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Frailty and Other Emerging Concepts in Care of the Aged

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ABSTRACT

Frailty has generated increased attention and scientific interest among health professionals because it offers an alternative frame of reference for quantification of risk and prognosis in the aged. However, considerable uncertainty remains about the definition of and criteria for frailty and effective interventions for prevention and treatment. A core feature of frailty is increased vulnerability to stressors resulting from accumulated decrements in multiple, inter-related cellular and organ systems. Subsequent diminished compensatory reserve and dysregulation leads to progressive decline in physiologic and physical function. Frailty is associated with adverse outcomes including morbidity, functional impairments, disability, and mortality, yet is potentially reversible. This review article addresses definitions, epidemiology, conceptual perspectives, and interventions for frailty, and implications for Gerontological nursing practice and research.

Keywords: frail elderly, aged, vulnerability, geriatric syndrome, allostatic load, Gerontological nursing

Frailty and Other Emerging Concepts in Care of the Aged

The differences between an elderly person who is fit and robust and one who is frail are intuitively and readily detectible based on observations of weakness, poor physical function, emotional withdrawal, fatigue, limited cognition, decreased biologic reserve, and high frequency of acute illness and hospitalizations (Studenski et al., 2004). Geriatric clinicians agree that frailty is easily recognized, “They know it when they see it,” but acknowledge significant ambiguity in its definition and diagnosis (Studenski et al., 2004, p. 1560). The definition of frailty continues to evolve but its defining feature is decreased resistance to stressors (Singh et al., 2008). Frailty exacts a high cost in terms of personal suffering, quality of life, excess disability, caregiver burden, health care utilization and costs. The personal and public health impact of extended lifespan underscores the need for a better understanding of frailty. Traditional approaches to appraisal of risk and prognosis are based upon chronological age, comorbidities, and functional status. Such approaches have limitations due to the heterogeneity of the aged and the mediating and moderating aspects of diverse lifestyles, socioeconomic resources, psychological coping, and life circumstances and events. Although age-related chronic diseases may interact to contribute to frailty risk, research suggests that frailty is not synonymous with aging nor is it omnipresent in the elderly (Hamerman, 1999). For instance, among elders with similar comorbidities, frailty status may differ. Although some functional loss is inevitable in aging, chronological age is a poor marker for estimating the level of fitness or frailty (Bergman et al., 2007). As the aging population increases, it is becoming increasingly important to discover why some elders develop frailty and others do not (Szanton et al., 2009). An understanding of factors beyond age is needed to explain the variability in morbidity and mortality of older adults. The concept of frailty may be an effective frame of reference for determination of risk, prognosis and functional age in older adults (Bergman et al., 2007; Hastings et al., 2008; Mitnitski et al., 2002). Increased understanding of frailty will inform interventions for prevention and treatment of chronic illness and factors associated with frailty risk (Bergman et al., 2007; Fried et al., 2001; Fries, 2005; Ravaglia et al., 2008; Walston et al., 2006; Walston, 2008).

Frailty Defined

There is no single best definition of frailty (Singh et al., 2008). The vernacular term frailty has been used to describe those who are feeble, weak, the most debilitated, and the oldest old. Synonyms of frailty include decrepitude, defect, deficiency, error, failing, fallibility, imperfection, infirmity, and susceptibility (Thesaurus.com, n.d.). In medicine, the term “frail elderly” has been a Medline MeSH term since 1991 and is defined as “older adults or aged individuals who are lacking in general strength and are unusually susceptible to disease or to other infirmity” (Hogan et al., 2003). The opposite of frailty is vigorousness and fitness (Mitnitski et al., 2002; Speechley & Tinetti, 1991). Although there is uncertainty about what frailty actually means, there is general agreement that frailty 1) conveys a state of physiologic vulnerability and high risk, 2) describes the heterogeneity and variability in functional decline and morbidity observed with

chronological age, and 3) allows for more direct quantification of risk and prediction of adverse outcomes that could be averted with targeted interventions. A better understanding of frailty will help identify why some elders in their 70s appear to be frail when others in their 90s do not evidence frailty at all.

Numerous scientific and clinical definitions have been proposed for frailty (see Table 1). Definitions focus on the influence of age, disease states, biochemical modulators, or the interplay of frailty, dependence and disability (Bortz, 2002). Different perspectives and purposes of researchers and clinicians in nursing, medicine and other health professions contributes to lack of consensus because conceptions of frailty do not fully equate to what each of these professionals has in mind when thinking about frail elders (Whitson et al., 2007). Contrasting viewpoints about the nature of frailty extend along a continuum. One end interprets frailty as a process of accelerated aging while other end emphasizes frailty as an entity with its own distinct pathophysiology (Fried et al., 2005; Mitniski et al., 2002). Recent position statements and concept papers (Bergman et al., 2007; Walston et al., 2006) suggest that the core feature of frailty is increased physiologic vulnerability to stressors resulting from accumulated decrements in multiple inter-related cellular and organ systems. Subsequent dysregulation and diminished compensatory reserve across systems leads to progressive decline in physiologic and physical function (Bergman et al., 2007; Bortz, 1993; Fried et al., 2001). Furthermore, no single altered system or etiology defines frailty (Fried et al., 2004; Fried et al., 2005; Whitson et al., 2007). Age is an important feature, but frailty can develop at any age, and chronological age correlates loosely with biologic age (Singh et al., 2008). A distinction between frailty due to physiologic vulnerability and frailty associated with biopsychosocial and environmental interactions, comorbidities and functional limitation has also been posited (Whitson et al., 2007). A comprehensive view incorporating biopsychosocial contributions to frailty may be more sensitive to detecting vulnerability that exists before any recognized clinical manifestations, functional decline or disability.

Frailty and disability are often viewed as synonymous but their physiological and physical manifestations are distinctly different. Disability refers to the inability to fulfill customary and desired roles due to functional impairments in the ability to perform activities of daily living (ADL) and/or instrumental activities of daily living (IADL). In contrast to frailty, functional impairment and disability do not affect the body across multiple organ systems. Nor does the onset and progression of frailty mirror the progression of functional loss and disability. A physically frail state may be clinically detected before disability, and alternatively, a more advanced state of physical frailty that manifests some initial degree of functional disability may be observed (Ferrucci et al., 2004). Disability is a consequence of chronic disease and age-related changes in musculoskeletal function and other systems, but only a small proportion of individuals with chronic disease become disabled (Fried et al., 2005). Concordance between frailty and disability is modest. In one study, among the 28% who were frail, only 6% had disability,

whereas 46% had comorbidity, 22% had comorbidity and disability, and 27% had neither disability nor comorbidity (Fried et al., 2001). Research also indicates that only 28% of disabled elderly are frail, and among these, only 27% cannot complete ADLs, and 60% have difficulty with IADLs (Fried et al., 2004).

Measurement of Frailty

Formal measures or indices of frailty include criteria that have been associated with, but different from, measures of comorbidity and disability, and independently predict falls, fractures, disability, hospitalization, and death (Fried et al., 2001). Operational constructs in frailty models vary and may include biologic, psychologic or social factors and physical performance. The relationships among the constructs have not always been defined. The Frailty Working Group's recommendations for operational criteria for physical frailty include mobility, balance, muscle strength, motor processing, cognition, nutrition (nutritional status, weight change), endurance (fatigue, exhaustion) and physical activity (Ferrucci et al., 2004). The most commonly identified constructs in the literature are physical inactivity, aging, and disease, followed by decreased mobility and/or agility, decreased physical activity and its consequences, nutritional deficits, cognitive-psychological factors, socio-economic factors, and spiritual, residential and legal factors (Levers et al., 2006). From the perspective of older adults and their caregivers, the social and emotional aspects of frailty are important to consider in frailty models (Studenski et al., 2004). Some frailty measures calculate a score by summing the ratings that are calculated for criteria. Less quantitative estimations of frailty status employ clinician judgment of the relative impact of frailty criteria on function and medical stability and outcomes.

Frailty criteria and measurement

Fried and colleagues (2001) propose a "phenotype" of frailty based on criteria for five domains of function including mobility, strength, endurance, physical activity, and nutrition. Using data from the Cardiovascular Health Study (CHS) of community-living elderly, a frailty index was constructed from five criteria that included gait speed (slowness), grip strength (weakness), exhaustion, weight loss, and low physical activity (See Table 1). Frailty was classified as the presence of three of the five criteria. Two criteria classified intermediate frailty and one indicated a prefrail state. The aggregated measure for the CHS frailty criteria demonstrate predictive validity for frailty and risk for falls, hospitalizations, disability and death. The CHS frailty criteria are proposed for frailty screening in the elderly (Fried et al., 2001).

In a longitudinal study, the natural history of frailty in older nonfrail women enrolled in the Women's Health and Aging Study II (WHAS-II, $N=420$) was examined using the CHS frailty criteria (Xue et al., 2008). Two of the criteria were slightly modified: self-report of exhaustion or feeling unusually tired or weak most

or all of the time was rated on a 0-10 Likert scale, and low activity was rated for six activities (walking, strenuous household chores, strenuous outdoor chores, dancing, bowling and exercise).

To evaluate the validity of the CHS frailty criteria, a subsequent study using latent class analysis to determine if the five frailty criteria aggregate as a syndrome using data from the Women's Health and Aging Studies, WHAS I (>65 years, more disabled, N=1002) and II, (70-79 years, least disabled, N=436) (Bandein-Roche et al., 2006). There was close agreement in frailty and robust status across the two datasets. The individual CHS frailty criteria and the overall index demonstrated similar distributions in the two groups and predicted disability and mortality independent of disease and other factors.

Despite its predictive strengths of the CHS frailty criteria, its focus on biological or physical frailty exclusion of cognitive or psychological factors which are associated with functional decline and disability has been questioned. Some investigators propose that several CHS frailty criteria are integrally related to cognitive impairment and form a composite summary that reflects integration of biological and cognitive functions (Purser et al., 2006; Sarkisian et al., 2008). Other investigators support that cognitive impairment has distinct influence on frailty risk which has led to development of more comprehensive measures to determine if predictive ability is increased (Fillit & Butler, 2009). Rothman and colleagues (2008) utilized the CHS frailty criteria and measures for cognitive impairment and depressive symptoms to determine their independent prognostic effect. Findings indicate that only three of the five CHS frailty criteria, slow gait speed, low physical activity, weight loss, were independently associated with frailty and other outcomes. In the model, cognitive impairment was independently associated with frailty. The validity of self-reported exhaustion and hand grip strength was questioned since they were not strong predictors of frailty, although better measures may improve their sensitivity (Rothman et al., 2008). Avila-Funes and colleagues (2009) used two measures for cognitive function with the CHS frailty criteria and found that the addition of cognitive assessment increased the ability to stratify frailty risk. In another study, three of the five CHS frailty criteria: weight loss, poor energy, and chair stands (proxy measure for gait speed) were used to evaluate the sensitivity and predictive ability of a more parsimonious approach to frailty assessment (Ensrud et al., 2008). These three criteria predicted frailty status similarly to the Cardiovascular Health Study (Ensrud et al., 2008).

Using factor analysis, Sarkisian and colleagues (2008), used modified CHS frailty criteria and five additional criteria for cognitive impairment and weakness and anorexia, and laboratory measures for interleukin-6 and C-reactive protein. Principal components analysis (PCA) of the CHS frailty criteria identified two sub-dimensions of frailty. Sub-dimension one included slower gait speed, weaker grip, and lower physical activity. Sub-dimension two included exhaustion and weight gain. The PCA of the expanded model which included the CHS frailty

criteria and the five additional criteria revealed four sub-dimensions: 1) higher interleukin-6 and C-reactive protein, 2) exhaustion and subjective weakness, 3) slower gait, weaker grip, lower physical activity, low cognitive function, and 4) weight loss and anorexia. The sub-dimension that included cognitive impairment, slow gait, weaker grip, and low physical activity provides support for the hypothesis that cognitive impairment is intrinsic to frailty and integrally related to these physical frailty criteria.

In the accumulated deficit framework, frailty is described as a combination of aging, disease, nutrition, activity and fitness, and other factors that render some elders more vulnerable (Rockwood et al, 1999). In community-living older adults (N=9008), baseline data were collected for a frailty scale classified in four levels: 0 = independence in ambulation and ADLs, continent, and cognitively intact, 1= bladder incontinence only, 2= one (two if incontinent) or more of needing mobility or ADL assistance and cognitive impairment but no dementia, and 3= two (three if incontinent) or more of totally dependence in mobility and transfers and one or more ADLs, incontinent of bowel or bladder, and dementia (Rockwood et al., 1999). Frailty status was classified as increasing dependency in ADLs and cognitive impairment.

Further development of the accumulated deficit model involved numerical counts of deficits listed in a frailty index that include functional performance, diagnoses, and self-rated health (Kulminski et al., 2007). Deficits were rated and summed, then analyzed to derive a proportion of deficits (Rockwood et al., 2007). Cross-sectional data supported that accumulated deficits increase with age in a nonlinear pattern. At younger ages, there are slow increases in the mean number of deficits, which increase with aging but decrease in old age. The accumulated deficit frailty index is predictive of mortality, hospitalization and institutionalization (Kulminski et al., 2007). Mitnitski and colleagues (2005) found that community elders accumulated deficits at about 3% per year, and women at any age were more frail.

Increased attention has focused on biological and physiological measures that reflect accumulated physiologic risk across cellular and organ systems over time, resulting in differential risks for morbidity, disability and frailty (McEwen & Stellar, 1993). The premise is that progressive physiologic wear-and-tear that occurs from repeated exposures to stress and other life challenges increases risks for precursors to disease and to development of disease. The initial conceptualization of allostatic load was based on analysis of available data from the MacArthur Study of Successful Aging and included ten biological parameters for cardiovascular function, metabolic and glucose metabolism, and neurohormonal and endocrine systems (Seeman et al., 2004). In contrast to traditional multifactorial models for estimating disease risk using single biologic markers, allostatic load is an aggregated sum of the parameters whose combined effects represent dysregulation across a range of body systems (Seeman et al., 2002). Allostatic load biomarkers that may be used in research

studies include systolic and diastolic blood pressure, HDL cholesterol, glycosylated hemoglobin, urinary cortisol, urinary norepinephrine, urinary epinephrine, fibrinogen, C-reactive protein, interleukin-6, dehydroepiandrosterone sulfate (DHEA), heart rate variability, and waist-hip ratio (Geronimus et al., 2006; Seeman et al., 2002; Szanton et al., 2009; Varadhan et al., 2009). Additional indicators have included measures for renal function and lung capacity (Seeman et al., 2004). Initial calculation of allostatic load was based on a count of the markers for which the subject scored in the upper 25% of the distribution. Subsequent analyses to explore whether individual indicators differentially contribute to risk to determine optimal weighting of components have not found major differences and support the concept of a summed measure for allostatic load. Research supports that allostatic load is associated with significant risk for frailty (Szanton et al., 2009).

Frailty assessments often include performance measures such as gait speed, handgrip strength, or chair stands. These performance measures may provide greater precision in detecting frailty status, since these tasks reflect an integration of physiologic function across systems (Purser et al., 2006). In the Health, Aging and Body Composition Study, frailty status was determined by low gait speed, and the ability to rise from a chair with the arms folded (Peterson et al., 2009). Elders with one impairment were considered moderately frail, and with both impairments, frail. Slow gait speed has been shown to be a strong independent predictor of frailty and mortality (Purser et al., 2006; Rothman et al., 2008).

In a departure from the use of frailty measures that require special procedures, equipment, and calculations, several studies report on the use of information readily available in geriatric practice to stratify frailty risk. Ravaglia and colleagues (2008) developed a frailty score for nine predictors that were analyzed in elders age 65 and over ($N=1,007$) who were followed over four years. Predictors included age >80 , male, low activity, two or more chronic conditions, sensory deficits, physical function (gait and balance), disability (ADL, IADL), calf circumference, and pessimism about one's health. Patients scoring >3 , were classified as frail. Similarly, Retornaz and colleagues (2008) calculated a frailty index in an elderly sample of cancer patients ($N=50$) for seven frailty measures that include nutritional status (BMI, weight loss, food intake), mobility (falls in past six months, Timed Up and Go test), strength (grip strength), energy (visual analogue scale), physical activity (self report), mood (Hospital Anxiety and Depression Scale) and cognition (Mini-mental State Examination and Montreal Cognitive Assessment, ADL and IADL).

Geriatric clinicians rely on clinical judgment in determining frailty status, but assessment methodologies vary widely. The use of algorithms, complex standardized instruments, and summative impairment lists can be cumbersome, time consuming, and impractical in clinical settings (Rolfson et al., 2006). One measure, the Clinical Global Impression of Change in Physical Frailty (CGIC-PF),

was designed to represent a geriatric clinician's global opinion about frailty (Studenski et al., 2004). The CGIC-PF consists of six domains (mobility, balance, strength, endurance, nutrition, and neuromotor performance) and seven consequences domains (medial complexity, healthcare utilization, appearance, self-perceived health, activities of daily living, emotional status, social status). Each domain has two to four clinical indicators. Indicators are rated subjectively on a seven point scale anchored by markedly worse to markedly improved, and summed. Certain areas are considered intrinsic to frailty and are highlighted. This measure is able to discriminate magnitude and direction of change in frailty risk, and capture different patterns of physical impairment and psychosocial change. Similarly, the Edmonton Frail Scale is a multidimensional tool that utilizes data accessible in a typical clinical encounter (Rolfson et al., 2006). The assessment domains include general health status, cognition, functional independence, social support, medication use, nutrition, mood, continence, functional performance, and quality of life. A maximum score of 17 indicates the highest level of frailty.

Clinical tools for the assessment of frailty must be practical, easy to understand and administer, not require special equipment, time-efficient, scientifically valid and reliable, clinically meaningful, and comparable across patient populations. Despite validation of the CHS frailty criteria in multiple research studies, widespread use is hindered by practical limitations related to the time and equipment needed to administer the test and calculate risk status. Criteria used in composite measures that incorporate available data and performance tests vary widely. Some measures, while practical and clinically meaningful, may fail to capture the complex interactions between physiologic and physical function, cognition, mood, social support and the environment, as these are not easily assessed. Nevertheless, incorporation of frailty criteria into geriatric assessment would bring attention to patient deficits and highlight care needs. Frailty assessment and risk stratification can identify vulnerable elders for intervention and protection. Additionally, frailty assessment may improve detection of higher functioning elders with subclinical risk factors or precursors that may predispose them to adverse events, poor outcomes, and risk for higher levels of frailty for which intervention can be directed.

Epidemiology of Frailty

The prevalence of frailty varies across studies due to considerable differences in definition, measurement, domains and criteria, and population characteristics (community-dwelling, nursing home) (Singh et al., 2008). Research indicates that 3% to 7% of older adults 65 to 75 years of age are frail. Although frailty increases with age, it is not universal (Walston, 2008). Elders may be classified as prefrail or intermediate frail, where fewer frailty criteria are evidenced. The presence of single criteria or other precursors or risk factors presumes risk for progression to a higher level of frailty.

In the Cardiovascular Health Study, the prevalence of frailty based on the CHS frailty criteria was 6.9% in those over age 65 years, and 25% in those over age 85. Forty-five percent met intermediate frailty criteria and 48% were nonfrail. A higher proportion of cardiovascular disease and frailty occurred among women and Blacks. Cardiovascular disease was significantly associated with frailty, where the odds ratio for intermediate frailty was 2.4 and for frailty was 7.51 ($p < 0.001$) in adjusted models (Newman et al., 2001).

In the Women's Health and Aging Studies, the prevalence of frailty in the WHAS-I and II cohort was 11.3%, compared to 11.6% in the CHS cohort (Bandeem-Roche et al., 2006). In the more disabled WHAS-I cohort, a higher percentage of women (25.4%) met frailty criteria than in the WHAS II or CHS cohorts. Xue and colleagues (2008) examined frailty in the WHAS-II cohort. The prevalence of frailty was 3%, 35% were classified as prefrail, and 62% were nonfrail. Of the women who were nonfrail at baseline, 44% had weak strength, 23% slow walking speed, and 29% low physical activity, single indicators in the CHS frailty criteria. The incidence of frailty based on a 7.5 year follow-up was 9% among women who were nonfrail at baseline, and 66% became prefrail. Of those who were prefrail at baseline, 23% developed frailty over 7.5 years. Weakness, slow gait, and low physical activity were the most common initial manifestations frailty. Study findings support partially hierarchical patterns in frailty onset. Weight loss and exhaustion signaled a transition to frailty in 80% of women.

In the Women's Health and Aging Studies I and II, allostatic load was associated with frailty (Szanton et al., 2009). About 10% of women were frail and 46% were prefrail. Allostatic load scores ranged from 0 to 8, with the vast majority (91%) scoring between 0-4. In regression analysis, a unit increase in the allostatic load score was associated with increasing frailty, when controlling for race, age, education, smoking, and comorbidities.

In a prospective cohort study in community-living elders examining the independent predictive ability of the CHS frailty criteria plus measures for cognitive impairment and depression, the prevalence of individual frailty criteria was highest for slow gait speed (43%), followed by low physical activity (93%), weight loss (23%), self-reported exhaustion (13%), cognitive impairment (11%), and depressive symptoms (22%) (Rothman et al., 2008).

In a study of community-dwelling elders, using the CHS frailty criteria and measures for cognitive impairment, 7% were frail (Avila-Funes et al., 2009). In adjusted models, frailty alone was not a significant predictor of mortality. Cognitive impairment was detected in 10% who were classified as nonfrail, 12% who were prefrail, and 21.9% who were frail. The addition of cognitive assessment increased ability to stratify risk. Frail elders with cognitive impairment were significantly more likely to develop adverse outcomes such as disability and hospitalization

In the MacArthur Study of Successful Aging, factor analysis of the CHS frailty index criteria found two sub-dimensions that explained 48% of the variance: the first included slower gait, weaker grip, and lower physical activity, and second, exhaustion and weight gain. Elders scored with the CHS frailty index criteria had an adjusted odds ratio of 4.4 for disability in 4 years and of 2.1 for mortality in 9 years. Those with the expanded frailty criteria had an adjusted odds ratio of 5.9 for disability and 2.7 for mortality (Sarkisian et al., 2008).

In the Health, Aging, and Body Composition study, 2% of men and 3% of women were classified as moderately or severely frail using two performance measures (Peterson et al., 2008). At three years, 5% of the men and 9% of the women were frail, and at five years, 13% and 17% of the men and women were frail, respectively. At three years, women had double the incidence of moderate frailty compared to men. The strongest predictor of frailty in adjusted models was the number of diagnoses, which was independent of exercise, activity level, and lifestyle. Increased age, male gender, black race, and low education were associated with frailty.

In a study comparing the CHS frailty criteria with the accumulated deficits index in hospitalized older adults with coronary artery disease, the prevalence of frailty was 27% using the CHS criteria, and 63% using the accumulated deficit criteria (Purser et al., 2006). Slow gait speed was a stronger predictor of six-month mortality than either of the two frailty models. The highest mortality was associated with slow gait speed (14.1%), followed by the CHS model (11.9%) and the accumulated deficit model (11.9%).

A frailty index including nine predictors (age >80, male, low activity, >2 chronic conditions, sensory deficits, gait and balance, ADL, IADL disability, calf circumference, and pessimism about health, patients scoring >3 (37.6%), were classified as frail (Ravaglia et al., 2008). Frailty status predicted hospitalizations, fracture, new or worsening of disability, and mortality. A one point increase in the score was associated with increased risk of adverse events, and doubling of mortality risk. The use of seven frailty markers in another study detected frailty in 42% of cancer patients (Retornaz et al., 2008). In the sample, 88% had at least one frailty marker, 52% had three or more, and the most prevalent markers were for nutrition, mobility, physical activity, and cognition (42%).

In a study comparing four frailty measures that included gait speed, handgrip strength, the CHS frailty Index, and the accumulated deficits index, frailty prevalence ranged from 23% to 88.8% (van Iersel & Rikkert, 2006). Frailty prevalence for hand grip strength was 36%, 48% for the accumulated deficits index, 62.4% for the CHS frailty index, and 88.8% for gait velocity. There was substantial overlap, and only 23% of older adults were considered frail according to all four frailty measures. Concordance in classifying patients as frail or nonfrail was poor to moderate. Dementia prevalence was 51-73% in the frail group, compared to 22-45% in the nonfrail group. In addition, dementia prevalence was

statistically significant for the accumulated deficits index and handgrip strength, but not for the CHS frailty Index and gait velocity.

There are considerable methodological and conceptual challenges in frailty research that hinders accurate estimates of prevalence. The varying definitions, defining characteristics, criteria, and measurement approaches to frailty risk assessment may delineate subgroups of elders associated with frailty risk and highlight sub-dimensions of frailty with potentially distinct etiologies and pathways. Since much research utilizes available data or is constrained by practical limitations, prospective research that utilizes theory-driven approaches is needed to explore the multiple dimensions of frailty.

Perspectives and Emerging Concepts on Frailty

Studies examining aging trajectories reveal marked variability suggesting a highly dynamic processes and interactions between biologic, psychologic, social, and environmental factors and risk for frailty (Kuh, 2007; Whitson et al., 2007). This section describes diverse perspectives and new concepts about frailty.

Biologic frailty and the aging process

Many different organ systems undergo decline in functional capacity and become dysregulated on an anatomic, molecular and physiologic level with increasing age (Wilson, 2004). While all organ systems undergo some degree of diminished function with age, there are complex physiological reserve mechanisms and redundancies that create reserve capacity and countering mechanisms to maintain survival. Bortz (2005) describes aging as “wear and tear minus repair” (p. 391). Organ systems can undergo substantial structural and functional loss but still be capable of normal function. In most organ systems, there can be a 70% margin of loss before evidence of failure is manifested (Bortz, 2002). Symptomatic impairment in organ function may not be evidenced until there have been substantial declines within organ structures among interacting organ systems (Bortz, 2002). Despite considerable capacity, comorbidities, exposure to illness and injury, and other physiologic stressors can deplete vital physiologic reserves and lead to a “cycle of frailty” (Bortz, 2005; Singh et al., 2008, p. 1149). Research suggests that organ system dysregulation advances more quickly in elders who are frail (Wilson, 2004).

The exact role of the aging process and the degree to which certain comorbidities and vulnerabilities share common causes and are related to frailty is yet undetermined (Walston et al., 2006). Two prominent indicators of biologic frailty are sarcopenia and cachexia. Sarcopenia, a state of marked loss of lean muscle mass, is considered a clinical hallmark of frailty (Walston et al., 2006). Sarcopenia may represent the net effect of multi-organ dysregulation since maintenance of skeletal mass is a function of hormonal, inflammatory, neurological, nutritional, and physical activity states (Walston et al., 2006).

Cachexia is characterized by muscle wasting, weight loss, anorexia, and inability to absorb nutrients. Cytokines that induce sarcopenia and cachexia may explain the “loss of energy” that is a central feature of frailty (Fillit & Butler, 2009, p. 349). Paradoxically, obesity may be associated with frailty through induction of an inflammatory state that contributes to development of sarcopenia (Jarosz & Bellar, 2009; Walston et al., 2006).

Frailty as a syndrome

In geriatric medicine a syndrome refers to multifactorial health conditions that occur with an accumulation of deficits and impairments in multiple systems resulting in increased vulnerability and adverse outcomes (Bergman et al., 2007; Inouye et al., 2007). Manifestations of a syndrome occur in combination, and no single manifestation stands out to distinguish those with the syndrome (Walston et al., 2006). Various definitions of frailty as a syndrome have included combinations of signs and symptoms such as weakness, fatigue, weight loss, decreased balance, low physical activity, slowed mobility, social withdrawal, cognitive changes, and increased vulnerability to stressors (Walston et al., 2006). Frailty is also described as a “final common pathway” or “precursor state” that results from altered processes and changes from multiple contributors. Given this, the search for underlying etiologies may not always be appropriate, diagnosis may remain elusive, and treatment may not be effective (Buckner & Wagner, 1992; Inouye et al., 2007).

Another view of frailty as a syndrome is that it may not be a single syndrome representing a final common pathway, but a constellation of syndromes, each with different contributors and different pathways (Bergman et al., 2007; Sarkisian et al., 2008). Research on geriatric syndromes such as falls, delirium, incontinence, functional decline and immobility, termed the “geriatric giants,” (Rockwood et al., 1994, p. 490) suggests that there are shared risk factors among these syndromes and to the overarching syndrome of frailty (Inouye et al., 2007). Characteristics of geriatric syndromes suggest there might be common etiologic factors, and that these syndromes are marker conditions for frailty. However, their onset and progression is not simultaneous. Cellular and organ system decompensation may advance at different rates and provoke deficits at different points on the frailty trajectory. Different multidimensional models conceptualizing frailty in non-linear patterns may better elucidate the distinct physiologic processes and pathways that contribute to the variable expressions of frailty. Research on frailty sub-dimensions suggests variability in frailty level, disability and comorbidity and a potential intrinsic role of cognitive impairment (Sarkisian et al., 2008). Some sub-dimensions of frailty may be more lethal and have a worse prognosis than others (Sarkisian et al., 2008). Interventions developed to prevent and treat frailty can be targeted to sub-dimensions of frailty that are most responsive or minimize adverse sequela (Fried et al., 2004; Inouye et al., 2007; Sarkisian et al., 2008).

Frailty as a trajectory

Frailty may be viewed as a process that occurs along the age continuum in dynamic interaction with age-related physiologic changes, chronic and acute illness, and physical function. Even in the presence of comorbidities and disability, some elders will develop significant physiologic vulnerability and frailty, while others remain independent and age well (Gill et al., 2006; Walston et al., 2006).

Figure 1 depicts the frailty trajectory which illustrates pathways along the age continuum for biologic function and physiologic vulnerability along one slope and physical function and independence along the other slope. The natural history of frailty is nonlinear, with transitions between levels. Although transitions may often shift towards greater frailty, transition to lesser states of frailty occurs in about 23% of frail elders (Gill et al., 2006). A direct, causal relationship between progressive physiologic decline and advancement to higher levels of frailty cannot be presumed. The dynamic interaction between physiologic and physical function along the age continuum will unfold and manifest in different patterns among elders. Some may experience rapid, progressive physiologic decline and dysregulation and develop physical function limitations that rapidly escalate to incapacitation. Others may experience slower progression of physiologic dysregulation and losses. Research suggests that many elders will spend months or years in a state of progressive decline (Fillit & Butler, 2009). The context in Figure 1 is especially important in the frailty trajectory. The physical, social, and neighborhood environment, economic resources, and health and social services can mediate or moderate the onset and progression of frailty, and the duration of disability and dependency in later stages.

The frailty trajectory can be examined from a life course perspective in contrast to views of frailty as a geriatric phenomenon. Longitudinal studies utilizing a life course framework consider frailty an expression of accelerated aging from lifetime exposure to physiologic, psychosocial, and environmental factors that have a differential impact on health status (Kuh, 2007). This perspective contrasts with conventional frailty research that is designed to study the oldest individuals to distinguish those who exhibit frailty from those who do not (Fried et al., 2001). Life course researchers propose that problems of childhood growth patterns and development are relevant to frailty and comparable to the atrophy, degeneration and decline that occurs in the aged (Kuh, 2007). For instance, prenatal and postnatal development of muscle fibers and growth during puberty may have important effects on musculoskeletal aging and risk for frailty (Kuh, 2007). Studies of resilience identify elders who maintain higher biologic and physical function than would be expected considering their lifetime risk exposure (Kuh, 2007). Studies on psychological resilience indicate that positive affect and coping behaviors over the life course may attenuate the physical decline in aging and moderate the negative effects of frailty (Fillit & Butler, 2009).

Cumulative risk and allostatic load

Cumulative biologic risk has been explored as a factor affecting health and illness. A defining feature of healthy functioning is the body's adaptive capacity to respond to stressful stimuli through cognitive, emotional, behavioral, and physiologic responses (Carlson & Chamberlain, 2005; Clark, et al., 2007). In aging, there is an accumulation of health deficits that may result in decreased physiologic adaptive reserve, organ system decline, and development of chronic disease. Research supports the detrimental effects of stress on the development, progression, and severity of chronic disease (Clark et al., 2007). This process of weathering, or wear-and-tear, leads to cumulative stress and damage to organs and systems through sustained physiologic arousal and dysregulated function (Geronimus, 2001). The adverse effects of weathering begin at an early age and accrue throughout lifetime to exert a physiologic cost in early health deterioration and onset of chronic disease, disability, and mortality (Geronimus, 2001).

Allostatic load describes the physiologic responses to persistent stress in daily life through adaptation processes of complex physiologic systems (Glei et al., 2007; Logan & Barksdale, 2007). Allostasis refers to the process of internal regulation to accommodate external demands. Repeated or constant states of stress-induced arousal lead to persistent derangements in neurohormonal feedback mechanisms in the hypothalamic-pituitary-adrenal axis, sympathetic nervous system, and immune system (Carlson & Chamberlain, 2005). Individual differences in disease occurrence over time may be related to the damaging effects of life stressors, where the release of physiologic mediators such as adrenalin, cortisol, and cytokines act upon receptors in tissues and organs. In the short run, these processes are adaptive, but in the context of unremitting physiologic stressors and responses that are overactive or inefficient, damage occurs in multiple organs and across multiple systems (McEwen, 2002). Allostatic load therefore is a cumulative measure of dysregulation across multiple physiologic systems that is associated with stressors (Glei et al., 2007), age-associated declines in health status and function, morbidity and mortality (Geronimus et al., 2006; Karlamangla et al., 2002; Seeman et al., 2004) and frailty (Szanton et al., 2009).

Psychosocial aspects of frailty

A biologic/physiologic view of frailty has dominated much of the research but clinicians hold to the premis that frailty is multi-dimensional and includes the psychosocial domain. The psychological aspects of frailty and the psychological effects of the transition from a healthy state to frailty is a topic that has received little attention in the literature (Fillit & Butler, 2009). The incorporation of psychosocial factors has been limited due to difficulty identifying which factors are most influential. Psychological problems such as depression and loneliness may predispose to frailty through activation of psychoneuroimmunological mechanisms (Fillit & Butler, 2009; McEwen, 2002). In a longitudinal study, high

positive affect was found to significantly lower the risk of frailty (Ostir et al., 2004). Other research indicates that isolation, lack of social support, participation in social activities or involvement with family and friends had a negative relationship with frailty. In a study of community dwelling elderly, a social vulnerability index for living situation, language, social support, social and leisure activities, relationships, and socio-economic status (Andrew et al., 2008) was weakly correlated with a frailty index (Rockwood et al., 2007).

In the absence of documented decline in physiologic processes or physical function, frailty may also arise from psychosocial and environmental demands leading to changes in physical activity and lifestyle. For example, lifestyle restrictions in response to environmental barriers or psychosocial factors such as fear of falling, anxiety, loneliness, and depression can lead to deterioration in physical function, progressive muscle deconditioning, functional losses, and risk for frailty. The experience of deteriorating health status, transitions along the frailty trajectory, and accompanying loss of independence may provoke a “frailty identity crisis” and passive acceptance of frailty and disability (Fillit & Butler, 2009).

Interventions for Frailty

The evidence-base for interventions to reduce or reverse frailty is limited. Frail elders are often excluded from intervention research based on assumptions that they would not tolerate testing or intervention protocols or they may not benefit from treatment (Ferrucci et al., 2004). The Frailty Working Group suggests that elders who are most likely to benefit from interventions are frail elders who are not yet disabled and those with early disability who are at high risk for progression to advanced levels of frailty (Ferrucci et al., 2004). Interventions for frailty may also be stratified according to three stages of frailty: prevention of frailty risk factors and precursors, treatment and management of clinical syndromes associated with frailty, and treatment of adverse outcomes of frailty (Buchner & Wagner, 1992; Fried, 1994). Intervention at different points on the frailty trajectory may require shifting the focus to function rather than survival, and quality of life rather than longevity (Rockwood et al., 1994). Interventions can also extend the focus from physical frailty to psychological needs and life stage challenges that evolve during transitions in frailty status (Fillit & Butler, 2009). Attention to psychological, social, and spiritual needs may moderate the negative effects of frailty on physical and emotional health.

Most intervention research has focused on nutrition and physical activity to address frailty risk factors or correlates. In a review of treatments for frailty, Walston and colleagues (2006) summarize nutritional enhancements using micronutrients and anabolic steroids such as megestrol for appetite, and growth hormone, testosterone and DHEA to prevent or treat sarcopenia. Erythropoietin has neuroprotective and regenerative effects and may be useful in stroke, myocardial infarction, sarcopenia, and osteoporosis. Angiotensin converging

enzyme inhibitors may improve muscle mass and strength, and statin treatment may have anti-inflammatory properties (Walston et al., 2006). Increased caloric intake combined with exercise may offer increased health benefits (Ahmed et al., 2007).

Exercise interventions influence a broad range of physiologic systems, disease risk factors, chronic illness states, and psychologic functioning (Binder et al., 2002; Chodzko-Zajko et al., 2009; Garg et al., 2009; Walston, 2008). The protective and restorative effects of physical activity and exercise on physiologic processes (inflammation, metabolism, energetics) may delay or prevent sarcopenia, functional decline and disability and slow biologic aging (Ahmed et al., 2007; Berk et al., 2006; Garg et al., 2009; Gu & Conn, 2008; Nelson et al., 2005). Unfortunately, there are few well designed exercise intervention studies in the elderly. In a meta-analysis of clinical trials (N=19), the median sample size was 67 (range, 21-486). Most studies were conducted with elderly living at home (94.7%), while two were conducted in long term care facilities (Gu & Conn, 2008). The majority of interventions employed strength or resistance training (76.7%) either alone (36.7%) or in combination with another form of exercise (40%). Eight studies recruited healthy elderly, but six studies enrolled elders with functional limitations, two studies enrolled frail elders, and three targeted inactive elders. The meta-analysis found that exercise intervention had a statistically significant impact on physical performance measures. In particular, strength training in combination with exercises that address specific deficits, such as balance, was most effective. A systematic review of exercise intervention in moderately frail community-living elders found that high-intensity multi-component exercise programs can have a positive effect on function (Daniels et al., 2008). Several randomized controlled trials enrolling sedentary elders at risk for disability or frailty found that walking speed and other performance measures were significantly improved in the intervention group (Binder et al., 2002; LIFE-P Study Investigators et al., 2006). Research suggests that exercise interventions may be beneficial even when begun in late life for maintaining or improving function and preventing or postponing frailty (Berk et al., 2006; Binder et al., 2002; Nelson et al., 2007; Peterson et al., 2009).

There is a need for greater understanding of the types of exercise programs that are the most effective for frailty subgroups, as approaches may be distinctly different. Exercise programs designed broadly for independent-living elders may not be appropriate for elders with functional or cognitive impairment, chronic illnesses, or frailty (Ferrucci & Simonsick, 2006; Stewart, 2001). For example, since many older adults manage chronic illnesses, a combination program that assesses and manages symptoms such as weakness, fatigue, dyspnea, pain and depression can improve function and well-being and enable participation in physical activity that meet exercise recommendations (Peterson et al., 2009; Sullivan-Marx et al., 2008; Xue et al., 2008). Many elders have a fear of falling, which may deter physical activity and exercise (Arfken et al., 1994; Bruce et al., 2002). Interventions that address fear of falling (Dukyoo et al., 2009) and offer

techniques to improve balance can increase physical function and foster the self-confidence needed for safe participation in exercise programs. Interventions may also need to address psychological barriers stemming from a person's beliefs about exercise and one's identity in "old age" (Fillit & Butler, 2009, p.349) since negative stereotypes about exercise efficacy may block opportunities for achievement of exercise's health benefits.

Nursing Implications for Practice and Research

Frailty is increasingly viewed as a prevalent and potentially preventable and modifiable syndrome, and not an absolute accompaniment to aging (Bortz, 2002; Rothman et al., 2008). Despite a strong biomedical approach in frailty research, Gerontological perspectives that influence views of frailty are broadening to include a focus on function over impairment, holism and integration versus a mechanistic separation of the organism into parts, the interconnectedness of the biologic, psychologic, social, and spiritual realms, and the influence of the physical and social environment on health status and wellbeing. Nursing's role in assessment, prevention, and treatment of frailty is pivotal.

A comprehensive approach to frailty includes 1) monitoring of health status and indicators of frailty, 2) optimizing biologic and psychosocial function (physical activity, nutrition, chronic disease management, polypharmacy, social support), 3) prevention of physiologic loss during acute illness, bedrest, treatments, surgery (nutrition, hydration, mobilization, pain, sleep, cognitive stimulation), and 4) implementation of restorative interventions when physiologic loss has occurred (rehabilitation and support services).

Comprehensive geriatric assessment and interdisciplinary collaboration provide a rational foundation for Gerontological nursing care of frail elders where a specific etiology is undetermined. Due to the multiple etiologic pathways that underlie frailty, extensive diagnostic testing may not yield helpful information (Inouye et al., 2007). The dynamic interactions of age-related changes, functional status, and chronic and acute illness along the frailty trajectory require careful nursing assessment and monitoring. Incorporation of frailty measures in the nursing assessment is the first step to determining frailty status. Although simple multidimensional frailty scoring systems are lacking (Ravaglia et al., 2008), the incorporation of a performance tests (i.e., Timed Get Up and Go, gait speed) into assessment, and attention to other frailty indicators that are already included in comprehensive geriatric assessment is a feasible approach to stratify frailty risk (Studenski et al., 2004; van Iersel et al., 2008).

Therapeutic treatment of chronic illness and the clinical manifestations of frailty can be beneficial even in the absence of definitive diagnoses (Inouye et al., 2007). Interventions that target specific components of frailty such as poor nutrition, deconditioning, poor balance, depression, and sensory deficits, may improve or preserve function, prevent comorbidities and delay progression of

frailty. For example, a frail older person who is admitted to an acute care setting with urinary incontinence, urinary tract infection and fever, and also presents with delirium, dehydration, perineal skin rash, weight loss, and arthritic hip and knee pain will require host of interventions that could improve health status across a range of systems. In this case, interventions should include not only antimicrobial treatment, antipyretics, and hydration, but should also address nutritional support, skin care, pain management, physical reconditioning, falls prevention, cognitive stimulation, and sleep hygiene. When cognitive function improves, the plan of care can be modified to increase self-care and prevent the adverse consequences of immobility associated with acute illness (Olson et al., 1990). Periods of immobilization or “taking to bed”, even if short term, can have deleterious and irreversible consequences in the elderly (Clark et al., 1990; Carnevali & Brueckner, 1970). Environmental modifications, adjustments in social support and care giving, and training in different types of assistive devices and other prosthetics can promote recovery and independence and counteract dependency. For older adults in poor health or disadvantaged socioeconomic conditions, referral for consultation on accessing available health and social services could improve complex or impoverished living situations. Many older adults do not receive services that are available, and removing barriers would help promote independence, meet daily needs, and optimize chronic illness care (Kuh, 2007). Timely and appropriate intervention may modify the frailty trajectory (Bergman et al., 2007; Purser et al., 2006).

Encouragement and goal setting for gradually increasing physical activity, including bed and chair exercises and range of motion (a highly under-rated intervention), is important in Gerontological nursing care. In addition, optimal symptom management may improve comfort and mobility, and enable higher levels of physical effort. Some older adults may express reluctance or aversion to physical activity and exercise Nurses can help reframe the older person’s mental model, since once the value, health benefit and safety of different types of activities is appreciated, and issues of pain, injury, or fatigue are addressed, then small behavior changes can be introduced and become habitual. Rejeski (2008) suggests a mindfulness-based approach to physical activity that integrates the person’s priorities, goals and daily behavior in a framework that minimizes negative emotions and physical symptoms. Physical activity can then become a part of daily routine that produces a sense of well being (Rejeski, 2008). Nurses can coach and support elders in developing physical activity and exercise habits that are personally meaningful so that achievements can be recognized and behavior changes rewarded (Hamerman, 1999).

There is a genuine need for nursing research in frailty to elucidate this complex, poorly understood phenomenon from a variety of theoretical perspectives (Ferruci et al., 2004; Fisher, 2005). Both qualitative and quantitative methodologies need to explore frailty and its trajectory in the aging process using theoretical models that capture the diversity of the aging experience from a multidimensional perspective. Prime areas for nursing research include the

following: 1) identify criteria for frailty and frailty subgroups, 2) characterize the natural history of frailty, 3) determine if frailty is a syndrome with defined risk factors and a common underlying cause, or defined by multiple clusters of risk factors and etiologies, 4) explore the role and impact of cognitive impairment and neurological degeneration in frailty, 5) explore theoretical models and methodologies such as the life course and allostatic load in longitudinal studies to understand the influence of life history, adverse life events, chronic stress, and biopsychosocial factors and frailty risk and its rate of progression, 6) examine health behaviors in well elders and in those who exhibit physical and psychological resilience, especially noting geriatric syndromes such as falls, delirium and incontinence that are considered markers of frailty, 7) conduct qualitative studies to explore frailty experience and the biopsychosocial and spiritual factors associated with coping with interdependency and dependency along the frailty trajectory, 8) identify key time points for targeted interventions for primary, secondary and tertiary prevention, 9) develop multidisciplinary programs to study frailty and mind-body interactions, and 10) develop effective models for dissemination of frailty assessment methods and interventions into practice (Ferrucci et al., 2004; Fillit & Butler, 2009; Inouye et al., 2007; Walston et al., 2006).

Conclusion

The concept of frailty provides a more integrative and holistic perspective to view the heterogeneity in health risk status of the older population that departs from organ- and disease-based approaches in traditional medicine (Bergman et al., 2007). Older adults experience different trajectories and pathways to frailty (Sarkisian et al., 2008). A better understanding of frailty will guide new directions for health promotion and improved care for subgroups of elders with different frailty status. Nurses can be influential in preventing and ameliorating frailty through comprehensive geriatric assessment and interventions to prevent frailty and promote optimal biopsychosocial and physical functioning, chronic illness and symptom management, and spiritual and psychosocial support. Nurses need to be fully engaged in the scientific work on frailty in clinical practice and research to improve care and quality of life in this vulnerable group of elders.

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Table 1

Definitions of frailty

Definition	Source
Those elderly persons over age 65 years who depend on others for activities of living and may require institutional care.	Woodhouse, 1988
A state of reduced physiological reserve associated with increased susceptibility to disability.	Buchner & Wagner, 1992
Diminished energy flow (interaction) between the individual and their environment.	Bortz, 1993
Unable to integrate responses in the face of stress.	Rockwood et al., 1994
A diminished ability to carry out the practical and social activities of daily living.	Brown et al., 1995
Excess demand imposed upon reduced capacity.	Powell, 1997
A syndrome involving deficiencies in two or more domains involving physical, nutritive, cognitive and sensory capabilities.	Strawbridge, 1998
Frailty is diminished functioning combined with diminished self-rated health.	Dayhoff et al., 1998
A state of age-related physiologic vulnerability resulting from impaired homeostatic reserve and reduced capacity of the organism to withstand stress.	Fried & Walston, 1999
A midpoint between independence and pre-death.	Hamerman, 1999
Frailty as a consequence of high allostatic load, an index of wear and tear on the body over time by efforts to adapt to life experiences and persistent stressors.	Seeman et al., 1999
Frailty is based on a phenotype of 5 characteristics, any three of which mark frailty, 1-2 mark prefrail or intermediate frailty.	Fried et al., 2001
Loss of adaptive capacity due to a loss of complexity.	Lipsitz, 2002
A state of muscular weakness and other secondary widely	Bortz, 2002

distributed losses in function and structure.	
An age related alteration in physiology and pathology that leads to vulnerability, loss of physiological reserve, and a range of poor medical and functional outcomes, a final common pathway, where the effect of disease, disuse, and aging across organ systems contribute to decline and adverse events.	Studenski et al., 2004
Increased vulnerability to stressors due to impairment in multiple, inter-related systems that lead to decline in homeostatic reserve and resilience, with the main consequence as increased risk for multiple adverse health-related outcomes.	Bergman et al., 2007
Frailty is based on a count of accumulated deficits that accrue over time which are weighted equally, and is considered a state variable that characterizes overall health, and is not a syndrome.	Rockwood et al., 2007
The psychological domain of frailty is defined as “Frailty identity crisis” to characterize a psychological syndrome that may accompany the transition from independence and robust health status to frailty status, which can be adaptive or maladaptive.	Fillit & Butler, 2009

Table 2

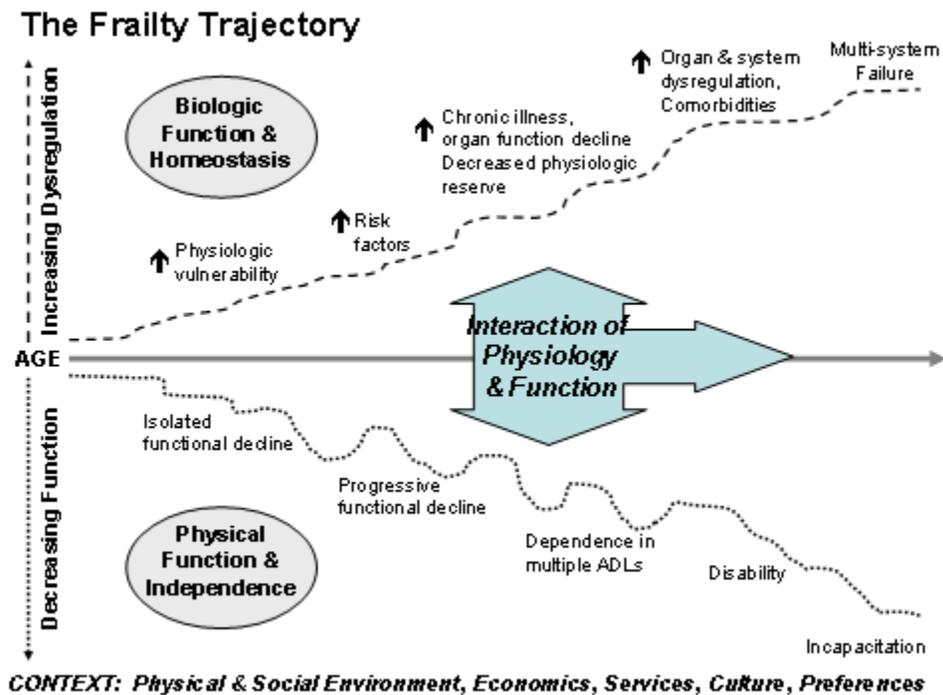
Criteria used to define physical frailty (Adapted from Fried et al., 2001, pp. M156 and Walston et al., 2006).

One must have 3 of the 5 following criteria for frailty, 2 for intermediate frailty, and 1 for prefrail				
Frailty Criteria	Male		Female	
15 foot walk time- “slowness”	Height < 173	> 7 seconds	Height < 159	> 7 seconds
	Height > 173	> 6 seconds	Height > 159	> 6 seconds
Hand grip strength – “weakness”	BMI < 24	< 29	BMI < 23	< 17
	BMI 24.1-26	< 30	BMI 23.1-26	< 17.3
	BMI 26.1-28	< 30	BMI 26.1-29	< 18
	BMI > 28	< 32	BMI > 29	< 21
Unintentional weight loss- “shrinking”	Greater than 10 lbs or 5% weight loss in the last year not due to dieting or exercise, calculated as: (weight in prior year – current measured weight)/(weight in prior year); frail for weight loss if calculation is > 0.05.			
Physical activity*- “low activity”	<383 kilocalories/wk		< 270 kilocalories/wk	
Exhaustion- “fatigue”	A score of 2 or 3 on either question of the CES-D			

	<p>How often in the last week did you feel this way?</p> <p>“I felt that everything I did was an effort.”</p> <p>“I could not get going.”</p> <p>0 = 1 day, 1 = 1-2 days, 2 = 2-3-4 days, 3 = more than 4 days.</p>
<p>*Calculated from short version of the Minnesota Leisure Time self-report questionnaire asking about walking, chores, mowing, swimming, hiking, dancing, cycling, etc. Kilocalories per week expended are calculated using a standardized algorithm.</p>	
<p>CES-D = Center for Epidemiologic Studies Depression Scale.</p>	
<p>BMI = body mass index (calculated by kilograms divided by meters squared, or pounds x 703/ height in inches).</p>	

Figure 1

The Frailty Trajectory



Editor's note: Due to technical difficulties, a previous version of this manuscript was found to contain some errors. This version of the manuscript replaces the earlier version.