WDMAC before starting the study and re-certified yearly (below). After certification, the primary examiner/trainer can train and certify other examiners at his/her site.
7. Re/certifications should occur each year prior to the visit at which the frailty assessments are conducted so that all staff are re/certified in time for the start of the visit.

4. CERTIFICATION REQUIREMENTS

1. Complete training requirements.
2. Primary examiner: Conduct exam on two volunteers, according to protocol. A **video** of the performance of the full battery of performance measures (repeated chair stands, grip strength, 4-meter walk) should be recorded on two volunteers by each primary examiner. The video should be recorded by site staff on low resolution and sent to WDMAC by site staff. The performance video will be reviewed and comments provided. Videos should be sent to Christine Alden at WDMAC. They can either be emailed to calden@jhu.edu, or mailed on CD/DVD to:

Christine Alden
 JHSPH, Department of Epi
 111 Market Place, Suite 906
 Baltimore, MD 21202

The certified primary examiner at each site should be the trainer for other examiners at the site. He/she at each site can certify other examiners by evaluating performance of tests by the trainee on two participants or volunteers. Certification will be achieved by successful demonstration of the tests as documented on QC checklists.

3. An annual recertification of the primary examiner that will be performed through uploading a video of the functional performance tests on one subject for WDMAC review.

The primary examiner will recertify other examiners at his/her site on an annual basis by evaluating the performance of tests on one participant or volunteer; annual recertification will be achieved by successful demonstration of the tests as documented on a QC checklist.

Quality Assurance/Certification Checklists are in the **Appendix A**.

5. FRAILTY

A phenotypic assessment of frailty (Fried) has been implemented in many studies of aging in the general population^{9,10} as well as in the MACS^{11,12} and WIHS¹³. It consists of five components:

1. **Physical shrinking:** Defined as unintentional weight loss of ≥ 10 lbs lasting more than one month since last visit, using core WIHS self-reported data from Form 22/22HX, variable name SYWLMH.

2. **Poor endurance and energy:** This will be measured by self-report of 'health keeping her from working past 4 weeks all or some of the time' from Form 26, variable name HWRKPS.
3. **Low physical activity level:** Defined as 'health limiting vigorous activities' self-reported from Form 26, variable name VACTPS.
4. **Slowness:** This will be measured by the time to walk 4 meters, adjusted for standing height.
5. **Weakness:** Defined as grip strength in the lowest 20% at baseline, adjusted for gender and body mass index. Handgrip strength will be measured by a hand dynamometer such as the JAMAR dynamometer (Model BK-7498, Fred Sammons Inc, Brookfield, IL). Grip strength will be measured three times for the participant's dominant hand only. The best measure in the dominant hand will be used.

Frailty will be calculated during analysis based on data collected during the WIHS visit.

APPENDIX A: Quality Assurance/Certification Checklist

1. Chair stands

- Back of chair against a wall
- Script correctly and clearly delivered
- Correctly demonstrates single stand, emphasizing keeping arms tight across chest
- Correctly demonstrates two stands, emphasizing full stand and return to complete sit
- Says "**Ready? Go**" for each test
- Counts each chair stand, takes a split time after participant stands upon the fifth stand and records final time after participant stands up on the tenth stand
- Records and explains unusual values
- If task was not performed, codes and explains reasons

2. Grip Strength

- Participants properly positioned
- Script correctly and clearly delivered
- Correctly demonstrates measurement technique
- Says "**Ready? Go**" for each test
- Has participant maintain proper positioning during 3 attempts
- Records and explains unusual values
- If task was not performed, codes and explains reasons

3. 4-meter walk

- Script correctly and clearly delivered
- Toes touching start line
- Time stopped with first footfall over finish line
- Records and explains unusual values
- If task was not completed, codes and explains reasons

APPENDIX B: How to use Stopwatch

You will use an Oslo/Robic 30 lap memory stopwatch.

A: LAP/RESET
B: RECALL
C: MODE
D: START/STOP
E: EL LIGHT



Press button **C** to go into lap mode (the word lap should be visible on the left upper corner of the LCD screen)

- A. For the **Chair Stand Test**, you will use a lap measurement to get time to completion of the fifth chair stand and the tenth chair stand.
1. To start measurement, press **D** once, and say "GO."
 2. When participants stands up for the **fifth** time, press **A** once.
 3. When participant stands up for the **tenth** time, press **D** once.
 4. Record the time to completion of five stands by recording the split for lap 1. Press **B** (small round black button) once until the lap number in the parentheses in the left upper corner of the LCD screen reads 1. Record the time on the upper line of the display.
 5. Next record the time for completion of 10 stands. Press **B** again, and the lap number should read 2. Now record the time on the lower line of the display, this is the cumulative time, which represents the time from start to the completion of 10 stands.
 6. Once you have recorded all the information, you can reset the stopwatch and erase the lap memory by pressing **B** once then **A** once.
- B. For the **4-meter walk**, you will use a simple time measurement.
1. To start measurement, press **D** once, and say "GO."
 2. At the first footfall past the 4 meter line, press **D** again.
 3. Record time on lower line of display.
 4. To reset timer, press **A** once.

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