

A REVIEW OF FRAILTY IN DEVELOPING COUNTRIES

T.N. NGUYEN^{1,2}, R.G. CUMMING¹, S.N. HILMER²

1. Sydney School of Public Health, University of Sydney, NSW, Australia; 2. Departments of Clinical Pharmacology and Aged Care, Royal North Shore Hospital and Kolling Institute of Medical Research, Sydney Medical School, University of Sydney, NSW, Australia. Corresponding author: Tu Nguyen, MD, PhD Candidate, Room 121A Edward Ford Building, School of Public Health, The University of Sydney NSW 2006 Australia, Phone. (+61) 02 93516898 Email: nngu9517@uni.sydney.edu.au

Abstract: *Background:* As the population ages, the prevalence and clinical importance of frailty are increasing. There have been few published studies about frailty in developing world. This study aims to review the evidence from developing countries on the prevalence of frailty, definition of frailty and factors associated with frailty. *Method:* A literature search was conducted via MEDLINE and EMBASE. Keywords included “frail”, “frailty”, “prevalence”, “criteria”, “definition”, “risk factors”, “outcomes”, “developing country”, “developing world”, and names of low and middle income countries according to the classification of the World Bank. *Result:* A total of 14 articles were reviewed from Brazil (n=6), China (n=3), Mexico (n=2), and one each from Russia, India, and Peru. There were 9 articles from community-based studies and 5 articles from hospital-based studies. Fried’s phenotype for frailty was used to define frailty in the majority of studies. The prevalence of frailty in community-dwelling older people was 17%-31% in Brazil, 15% in Mexico, 5%-31% in China, and 21%-44% in Russia. The prevalence of frailty was 49% in institutionalized older patients in Brazil and 32% in hospitalized older patients in India. The prevalence of frailty in outpatient clinics was 55%-71% in Brazil and 28% in Peru. Frailty was associated with increased mortality and comorbidities, decreased physical and cognitive function, and poor perceptions of health. *Conclusion:* The limited studies available suggest that frailty occurs frequently in older people in the developing world and it appears to be associated with adverse outcomes. This has implications for policy and health care provision for these ageing populations.

Key words: Frailty, prevalence, outcome, developing countries, low and middle income countries.

Introduction

The world’s population is ageing, not only in developed countries but also in developing countries. In 2010 about two third of the world’s population 60 years and older lived in less developed countries and it is estimated that the speed of aging in middle- and low-income countries will outpace that of the high-income countries (1). As the population ages, the prevalence and clinical importance of frailty are increasing.

Frailty is a clinical syndrome resulting from multisystem impairments and characterized by increased vulnerability and disabilities (2). Frailty occurs as a result of impacts from multiple physical, social and environmental factors, and is a changeable condition. Multiple physiological factors are thought to be involved in the development of frailty, including the immune, cardiovascular, metabolic and nervous systems. Frailty is also consistently associated with inflammation and activation of thrombotic pathways. Frailty predicts adverse outcomes for older people, such as comorbidities, polypharmacy, loss of independence, increasing hospitalizations, and mortality. Clinically, frailty may have an impact on treatment strategies and responses to therapy and prognosis. For hospitalized patients, frailty status prior to admission has been shown to predict poor outcomes (3). Understanding the etiology, prevalence and outcomes of frailty informs research and policy to optimize care for older people (2).

Although the concept of frailty has been emerging in geriatric medicine for many years, there is no gold standard

for the definition of frailty. The two most commonly used definitions in research revolve around deficit accumulation and around the frailty phenotype (2). Rockwood et al used an accumulation of deficits which include physical dysfunction, cognitive deficits, comorbidities and socio-economic conditions to calculate a Frailty Index (FI) (2). On the other hand, Fried et al defined frailty with five criteria: unintentional weight loss (more than 10 pounds in prior year), weakness (measured by grip strength), self-report exhaustion, slowness (measured by walking speed) and low physical activity (measured by energy expenditure). Having three or more criteria indicates a frailty phenotype, while one or two criteria indicate intermediate or prefrail (2). Recently, the Edmonton Frail Scale has been applied in many studies. This scale, which was elaborated by Rolfson in Canada, involves 9 frailty domains (cognition, general health status, functional independence, social support, medication use, nutrition, mood, continence and functional performance). With a maximum score of 17, 0 to 4 score indicates robust, 5 to 6 scores indicates apparently vulnerable status, 7 to 8 mild frailty, 9 to 10 moderate frailty and 11 or more indicates severe frailty (4). In terms of feasibility, the Edmonton Frail Scale seems to be the quickest, FI requires simple measures, while phenotype requires specific equipment. The FI can be done retrospectively, others need specific data collection or modification of the tools. The frailty phenotype seems to be the most affected by acute illness for studies in acute setting.

Many studies have reported the prevalence of frailty in Western countries. The prevalence of frailty in the community

A REVIEW OF FRAILTY IN DEVELOPING COUNTRIES

Table 1
 Studies of frailty in community-dwelling older adults

Authors and year of publication	N	Participants	Sampling method and time period	Prevalence of frailty/ Mean FI	Definition of frailty
Brazil					
Asmar Alencar et al, 2012 (6)	207	Aged 65 years or older. Mean age \pm SD: 74.5 \pm 6.4 (non-frail) 78.3 \pm 8.0 (pre-frail) 82.3 \pm 7.1 (frail)	Simple random probabilistic sampling, response rate not provided in the paper. Data collected 2009	23.2%	Fried's criteria
Fabricio-Wehbe et al, 2009 (7)	137	Aged 65 years or older 65-79: 67% \geq 80: 33%	Representative sample based on a probabilistic double-stage sampling process in the population. Response rate 80%. Data collected 2007-2008.	31.4%	The Edmonton Frail Scale
The FIBRA Study, 2011 (8)	391	Aged 65 years or older. 65-74: 60% 75-84: 33% \geq 85: 7%	Representative sample based on a probabilistic multi-stage sampling process in the population. Response rate not provided in the paper. Data collected 2007-2008.	17.1%	Fried's criteria
Mexico					
Mexican Study on Nutritional and Psychosocial Markers of Frailty, 2012 (9)	838	Aged 70 years or older. Mean age \pm SD: 77.9 \pm 6.3	Representative sample based on a random sampling process in the population, stratified by age and gender. Response rate 86.9%. Data collected 2008-2009.	15%	Fried's criteria
The Mexican Health and Aging Study, 2009 (10)	4082	Aged 65 years or older. Mean age: 73.0	Representative sample. Response rate 84.2%. (Participants and their spouse/partners were selected from a nationally representative sample of non-institutionalized Mexicans who had previously participated in the fourth quarter of 2000 in an employment survey). Data collected 2001.	Mean FI: 0.16 \pm 0.11	Frailty Index (34 deficits)
China					
Lee et al, 2011 (11)	4000	Aged 65 years or older. Mean age \pm SD: 72.3 \pm 5.0 (men) 72.5 \pm 5.3 (women)	Sample may be not representative (recruiting by placing recruitment notices in community centers for older persons and housing estates). Response rate not provided in the paper. Data collected 2001-2003	5.4% 1.8% in people from 65-69 years old 3% in people 70-74 years old 11.8% in people \geq 75 years old	Fried's criteria
The Beijing Longitudinal Study of Ageing, 2011 (12)	3257	Aged 55 years or older. 55-64: 32.0% 65-74: 34.0% 75-84: 28.6% 85-94: 5.2% \geq 95: 0.2%	Representative sample based on a random sampling process in the population. Response rate 91.2%. Data collected 1992-2000.	Mean FI: 0.11 \pm 0.1 in men and 0.14 \pm 0.11 in women. Prevalence of frailty (cut-off 0.22): 28.9% in men and 30.8% in women	Frailty Index (35 deficits)
The Chinese Longitudinal Healthy Longevity Survey, 2009 (13)	13717	Aged 65 years or older. 65-79: 30.7% 80-89: 26.8% 90-99: 23.7% \geq 100: 18.8%	Representative sample based on a random sampling process in the population. Response rate 88%. Data collected 2002 -2005.	Mean FI: 0.19 in men 0.26 in women	Frailty Index (39 deficits)
Russia					
Gurina et al, 2011 (14)	611	Aged 65 years or older. 65-74: 50% (mean \pm SD: 69.7 \pm 2.4 for male, 70.2 \pm 2.3 for female) \geq 75: 50% (mean \pm SD: 78.8 \pm 3.2 for male, 80.5 \pm 2.4 for female)	Representative sample based on a random sampling process in the population, stratified by age. Response rates: 59.5% in male aged 65-74 70.1% in female aged 65-74 61.3% in male aged \geq 75 70.3% in female aged \geq 75 Data collected 2009.	21.1% (Fried's criteria) 32.6% (Steinerink-Slaets model) 43.9% (Puts model)	Fried's criteria Steinerink-Slaets model Puts model

has ranged from 4% to 10% in studies in the United States, 6.5% in Italy, 7% in France, 8.1% in the United Kingdom (using Fried's phenotype) (3, 5). In Australia, the prevalence of frailty has ranged from 9.4% (using Fried's phenotype) to 15.2% (using FRAIL scale) in community-dwelling older men and up to 64% in older patients admitted to hospital with atrial fibrillation (using the Reported Edmonton Frail Scale) (3). However, there have been few published studies about frailty in the developing world. Therefore, the aim of this paper is to systematically review the evidence from developing countries on the prevalence of frailty, definitions of frailty and outcomes associated with frailty.

Methods

A literature search was conducted via MEDLINE and EMBASE (from 1990 to January 2014). Keywords used for searching included "frail", "frailty", "prevalence", "criteria", "definition", "risk factors", "outcomes", "developing country", "developing world", and the names of low and middle countries according to the classification of the World Bank. The articles attained by this method of searching were screened by title and relevant papers were retrieved. Both community and hospital/institutional-based studies were included. Studies were stratified by study population into those that studied prevalence of frailty in the community and those that studied prevalence in institutionalized or hospitalized older people. In cases where there were many publications based on one study, the first publication was chosen and full papers were chosen instead of letters to the editor. Language was restricted to English. Information extracted from papers included sample size, sampling methodology, prevalence of frailty, definition of frailty and outcomes. When necessary, percentages were calculated from data reported in published studies.

Results

A total of 110 abstracts was obtained. After further screening for prevalence, definition, and outcomes of frailty, 79 abstracts were rejected. Another 6 abstracts were rejected because full texts in English could not be obtained, leaving 25 papers. Among these 25 papers, there were some studies with several reports. In these cases, the first publication was chosen and full papers were chosen instead of letters to the editor, leaving a total of 14 papers from 14 studies included in this review (6-19). There were 6 studies from Brazil, 3 from China, 2 from Mexico, and one each from Russia, India, and Peru. There were 9 studies from community-based studies (3 in Brazil, 3 in China, 2 in Mexico, and one from Russia). The remainder were in institutions or hospitals. Most of the publications in Brazil, Mexico and China were based on large cohort studies about ageing and frailty, such as the study on Frailty in Elderly Brazilians (the FIBRA study), the Mexican Study on Nutritional and Psychosocial Markers of Frailty, the

Mexican Health and Aging Study, the Beijing Longitudinal Study of Ageing and the Chinese Longitudinal Healthy Longevity Survey.

The 14 reviewed papers were all published between 2009 and 2014 and, apart from the Beijing Longitudinal Study of Ageing (12), the studies were conducted after 2000. All the studies of community-dwelling older people used a probability sampling methodology except the study from China by Lee et al, which involved volunteers recruited via advertisements on noticeboards (11). Response rates were reported in 6 of the community studies and were above 80% in all but the study from Russia (14). It is difficult to compare age distributions between studies because of differences in reporting; however, it appears that most subjects in the community studies were in their 70s. The exception is the Chinese Longitudinal Healthy Longevity Survey, where more than 40% of subjects were aged 90 years and over.

Prevalence of frailty in community-dwelling older adults, outpatients and institutionalized patients varied between countries. The prevalence of frailty in older people in the community ranged from 17.1% to 31.4% in Brazil (data from 2 studies), 15% in Mexico (from 1 study), 5.4% to 30.8% in China (2 studies), and 21.1% to 43.9% in Russia (from 1 study) (Table 1). The low prevalence of 5.4% was from the only study involving a convenience sample (11). Three studies in geriatric medicine outpatients found that the prevalence of frailty was 55.3% to 71.3% in Brazil and 27.8% in Peru. The prevalence of frailty in older people in long stay institutions was 49.3% in one study in Brazil and the prevalence in older inpatients was 32.3% in one study in India (Table 2).

Fried's phenotype was used to define frailty in the majority of studies. Only one study (from Brazil) used the Edmonton Frail Scale, one from Russia reported the Steverink-Slaets and Puts score. The Frailty Index was used in 3 community-based studies: the Beijing Longitudinal Study of Ageing (35 deficits, mean FI 0.11±0.1 in men and 0.14±0.11 in women), the Chinese Longitudinal Healthy Longevity Survey (39 deficits, mean FI 0.19 in men and 0.26 in women) and The Mexican Health and Aging Study (34 deficits, mean FI 0.16±0.11).

Outcomes of frailty were inconsistently assessed in the reviewed studies (6-19). Cross-sectional approach for examining the relationship between frailty and the various outcomes was applied in seven out of the fourteen studies (7-9, 15-18). In the reviewed studies, frailty was associated with increased health care utilization, increased mortality and comorbidities such as cardiovascular diseases, depression, falls and fractures, incontinence, anemia, increased hospitalizations, increased number of medications, increased use of medical and dental services, increased physical dependence and decreased physical and cognitive function, and poor perception of health. One publication from the Mexican Study on Nutritional and Psychosocial Markers of Frailty reported that frailty was not associated with quality of social networks (9).

A REVIEW OF FRAILTY IN DEVELOPING COUNTRIES

Table 2
Studies of frailty in health care settings

Authors and year of publication	N	Participants	Sampling Method	Definition of frailty	Prevalence of frailty
Nobrega et al, 2013 (15) (Brazil)	69	Older residents of six long stay institutions.	Representative sample based on a random sampling process. Response rate 80%.	Fried's criteria	49.3%
Batista et al, 2012 (16) (Brazil)	150	Older patients aged 80 years or older, or patients aged 60 years or older with functional impairment at the outpatient clinic.	Non-probabilistic convenience sampling method.	Fried's criteria	55.3%
Da Silva et al, 2011 (17) (Brazil)	100	Older patients aged 80 years or older, or patients aged 60 years or older with functional impairment at the outpatient clinic.	Non-probabilistic convenience sampling method.	Fried's criteria	71.3%
Runzer-Colmenares et al, 2014 (18) (Peru)	311	Older patients aged 60 years or older at the outpatient clinic (mostly men and retired military personnel).	Random sampling method. Response rate 52.5%.	Fried's criteria	27.8%
Khandelwal et al, 2012 (19) (India)	250	Hospitalized patients aged 60 years or older.	Consecutive series of patients were recruited.	Fried's criteria	32.3%

Discussion

A total of 14 articles describing 14 studies about frailty in developing countries were included in this review. Most of the studies of community-dwelling older adults were conducted using probability sampling methods and achieved high response rates. The quality of the sampling methods for the studies in health care settings was more variable. The prevalence of frailty in older people in developing countries was quite variable, from 5.4% to 44% in community-dwelling older adults, 27.8% to 71.3% in geriatric outpatients and 32.3% to 49.3% in institutionalized older patients.

Fried's phenotype was the most common approach used to determine frailty, not only in community setting but also in hospital based studies in these developing countries. This finding is rather consistent with studies from developed countries. The phenotypic approach to frailty is the most widely used approach and it has been shown to correlate well with both the risk of adverse outcomes and with many important clinical parameters (20). In studies using Fried's frailty phenotype, the prevalence of frailty in community-dwelling adults was variable, ranging from 5.4% in China, 17.1% to 23.2% in Brazil, 15% in Mexico, and 21.1% in Russia. Except for the study in China in which the sample may not be representative (participants were recruited by placing recruitment notices in community centers for the older persons and housing estates), the prevalence of frailty in the developing countries in this review prevalence was high compared to developed countries, in which the prevalence of frailty has ranged from 4% to 17% in the United States, Australia, Canada, the United Kingdom, France and Italy, and other European countries

(5). Poor nutritional health, high prevalence of physical labor during lifetimes and disability may contribute to this result. According to the Study on Global Ageing and Adult Health (SAGE), which was conducted in six countries - China, Ghana, India, Mexico, Russia, and South Africa- approximately 70% of the population aged 50 and over had some types of disability, with up to 90% of older Indians and Russians suffering from disabilities (1). In a recent published study based on the SAGE study data, average walking speeds were slower in SAGE countries than commonly reported in Western countries (21). Variations in measurement when applying the frailty phenotypes in these countries may also explain why the prevalence of frailty in developing countries was more variable and generally higher compared to Western countries.

Only three studies, all in the community, used the Frailty Index to define frailty. All Frailty Indices included symptoms, diseases and physical function. The Beijing Longitudinal Study of Ageing also included cognitive function. The mean Frailty Index in these studies is consistent and rather similar to studies in developed countries. In the Survey of Health, Ageing and Retirement in 12 European countries (based on 40 deficits), the mean FI was 0.08 for those aged 50, 0.10 for those aged 60, 0.14 for those aged 70, 0.21 for those aged 80, 0.30 for those aged 90, and 0.43 for those aged 100 (22). According to the National Population Health Survey of Canada, the mean values of the Frailty Index were 0.046 for non-frail, 0.156 for pre-frail, and 0.310 for frail people (23).

The number of institution-based and hospital-based studies in this review was small and all used Fried's frailty phenotype. There were three studies in geriatric outpatient clinics. One study in Peru in participants aged 60 years or older found that

the prevalence of frailty was 27.8% (18) while two separate studies in Brazil in older outpatients aged ≥ 80 years or aged ≥ 60 years with functional impairment found the prevalence of 55.3% and 71.3% (16, 17). One study in India found that the prevalence of frailty in hospitalized older patients was 32.3% and one study in Brazil showed that frailty was present in 49.3% of older residents of long stay institutions (Table 2).

Frailty has been reported to be associated with many adverse outcomes (3). The outcomes for frail people in the studies reviewed in this paper are consistent with reports from the developed world.

Most of the studies in this review were from Latin America and Asia and all were middle income countries. The prevalence of frailty was variable among these regions. There was no data from low income countries where the prevalence of frailty may be higher. A recent study in Europe found that a country's level of frailty and fitness in older adults was strongly correlated with national economic indicators, such that lower income countries had higher levels of frailty and lower levels of fitness when compared with the higher-income countries (24). There appear to have been no studies on frailty from Africa. In the United States, studies have found that African Americans have a higher prevalence of frailty than Caucasians using Fried's frailty phenotype model (25).

The Fried's phenotype and the Frailty Index can identify older people at high risk of death and correlate well with each other, with the deficit accumulation approach predicting mortality better (26). Although the Frailty Index has been shown to be more applicable for predicting mortality than the phenotypic criteria, in this review there were no studies in hospital settings using the Frailty Index. These findings raise a question regarding the most feasible approaches for frailty research in developing countries. The newer deficit accumulation scales, The Edmonton Frail Scale (4), and the Reported Edmonton Frail Scale that was adapted from the Edmonton Frail Scale for use with Australian acute inpatients (27), are both based on a questionnaire and seem to be easy to apply. This scale is less time-consuming and may be practical for both outpatients and inpatients in the developing world where there are limited resources for conducting research.

This review has some limitations. First, the articles were restricted to English only. We may have missed some papers that were not available in English fulltext or in journals that were not indexed on MEDLINE and EMBASE. Secondly, there may be bias due to inadequate sampling techniques, including use of convenience samples. Thirdly, comparison of prevalence between studies using different frailty assessment methods is complicated by the fact that, even within the same population, different frailty assessments classify different participants as frail (3). Since within populations the prevalence of frailty increases with age (3, 23), another limitation of this study was comparing studies that included people of different ages. The strength of our study is that it is a systematic review that comprehensively addresses the published English language

literature on prevalence, definition and outcomes of frailty in developing countries.

Conclusions

Frailty is an important issue in geriatric medicine. There is emerging evidence that frailty can be used clinically to individualise treatment plans, predict therapeutic outcomes and inform public policy for older people. At the societal level, understanding frailty can help to identify groups of people who need extra medical care. The limited studies available suggest that frailty occurs frequently in the developing world. This has implications for policy and health care provision for these ageing populations.

Conflict of interest: None

References

1. Fried LP, Tangen CM, Walston J, Newman AB, Hirsch C, Gottdiener J, et al. 1. He, W., M.N. Muenchrath, and P. Kowal, Wan He, Mark N. Muenchrath, and Paul Kowal, U.S. Census Bureau, *Shades of Gray: A Cross-Country Study of Health and Well-Being of the Older Populations in SAGE Countries, 2007–2010*, U.S. Government Printing Office, Washington, DC, 2012.
2. Clegg, A., et al., Frailty in elderly people. *The Lancet*, 2013. 381(9868): p. 752-762.
3. Hilmer, S.N. and D. Gnjjidic, Frailty: Chapter 12. In: Caplan G. ed. *Geriatric Medicine: An Introduction*. IP Communications, 2014:189-201.
4. Rolfson, D.B., et al., Validity and reliability of the Edmonton Frail Scale. *Age and Ageing*, 2006. 35(5): p. 526-529.
5. Collard, R.M., et al., Prevalence of frailty in community-dwelling older persons: A systematic review. *Journal of the American Geriatrics Society*, 2012. 60(8): p. 1487-1492.
6. Asmar Alencar, M., et al., Frailty and cognitive impairment among community-dwelling elderly. *Arquivos de Neuro-Psiquiatria*, 2013. 71(6): p. 362-367.
7. Fabricio-Wehbe, S.C.C., et al., Cross-cultural adaptation and validity of the «Edmonton frail scale - EFS» in a Brazilian elderly sample. *Revista Latino-Americana de Enfermagem*, 2009. 17(6): p. 1043-1049.
8. De Albuquerque Sousa, A.C.P., et al., Frailty syndrome and associated factors in community-dwelling elderly in Northeast Brazil. *Archives of Gerontology and Geriatrics*, 2012. 54(2): p. e95-e101.
9. Castrejon-Perez, R.C., et al., Oral health conditions and frailty in Mexican community-dwelling elderly: a cross sectional analysis. *BMC public health*, 2012. 12: p. 773.
10. Garcia-Gonzalez, J.J., et al., A frailty index to predict the mortality risk in a population of senior mexican adults. *BMC Geriatrics*, 2009. 9(1).
11. Lee, J.S.W., et al., Physical frailty in older adults is associated with metabolic and atherosclerotic risk factors and cognitive impairment independent of muscle mass. *Journal of Nutrition, Health and Aging*, 2011. 15(10): p. 857-862.
12. Shi, J., et al., Analysis of frailty and survival from late middle age in the Beijing Longitudinal Study of Aging. *BMC Geriatrics*, 2011. 11: p. 17.
13. Dupre, M.E., et al., Frailty and type of death among older adults in China: Prospective cohort study. *BMJ (Online)*, 2009. 338(7700): p. 924-927.
14. Gurina, N.A., E.V. Frolova, and J.M. Degryse, A roadmap of aging in Russia: The prevalence of frailty in community-dwelling older adults in the St. Petersburg District-The «crystal» study. *Journal of the American Geriatrics Society*, 2011. 59(6): p. 980-988.
15. Nobrega, P.V.D.N., et al., Sleep and frailty syndrome in elderly residents of long-stay institutions: A cross-sectional study. *Geriatrics and Gerontology International*, 2013. DOI: 10.1111/ggi.12144.
16. Batista, F.S., et al., Relationship between lower-limb muscle strength and frailty among elderly people. *Sao Paulo Medical Journal*, 2012. 130(2): p. 102-108.
17. Da Silva, V.A., K.L. de Souza, and M.J. D'Elboux, Urinary incontinence and the criteria of frailness among the elderly outpatients. *Revista da Escola de Enfermagem*, 2011. 45(3): p. 672-678.
18. Runzer-Colmenares, F.M., et al., Prevalence and factors associated with frailty among Peruvian older adults. *Archives of Gerontology and Geriatrics*, 2014. 58(1): p. 69-73.
19. Khandelwal, D., et al., Frailty is associated with longer hospital stay and increased mortality in hospitalized older patients. *Journal of Nutrition, Health and Aging*, 2012: p. 1-4.

A REVIEW OF FRAILTY IN DEVELOPING COUNTRIES

20. Rockwood, K. and A. Mitnitski, Frailty Defined by Deficit Accumulation and Geriatric Medicine Defined by Frailty. *Clinics in Geriatric Medicine*, 2011. 27(1): p. 17-26.
21. Capistrant, B.D., M.M. Glymour, and L.F. Berkman, Assessing mobility difficulties for cross-national comparisons: Results from the world health organization study on global ageing and adult health. *Journal of the American Geriatrics Society*, 2014. 62(2): p. 329-335.
22. Romero-Ortuno, R., An alternative method for Frailty Index cut-off points to define frailty categories. *European Geriatric Medicine*, 2013. 4(5): p. 299-303.
23. Song, X., A. Mitnitski, and K. Rockwood, Prevalence and 10-Year outcomes of frailty in older adults in relation to deficit accumulation. *Journal of the American Geriatrics Society*, 2010. 58(4): p. 681-687.
24. Theou, O., et al., Exploring the relationship between national economic indicators and relative fitness and frailty in middle-aged and older europeans. *Age and Ageing*, 2013. 42(5): p. 614-619.
25. Hirsch, C., et al., The Association of Race With Frailty: The Cardiovascular Health Study. *Annals of Epidemiology*, 2006. 16(7): p. 545-553.
26. Rockwood, K., M. Andrew, and A. Mitnitski, A comparison of two approaches to measuring frailty in elderly people. *Journals of Gerontology - Series A Biological Sciences and Medical Sciences*, 2007. 62(7): p. 738-743.
27. Hilmer, S.N., et al., The assessment of frailty in older people in acute care. *Australasian Journal on Ageing*, 2009. 28(4): p. 182-188.