Assessment of geriatric syndromes and physical function in people living with HIV

Meredith Greene, Amy C. Justice, and Kenneth E. Covinsky

ABSTRACT
As the number of older adults living with HIV continues to increase, understanding how to incorporate geriatric assessments within HIV care will be critical. Assessment of geriatric syndromes and physical function can be useful tools for HIV clinicians and researchers to help identify the most vulnerable older adults and to better understand the aging process in people living with HIV (PLWH). This review focuses on the assessment of falls, frailty, and physical function, first in the general population of older adults, and includes a specific focus on use of these assessments in older adults living with HIV.

Overview of geriatric syndromes
With advances in antiretroviral therapy, HIV has transformed into a chronic illness. As a result, people living with HIV (PLWH) are living substantially longer. As the population of PLWH ages, many are facing increased medical complexity including multiple chronic conditions or multimorbidity, polypharmacy, and significant psychosocial challenges including mental health conditions and isolation. With this increasing complexity, clinicians and researchers need tools to help identify the most vulnerable older adults who may need the most resources as they age. Drawing on assessments used in geriatrics and gerontology, assessment of physical function and geriatric syndromes could help to better define aging trajectories in older adults living with HIV. Understanding how to assess for these conditions is critical given the increasing numbers of older adults living with HIV in the US and worldwide. The focus of this review is on the assessment of geriatric syndromes and physical function and how these assessments may be applied to HIV settings. Although a brief overview of geriatric syndromes is included, this review will focus on the specific geriatric syndromes of falls, frailty and assessment of physical function as these have been most studied in HIV.

Methods: PubMed was searched for articles using terms “geriatric syndrome,” “frailty,” “falls,” “physical function,” “functional status” with limits of aged, middle aged, aged 80 and older with and without addition of “HIV” search terms. Searches were also conducted pertaining to specific assessments such as VACS index. Additionally, key articles and references pertaining to geriatric syndromes in the general population and key articles pertaining to HIV and geriatric syndromes known to the authors were also included.

The term “geriatric syndrome” itself is often confusing, in part because of multiple definitions used and the distinction between traditional medical syndromes and geriatric syndromes. In an attempt to standardize the definition of geriatric syndromes, a 2007 paper by Inouye et al defined geriatric syndromes as “multifactorial health conditions that occur when the accumulated effects of impairments in multiple systems render [an older] person vulnerable to situational challenges.” The key distinction with geriatric syndromes is the multifactorial etiology; this is the opposite of the traditional medical syndrome, defined as a collection of signs and symptoms stemming from a single etiology. Rarely can one identify a single cause for a geriatric syndrome; the multiple deficits can occur from impairments in different organ systems as well as social and environmental factors. Classic examples of geriatric syndromes include falls, urinary incontinence, frailty and delirium. General texts of geriatrics include additional syndromes such as dizziness, sleep disorders, pressure ulcers, and syncope. Cognitive impairment and dementia, malnutrition, sensory impairment (hearing and vision), gait disorders, depressive symptoms, elder mistreatment and osteoporosis have also been considered geriatric syndromes.

ARTICLE HISTORY
Received 29 April 2016
Revised 20 September 2016
Accepted 1 October 2016

KEYWORDS
aging; disability; falls; frailty; geriatric syndrome; HIV
Geriatric syndromes often share risk factors such as specific medication use (e.g., sedative hypnotic medications contributing to falls and delirium), cognitive impairment, as well as gait and sensory impairment. In one study, both upper and lower extremity impairment, sensory impairment (hearing and vision impairments) and affective impairment (high depression or anxiety scores) were associated with falls, urinary incontinence and functional dependence. In a review of geriatric syndromes, older age, baseline functional impairment, as well as cognitive and mobility impairments were risk factors found to be common to 5 geriatric syndromes. Fig. 1 illustrates the multifactorial nature of geriatric syndromes and shows how these conditions can share risk factors.

In addition to having potential shared risk factors, geriatric syndromes tend to co-occur and are interrelated. Falls contributing to functional decline and cognitive impairment contributing to falls and urinary incontinence illustrate how syndromes can be interrelated. Another example is the scenario when an individual with mobility impairment rushes to get to the bathroom due to urinary incontinence and falls. The reality is that the relationship between syndromes is complex and intertwined.

**Importance of geriatric syndrome assessment and relevance to HIV**

The first argument for assessment is the increasing complexity of medical care for older adults living with HIV. The focus of health care for the aging population with HIV is no longer focused on HIV alone but rather on HIV and other chronic conditions, including HIV-associated non-AIDS (HANA) conditions such as liver, renal and cardiovascular disease as well as certain types of cancers. PLWH often face multiple comorbid conditions, or multimorbidity and patterns of multimorbidity among PLWH may be influenced by duration of HIV infection, obesity, degree of immunosuppression, substance use and other factors. Yet assessment of comorbidities alone does not reflect the entirety of the aging process. Two people with the same exact comorbid conditions can have very different aging trajectories. In the general population of older adults, geriatric syndromes and measures of physical function are more predictive of self-reported health and mortality than diagnoses of chronic diseases alone. Geriatric syndromes also predict healthcare utilization, including nursing home placement, and mortality. Assessment of physical function and geriatric syndromes could serve as a better marker of the cumulative impact of HIV and both HIV related and non-related comorbidities.

Second, although geriatric syndromes may typically be thought of as conditions occurring in persons aged 65 and older, geriatric syndromes can identify vulnerability at younger ages. In addition to those living with HIV, geriatric syndromes have been identified in middle aged (50s) adults living with complex chronic illness like diabetes and dealing with complex social issues such as homelessness.

To further illustrate how assessment of geriatric syndromes and other elements of geriatric assessment can help identify vulnerability in PLWH, take the example of Mr. X and Mr. P. Mr. X is a 60 y/o male, living with HIV for 10 years, virally suppressed, who also has diabetes, COPD and coronary artery disease. Mr. P is a 62 y/o male, living with HIV infection for 12 years, also virally suppressed who has the same exact comorbid conditions. Both acquired HIV through sex with other men. However, Mr. X walks 1 mile daily with his dog and lives independently while Mr. P cannot walk as far as he used.

![Figure 1](image-url). Geriatric Syndromes are Multifactorial and Share Risk Factors. Causes of geriatric syndromes include multiple etiologies such as physiologic changes that occur with aging, specific disease states, medications, and the environment. Figure 1 shows shared risk factors (bolded) of 2 geriatric syndromes falls and urinary incontinence and highlights the multifactorial etiologies of these syndromes.
to and admits he is starting to have trouble with doing housework and even sometimes getting out of chairs. He fell 3 months ago. While they have the same exact comorbidities, they have different aging related needs.

Mr. X is beginning to have mobility and functional impairment, and the approach to the care of these 2 men should be different to help maintain their independence.

**Frailty assessment**

Frailty is generally defined as a state that puts an individual at increased risk of adverse outcomes when faced with stressors. In geriatrics and gerontology, there is no consensus on the best method to assess frailty. However, 2 main conceptual models exist which relate to assessment methods. One conceptualizes frailty as a distinct process defined by deficits in multiple physiologic systems referred to as the “Phenotypic definition” and the other emphasizes a state of vulnerability, conceptualizing frailty as the accumulation of multiple health deficits referred to as the “Cumulative Deficits Model.”

Many different assessment tools exist, which differ by focus on specific domains including whether the focus is on physical frailty domains (often includes the phenotypic definition) or includes social (e.g., loneliness) and psychological (e.g., depressive symptoms) frailty domains. Some frailty scales include physical measurements, such as the Fried frailty phenotype, while others are based solely on self-report, such as the Tilberg Frailty Index. The phenotypic model developed by Fried et al in the Cardiovascular Health Study (CHS) and the Cumulative Deficit Model developed by Rockwood et al in the Canadian Study of Health and Aging (CSHA) have the most data and will be the focus here.

The Fried model includes 5 components with biological basis: 1) shrinking (e.g., baseline unintentional weight loss of 10 or more lbs.), 2) weakness (grip strength), 3) poor endurance and energy (self-report from CES-D) 4) slowness (gait speed) 5) low physical activity (kcal expended based on Minnesota Leisure Time Survey). The presence of 3 of the 5 components is considered frail and 1 or 2 components pre-frail. Cut points were defined using the lowest 20% of measurements for grip strength and gait speed, and the lowest quintile of physical activity, per gender. The use of this model has been widespread, although one challenge is that many survey based studies do not collect gait speed and grip strength. As such, large cohort studies have tried to find ways to capture the frailty phenotype through self-report as opposed to objective measurements. Many argue that a cognitive domain should be added to the frailty phenotype and data suggest that including cognitive impairment improved predictive validity of the phenotype.

The Fried index developed by Rockwood et al can include up to 75 components, but needs to include at least 30 for best validity. This index measures cumulative burden of health deficits including diseases, symptoms and disability which must incorporate different domains (e.g. cognitive, physical health). Each item is scored 0 (absent) or 1 (present) and then a summary score is created between 0 and 1, often with cutoffs of 0.20 or 0.25 used to distinguish frailty. This model has also been frequently utilized, although the number of items required for inclusion could be challenging to assess. Both assessment tools are valid ways of measuring frailty, with some degree of overlap, although may identify slightly different subgroups of older adults as was seen in a study of HIV-negative older adults which compared frailty measurements. Discussion of standard definitions of frailty and assessment tools is an ongoing area of research.

**Frailty assessment in PLWH**

The Fried phenotype definition of frailty has been the most commonly used assessment of frailty among PLWH. Many of the large cohort studies including MACS, WIHS, ALIVE and VACS have utilized a modified version of the frailty phenotype relying on self-report measures and in some cases excluding weakness as one of the components. Importantly, these studies demonstrated that frailty occurs at higher rates and younger ages in PLWH compared to HIV-negative persons and demonstrated criterion validity through prediction of mortality and progression to AIDS. Only one study from Italy has examined a frailty index as originally conceived by Rockwood et al. The frailty index utilized consisted of 37 items including lipodystrophy, BMI, polypharmacy, and biomarkers and was shown to predict mortality and incident multimorbidity. The authors also examined indices which added HIV related variables and comorbidities, but found the indices performed similarly.

In addition to the phenotypic and cumulative deficits models of frailty, the VACS index has also been proposed as a tool to assess the level of physiologic frailty or cumulative organ system injury in PLWH. The VACS index includes routine clinical HIV and general organ system biomarkers as well as age and has been shown to predict mortality and hospitalization, among other outcomes and has been shown to predict outcomes in HIV-negative populations as well. Its relevance as a frailty index includes its association with biologic markers of inflammation and frailty such as IL-6, d-dimer as well as associations with neurocognitive performance, functional performance, and an ability to predict...
Table 1. Frailty assessment in older adults with HIV.

| Frailty Measurement: |
|----------------------|
| Frailty Phenotype     |
| Frailty Index         |
| VACS Index            |

**Components:**
- 5 Criteria:
  1. Shrinking (Weight loss)
  2. Exhaustion (self-report CES-D)
  3. Weakness (grip strength)
  4. Slowness (gait speed)
  5. Low activity (Minnesota Leisure Time Scale)

**Scoring/Criteria:**
- 3/5 criteria=frail
- 1 or 2/5 criteria=pre-frail
- Binary yes/no to each item and then generate total frailty index score

**Brief Summary Comments:**
- Model used in majority of studies in HIV; shown to predict mortality and AIDS progression
- Examined in only 1 study; shown to predict mortality and incident multimorbidity

**Items:**
- 1. Age
- 2. CD4 count
- 3. HIV viral load
- 4. Hemoglobin (anemia)
- 5. FIB-4 (liver tests, platelets)
- 6. eGFR (renal function)
- 7. Hepatitis C Co-infection

**Measurement:**
- Frailty Phenotype
- Frailty Index
- VACS Index

**Scoring/Criteria:**
- 3/5 criteria=frail 1 or 2/5 criteria=pre-frail
- Binary yes/no to each item and then generate total frailty index score

**Examine items included in HIV Frailty index: Lipatrophy, Hepatitis C co-infection, polypharmacy, low physical activity, abnormal lab values (CRP, lipids, liver tests, anemia, platelets)

**Note:** Bolded items are common items across assessments; VACS= Veterans Aging Cohort Study

Falls assessment

Different definitions of falls are utilized, although they share the components of being “unintentional,” e.g. not pushed, and involve “coming to a lower level.” For example, the Prevention of Falls Network Europe (ProFaNE) definition is “an unexpected event in which the participants come to rest on the ground, floor, or lower level.” A distinction is also made with injurious falls due to the increased impact on quality of life and healthcare utilization of these events. Less consensus exists in how to define “injurious” which may include aspects of severity of injury (e.g., bruises to fractures) as well as degree of healthcare utilization (e.g., clinic visit vs. hospital visit).

Falls are commonly measured by self-report. With new technological developments in monitors and sensors, falls may be assessed by direct measurement in the future, although the intermittent nature of falls could make measurement challenging. Self-report can be measured by simple recall such as “In the past month, have you had any fall including a slip or trip in which you lost your balance and landed on the floor or ground or lower level” or can be measured by detailed daily fall diaries. Simple recall of falls (single item question) has similar specificity but poorer sensitivity than weekly and monthly fall calendars or diaries, but the intensity of these latter assessments remains practical primarily for research settings where falls are a primary outcome. The ideal timeframe to assess with simple recall questions has been debated given concern for under-reporting of fall events. However in one study, recall of falls in a one year timeframe was better than shorter 3 or 6 month recall periods. Algorithms for fall screening and assessment in the clinical setting have been developed including a joint guideline by the American Geriatrics Society/British Geriatrics Society (AGS/BGS).
BGS), the STEADI (Stopping Elderly Accidents, Deaths & Injuries) initiative developed by the Centers for Disease Control and Prevention (CDC), and the Elderly Falls Screening Test (EFST) originally developed in Israel. Each stratifies older adults into different risk categories for falls with the highest risk groups receiving a multifactorial risk assessment including physical exam and history components to assess contributing etiologies. The initial components of the CDC and AGS/BGS algorithms are all based on self-report while the initial EFST components include direct observation of gait speed and style. All three tools include assessment of balance and gait which are key risk factors for falls.

**Falls assessment in PLWH**

Few articles have described falls and risk factors in PLWH. Studies have focused on fractures, although not all of these may be attributable to falls. Traditional assessment of falls should also be relevant to PLWH, although as associations with antiretroviral history and adherence have been seen with falls, inclusion of these more HIV specific factors as potential contributors to falls should be considered. Guidelines for clinical care of PLWH have recommended screening for osteoporosis at earlier ages (age 50 and older), and screening for falls at this age should also be considered.

**Physical function assessment: Assessment of functional limitations and disability**

The disability process is often conceptualized as the following: a pathology or injury leading to impairment leading to functional limitation leading to disability. For example, a trauma or injury to the arm causes an impairment in one of the arm muscles, which leads to a functional limitation of inability to fully extend the arm, causing disability in being able to perform specific job or basic self-care tasks. In reality, distinctions as in this example are not always so clear and often assessments can include elements of both functional limitations and disability. Functional limitations are sometimes described as “limitations at the level of the person” and disability as “limitation in tasks at the level of the environment.” Disability specifically involves the interaction with the individual and the environment; it requires environmental demands that cannot be met by the individual’s intrinsic capabilities. Both can be measured by objective and subjective (or self-report) assessments. Self-report and objective assessments are considered complementary and both have been shown to predict outcomes although may not always measure the same physical function constructs. Depression can affect self-report of disability although the use of objective measurement of functional limitations also demonstrated a relationship between depressive symptoms and functional decline.

Measurement of functional limitations may identify earlier opportunities to intervene to prevent progression to disability. Examples of both subjective and objective measurements are listed in Table 2 but can include measurements of single movements (like reaching for object) or more complicated, coordinated movements like gait speed, as well as tests of balance and strength. Another example is the Short Physical Performance Battery (SPPB), developed by the National Institute on Aging (NIA), which measures lower extremity physical function, including balance, chair stands and gait speed. While these are all examples of objective assessments, self-report of functional limitations are also utilized.

| Examples of Functional Limitation Assessments | Examples of Disability Assessments: |
|---------------------------------------------|-----------------------------------|
| Self-Report: Individual questions about reaching, pulling, kneeling | Self-report of ADL, IADL* |
| Self-Report: Late life Function and Disability Instrument | Performance ADL test |
| Chair rise | Cess study test |
| Gait Speed | |
| Get Up and Go Test | |
| Short Physical Performance Battery (SPPB) | |
| Functional Reach Test | |

**Examples of Questions Used to Assess Difficulty with ADL, IADL:**

- Because of a health or memory problem, do you have difficulty with...? If yes, followed by yes/no question about help with activity (to assess dependence)*
- By yourself, without help from another person or special equipment, do you have any difficulty with...? “If yes, “How much difficulty do you have?” “A little, some, a lot, Not able to do at all”
- Because of a physical or mental health condition, [do you] have difficulty doing any of the following by yourself? (yes/no response)*

**Considerations when Assessing Functional Limitations and Disability in PLWH:**

In more middle aged populations:

Functional Limitation Assessments can detect earlier spectrum of disability; can modify many assessments to avoid ceiling effects Ask about “difficulty with” ADL and IADL, instead of focusing just on “dependence”

Note: ADL = Activities of Daily Living, IADL = Instrumental Activities of Daily Living

For some measurements, context is critical as can measure both functional limitations and disability

*Health and Retirement Study (HRS), http://hrsonline.isr.umich.edu; Women’s Health and Aging Survey (WHAS) ADL questions; IADL questions similar to HRS, http://coah.jhu.edu/research/projects/whas_i.htm; Survey of Income and Program Participation (SIPP), https://www.census.gov/sipp/
Selecting the test depends on the desired measurements and goals of assessments including correlations with upper extremity or lower extremity tasks, measuring strength, or needing a more integrated assessment like gait speed. Measurements of functional limitations have the advantage of being more sensitive to higher functioning individuals compared to disability measurements. Functional limitation measures can be analyzed as predictors of outcomes including full disability, nursing home placement, or mortality, or analyzed as a more proximal measure of disability.

For assessment of disability, the classic method in the geriatric literature is by self-report of difficulty with Activities of Daily Living (ADLs) and Instrumental Activities of Daily Living (IADLs). ADLS (sometimes also called BADLs) are basic tasks required for self-care like bathing and dressing while IADLs are tasks like shopping and managing medications. As disability can also occur in settings of hobbies, volunteer work and occupational tasks, assessment may also extend to these tasks, known as Advanced Activities of Daily Living. Although historically geriatrics has focused on ADL dependence because of its relationship with nursing home entry, disability, especially in more middle aged persons, should not be assessed solely by asking about “dependence” or “help with” activities alone. Instead, it can be assessed by asking about “difficulty with” each activity either as degree of difficulty (none, some, a lot, or unable to do activity) or a dichotomous question of “any” difficulty. Examples of how large gerontologic studies ask about disability are listed in Table 2. The reality is that assessment of disability is nuanced and asking about modifications (adaptive equipment) in the environment, as well as confirming motivation and traditional roles (e.g. older men may have never cooked) will provide more detailed assessment. Similar to functional limitation measurements, both objective and self-reported measurements of disability with ADLs and IADLs can be used (Table 2); although direct observation of tasks like filling a medication set or watching someone prepare a meal are time consuming and may not be practical for all clinical settings. However, observing someone unbutton a coat or get out of a chair in an exam room can provide objective data on ADLs within the usual length of a clinical visit.

### Functional limitations and disability assessment in PLWH

Both functional limitations and disability assessments have been utilized in PLWH. Terminology is important; as disability has sometimes been used interchangeably with frailty in the HIV literature as well as aging literature; an issue that has been discussed by Erlandson et al. Although some studies in HIV utilize the classic geriatric assessment of asking about ADLs and IADLs to assess disability, other studies utilize questions from MOS-HIV or SF-36 which include self-report of functional limitations and disability. Different methodology utilized can make comparisons between studies difficult. While self-report of functional limitations are included in questionnaires like the MOS-HIV utilized by many studies, recent emphasis has focused on objective assessments of gait speed, grip strength, chair stands, and the Short Physical Performance Battery (SPPB). The SPPB in particular has been used in multiple cross sectional studies and was recently shown to predict mortality.

Given the relatively younger age of older populations of PLWH, asking about “difficulty with” ADLs and IADLs and not just dependence to assess disability will be critical. Assessment of functional limitations to capture the spectrum before full disability (like SPPB, gait speed) may have more of a role in this more middle aged population. In the general population, physical performance based assessments of functional limitations have been modified and validated for relatively younger or higher functioning populations to avoid ceiling effects, such as using “fastest” walking speed vs “usual” walking speed or adding difficulty to chair rises. These techniques may also be relevant especially in cohort studies which include PLWH under age 50. Use of higher cutoffs for assessments like the SPPB in more middle aged adults, as was done by Greene et al in the ALIVE cohort may also be appropriate, as the test was originally designed for people 75 and older.

Table 3 highlights the key findings of articles focused on assessment of frailty, falls and physical function in PLWH cited in this article.

### General considerations for assessment of geriatric syndromes and physical function

The first and foremost principle is simply asking or assessing for syndromes. Many older adults will not volunteer information about falls or incontinence as unfortunately these conditions are often viewed as a normal consequence of aging. The timeframe of assessment is also important to consider. Not only can geriatric syndromes occur intermittently (e.g., falls), but recall (self-report) can be affected by the timeframe chosen. Transitions along the disability continuum also occur including periods of recovery and progression of disability. While these transitions were originally demonstrated in monthly assessments, a timeframe that may not be feasible for many purposes, acknowledging the role of hospitalization in contributing to disability.


### Table 3. Key findings of articles pertaining to assessment of frailty, falls and physical function in people living with HIV.

| Reference Number | Reference Citation | Assessments Utilized and Key Findings of Article |
|------------------|-------------------|-------------------------------------------------|
| 32               | Desquilbet L, Jacobson LP, Fried LP, et al. HIV-1 infection is associated with an earlier occurrence of a phenotype related to frailty. J Gerontol A Biol Sci Med Sci. 2007;62(11):1279-1286. | Frailty Related Phenotype (FRP): Modified Fried frailty criteria: Included shrinking and exhaustion (as measured in original Fried criteria), self-report of slowness, self-report of physical activity, did not have measure of weakness. Frailty defined as 3 out of the 4 criteria. Study of HIV+ and HIV- men in Multicenter AIDS Cohort Study (MACS)-Prevalence of FRP ranged between 1-4.4% overall (with increasing age), HIV+ men in 55 y age range had similar prevalence of HIV- men age ≥65. |
| 33               | Piggott DA, Muzzaale AD, Mehta SH, et al. Frailty, HIV infection, and mortality in an aging cohort of injection drug users. PloS One. 2013;8(1):e54910. | Utilized Fried Criteria: Included all 5 criteria with physical activity measured by self-report as in MACS study. Study of HIV+ and HIV- IDU in ALIVE cohort. Frailty prevalence 12.3% overall with HIV+ adults having increased odds of frailty, especially with advanced HIV, Frailty independently associated with mortality. |
| 34               | Terzian AS, Holman S, Nathwani N, et al. Factors associated with preclinical disability and frailty among HIV-infected and HIV-uninfected women in the era of cART. Journal of women's health (2002). 2009;18(12):1965-1974. | Utilized Fried Criteria: Included all 5 criteria (did adjust some cut points given younger age of participants; Study of HIV+ and HIV- women in Women's Interagency HIV Study (WIHS). Frailty prevalence 8% in HIV-women, no difference in HIV+ women with intact immunity; HIV+ women with AIDS had higher risk (14% prevalence) of frailty especially if CD4 <100 (20% frailty prevalence). |
| 36               | Akgun KM, Tate JP, Crothers K, et al. An adapted frailty-related phenotype and the VACS index as predictors of hospitalization and mortality in HIV-infected and uninfected individuals. J Acquir Immune Defic Syndr. 2014;67(4):397-404. | Utilized adapted Frailty Related Phenotype (aFRP) with 4 out of 5 Fried criteria similar to FRP in MACS (leaving out weakness, other 4 domains all self-report from surveys); utilized different but related self-report questions for each of 4 domains than MACS; Frailty defined as 3-4 out of 4 criteria. Study of HIV+ and HIV-veterans; HIV- had prevalence aFRP of 2.8%, HIV+ with virologic control had 2.0%, HIV+ with viral load >400 copies 3.9% aFRP. aFRP independently associated with hospitalization and mortality; compared prediction of aFRP with VACS Index. |
| 38               | Guaraldi G, Brothers TD, Zona S, et al. A frailty index predicts survival and incident multimorbidity independent of markers of HIV disease severity. AIDS. 2015;29(13):1633-1641. | Utilized Rockwood cumulative deficit model--frailty index. Study of HIV+ adults from Modena HIV Metabolic Cohort; Frailty Index included 37 variables. Baseline scores ranged from 0.0-0.63 (out of scale 0-1), scores increased with age. Frailty index predicted survival and incident multimorbidity. |
| 49               | Escota GV, Patel P, Brooks JT, et al. Short communication: The Veterans Aging Cohort Study Index is an effective tool to assess baseline frailty status in a contemporary cohort of HIV-infected and human retroviruses. 2015;31(3):313-317. | Examined VACS index and association with baseline frailty status, using the 5 Fried criteria (with physical activity questions modified from original Fried criteria), as well as association with VACS index and transitions in frailty status within the SUN study. VACS index was independently associated with frailty and persons identified as frail had higher VACS scores; scores did not change with transitions in frailty status; those who stayed frail still had higher VACS scores. |
| 59               | Erlandson KM, Allshouse AA, Jankowski CM, et al. Risk factors for falls in HIV-infected persons. J Acquir Immune Defic Syndr. 2012;61(4):484-489. | Defined falls “as unintentionally coming to rest on the ground or other lower level, not as a result of a major intrinsic event or external hazard,” examined over 1 y period. Also distinguished recurrent fallers. Study of patients in Infectious Diseases clinic at University of Colorado; 30% had a fall, 18% were recurrent fallers. Examined predictors of falls with emphasis on comorbidities and medications. Female gender, diabetes, antidepressants, sedatives, opiates, didanosine, exhaustion,weight loss, and difficulty with balance were the most significant predictors of falls. |
| 60               | Ruiz MA, Reske T, Cefalu C, Estrada J. Falls in HIV-infected patients: a geriatric syndrome in a susceptible population. Journal of the International Association of Providers of AIDS Care. 2013;12(4):266-269. | Fall was defined as a situation where patients landed on the ground without accidental intervention; falls abstracted from medical record. Study of patients at Louisiana State University HIV clinic. Found incidence rate 16 x 1000 patients per year. Falls associated with number of medications, having 3 or more comorbidities, and noncompliance with ART. |
| 61               | Greene M, Cousin FS, Varchek Y, et al. Geriatric Syndromes in Older HIV-Infected Adults. J Acquir Immune Defic Syndr. 2015;69(2):161-167. | Examined frailty, falls, and physical function. Utilized original Fried criteria; falls assessed by “Have you fallen in the past year?—A fall can include a slip or trip in which you lost your balance and landed on the floor or ground or lower level?.” Physical function assessed by self report of ADLs and IADLs. Study within SCOPE cohort in San Francisco, 9% were frail, 26% had at least one fall, 47% had difficulty with at least 1 IADL. |
| 63               | Erlandson KM, Plankey MW, Springer G, et al. Fall frequency and associated factors among men and women with or at risk for HIV infection. HIV Med. 2016. | Falls assessed by “During the past 12 months, about how many times have you fallen?,” with a fall defined as unexpectedly dropping to the floor or ground from a standing, walking or bending position. Study of HIV+ and HIV- men in MACS cohort; HIV+ men had 24% fall prevalence compared to 17% in HIV- men which was not a statistically significant difference. Balance problems were more common in HIV+ men. Smoking, balance problems, and number of medications were associated with falls in HIV+ men. |
| 80               | Morgan EE, Iudicello JE, Weber E, et al. Synergistic effects of HIV infection and older age on daily functioning. J Acquir Immune Defic Syndr. 2012;61(3):341-348. | Utilized self-report of ADLs and IADLs to assess physical function as well as Kamofsky Scale of Performance Status and SF-36 and HIV+ and HIV-younger (<40) and older (<50) patients in San Diego; interaction seen with HIV serostatus and age with older HIV+ adults having worse physical function. Major depressive disorder, comorbidities, neurocognitive impairment, nadir CD4 T Cell count were associated with worse function. |

(Continued on next page)
Table 3. (Continued).

| Reference Number | Reference Citation | Assessments Utilized and Key Findings of Article |
|------------------|--------------------|--------------------------------------------------|
| 82               | Balderson BH, Grothaus L, Harrison RG, McCoy K, Mahoney C, Catz S. Chronic illness burden and quality of life in an aging HIV population. AIDS Care. 2013;25(4):451-458. | Utilized physical functioning SF-36 subscale to measure physical function; Study of HIV+ participants from larger PRIME trial; recruited from AIDS Service Organizations in 9 US States; Additional comorbidities associated with lower physical function scores. Utilized Short Physical Performance Battery as objective measure of physical function with abnormal function considered score of <10. Study of HIV+ and HIV- IDU in ALIVE cohort with 33% of both groups having abnormal physical function. HIV+ participants had 30% increased odds of lower physical function. HIV+ adults with poor physical function had highest mortality risk compared to HIV- adults and HIV+ adults with normal physical function. |

Note. ADLs= Activities of Daily Living; IADLs= Instrumental Activities of Daily Living; HRQoL= Health Related Quality of Life.

could trigger a more detailed record review or assessment for change in disability status. Transitions in frailty states (pre-frail, frail) have also been seen when assessed in 18 month intervals, although the majority of transitions were progression of frailty and only 2 persons went from frail to non-frail.89

Finally, the setting, both of where the patient resides, as well as whether the assessment is occurring in the research or clinical setting is another important consideration. Older adults residing in long term care facilities will have higher prevalence of geriatric syndromes and disability with ADLs. Studies should compare patients from similar settings (e.g. community vs. long-term care). Assessment among community dwelling older adults will capture earlier degrees of impairment such as “difficulty with” daily activities as opposed to full dependency especially compared to assessment in residents of long term care facilities. Multiple IADL difficulties will be seen more commonly in community dwelling older adults than ADL difficulties. Whether the assessment is taking place in a clinical or research setting is also a practical consideration; more detailed assessments can take place in a research setting where there are fewer time constraints.

General considerations for PLWH

Many of the same assessments used in geriatrics and gerontology should apply to PLWH and the same general considerations should be utilized. Yet consideration should also be given to incorporating HIV specific factors (e.g., viral load, CD4 T cell count, length of infection, antiretroviral medications) into assessments, for example when trying to define frailty domains. As the population of PLWH is still predominately middle-aged, including assessment of both pre-frailty and frailty, earlier stages of the disability spectrum such as functional limitations, and asking about “difficulty with” IADLs and ADLs in addition to dependence may be more useful. As an example, in a study of geriatric syndromes among PLWH with a median age of 57, 56% met criteria for pre-frailty while only 9% met the full frailty criteria. In the same study, 47% reported “difficulty with” ≥1 IADLs, with 30% reporting dependence in ≥1 IADLs, 25% reported “difficulty with” ≥1 ADL and only 10% reported dependence in ≥1 ADLs.61

Even when traditional geriatric assessments are utilized, the results in PLWH may not be the same. As an example, the traditional pattern of ADL deficits in adults 65 and older often starts with bathing, then dressing followed later by transfers and feeding. In a study of geriatric syndromes in PLWH, transfers were the most common ADL impairment, a similar finding in a study of homeless older adults with a median age of 56.61,91 This suggests that the pattern of disability may vary in middle aged adults dealing with complex illness and social situations compared to the general population of adults 65 and older and warrants further exploration. Ongoing validation studies of specific assessments from geriatrics applied to PLWH are needed.

Conclusion

Assessment of physical function and geriatric syndromes should be considered as an important tool for clinicians and researchers to understand more about aging in PLWH and to identify the most vulnerable older adults to help target resources. Determining if assessing all older adults living with HIV is appropriate and identifying ways to target which PLWH should undergo assessments is an important consideration in clinical settings. More research is needed to continue to validate geriatric assessments designed for significantly older populations in PLWH. Research should also consider identifying shared risk factors for syndromes, which may include both HIV related and traditional risk factors, in order to help develop multifactorial interventions. Working together with geriatricians and gerontologists will be critical; and what is learned from HIV may also help to inform the field of aging research.
Disclosure of potential conflicts of interest

No potential conflicts of interest were disclosed.

Funding

Each of the authors received funding from the NIH during the time period worked on this review. Dr. Greene received support from the NIA (R33 AG044281) and Dr. Justice received support from the NIAAA (R01-AA020790, U24-AA020794, U01-AA020790, U24-AA022001, R01-AA023733), the NIAID (2U01-AI069918), the NCI (R01-CA035616), and the NHLBI (R01-HL125032), all specific to HIV and aging.

References

[1] Deeks SG, Lewin SR, Havlir DV. The end of AIDS: HIV infection as a chronic disease. Lancet 2013; 382 (9903):1525-33; PMID:24152939; https://doi.org/10.1016/S0140-6736(13)61809-7
[2] Greene M, Justice AC, Lampiris HW, Valcour V. Management of human immunodeficiency virus infection in advanced age. Jama 2013; 309 (13):1397-405; PMID:23549585; https://doi.org/10.1001/jama.2013.2963
[3] Inouye SK, Studenski S, Tinetti ME, Kuchel GA. Geriatric syndromes: clinical, research, and policy implications of a core geriatric concept. J Am Geriat Soc 2007; 55 (5):780-91; PMID:17493201; https://doi.org/10.1111/j.1532-5415.2007.01156.x
[4] Tinetti ME, Inouye SK, Gill TM, Doucette JT. Shared risk factors for falls, incontinence, and functional dependence. Unifying the approach to geriatric syndromes. Jama 1995; 273 (17):1348-53; PMID:7715059; https://doi.org/10.1001/jama.1995.03520410042024
[5] Flacker JM. What is a geriatric syndrome anyway? J Am Geriat Soc 2003; 51 (4):574-76; PMID:12657087; https://doi.org/10.1046/j.1532-5415.2003.51174.x
[6] Halter JB, Ouslander JG, Tinetti ME, Studenski S, High KP, Asthana S. Hazzard’s Geriatric Medicine and Gerontology. 6e. New York, NY: McGraw-Hill; 2009.
[7] Pacala JT, Sullivan GM, eds. Geriatrics Review Syllabus: A Core Curriculum in Geriatric Medicine. 7th ed. New York: American Geriatrics Society; 2013.
[8] Cigolle CT, Lee YY, Tian Z, Blaum CS. Geriatric conditions develop in middle-aged adults with diabetes. J Gen Intern Med 2011; 26 (3):272-79; PMID:21879368; https://doi.org/10.1001/jama.2013.29602246
[9] Brown RT, Kiely DK, Barel M, Mitchell SL. Geriatric syndromes in older homeless adults. J Gen Intern Med 2012; 27 (1):16-22; PMID:21879368; https://doi.org/10.1007/s11606-011-1848-9
[10] Fried LP, Tangen CM, Walston J, Newman AB, Hirsch C, Gottesdiener J, Seeman T, Tracy R, Kop WJ, Burke G, et al. Frailty in older adults: evidence for a phenotype. J Gerontol A Biol Sci Med Sci 2001; 56 (3):M146-156; PMID:11253156; https://doi.org/10.1093/gerona/56.3.M146
Searle SD, Mitnitski A, Gahbauer EA, Gill TM, Rockwood K. A standard procedure for creating a frailty index. BMC Geriatr 2008; 8:24; PMID:18826625; https://doi.org/10.1186/1471-2318-8-24

Gobbens RJ, van Assen MA. Frailty and its prediction of disability and health care utilization: the added value of interviews and physical measures following a self-report questionnaire. Arc Gerontol Geriat 2012; 55 (2):369-79; https://doi.org/10.1016/j.archger.2012.04.008

Rockwood K, Andrew M, Mitnitski A. A comparison of two approaches to measuring frailty in elderly people. J Gerontol A Biol Sci Med Sci 2007; 62 (7):738-43; PMID:17634321; https://doi.org/10.1093/gerona/62.7.738

Woodes NF, LaCroix AZ, Gray SL, Aragaki A, Cochrane BB, Brunner RL, Masaki K, Murray A, Newman AB Women’s Health Initiative. Frailty: emergence and consequences in women aged 65 and older in the women’s health initiative observational study. J Am Geriatr Soc 2005; 53 (8):1321-30; PMID:16078957; https://doi.org/10.1111/j.1532-5415.2005.53405.x

Gigoloe CT, Ofstedal MB, Tian Z, Blaum CS. Comparing models of frailty: the health and retirement study. J Am Geriatr Soc 2009; 57 (5):830-39; PMID:19453306; https://doi.org/10.1111/j.1532-5415.2009.02225.x

Rodriguez-Manas L, Feart C, Mann G, Vina J, Chatterji S, Chodzko-Zaja W, Gonzalez-Cola−ha−mand M, Bergman H, Caracillon L, Nicholson C, et al. Searching for an operational definition of frailty: a Delphi method based consensus statement: the frailty operative definition-consensus conference project. J Gerontol A Biol Sci Med Sci 2013; 68 (1):62-67; PMID:22511289; https://doi.org/10.1093/gerona/gls119

Walston J, Hadley EC, Ferrucci L, Guralnik JM, Newman AB, Studenski SA, Ershler WB, Harris T, Fried L. Research agenda for frailty in older adults: toward a better understanding of physiology and etiology: summary from the American Geriatrics Society/National Institute on aging research conference on frailty in older adults. J Am Geriatr Soc 2006; 54 (6):991-1001; PMID:16776798; https://doi.org/10.1111/j.1532-5415.2006.00745.x

Morley JE, Vellas B, van Kan GA, Anker SD, Bauer JM, Bernabei R, Cesari M, Chumlea WC, Doehner W, Evans J, et al. Frailty consensus: a call to action. J Am Med Dir Assoc 2013; 14 (6):392-97; PMID:23764209; https://doi.org/10.1016/j.jamda.2013.03.022

Desquilel L, Jacobson LP, Fried LP, Phair JP, Jamie−son BD, Holloway M, Margolick JB; Multicenter AIDS Cohort Study. HIV-1 infection is associated with an earlier occurrence of a phenotype related to frailty. J Gerontol A Biol Sci Med Sci 2007; 62 (11):1279-86; PMID:18000149; https://doi.org/10.1093/gerona/62.11.1279

Piggott DA, Muzzaele AD, Mehta SH, Brown TT, Patel KV, Leng SX, Kirk GD. Frailty, HIV infection, and mortality in an aging cohort of injection drug users. PloS one 2013; 8 (1):e54910; PMID:23382997; https://doi.org/10.1371/journal.pone.0054910

Terzian AS, Holman S, Nathwani N, Robison E, Weber K, Young M, Greenblatt RM, Gange SJ, Women’s Interagency HIV Study. Factors associated with preclinical disability and frailty among HIV-infected and HIV-uninfected women in the era of cART. J Women’s Health (2002) 2009; 18 (12):1965-74; PMID:20044858; https://doi.org/10.1089/jwh.2008.1090

Gustafson DR, Shi Q, Thurn M, Holman S, Minkoff H, Cohen M, Plankey MW, Havlik R, Sharma A, Gange S, et al. Frailty and constellations of factors in aging HIV-infected and uninfected women—the women’s interagency HIV study. J Frailty Aging 2016; 5 (1):43-48; PMID:26980368

Akgun KM, Tate JP, Crothers K, Crystal S, Leaf DA, Womack J, Brown TT, Justice AC, Oursler KK. An adapted frailty-related phenotype and the VACS index as predictors of hospitalization and mortality in HIV-infected and uninfected individuals. J Acquir Immune Defic Syndr 2014; 67 (4):397-404; PMID:25209291; https://doi.org/10.1097/QAI.0000000000000341

Desquilel L, Jacobson LP, Fried LP, Phair JP, Jamie−son BD, Holloway M, Margolick JB. A frailty-related phenotype before HAART initiation as an independent risk factor for AIDS or death after HAART among HIV-infected men. J Gerontol A Biol Sci Med Sci 2011; 66 (9):1030-38; PMID:21719610; https://doi.org/10.1093/gerona/gir097

Guaraldi G, Brothers TD, Zona S, Stentarelli C, Carli F, Malagoli A, Santoro A, Menozzi M, Mussi C, Mussini C, et al. A frailty index predicts survival and incident morbidities independent of markers of HIV disease severity. AIDS 2015; 29 (13):1633-41; PMID:26372273; https://doi.org/10.1097/QAD.0000000000000753

Justice AC, McGinnis KA, Skanderson M, Chang CC, Gilbert CL, Goetz MB, Rimland D, Rodriguez-Barradas MC, Oursler KK, Brown ST, et al. Towards a combined prognostic index for survival in HIV infection: the role of ‘non-HIV’ biomarkers. HIV Med 2010; 11 (2):143-51; PMID:19751364; https://doi.org/10.1111/j.1468-1293.2009.00757.x

Akgun KM, Gordon K, Pisani M, Fried T, McGinnis KA, Tate JP, Butt AA, Gilbert CL, Huang L, Rodriguez-Barradas MC, et al. Risk factors for hospitalization and medical intensive care unit (MICU) admission among HIV-infected Veterans. J Acquir Immune Defic Syndr 2013; 62 (1):52-59; PMID:23111572; https://doi.org/10.1097/QAI.0b013e318278f3fa

Tate JP, Justice AC, Hughes MD, Bonnet F, Reiss P, Moc−roft A, Nattermann J, Lampe FC, Bucher HC, Sterling TR, et al. An internationally generalizable risk index for mortality after one year of antiretroviral therapy. AIDS 2013; 27 (4):563-72; PMID:23095314; https://doi.org/10.1097/QAD.0b013e32835b8c7f

Justice AC, Modur SP, Tate JP, Althoff KN, Jacobson LP, Gebo KA, Kitahata MM, Horberg MA, Brooks JT, Buchacz K, et al. Predictive accuracy of the veterans aging cohort study index for mortality with HIV infection: a North American cross cohort analysis. J Acquir Immune Defic Syndr 2013; 62 (2):149-63; PMID:23187941; https://doi.org/10.1097/QAI.0b013e31827df36c
[43] Justice AC, Freiberg MS, Tracy R, Kuller L, Tate JP, Goetz MB, Fiellin DA, Vanasse GJ, Butt AA, Rodriguez-Barradas MC, et al. Does an index composed of clinical data reflect effects of inflammation, coagulation, and monocyte activation on mortality among those aging with HIV? Clin Infect Dis 2012; 54 (7):984-94; PMID:22337823; https://doi.org/10.1093/cid/cir989

[44] Williams B, Livak B, Bahk M, Keating SM, Adeyemi OM. SCD14 and SCD163 levels are correlated with VACS index scores: initial data from the blunted immune recovery in CORE patients with HIV (BIRCH) cohort. AIDS Res Hum Retroviruses 2016; 32(2):144-7; Epub; PMID:26366931

[45] Mooney S, Tracy R, Osler T, Grace C. Elevated biomarkers of inflammation and coagulation in patients with HIV are associated with higher framingham and VACS risk index scores. PLoS One 2015; 10 (12): e0144312; PMID:26641655; https://doi.org/10.1371/journal.pone.0144312

[46] Marquine MJ, Umlauf A, Rooney AS, Fazeli PL, Gouaux BD, Paul Woods S, Letendre SL, Ellis RJ, Grant I, Moore DJ, et al. The veterans aging cohort study index is associated with concurrent risk for neurocognitive impairment. J Acquir Immune Defic Syndr 2014; 65 (2):190-97; PMID:24442225; https://doi.org/10.1097/QAI.0000000000000008

[47] Erlandson KM, Allshouse AA, Jankowski CM, Duong S, Mawhinney S, Kohrt WM, Campbell TB. Comparison of functional status instruments in HIV-infected adults on effective antiretroviral therapy. HIV Clin Trials 2012; 13 (6):324-34; PMID:23195670; https://doi.org/10.1310/hct1306-324

[48] Womack JA, Goulet JL, Gibert C, Brandt CA, Skanderson M, Gulanski B, Rimland D, Rodriguez-Barradas MC, Tate J, Yin MT, et al. Physiologic frailty and fragility fracture in HIV-infected male veterans. Clin Infect Dis 2013; 56 (10):1498-504; PMID:23378285; https://doi.org/10.1093/cid/cit056

[49] Escota GV, Patel P, Brooks JT, Bush T, Conley L, Baker J, Kojic EM, Hammer J, Önen NF, SUN Study Investigators. Short communication: The veterans aging cohort study index is an effective tool to assess baseline frailty status in a contemporary cohort of HIV-infected persons. AIDS Res Hum Retroviruses 2015; 31 (3):313-17; PMID:25495766; https://doi.org/10.1097/AID.0000000000000008

[50] Lamb SE, Jorstad-Stein EC, Hauer K, Becker C, Prevention of Falls Network E, Outcomes Consensus G. Development of a common outcome data set for fall injury prevention trials: the Prevention of Falls Network Europe consensus. J Am Geriat Soc 2005; 53 (9):1618-22; PMID:16137297; https://doi.org/10.1111/j.1532-5415.2005.53455.x

[51] The prevention of falls in later life. A report of the Kellogg international work group on the prevention of falls by the elderly. Dan Med Bull 1987; 34 (Suppl 4):1-24.

[52] Cwikel JG, Fried AV, Biderman A, Galinsky D. Validation of a fall-risk screening test, the Elderly Fall Screening Test (EFST), for community-dwelling elderly. Disabil Rehabil 1998; 20 (5):161-67; PMID:9622261; https://doi.org/10.3109/09638289809166077

[53] Schwenk M, Lauenroth A, Stock C, Moreno RR, Oster P, McHugh G, Todd C, Hauer K. Definitions and methods of measuring and reporting on injurious falls in randomised controlled fall prevention trials: a systematic review. BMC Med Res Methodol 2012; 12:50; PMID:22510239; https://doi.org/10.1186/1471-2288-12-50

[54] Dinh A, Shi Y, Teng D, Ralhan A, Chen L, Dal Bello-Haas V, Basran J, Ko SB, McCrowsky C. A fall and near-fall assessment and evaluation system. Open Biomed Eng J 2009; 3:1-7; PMID:19662151; https://doi.org/10.2174/1874120700903010001

[55] Ganz DA, Higashi T, Rubenstein LZ. Monitoring falls in cohort studies of community-dwelling older people: effect of the recall interval. J Am Geriat Soc 2005; 53 (12):2190-94; PMID:16398908; https://doi.org/10.1111/j.1532-5415.2005.00509.x

[56] Cummings SR, Nevitt MC, Kidd S. Forgetting falls. The limited accuracy of recall of falls in the elderly. J Am Geriat Soc 1988; 36 (7):613-16; PMID:3385114; https://doi.org/10.1111/j.1532-5415.1988.tb00155.x

[57] Panel on Prevention of Falls in Older Persons, American Geriatrics Society and British Geriatrics Society. Summary of the updated American Geriatrics Society/British Geriatrics Society clinical practice guideline for prevention of falls in older persons. J Am Geriat Soc 2011; 59 (1):148-57; PMID:21226685; https://doi.org/10.1111/j.1532-5415.2010.03234.x

[58] Stevens JA, Phelan EA. Development of STEADI: a fall prevention resource for health care providers. Health Promot Pract 2013; 14 (5):706-14; PMID:23159993; https://doi.org/10.1177/1524839912463576

[59] Erlandson KM, Allshouse AA, Jankowski CM, Duong S, Mawhinney S, Kohrt WM, Campbell TB. Risk factors for falls in HIV-infected persons. J Acquir Immune Defic Syndr 2012; 61 (4):484-89; PMID:23143526; https://doi.org/10.1097/QAI.0b013e3182716e38

[60] Ruiz MA, Reske T, Cefalu C, Estrada J. Falls in HIV-infected patients: a geriatric syndrome in a susceptible population. J Int Assoc Provid AIDS Care 2013; 12 (4):266-69; PMID:23719236; https://doi.org/10.1177/1524839913488204

[61] Greene M, Covinsky KE, Valcour V, Miao Y, Madamba J, Lampiris H, Cenzer IS, Martin J, Deeks SG. Geriatric syndromes in older HIV-infected adults. J Acquir Immune Defic Syndr 2015; 69 (2):161-67; PMID:26009828; https://doi.org/10.1097/QAI.0000000000000556

[62] Bates J, Fodeh SJ, Brandt CA, Womack JA. Classification of radiology reports for falls in an HIV study cohort. J Am Med Infor Assoc 2016; 23(e1):e13-7.

[63] Erlandson KM, Plankey MW, Springer G, Cohen HS, Cox C, Hoffman HJ, Yin MT, Brown TT. Fall frequency and associated factors among men and women with or at risk for HIV infection. HIV Med 2016; 17:740-48; PMID:27028463

[64] Triant VA, Brown TT, Lee H, Grinspoon SK. Fracture prevalence among human immunodeficiency virus (HIV)-infected versus non-HIV-infected patients in a large U.S. healthcare system. J Clin Endocrinol Metab 2008; 93 (9):3499-504; https://doi.org/10.1210/jc.2008-0828

[65] Aberg JA, Gallant JE, Ghanem KG, Emmanuel P, Zingman BS, Horber MA, Infectious Diseases Society of America. Primary care guidelines for the management of
persons infected with HIV: 2013 update by the HIV Medicine Association of the Infectious Diseases Society of America. Clin Infect Dis 2014; 58 (1):1-10; PMID:24343580; https://doi.org/10.1093/cid/cit757

[66] Verbrugge LM, Jette AM. The disablement process. Soc Sci Med 1994; 38 (1):1-14; PMID:8146699; https://doi.org/10.1016/0277-9536(94)90294-1

[67] Pope AM, Tarlov AR “Front Matter.” Institute of Medicine. Disability in America: Toward a National Agenda for Prevention. Washington, DC: National Academy of Science; 1991.

[68] Guralnik JM, Ferrucci L. Assessing the building blocks of function: utilizing measures of functional limitation. Am J Prevent Med 2003; 25 (3 Suppl 2):112-21; https://doi.org/10.1016/S0749-3797(03)00174-0

[69] Suthers, K, Seeman T. The measurement of physical functioning in older adult populations: summary of BSR physical performance meeting. National Institute on Aging; Baltimore, MD, 2004.

[70] Reuben DB, Siu AL, Kimpaui S. The predictive validity of self-report and performance-based measures of function and health. J Gerontol 1999; 47 (4):M106-110; PMID:1624692; https://doi.org/10.1093/geront/47.4.M106

[71] Penninx BW, Guralnik JM, Ferrucci L, Simonsick EM, Deeg DJ, Wallace RB. Depressive symptoms and physical decline in community-dwelling older persons. Jama 1998; 279 (21):1720-26; PMID:9624025; https://doi.org/10.1001/jama.279.21.1720

[72] Guralnik JM, Simonsick EM, Ferrucci L, Glynn RJ, Berkman LF, Blazer DG, Scherr PA, Wallace RB. A short physical performance battery assessing lower extremity function: association with self-reported disability and prediction of mortality and nursing home admission. J Gerontol 1994; 49 (2):M85-94; PMID:8126356; https://doi.org/10.1093/geronj/49.2.M85

[73] Guralnik JM, Ferrucci L, Simonsick EM, Salive ME, Wallace RB. Lower-extremity function in persons over the age of 70 years as a predictor of subsequent disability. N Eng J Med 1995; 332 (9):556-61; https://doi.org/10.1056/NEJM199503023320902

[74] Guralnik JM, Ferrucci L, Pieper CF, Leveille SG, Markides KS, Ostir GV, Studenski S, Berkman LF, Wallace RB. Lower extremity function and subsequent disability: consistency across studies, predictive models, and value of gait speed alone compared with the short physical performance battery. J Gerontol A Biol Sci Med Sci 2000; 55 (4):M221-231; PMID:10811152; https://doi.org/10.1093/gerona/55.4.M221

[75] Ferrucci L, Penninx BW, Leveille SG, Corti MC, Pahor M, Wallace R, Harris TB, Havlik RJ, Guralnik JM. Characteristics of nondisabled older persons who perform poorly in objective tests of lower extremity function. J Am Geriat Soc 2000; 48 (9):1102-10; PMID:10983911; https://doi.org/10.1111/j.1532-5415.2000.tb04787.x

[76] Katz S, Ford AB, Moskowitz RW, Jackson BA, Jaffe MW. Studies of illness in the aged. The index of ADL: A standardized measure of biological and psychosocial function. Jama 1963; 185:914-19; PMID:14044222; https://doi.org/10.1001/jama.1963.03060120024016

[77] Lawton MP, Brody EM. Assessment of older people: self-maintaining and instrumental activities of daily living. The Gerontologist 1969; 9 (3):179-86; PMID:5349366; https://doi.org/10.1093/geront/9.3_Part_1.179

[78] Huisings-Sheetz M, Kocherginsky M, Schumm PL, Engelman M, McClintock MK, Dale W, Maggett E, Rush P, Waite L. Geriatric syndromes and functional status in NSHAP: Rationale, measurement, and preliminary findings. J Gerontol B Psychol Sci Soc Sci 2014; 69 (Suppl 2):177-190; PMID:25360019; https://doi.org/10.1093/geronb/gbu091

[79] Erlandson KM, Schrack JA, Jankowski CM, Brown TT, Campbell TB. Functional impairment, disability, and frailty in adults aging with HIV-infection. Curr HIV/AIDS Rep 2014; 11 (3):279-90; PMID:24966138; https://doi.org/10.1007/s11907-014-0215-y

[80] Morgan EE, Judiciello JE, Weber E, Duarte NA, Riggs PK, Delano-Wood L, Ellis R, Grant I, Woods SP, HIV Neurobehavioral Research Program (HNRP) Group. Synergistic effects of HIV infection and older age on daily functioning. J Acquir Immune Defic Syndr 2012; 61 (3):341-48; PMID:22878422; https://doi.org/10.1097/QAI.0b013e31826bf5c3

[81] Balderson BH, Grothaush L, Harrison RG, McCoy K, Mahoney C, Catz S. Chronic illness burden and quality of life in an aging HIV population. AIDS Care 2013; 25 (4):451-58; PMID:22894702; https://doi.org/10.1080/09540121.2012.712669

[82] Greene MCK, Astemborski J, Piggott DA, Brown T, Leng S, Galai N, Mehta S, Guralnik J, Patel KV, Kirk GD. The relationship of physical performance with HIV disease and mortality: A cohort study. AIDS 2014; 28(18):2711-9; PMID:25493597

[83] Guralnik JM, Seeman TE, Tinetti ME, Nevitt MC, Berkman LF. Validation and use of performance measures of functioning in a non-disabled older population: MacArthur studies of successful aging. Aging (Milan, Italy) 1994; 6 (6):410-19; PMID:7748914

[84] Simonsick EM, Newman AB, Nevitt MC, Kritchevsky SB, Ferrucci L, Guralnik JM, Harris T, Health ABC Study Group. Measuring higher level physical function in well-functioning older adults: expanding familiar approaches in the Health ABC study. J Gerontol A Biol Sci Med Sci 2001; 56 (10):M644-649; PMID:11584038; https://doi.org/10.1093/gerona/56.10.M644

[85] Shinkai S, Watanabe S, Kumagai S, Fujiwara Y, Amano H, Yoshida H, Ishizaki T, Yukawa H, Suzuki T, Shibata H. Walking speed as a good predictor for the onset of functional dependence in a Japanese rural community population. Age Ageing 2000; 29 (5):441-46; PMID:11108417; https://doi.org/10.1093/ageing/29.5.441

[86] Gill TM, Kurland B. The burden and patterns of disability in activities of daily living among community-living older persons. J Gerontol A Biol Sci Med Sci 2003; 58 (1):70-75; PMID:12560415; https://doi.org/10.1093/gerona/58.1.M70

[87] Hardy SE, Dublin JA, Holford TR, Gill TM. Transitions between states of disability and independence among older persons. Am J Epidemiol 2005; 161 (6):575-84; PMID:15746474; https://doi.org/10.1093/aje/kwi083

[88] Gill TM, Allore HG, Gahbauer EA, Murphy TE. Change in disability after hospitalization or restricted activity in older persons. JAMA 2010; 304 (17):1919-28; PMID:21045098; https://doi.org/10.1001/jama.2010.1568
[89] Gill TM, Gahbauer EA, Allore HG, Han L. Transitions between frailty states among community-living older persons. Arch Intern Med 2006; 166 (4):418-23; PMID:16505261; https://doi.org/10.1001/archinte.166.4.418

[90] Gill TM, Robison JT, Tinetti ME. Difficulty and dependence: two components of the disability continuum among community-living older persons. Annal Int Med 1998; 128 (2):96-101; https://doi.org/10.7326/0003-4819-128-2-199801150-00004

[91] Cimino T, Steinman MA, Mitchell SL, Miao Y, Bharel M, Barnhart CE, Brown RT. The course of functional impairment in older homeless adults: Disabled on the street. JAMA Inter Med 2015; 175 (7):1237-39; PMID:26011591; https://doi.org/10.1001/jamainternmed.2015.1562