Frailty in Older Adults with Heart Failure

By

Boqin Xie

**A dissertation submitted in partial fulfillment
of the requirements for the degree of
Doctor of Philosophy
(Nursing)
in the University of Michigan
2015**

Doctoral Committee:

**Associate Professor Cynthia M. Arslanian-Engoren, Chair
Professor Richard D. Gonzalez
Professor Janet L. Larson
Associate Professor Cindy A. Lustig
Professor Susan J. Pressler**

DEDICATION

To My Parents for Their Continuous Support, Unconditional Love and Persistent Encouragement

ACKNOWLEDGEMENTS

I would like to express my deepest appreciation to my PhD advisor, Dr. Cynthia Arslanian-Engoren, for supporting me throughout these four years. It has been an honor to be her Ph.D. Student. She has taught me, both consciously and unconsciously, the importance of scientific rigor and scholarly standard. Without her support and persistent help, this dissertation would not have been possible.

I would like to thank my committee members, Dr. Richard Gonzalez, Dr. Janet Larson, Dr. Cindy Lustig, and Dr. Susan Pressler for their time and valuable comments and feedback. I am very grateful to Dr. Larson, Dr. Lustig and Dr. Pressler for providing insightful discussions about dissertation proposal and research. I would particularly like to acknowledge Dr. Gonzalez for his statistical expertise, scientific advice and many insightful discussions and suggestions.

A special thank to the instructors, Christine Feak and John Swales, in the English Language Institute for their help and support in dissertation writing. Beyond their supports in academic writing, I appreciate for their continuous emotional support and encouragement. I also would like to thank Brady West and Missy Plegue in the Center for Statistical Consultation and Research for assistance with statistical analyses.

I would like to thank my colleagues An-Yun Yeh, Celia Bridges, and Celeste Schultz for editorial helps, scientific discussions, emotional supports, and friendship that I needed and valued. A special thank to my friend Ziyong Lin who spent lots of sleepless nights working with me and incented me when I were down. I couldn’t have survived this dissertation venture without her friendship.

I would like to thank my parents for their constant support and unconditional love. I would like to thank my partner Jianyou Ni. He stood by me through the good times and bad.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

Frailty in Older Adults with Heart Failure

By

Boqin Xie

Abstract

Frailty is prevalent in older adults with heart failure (HF), which increases their risk for basic and instrumental activities of daily living (ADL/IADL) disability and a diminished quality of life (QOL). However, the issue of conceptualizing frailty remains unresolved. To date, the two predominant frailty models are the Fried model, which defines frailty as purely physical, and the Gobben model, which defines frailty as multi-domain with physical, psychological, and social domains.

An integrative literature review of frailty components in existing frailty measures was conducted. The most commonly used frailty components were mobility and balance, nutrition, and cognitive function.

Next, a cross-sectional, secondary data analysis was conducted using data from the Health and Retirement Study (HRS) to compare the capacity of the Fried model and the Gobbens model to predict ADL/IADL disability and QOL. Compared to the Fried physical frailty model, the inclusion of psychological components from the Gobbens model significantly increased the power to predict ADL/IADL disability, while the psychological and social components from the Gobbens' model significantly increased the ability to predict QOL. These findings support the view that frailty is a multidimensional syndrome with three domains (physical, psychological, and social). The levels of the three frailty domains were then compared, and older adults with HF

were found to have higher levels of frailty across all three domains compared to older adults without HF.

Lastly, a longitudinal examination of multidimensional frailty in older adults with HF was conducted, using HRS data collected at two time-points (2006/2008 to 2010/2012) from two cohorts. Across the two time-points, older adults with HF had higher levels of frailty across all three domains compared to older adults without HF. All HF and three frailty domains were associated with increased risks of ADL/IADL disability and decreased QOL. Each frailty domain mediated the relationship between HF and outcomes (ADL/IADL disability and QOL).

The findings in this dissertation support frailty as a multidimensional syndrome. These findings have implications for the development of tailored, broad-based intervention aimed at preventing frailty or delaying its onset to reduce adverse outcomes of ADL/IADL disability and decreased QOL.

CHAPTER I

INTRODUCTION

Statement of the Problem

Frailty is a state of increased vulnerability and deceased reserve capacity that affects many older adults (Clegg, Young, Iliffe, Rikkert, & Rockwood, 2013; Fried et al., 2001b; Fulop et al., 2010; Morley et al., 2013). The prevalence of frailty increases with aging (Fried et al., 2001; Mitnitski, Mogilner, & Rockwood, 2001; Rockwood et al., 2004). According to the Cardiovascular Health Study (CHS), the prevalence of frailty reported for every five years of life beyond age 65 is: 3.2% (age 65-70), 5.3% (age 70-75), 9.5% (age 75-80), 16.3% (age 80-85), and 25.7% (age 85-90) respectively (Fried et al., 2001). A recent meta-analysis (Collard, Boter, Schoevers, & Oude Voshaar, 2012) reported the prevalence of frailty to be as high as 59.1% in community-dwelling adults age 65 and older. Older adults with heart failure (HF) are particularly vulnerable to the development of frailty (Boxer, Dauser, Walsh, Hager, & Kenny, 2008; Cacciatore et al., 2005; McNallan et al., 2013; Newman et al., 2001; Woods et al., 2005). With increasing age, approximately 40% of older adults with HF experience concurrent frailty with the prevalence ranging from 15% to 74%, depending on the study population and the frailty measures used (Harkness, Heckman, & McKelvie, 2012; Uchmanowicz, Loboz-Rudnicka, Szelag, Jankowska-Polanska, & Loboz-Grudzien, 2014). Coexisting frailty in older adults with HF increases the risk for hospitalization, disability and mortality and diminishes quality of life (QOL) (Buck & Riegel, 2011; Cacciatore et al., 2005; Khandelwal et al., 2012).

Heart failure in older adults

Approximately 5.7 million Americans are living with HF, with its incidence and prevalence increasing with age (Mozaffarian et al., 2015). In spite of diagnostic and treatment improvements, the prognosis of adults living with HF is still poor, with 5-year mortality rates between 45% and 60% (Bui, Horwich, & Fonarow, 2011). In addition to its high mortality, HF contributes to functional limitations and disabilities (Alosco et al., 2012; Norberg, Boman, & Lofgren, 2008), ultimately decreasing QOL (Heo, Moser, Lennie, Zambroski, & Chung, 2007). A study using a nationally representative sample of community-dwelling adults with HF reported that more than half (57%) of older adults (≥60 years) with HF had difficulty in walking and 11% were unable to perform activities of daily living (ADL) (Wong, Chaudhry, Desai, & Krumholz, 2011). The ability to perform basic and instrumental activities of daily living (ADL/IADL) is essential for an older adult to live independently and engage in self-care. Difficulties in performing ADLs/IADLs are associated with increased risks for hospitalization, institutionalization in a nursing home and mortality (Dunlay et al., 2015; Gure, Kabeto, Blaum, & Langa, 2008). Another important health outcome in older adults with HF is QOL. Quality of life is a subjective self-evaluation of both positive and negative aspects of one's life (e.g. physical, psychological, cultural, social and environmental) (Harper et al., 1998). Older adults with HF report significantly lower QOL than age-matched older adults without HF (Heo et al., 2007). Declines in QOL among older adults with HF are associated with hospital readmission and mortality (Mejhert, Kahan, Persson, & Edner, 2006).

As the population ages, an increasing number of older adults with HF also experience concurrent frailty (Harkness et al., 2012). Coexisting frailty in older adults with HF increases their vulnerability for poor clinical outcomes and decreases QOL (Harkness et al., 2012). The failure of health providers and nurses to identify frailty and consider its impact may interfere with their ability to provide effective health care to improve QOL and enhance the ability of older adults with HF to engage in ADL/IADL. To mitigate the adverse outcomes experienced by older adults with HF and to potentially delay the onset of concurrent frailty, a better understanding of frailty in this vulnerable population is needed and will be examined in this dissertation.

Concurrent frailty and heart failure

Several cross-sectional studies show the strong association between HF and frailty (Boxer et al., 2008; Cacciatore et al., 2005; McNallan et al., 2013; Newman et al., 2001; Woods et al., 2005). Older adults with HF in the CHS were more than seven times more likely to be frail than older adults without HF (Odds ratio [OR] =7.51, 95% CI=4.66-12.12) (Newman et al., 2001). Similarly, older women with HF in the Women's Health Initiative Observational Study (WHI-OS) were six times more likely to develop frailty than women without HF (OR=6.16, 95%CI= 4.97-7.64) (Woods et al., 2005). McNallan et al. (2013) recently reported that among 223 older adults with HF (mean age=71,SD=14, 61% male), 21% of participants were identified as frail using the frailty phenotype measure (McNallan et al., 2013). Similarly, Cacciatore et al (2005) and Boxer et al. (2008) found high rate of frailty among older adults with HF (54% and 25% respectively).

The relationship between frailty and HF is bidirectional and frail older adults are at increased risk for the development of HF. A recent longitudinal study of 2,825 older adults without a diagnosis of HF at baseline (age=74, SD=3; 48% male) reported that physical frailty (measured by Short Physical Performance Battery, [SPPB]) was independently associated with

HF up to 11 years later (Khan et al., 2013). Compared to non-frail older adults, moderate (one of the two tests in SPPB being abnormal) and severe (both of two tests in SPPB being abnormal) physical frailty in older adults was associated with a higher risk of the development of HF (HR=1.36 and 1.88, respectively) (Khan et al., 2013). This association remained significant even after adjustment using the Health Aging and Body Composition (ABC) HF Risk Score (HR=1.24[1.13, 1.36]). Results remained consistent, even when excluding HF events in the first year of follow-up, indicating that frailty was an independent predictor of the development of HF in older adults. This lends support for the conceptualization of frailty and HF as two separate and distinct concepts.

Consequence of coexisting frailty and heart failure

The co-occurrence of frailty and HF increases the risk of hospitalization and mortality and diminishes QOL among older adults (Buck & Riegel, 2011; Cacciatore et al., 2005; Khandelwal et al., 2012). Khandelwal et al. studied 250 older hospitalized adults with HF and found that frail older adults with HF had higher median hospital stay compared with their non-frail counterpart (14 days vs. 8 days, $p<.001$). The presence of frailty increased the likelihood of death during hospitalization (5 deaths in frail subjects vs. 0 death non-frail subjects; $p=.004$). Similarly, Cacciatore et al. reported that frailty remained a strong predictor of mortality in older adults with HF, even after adjusting for age and gender (Hazard Ratio =1.48, 95% CI=1.04-2.11). In a secondary analysis of 130 older adults with HF (median age =72), Buck and Riegel reported that frailty explained 13% and 25% of variance in QOL in two different samples of patients with HF. While informative, these studies focused only on the relationships between physical frailty and HF. It is also unclear if or how frailty mediates the relationship between HF and adverse health outcomes (QOL and ADL/IADL disability).

Risk factors of frailty

Demographic factors. The impact of individual demographics on frailty in older adults with HF remains unclear. While women have high levels of frailty with aging than men (Fried et al., 2001), results do not always reach statistical significance (Goggins, Woo, Sham, & Ho, 2005; Strawbridge, Shema, Balfour, Higby, & Kaplan, 1998). Frailty in women is associated with increased risk of mortality compared to age-matched men, but this effect is attenuated by disability and chronic diseases (Puts, Lips, & Deeg, 2005). Additionally, inconsistent differences in frailty based on race have been reported. The CHS reported that African Americans have higher rates of frailty compared to Caucasians (Fried et al., 2001). However, minimal racial difference in frailty was reported in the Alameda County Study conducted in northern California (Strawbridge et al., 1998), possibly because the study was conducted in one geographic area with a largely Caucasian population.

Socioeconomic status and comorbidity status are additional individual characteristics related with frailty. Older adults with lower educational level and lower income levels are more likely to be frail (Andrew, Mitnitski, & Rockwood, 2008; Fried et al., 2001). Among 14,424 community-dwelling adults aged $\geq$ 55 years living in Europe, Etman et al. (2012) found that adults with formal education of 10 years or less had an increased risk of frailty compared to adults who had 11-25 years of formal education (OR=1.40 [1.28,1.54]). It is possible that education affects work and economic status and low income/poverty may further impede access to health care (Gaskin, Early, Olsen, & Roberts, 2012). In addition, the number of chronic illnesses is associated with an increased risk of frailty in older adults (Fried et al., 2001b). Similarly, Woods et al. (2005) reported that chronic illness (history of coronary heart disease, stroke, hip fracture, chronic obstructive pulmonary disease, diabetes, and arthritis) increased the risks of frailty in older adults. The possible reason may lie in the shared risk factors for these chronic illnesses and frailty (Fulop et al., 2010).

Behavioral factors. In addition to socio-demographic factors, lifestyle factors and life events also influence the development of frailty in older adults. Smoking (Woods et al., 2005) and heavy drinking (Strawbridge et al., 1998) are associated with increased risk of frailty (OR=2.90 [2.35, 3.57], and OR=1.97 [$p<.01$], respectively). Similarly, Gobbens et al. (2010) reported that self-reported unhealthy lifestyles were associated with greater frailty (total in physical, psychological and social domains) after adjustment of other life-course determinants (e.g. age, gender and education) (*Beta*=1.77, $p<.001$). They also found that life events (death of loved one, serious illness, serious illness of loved one, end of important relationship, traffic accident, and crime) were significantly associated with frailty in psychological domain (*Beta*=0.31, p=.009). Although these studies demonstrated that individual characteristics (gender, race, socioeconomic status, comorbidities, life style factors and life events) influence the level of frailty in older adults, it remains unknown whether these individual characteristics influence the development of frailty in older adults with HF. More importantly, it remains unknown if the association between individual characteristics and frailty change over the time.

Theoretical Framework

Frailty models: physical vs. multidimensional

Although frailty has been increasingly recognized as a critical health problem in older adults (Clegg et al., 2013; Heppenstall, Wilkinson, Hanger, & Keeling, 2009; Morley et al., 2013), especially in those with HF, consensus is still lacking regarding a universally accepted frailty model (Bergman et al., 2007). Depending on the population studied and research design and method used, the models of frailty vary considerably. The components of frailty in these models vary considerably. To date, despite these variations, two models for conceptualizing frailty are commonly used. One, defining frailty using a physical phenotype, is best typified by Fried's frailty model (Fried et al., 2001a). The other defines frailty as a multidimensional syndrome that includes deficits in three different domains (physical, psychological, and social). One such model that examines this multidimensional concept of frailty is Gobbens et al.'s (2010) Integral Conceptual Model of Frailty (ICMF). Discussion of these two models follows.

Physical frailty model. Fried's frailty model (Fried et al., 2001b), which focuses on cumulative declines in physical domains, has been widely used in geriatrics (Walston et al., 2006). In this model, physical frailty has five components: shrinking/loss of muscle mass, weakness/decreased strength, poor endurance/ poor energy expenditure, slowness/decreased walking speed, and low activity (Appendix A). Muscle function and mobility play a central role in this conceptualization of physical frailty.

The Fried model, initially developed and tested in the Cardiovascular Health Study (CHS), showed the ability to predict ADL disability (Hazard Ratio [HR] =1.98, $p<.0001$), hospitalization (HR=1.29, $p=.004$) and death (HR=2.24, $p=.0001$) (Fried et al., 2001b). The model, replicated and validated in the Women's Health and Aging Studies (WHAS), had construct validity and the ability to predict ADL disability (HR=15.79 [5.83, 42.78]), IADL disability (HR=10.44 (3.51, 31.0), long-term stays in nursing home (HR=23.98[4.45, 129.2]), and three year mortality (HR=6.03 [3.0, 12.08]) (Bandeen-Roche et al., 2006). However, a major limitation of Fried's model is that it only focuses on the physical pathway to frailty and excludes other frailty pathways (psychological and social) associated with functional declines, disability and mortality (Rothman, Leo-Summers, & Gill, 2008; Sarkisian, Gruenewald, John Boscardin, & Seeman, 2008).

Multidimensional frailty model. The multidimensional frailty model developed by Gobbens'(Gobbens, Luijkx, et al., 2010) (Appendix B) describes multidimensional frailty pathways which occur over time and that are initiated by life course determinants and decreased physical reserves due to aging or disease. These pathways proceed to a frailty state, and ultimately end in adverse outcomes (e.g. disability, health care utilization, death and decreased QOL). Gobbens' model incorporates a holistic view of health that reflects the perspectives of physical, psychological and social frailty.

Gobbens' model was recently tested in a sample of 213 community-dwelling older adults (mean age=80.3 years [SD=3.7], 59.6% female) where it explained 20%, 6%, and 18% of the variance of disability, health utilization, and QOL, respectively (Gobbens, van Assen, Luijkx, & Schols, 2012). The physical domain of frailty was correlated with disability ($r = 0.67$, $p<.001$) and QOL ($r = -0.71$, $p<.001$) (Gobbens et al., 2012). Gobbens et al. (2013) later tested the ability of multidimensional domains of frailty (physical, psychological and social) to predict QOL in 1,031 adults aged 65 years and older. The Tilburg Frailty Indicator (TFI) was used to measure multidimensional frailty and the WHO Quality of Life-BREF was used to measure four aspects of QOL (physical health, psychological state, social relations, and environmental conditions). Together, psychological and social frailty explained 20.5% of variance in the QOL psychological aspect and 15.3% of variances in the QOL social relations aspect (Gobbens et al., 2013). Adding these psychological and social domains improved the ability of frailty to predict QOL. Psychological frailty was a significant predictor of disability (measured by the Groningen Activity Restriction Scale) after controlling for individual characteristics and physical frailty (*Beta*=1.16, $p<.05$) (Gobbens et al., 2012).

Comparisons of predictive abilities of frailty models. Although the aforementioned studies show that multidimensional frailty improves the ability to predict QOL and disability in older adults, inconsistencies in findings support the need for additional examination. Ament et al. (2014) examined the ability of multidimensional frailty to predict disability in IADLs and QOL among physically frail older adults (n = 334). The Groningen Frailty Indicator (GFI) was used to measure physical, cognitive, psychological, and social frailty. However, results indicated that only physical frailty was a significant predictor for IADL disability, while cognitive, psychological, or social frailty each failed to predict IADL disability (Ament et al., 2014). Additionally, when QOL was again measured one-year later, physical, cognitive, psychological and social frailty, failed to predict QOL, even after controlling for the baseline QOL (Ament et al., 2014). A possible reason for these findings was that data were collected via mailed questionnaires which can lead to nonresponse bias (Hébert, Bravo, Korner-Bitensky, & Voyer, 1996). Another possible reason is that cognitive frailty and QOL were measured by a single question. Reliability of these measures cannot be evaluated. Similarly, Gobbens et al (2010) also found that social frailty by itself did not predict disability, even after controlling for physical and psychological frailty.

Given these inconsistent findings, it remains unclear whether there is the added predictive value of including psychological and social domains in a frailty model. This uncertainty makes frailty models less reliable and useful for health providers and nurses. As a result, health care providers and nurses may lack clear theoretical guidance for developing interventions designed to minimize the negative consequences of frailty in older adults with HF. Future study is needed to determine whether the multidimensional frailty model (i.e. Gobbens' model) adds significantly more predictive value compared to purely physical frailty model (i.e. Fried's model).

Framework

The theoretical framework for this dissertation is presented in Figure 1.1. In light of a summary of the literature, this framework describes the pathway of frailty and variables related to frailty. Within this framework, frailty is viewed as dynamic with a number of factors influencing its development. Firstly, the framework depicts a relationship between HF and frailty. The findings in current literature support that frailty is prevalent in older adults with HF and that HF is associated with increased risk of developing frailty. Moreover, older adults with HF experience decreased reserve capacity due to declines in skeletal muscle and body composition (Persinger et al., 2003; Slettaløkken et al., 2012). Declines in reserve capacity resulting from HF also play an important role in the development of frailty (Bergman et al., 2004). Secondly, this framework depicts individual characteristics (e.g. demographics, comorbidity, life style factors, life events) as determinants of developing frailty in older adults with HF.

This framework also presents the relationship between frailty and adverse health outcomes of ADL/IADL disability and decreased QOL. It is hypothesized that frailty in older adults with HF is associated with declines in the ability to perform ADL/IADL and diminishes in QOL. It is further hypothesized that frailty mediates the relationship between HF and both ADL/IADL disability and decreased QOL.

Frailty within this framework will be characterized based on the results of the comparison of the two frailty models (Gobbens and Fried). The frailty models of Gobbens' and Fried will be statistically analyzed and compared. The one with the better ability to predict ADL/IADL disability and QOL will be incorporated and selected for use. Should the Fried model be selected, frailty will be operationalized by five physical components: physical activity, nutrition, mobility, strength and endurance. However, should the Gobbens model be selected, frailty will be operationalized using the 14 components with the three domains: physical domain (5 components referring to Fried's model and other 3 are balance, hearing and vision); psychological domain (cognition, depressive mood, anxious mood and coping); and social domain (social relationship and social support).

Summary of Knowledge Gaps

Frailty is a debilitating health problem affecting many older adults age 65 and older. Older adults with HF are more likely to be physically frail than their age-matched counterparts, and to have increased risk of depression (Moudgil & Haddad, 2013) and cognitive impairments (Hajduk, Kiefe, Person, Gore, & Saczynski, 2013), which suggest they may have different pathway of frailty compared to older adults without HF. However, to date, no widely accepted frailty model exists from which to examine this important phenomenon. Inconsistencies exist in the frailty components and corresponding indicators. Moreover, although frailty has been recently conceptualized as a multidimensional syndrome (Bergman et al., 2007; Gobbens, Luijkx, et al., 2010; Markle-Reid & Browne, 2003), the added predictive value of multidimensional frailty compared to physical frailty remains inconclusive. Current studies have primarily focused on the relationship between HF and physical frailty (as measured by frailty phenotype (Fried et al., 2001) and no studies were found that described multidimensional frailty in older adults with HF. As such, little is known about the impact of the multiple frailty domains (physical, psychological and social) on disability or QOL in older adults with HF or the factors (demographics, medical history, lifestyle behaviors and life events) which predispose these older adults to frailty (Andrew et al., 2008; Fried et al., 2001b; Gobbens et al., 2012; Goggins et al., 2005; Strawbridge et al., 1998). No longitudinal study has examined changes in frailty in older adults with HF and little is known about the dynamics and heterogeneity of frailty among older adults with HF. A better understanding of the impact of frailty on the health outcomes of ADL/IADL ability and QOL and the individual differences in the changes in frailty in older adults with HF is urgently needed to guide the development of tailored interventions to prevent or delay the onset of frailty, decrease the risk of disability, and, to ultimately, improve QOL.

Statement of Purposes

Therefore, the purpose of this dissertation study is to evaluate frailty in older adults with HF. Given the lack of consistency in frailty measures and its components, the first part of this dissertation (Chapter 2) is an integrative literature review to examine the components of frailty and the corresponding indicators described in existing frailty measures. The aims of literature review are to: 1) describe the frailty components and corresponding indicators within three domains (physical, psychological, and social); and 2) identify limitations in current frailty measures. After conducting the literature review, an evaluation of frailty in older adults with HF will be conducted using a nationally representative population sample from the Health and Retirement Study (HRS). The HRS is currently the foremost database to assess health disparities in the United States as it contains long-running panel data of physical health, affective and cognitive functioning, and health risk behaviors [1992-present] (Hayward, 2002). Data from the 2006 wave to the 2012 wave are used in this study.

This dissertation will examine the ability of two frailty models [Fried's model (Fried et al., 2001) and Gobbens' model (Gobbens, Luijkx, et al., 2010)] to predict QOL and ADL/IADL disability in older adults. These results will be compared and used to guide the operationalization of frailty in the subsequent analysis of HRS data. If it is found that adding the psychological and social domains (Gobben's model) significantly increases the prediction of QOL or ADL/IADL, the operationalization of frailty will be guided by the Gobben's model. However, if no significant increase in prediction of QOL or ADL/IADL is found, then the Fried model will be used to operationalize frailty and to guide the study. The specific aims of this study are:

Specific Aim 1: To compare the abilities of the Gobbens' multidimensional frailty model and the Fried's physical frailty model to predict ADL/IADL disability and QOL among older adults.

Hypothesis 1.1*: Multidimensional frailty (physical, psychological, and social domains) measured using the Gobbens' model will account for more variance in ADL/IADL disability and quality of life among older adults compared to the Fried's* model.

Specific Aim 2: To assess frailty in older adults with HF and compare it to older adults without HF using the HRS 2006 wave data as baseline and controlling for demographics.

Hypothesis 2.1: *Older adults with HF will have greater level of frailty than older adults without HF when controlling for demographics.*

Specific Aim 3: To longitudinally compare levels of frailty and changes in frailty between older adults with HF and older adults without HF over a 4-years period (2006/2008 to 2010/2012).

Hypothesis 3.1: *Older adults with HF will have higher levels of frailty over the 4-years period, compared to older adults without HF,.*

Hypothesis 3.2: *Older adults with HF will have steeper rates of changes in frailty over the 4-years period, compared to older adults without HF.*

Specific Aim 4: To longitudinally assess the relationships among HF, frailty and ADL/IADL ability and QOL.

Hypothesis 4.1: *Frailty and HF will predict a decrease in ADL/IADL ability and QOL over the 4-year period* (2006/2008 to 2010/2012).

Hypothesis 4.2: *Frailty will mediate the relationship between HF and health outcomes (both ADL/IADL ability and QOL).*

Specific Aim 5: To assess the impact of individual characteristics (demographics, medical history, lifestyle behaviors and life events) on frailty and to determine how changes in frailty differs by individual characteristics among older adults with HF.

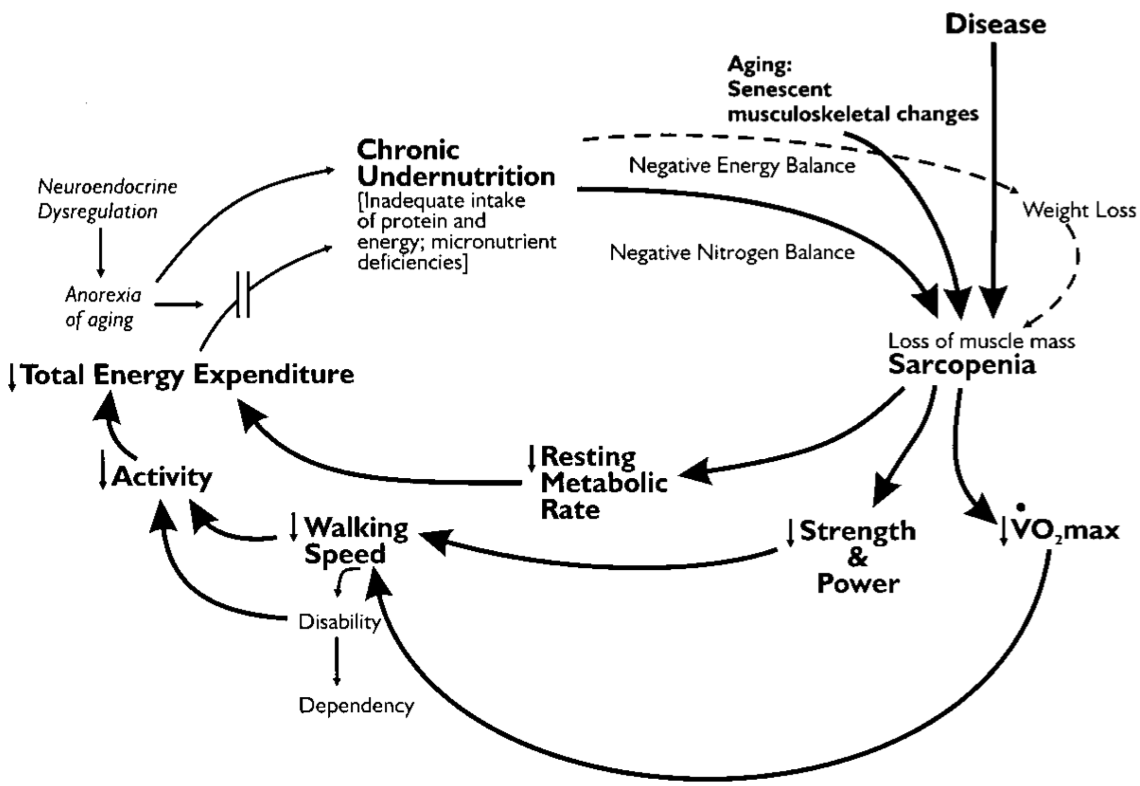
Hypothesis 5.1: *Older adults with HF who are female, African American, of low SES, have more than one comorbidity (e.g. hypertension), unhealthy lifestyle (drinking and smoking), or experiencing stressful life events (e.g. death of child, nature disaster, serious assault) will have a higher level of frailty compared to those older adults with HF but without these characteristics.*

Hypothesis 5.2: *Older adults with HF who are female, African American, of low SES, have more than one comorbidity (e.g. hypertension), unhealthy lifestyle (drinking and smoking), or experiencing stressful life events (e.g. death of child, nature disaster, serious assault) will have a steeper rate in frailty than older adults with HF but without these characteristics*

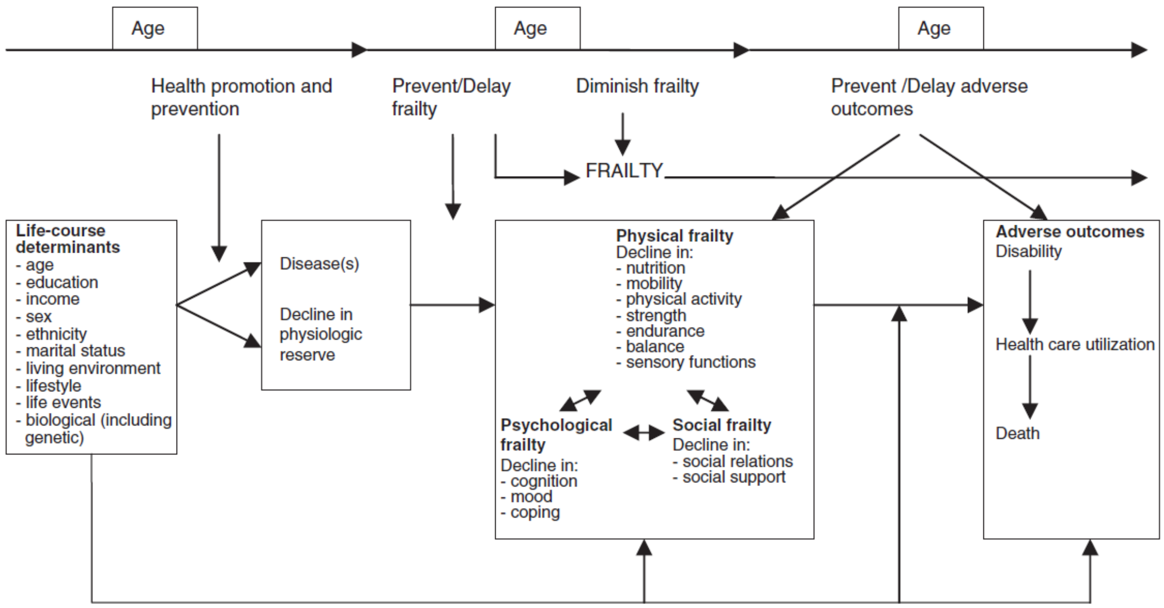
Structure of Dissertation

Using a three-manuscript format, this dissertation consisted of five chapters: an introduction, three manuscript-type papers, and a conclusion. In the first chapter, the background literature, statement of the problem, and theoretical framework are presented. Chapter 2 presents a literature review, which focuses on the components and indicators of frailty in current frailty measure. Chapter 3 presents the results of a cross-sectional analysis comparing the ability of two frailty models (Fried's physical frailty model and Gobbens' multidimensional frailty model) to predict ADL/IADL disability and QOL. Chapter 3 also presents the results of comparisons of frailty levels in older adults with and without HF. Chapter 4 describes the results of a longitudinal examination of frailty in older adults with HF over time; compares levels of frailty and its changes over 4-year period. It also examined the impacts of individual characteristics on frailty levels and investigates the relationships among HF, frailty and health outcomes (ADL/IADL and QOL). Chapter 5 provides a summary of results, limitations, recommendations for future studies, implications for nursing science and practice, and an overall conclusion.

Appendix A. Fried's Frailty Model (Fried et al., 2001)



Appendix B. Gobbens' Frailty Model (Gobbens, Luijkx, et al., 2010)



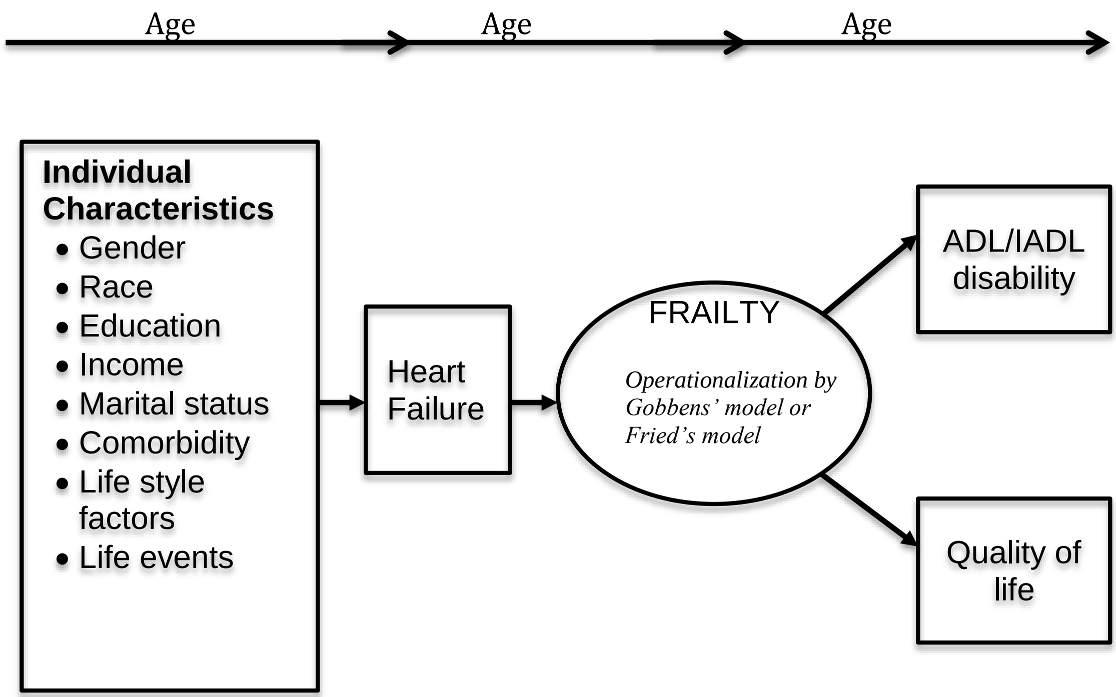


Figure 1.1. Theoretical Framework of Frailty

References

Alosco, M. L., Spitznagel, M. B., Cohen, R., Sweet, L. H., Colbert, L. H., Josephson, R., . . . Gunstad, J. (2012). Cognitive impairment is independently associated with reduced instrumental activities of daily living in persons with heart failure. *The Journal of Cardiovasc Nursing, 27*(1), 44-50. doi: 10.1097/JCN.0b013e318216a6cd

Ament, B.H. L., de Vugt, M. E., Verhey, F.R. J., & Kempen, G. (2014). Are physically frail older persons more at risk of adverse outcomes if they also suffer from cognitive, social, and psychological frailty? *European Journal of Ageing, 11*(3), 213-219.

Andrew, M. K., Mitnitski, A. B., & Rockwood, K. (2008). Social vulnerability, frailty and mortality in elderly people. *PLoS One*, *3*(5), e2232. doi: 10.1371/journal.pone.0002232

Bandeen-Roche, K., Xue, Q.L., Ferrucci, L., Walston, J., Guralnik, J.M., Chaves, P., . . . Fried, L. P. (2006). Phenotype of frailty: characterization in the women's health and aging studies. *The Journals of Gerontology. Series A, Biological sciences and medical sciences, 61*(3), 262-266.

Bergman, H., Ferrucci, L., Guralnik, J., Hogan, D. B., Hummel, S., Karunananthan, S., & Wolfson, C. (2007). Frailty: an emerging research and clinical paradigm--issues and controversies. *The Journals of Gerontology Series A: Biological Sciences and Medical Sciences, 62*(7), 731-737.

Bergman, H., Béland, F., Karunananthan, S., Hummel, S., Hogan, D., & Wolfson, C. (2004). English translation of article published in “Gérontologie et société”: Développement d'un cadre de travail pour comprendre et étudier la fragilité. *Gérontologie et société, n 109*(2), 15.

Boxer, R. S., Dauser, D. A., Walsh, S. J., Hager, W. D., & Kenny, A. M. (2008). The association between vitamin D and inflammation with the 6-minute walk and frailty in patients with heart failure. *The Journal of the American Geriatrics Society, 56*(3), 454-461. doi: 10.1111/j.1532-5415.2007.01601.x

Buck, H. G., & Riegel, B. (2011). The impact of frailty on health related quality of life in heart failure. *European Journal of Cardiovascular Nursing, 10*(3), 159-166. doi: 10.1016/j.ejcnurse.2010.06.001

Bui, A. L., Horwich, T. B., & Fonarow, G. C. (2011). Epidemiology and risk profile of heart failure. *Nature Reviews Cardiology, 8*(1), 30-41. doi: 10.1038/nrcardio.2010.165

Cacciatore, F., Abete, P., Mazzella, F., Viati, L., Della Morte, D., D'Ambrosio, D., . . . Rengo, F. (2005). Frailty predicts long-term mortality in elderly subjects with chronic heart failure. *European Journal of Clinical Investigation, 35*(12), 723-730. doi: 10.1111/j.1365-2362.2005.01572.x

Clegg, A., Young, J., Iliffe, S., Rikkert, M. O., & Rockwood, K. (2013). Frailty in elderly people. *Lancet, 381*(9868), 752-762. doi: 10.1016/s0140-6736(12)62167-9

Collard, R. M., Boter, H. Schoevers, R.A., & Oude Voshaar, R. C. (2012). Prevalence of Frailty in Community-Dwelling Older Persons: A Systematic Review. *Journal of the American Geriatrics Society, 60*(8), 1487.

Dunlay, S. M., Manemann, S. M., Chamberlain, A. M., Cheville, A. L., Jiang, R., Weston, S. A., & Roger, V. L. (2015). Activities of daily living and outcomes in heart failure. *Circulation: Heart Failure, 8*(2), 261-267. doi: 10.1161/circheartfailure.114.001542

Etman, A. Burdorf, A., Van der Cammen, T., Mackenbach, J. P., & Van Lenthe, F.J. (2012). Socio-demographic determinants of worsening in frailty among community-dwelling older people in 11 European countries. *Journal ofEpidemiology and Community Health, 66*(12), 1116-1121.

Fried, L. P., Tangen, C. M., Walston, J., Newman, A. B., Hirsch, C., Gottdiener, J., . . . McBurnie, M. A. (2001). Frailty in older adults: evidence for a phenotype. *The Journals of Gerontology Series A: Biological Sciences and Medical Sciences, 56*(3), M146-156.

Fulop, T., Larbi, A., Witkowski, J. M., McElhaney, J., Loeb, M., Mitnitski, A., & Pawelec, G. (2010). Aging, frailty and age-related diseases. *Biogerontology, 11*(5), 547-563. doi: 10.1007/s10522-010-9287-2

Gaskin, D.J., Early, D.W., Olsen, E.O., & Roberts, E.T. (2012). Poverty, Health, and Healthcare. *The Oxford Handbook of the Economics of Poverty* (Vol. 1): Oxford University Press.

Gobbens, R. J., Luijkx, K. G., Wijnen-Sponselee, M. T., & Schols, J. M. (2010). Towards an integral conceptual model of frailty. *The Journal of Nutrition, Health & Aging. , 14*(3), 175-181.

Gobbens, R. J., Luijkx, Katrien G., & van Assen, Marcel A. L. M. (2013). Explaining quality of life of older people in the Netherlands using a multidimensional assessment of frailty. *Quality of Life Research : An International Journal of Quality of Life Aspects of Treatment, Care and Rehabilitation, 22*(8), 2051-2061.

Gobbens, R. J., van Assen, M. A., Luijkx, K. G., & Schols, J. M. (2012). Testing an integral conceptual model of frailty. *Journal of Advanced Nursing, 68*(9), 2047-2060. doi: 10.1111/j.1365-2648.2011.05896.x

Gobbens, R. J., van Assen, M. A., Luijkx, K. G., Wijnen-Sponselee, M. T., & Schols, J. M. (2010). Determinants of Frailty. *Journal of the American Medical Directors Association, 11*(5), 356-364.

Goggins, W. B., Woo, J., Sham, A., & Ho, S. C. (2005). Frailty index as a measure of biological age in a Chinese population. *The Journals of Gerontology Series A: Biological Sciences and Medical Sciences, 60*(8), 1046-1051.

Gure, T. R., Kabeto, M. U., Blaum, C. S., & Langa, K. M. (2008). Degree of disability and patterns of caregiving among older Americans with congestive heart failure. *The Journal of General Internal Medicine, 23*(1), 70-76. doi: 10.1007/s11606-007-0456-1

Hajduk, A.M., Kiefe, C. I., Person, S.D., Gore, J.G., & Saczynski, J.S. (2013). Cognitive change in heart failure: a systematic review. *Circulation. Cardiovascular quality and outcomes, 6*(4), 451.

Harkness, K., Heckman, G.A., & McKelvie, R.S. (2012). The older patient with heart failure: high risk for frailty and cognitive impairment. *Expert Review of Cardiovascular Therapy, 10*(6), 779.

Harper, A., Power, M.k, Orley, J., Herrman, H., Schofield, H., Murphy, B., . . . Sartorius, N. (1998). Development of the World Health Organization WHOQOL-BREF Quality of Life Assessment. *Psychological Medicine, 28*(3), 551-558.

Hayward, M.D. (2002). Using the Health and Retirement Survey to Investigate Health Disparities. Retrieved from http://hrsonline.isr.umich.edu/sitedocs/dmc/hrs_healthdisparities_hayward.pdf

Hébert, R., Bravo, G., Korner-Bitensky, N., & Voyer, L. (1996). Refusal and information bias associated with postal questionnaires and face-to-face interviews in very elderly subjects. *Journal of Clinical Epidemiology, 49*(3), 373-381.

Heo, S., Moser, D. K., Lennie, T. A., Zambroski, C. H., & Chung, M. L. (2007). A comparison of health-related quality of life between older adults with heart failure and healthy older adults. *Heart & Lung, 36*(1), 16-24. doi: 10.1016/j.hrtlng.2006.06.003

Heppenstall, C. P., Wilkinson, T. J., Hanger, H. C., & Keeling, S. (2009). Frailty: dominos or deliberation? *New Zealand Medical Journal, 122*(1299), 42-53.

Khan, H., Kalogeropoulos, A. P., Georgiopoulou, V. V., Newman, A. B., Harris, T. B., Rodondi, N., . . . Butler, J. (2013). Frailty and risk for heart failure in older adults: the health, aging, and body composition study. *American Heart Journal, 166*(5), 887-894. doi: 10.1016/j.ahj.2013.07.032

Khandelwal, D., Goel, A., Kumar, U., Gulati, V., Narang, R., & Dey, A. B. (2012). Frailty is associated with longer hospital stay and increased mortality in hospitalized older patients. *The Journal of Nutrition Health and Aging, 16*(8), 732-735. doi: 10.1007/s12603-012-0369-5

Markle-Reid, M., & Browne, G. (2003). Conceptualizations of frailty in relation to older adults. *Journal of Advanced Nursing, 44*(1), 58-68.

McNallan, S. M., Chamberlain, A. M., Gerber, Y., Singh, M., Kane, R. L., Weston, S. A., . . . Roger, V. L. (2013). Measuring frailty in heart failure: a community perspective. *American Heart Journal, 166*(4), 768-774. doi: 10.1016/j.ahj.2013.07.008

Mejhert, M., Kahan, T., Persson, H., & Edner, M. (2006). Predicting readmissions and cardiovascular events in heart failure patients. *International Journal of Cardiology, 109*(1), 108-113.

Mitnitski, A. B., Mogilner, A. J., & Rockwood, K. (2001). Accumulation of deficits as a proxy measure of aging. *Scientific WorldJournal, 1*, 323-336. doi: 10.1100/tsw.2001.58

Morley, J.E., Vellas, B., van Kan, G. A., Anker, S.D., Bauer, J.M., Bernabei, R., . . . Walston, J. (2013). Frailty consensus: a call to action. *Journal of the American Medical Directors Association, 14*(6), 392.

Moudgil, R., & Haddad, H. (2013). Depression in heart failure. *Current opinion in cardiology, 28*(2), 249.

Mozaffarian, D., Benjamin, E.J., Go, A.S., Arnett, D.K., Blaha, M.J., Cushman, M., . . . Turner, M.B. (2015). Heart Disease and Stroke Statistics—2015 Update: A Report From the American Heart Association. *Circulation, 131*(4), e29.

Newman, A. B., Gottdiener, J. S., McBurnie, M. A., Hirsch, C. H., Kop, W. J., Tracy, R., . . . Fried, L. P. (2001). Associations of subclinical cardiovascular disease with frailty. *The Journals of Gerontology Series A: Biological Sciences and Medical Sciences, 56*(3), M158-166.

Norberg, E. B., Boman, K., & Lofgren, B. (2008). Activities of daily living for old persons in primary health care with chronic heart failure. *Scandinavian Journal of Caring Science, 22*(2), 203-210. doi: 10.1111/j.1471-6712.2007.00514.x

Persinger, R., Janssen-Heininger, Y., Wing, S., Matthews, D., LeWinter, M., & Toth, M. (2003). Effect of heart failure on the regulation of skeletal muscle protein synthesis, breakdown, and apoptosis. *American Journal of Physiology - Endocrinology And Metabolism, 284*(5), E1001-1008.

Puts, M. T., Lips, P., & Deeg, D. J. (2005). Sex differences in the risk of frailty for mortality independent of disability and chronic diseases. *Journal of the American Geriatrics Society, 53*(1), 40-47. doi: 10.1111/j.1532-5415.2005.53008.x

Rockwood, K., Howlett, S. E., MacKnight, C., Beattie, B. L., Bergman, H., Hebert, R., . . . McDowell, I. (2004). Prevalence, attributes, and outcomes of fitness and frailty in community-dwelling older adults: report from the Canadian study of health and aging. *The Journals of Gerontology Series A: Biological Sciences and Medical Sciences, 59*(12), 1310-1317.

Rothman, M. D., Leo-Summers, L., & Gill, T. M. (2008). Prognostic significance of potential frailty criteria. *Journal of the American Geriatrics Society, 56*(12), 2211-2116. doi: 10.1111/j.1532-5415.2008.02008.x

Sarkisian, C.A., Gruenewald, T.L., John Boscardin, W., & Seeman, T. E. (2008). Preliminary evidence for subdimensions of geriatric frailty: the MacArthur study of successful aging. *Journal of the American Geriatrics Society, 56*(12), 2292-2297.

Slettaløkken, G., Rehn, T. A., Munkvik, M., Rud, B., Sökjer-Petersen, M., Lunde, P. K., . . . Hallén, J. (2012). Preserved metabolic reserve capacity in skeletal muscle of post-infarction heart failure patients. *Scandinavian journal of medicine & science in sports, 22*(2), 199-206.

Strawbridge, W. J., Shema, S. J., Balfour, J. L., Higby, H. R., & Kaplan, G. A. (1998). Antecedents of frailty over three decades in an older cohort. *The Journals of Gerontology Series B: Psychological Sciences and Social Sciences*, *53*(1), S9-16.

Uchmanowicz, I., Loboz-Rudnicka, M., Szelag, P., Jankowska-Polanska, B., & Loboz-Grudzien, K. (2014). Frailty in Heart Failure. *Current Heart Failure Reports*. doi: 10.1007/s11897-014-0198-4

Walston, J., Hadley, E. C., Ferrucci, L., Guralnik, J.M., Newman, A.B., Studenski, S. A., . . . Fried, L.P. (2006). Research agenda for frailty in older adults: toward a better understanding of physiology and etiology: summary from the American Geriatrics Society/National Institute on Aging Research Conference on Frailty in Older Adults. *Journal of the American Geriatrics Society, 54*(6), 991.

Wong, C. Y., Chaudhry, S. I., Desai, M. M., & Krumholz, H. M. (2011). Trends in comorbidity, disability, and polypharmacy in heart failure. *The American journal of medicine*, *124*(2), 136-143. doi: 10.1016/j.amjmed.2010.08.017

Woods, N. F., LaCroix, A. Z., Gray, S. L., Aragaki, A., Cochrane, B. B., Brunner, R. L., . . . Newman, A. B. (2005). Frailty: emergence and consequences in women aged 65 and older in the Women's Health Initiative Observational Study. *The Journal of the American Geriatrics Society, 53*(8), 1321-1330. doi: 10.1111/j.1532-5415.2005.53405.x

CHAPTER 2

Components and Indicators of Frailty: An integrative Literature Review

Abstract

Background: Frailty is a debilitating condition in older adults that is associated with increased risks for adverse outcomes. However, the issue of quantifying frailty remains elusive. There is a lack of consistency in the frailty components and the corresponding indicators used to quantify these components.

Purposes: 1) to describe the components of frailty and examine the corresponding indicators in existing measures of frailty; and 2) to identify current gaps in knowledge of frailty measures.

Methods: The PubMed, CINAHL, and Web of Science databases were searched. Each study was reviewed to determine its fit with inclusion/exclusion criteria.

Results: A total of 43 studies were identified and comprised the sample. Each study described one unique measure of frailty. The frailty components and corresponding indicators within three domains (physical, psychological, and social) were described. The most frequently reported components of frailty were mobility and balance, nutrition, and cognitive function. Only 10 of 43 frailty measures included components across all three domains. Current frailty measures were critiqued and important areas for future study are identified.

Conclusions: The frailty components and corresponding indicators vary considerably across different frailty measures. Future studies are needed to address inconsistences in frailty measures and models.

Key words: frailty, measures, components, indicators

Introduction

Frailty is a health problem characterized by a state of increased vulnerability and decreased reserve capacity (Morley et al., 2013). As age increases, the prevalence of frailty rises dramatically. According to the Cardiovascular Health Study (CHS) (Fried et al., 2001), the prevalence of frailty increases with every five years of life beyond age 65 by 3.2% (age 65-70), 5.3% (age 70-75), 9.5% (age 75-80), 16.3% (age 80-85), and 25.7% (age 85-90). As the number of older adults, and especially the oldest old (≥85 years), continues to increase worldwide, so does the cost of caring for these frail individuals (Kinsella & Phillips, 2005). In fact, frail older adults are the predominant consumers of healthcare across all healthcare delivery and social care settings (Rockwood & Hubbard, 2004). In addition to the economic costs, frail individuals also experience a diminished quality of life (Rizzoli et al., 2013) and increased risks of disability, hospitalization, institutionalization, and morbidity and mortality (Fried et al., 2001; Song, Mitnitski, & Rockwood, 2010). Given the economic and individual burdens, accurate identification of older adults who are frail is needed along with the delivery of proper health care to minimize the negative consequences associated with frailty.

Although the number of frailty studies has rapidly increased over the last two decades (Hogan, MacKnight, & Bergman, 2003), the issue of quantifying frailty remains unresolved (Abellan van Kan et al., 2008). Depending on the population studied and research design and method used, the measures of frailty may encompass different domains (e.g. physical, psychological, or social) with each domain including a number of components (e.g. mobility, nutrition) quantified by a variety of indicators (e.g. gait speed, weight loss). For instance, Frailty Phenotype measure, developed by Fried et al. (2001), assesses frailty within the physical domain as the presence of at least three of the following five components: shrinking, muscle weakness, endurance, mobility, and physical activity. These five components are quantified by five indicators: unintentional weight loss, grip strength, self-reported exhaustion, gait speed, and kilocalories expended per week. In contrast, the Frailty Index, developed by Mitniski et al. (2001), includes five different components of symptoms, signs, abnormal laboratory values, comorbidity, and disabilities within the physical and psychological domains. These components are quantified by 92 different indicators. The severity of frailty is computed by counting the number of deficits and dividing by the total number of indicators. Although frailty has recently been conceptualized as a multidimensional syndrome that includes physical, psychological, or social domains (Bergman et al., 2007; Fulop et al., 2010; Markle-Reid & Browne, 2003), research has focused primarily on physical frailty. The identification of the components of frailty within psychological and social domains remains elusive.

The inconsistencies in frailty components and corresponding indicators used to quantify these components pose challenges for clinicians in identifying older adults who are frail. These may also impede the development of focused interventions to prevent or delay the onset of frailty and to mitigate the adverse outcomes associated with frailty. Given the growing numbers of frail older adults, a comprehensive understanding of the components and indicators of frailty is needed to address the complex and multidimensional healthcare needs of this vulnerable population.

Therefore, this paper will examine the components of frailty and the corresponding indicators described in existing measures. More specifically, the aims of this paper are: (1) to describe the frailty components and corresponding indicators within the physical, psychological and social frailty domains; and (2) to critique existing measures of frailty.

Method

A comprehensive search of literature published between January 1, 1990 and December 31, 2014 was performed. The electronic databases of PubMed, CINAHL, and the Web of Science were searched using the following subject headings in combination and in isolation: *frailty elderly*, *frailty* and *older adult*, along with the words of *definition, concept* or *measure* in the abstract. Reference lists of the selected articles were also reviewed to identify relevant citations.

Studies were eligible for inclusion if they included: 1) original measures of frailty; 2) adults aged 65 years and older; and 3) were written in English. Studies were excluded if they used the same measures as in previously published studies or if animal subjects were included. Literature reviews, letters to the editor, commentaries, book chapters, case studies, master's theses and doctoral dissertations were also excluded.

Results

A total of 1512 published studies were initially identified. Based on the title and the abstract, 1179 studies were eliminated because they did not focus on frailty measures, included non-human subjects, and because they did not include empirical data. Twenty-two published studies were excluded because of duplicate titles. Of the remaining 311 published studies, 43 papers met the criterion of providing a unique measure of frailty and, therefore, comprised the sample for this literature review (Figure 2.1). In other words, each included study described one unique measure of frailty, resulting in a total of 43 different measures of frailty in the 43 published studies.

Characteristics of selected frailty measures

Of the 43 frailty measures, 26 (61%) contained the two domains of physical and psychological frailty; 7 (16%) focused only in the physical domain; and only 10 (23%) included all three frailty domains (physical, psychological and social). The types of frailty measures varied considerably among the 43 papers: 21 were a combination of self-reported and performance based (47%) (Table 2.1), 4 were objective performance-based (12%) (Table 2.2), 15 were participant self-report (35%) (Table 2.3), and 3 were clinician/researcher judgment (6%) (Gerdhem, Ringsberg, Magnusson, Obrant, & Åkesson, 2003; Rockwood et al., 2005; Studenski et al., 2004)(Table 2.4). The majority of the frailty measures (40/43) scores were either rule based (e.g. robust, pre-frail or frail) or indexes with equal weight for each frailty indicators (e.g. summative score or mean score). The three frailty measures scores (Carrière, Colvez, Favier, Jeandel, & Blain, 2005; Jung et al., 2014; Kamaruzzaman, Ploubidis, Fletcher, & Ebrahim, 2010) were assigned relative weights to indicate the importance of each frailty components.

Frailty components

The most frequently reported components of frailty across all three domains were mobility and balance (65%), nutrition (63%), and cognitive function (49%). Almost half of the frailty measures (46.5%) included overlapping, but distinct entities from frailty (Fried, Ferrucci, Darer, Williamson, & Anderson, 2004; Fried et al., 2001) (increasing age, disability, or comorbidity). The 43 measures are presented in detail along with the components and corresponding indicators of frailty by domains (Table 2.1, 2.2, 2.4, and 2.4).

Physical domain

Mobility and Balance. Deficits in mobility and balance were the most frequently reported (65%) components of physical frailty (Avila-Funes et al., 2009; Bielderman et al., 2013; Brehmer-Rinderer, Zeilinger, Radaljevic, & Weber, 2013; Brown, Sinacore, Binder, & Kohrt, 2000; Cacciatore, Abete, Mazzella, Viati, Della Morte, D’Ambrosio, et al., 2005; Carrière et al., 2005; De Witte et al., 2013; Freiheit, 2010; Fried et al., 2001; García-García et al., 2014; Gill et al., 2002; Gobbens, van Assen, Luijkx, Wijnen-Sponselee, & Schols, 2010; Hubbard, O'Mahony, & Woodhouse, 2009; Hyde et al., 2010; Jones, Song, & Rockwood, 2004a; Jung et al., 2014; Kamaruzzaman et al., 2010; Klein, Klein, Knudtson, & Lee, 2005; Opasich et al., 2010; Ravaglia et al., 2008; Robinson et al., 2013; Rockwood et al., 1999; Rolfson, Majumdar, Tsuyuki, Tahir, & Rockwood, 2006; Rothman, Leo-Summers, & Gill, 2008; Sarkisian, Gruenewald, John Boscardin, & Seeman, 2008; Strawbridge, Shema, Balfour, Higby, & Kaplan, 1998; Studenski et al., 2004; Sündermann et al., 2011). The indicators to assess mobility and balance included self-report measures and objective physical performance tasks. In the self-report questions, participants were asked if they had difficulties or needed assistance in walking or balance (Bielderman et al., 2013; Brehmer-Rinderer et al., 2013; Cacciatore et al., 2005; De Witte et al., 2013; Gobbens, van Assen, et al., 2010; Hyde et al., 2010; Kamaruzzaman et al., 2010; Strawbridge et al., 1998). One of most commonly used objective indicators for mobility (in 8 of the 43 studies) was gait speed, which was assessed by the time it takes to walk a set distance (e.g. 15 ft., or 6m) at usual speed or maximum speed (Brown et al., 2000; Cacciatore et al., 2005; Carrière et al., 2005; Freiheit, 2010; Fried et al., 2001; Klein et al., 2003; Rothman et al., 2008; Sündermann et al., 2011). Another objective indicator to quantify mobility was the Time Up and Go Test (TUG), which tests the time a person takes to raise from a chair, walk a certain distance, turn around, walk back to the chair and sit down (Hubbard et al., 2009; Opasich et al., 2010; Robinson et al., 2013; Rolfson et al., 2006) . The Tandem Position Test, which assesses the time to maintain the progressively more challenging positions (side-by-side position, semi tandem position, and tandem position), was used in five studies (Brown et al., 2000; Carrière et al., 2005; Freiheit, 2010; Opasich et al., 2010; Sündermann et al., 2011). Only one study (Jung et al., 2014) used the Short Physical Performance Battery (SPPB), which includes repeated chair stand, tandem position test and gait speed, to quantify both mobility and balance.

Nutrition. Twenty-eight studies (Amici et al., 2008; Avila-Funes et al., 2009; Bielderman et al., 2013; Brehmer-Rinderer et al., 2013; Chin A Paw, Feskens, Dekker, Kromhout, & Schouten, 1999; Ensrud et al., 2008; Freiheit, 2010; Fried et al., 2001; García-García et al., 2014; Gobbens, van Assen, et al., 2010; Hubbard et al., 2009; Hyde et al., 2010; Johansen et al., 2014; Jung et al., 2014; Kamaruzzaman et al., 2010; Kim et al., 2014; Puts, Lips, & Deeg, 2005; Ravaglia et al., 2008; Robinson et al., 2013; Rolfson et al., 2006; Rothman et al., 2008; Sarkisian et al., 2008; Strawbridge et al., 1998; Studenski et al., 2004; Sündermann et al., 2011Tocchi, Dixon, Naylor, Jeon, & McCorkle, 2014) described poor nutrition as a component of physical frailty (65%). Indictors to quantify poor nutrition included unintended weight loss and abnormal Body Mass Index (BMI) (<18.5 or >30 kg/m^2) (Avila-Funes et al., 2009; Bielderman et al., 2013; Brehmer-Rinderer et al., 2013; Chin A Paw, Feskens, Dekker, Kromhout, & Schouten, 1999; Ensrud et al., 2008; Freiheit, 2010; Fried et al., 2001; García-García et al., 2014; Gobbens, van Assen, et al., 2010; Hubbard et al., 2009; Hyde et al., 2010; Johansen et al., 2014; Kamaruzzaman et al., 2010; Puts, Lips, & Deeg, 2005; Rolfson et al., 2006; Rothman et al., 2008; Sarkisian et al., 2008; Strawbridge et al., 1998; Studenski et al., 2004) . Other indicators of nutrition included self-reported poor appetite (Brehmer-Rinderer et al., 2013; Strawbridge et al., 1998; Tocchi, Dixon, Naylor, Jeon, & McCorkle, 2014), Mini Nutritional Assessment (scores <23.5) (Kim et al., 2014), calf circumference (<31cm) (Ravaglia et al., 2008), mid-arm circumference (≤27cm) (Kim et al., 2014), waist circumference (men≥102cm /women ≥88cm) (García-García et al., 2014), waist-hip ratio (men>0.90 /women>0.85) (Kamaruzzaman et al., 2010), and low serum albumin level (various cutoff points across studies)

(Amici et al., 2008; Jung et al., 2014; Kim et al., 2014; Robinson et al., 2013; Studenski et al., 2004; Sündermann et al., 2011).

Muscle Weakness. In 19/43 (44%) of the studies, muscle weakness was reported as a component of frailty in the physical domain (Avila-Funes et al., 2009; Binder et al., 2002; Brehmer-Rinderer et al., 2013; Brown et al., 2000; Carrière et al., 2005; Ensrud et al., 2008; Fried et al., 2001; García-García et al., 2014; Gill et al., 2002; Gobbens, van Assen, et al., 2010; Hubbard et al., 2009; Johansen et al., 2014a; Jung et al., 2014; Klein et al., 2005; Rothman et al., 2008; Sarkisian et al., 2008; Strawbridge et al., 1998; Studenski et al., 2004; Sündermann et al., 2011). The indicators of muscle weakness included self-reported lack of strength or weakness in the arms or legs (Avila-Funes, 2009; Gobbens, van Assen, et al., 2010; Strawbridge et al., 1998), objective grip strength assessed by dynamotor (Brehmer-Rinderer et al., 2013; Carrière et al., 2005; Fried et al., 2001; García-García et al., 2014; Hubbard et al., 2009; Klein et al., 2005; Rothman et al., 2008; Sarkisian et al., 2008; Studenski et al., 2004; Sündermann et al., 2011), and the Chair Stand Test to assess lower extremity strength (Brown et al., 2000; Carrière et al., 2005; Ensrud et al., 2008; García-García et al., 2014; Gill, Gahbauer, Allore, & Han, 2006; Jung et al., 2014; Klein et al., 2005; Sündermann et al., 2011).

Additional physical performance. Three studies (Binder et al., 2002; Brown et al., 2000; Johansen et al., 2014) also reported additional physical performance as a component of frailty. The objective indicators of physical performance included the ability to: put on and take off a jacket; pick up a penny from the floor; lift a five-pound book overhead to a shelf; climb one flight of stairs; turn 360 degrees; and climb four flights of stairs (Binder et al., 2002; Brown et al., 2000). One study (Johansen et al., 2014) used the self-reported physical function scale of the Short Form (36) Health Survey (SF-36) to quantify physical performance.

Endurance. Endurance as a component of physical frailty was noted in 12 of the 43 (28%) studies. All of the corresponding indicators across these studies used self-reported exhaustion or low energy (Avila-Funes et al., 2009; Chin A Paw et al., 1999; Ensrud et al., 2008; Fried et al., 2001; Gobbens, van Assen, et al., 2010; Hyde et al., 2010; Johansen et al., 2014; Rothman et al., 2008; Sarkisian et al., 2008; Studenski et al., 2004; Sündermann et al., 2011; Tocchi et al., 2014) . In both the measures of Frailty Phenotype (Fried et al., 2001) and those measures expanded from the Frailty Phenotype (Avila-Funes, 2009; Rothman et al., 2008; Sündermann et al., 2011), endurance was similarly quantified using two questions from the Center for Epidemiologic Studies Depression Scale (CES-D): "felt everything an effort" and "could not get going".

Physical activity. Approximately, a quarter (26%) of the identified studies used physical inactivity as a component of physical frailty (Avila-Funes et al., 2009; Carrière et al., 2005; Chin A Paw et al., 1999; Fried et al., 2001; García-García et al., 2014; Gobbens, van Assen, et al., 2010; Johansen et al., 2014; Puts, Lips, & Deeg, 2005; Ravaglia et al., 2008; Rothman et al., 2008; Sarkisian et al., 2008). All of the indicators of physical activity were self-reported (e.g., self-reported moderate activity less than 4 hours/week (Ravaglia et al., 2008)). None of the included studies used an objective indicator of physical activity (e.g. pedometer, accelerometer).

Sensory function. Declines in sensory function (vision and hearing) were reported in 12 studies as components of physical frailty (Amici et al., 2008; Bielderman et al., 2013; Brehmer-Rinderer et al., 2013; Cacciatore et al., 2005; Gobbens, van Assen, et al., 2010; Jones et al., 2004; Kamaruzzaman et al., 2010; Klein et al., 2005; Puts et al., 2005; Ravaglia et al., 2008; Strawbridge et al., 1998; Sündermann et al., 2011). All, but one of the 43 studies (Klein et al., 2005), used self-reported declines in vision or hearing. Only Klein et al. quantified deficits in vision using the objective Distance Visual Acuity Test, which defines a deficit as best-corrected visual acuity of 20/40 or poorer in the better eye.

Disability. Sixteen of the 43 studies included disability-which should be a different entity from frailty (Fried et al., 2004)- as an indicator of frailty in the physical domain (Brehmer-Rinderer et al., 2013; Cacciatore et al., 2005; de Vries, Staal, Rikkert, & Nijhuis-van der Sanden, 2013; Johansen et al., 2014; Jones et al., 2004; Jung et al., 2014; Kamaruzzaman et al., 2010; Kanauchi, Kubo, Kanauchi, & Saito, 2008; Kim et al., 2014; Mitnitski, Mogilner, & Rockwood, 2001; Ravaglia et al., 2008; Robinson et al., 2013; Rockwood et al., 1999; Rolfson et al., 2013; Saliba et al., 2001; Tocchi et al., 2014). Disability was quantified as difficulties in performing activities of daily living (ADL) or instrumental activities of daily living (IADL).

Comorbidity. Comorbidity was included as a physical frailty measures in 11 studies (Amici et al., 2008; Bielderman et al., 2013; Brehmer-Rinderer et al., 2013; de Vries et al., 2013; Hyde et al., 2010; Kamaruzzaman et al., 2010; Kim et al., 2014; Mitnitski et al., 2001; Ravaglia et al., 2008; Robinson et al., 2013; Rolfson et al., 2006). Indicators of comorbidity included the Charlson Comorbidity Index (Kim et al., 2014; Robinson et al., 2013), the presence of a series of chronic conditions (e.g. hypertension, cardiac diseases, bronchitis/emphysema, diabetes, stroke) (Amici et al., 2008; de Vries et al., 2013; Kamaruzzaman et al., 2010; Mitnitski et al., 2001), self-report of five or more illnesses (Hyde et al., 2010), and self-report of three or more different types of medication (i.e. for different chronic diseases) (Bielderman et al., 2013; Brehmer-Rinderer et al., 2013; Ravaglia et al., 2008; Rolfson et al., 2006).

Other physical frailty components. Other components of frailty in the physical domain included aging (Carrière et al., 2005; Ravaglia et al., 2008; Saliba et al., 2001), living in a nursing home (Brody, 1997; Brody, Johnson, Ried, Carder, & Perrin, 2002), abnormal biomarkers/ laboratory values (e.g. calcium, creatinine, Interleukin-6) (Mitnitski et al., 2001; Sarkisian et al., 2008), self-reported declines in general health status (Bielderman et al., 2013; Brehmer-Rinderer et al., 2013; Carrière et al., 2005; de Vries et al., 2013; Rolfson et al., 2006; Saliba et al., 2001; Tocchi et al., 2014), and symptoms/signs (e.g. incontinence, sleepless, low peak expiratory flow rate) (Brehmer-Rinderer et al., 2013; Cacciatore et al., 2005; Hubbard et al., 2009; Jones et al., 2004; Kamaruzzaman et al., 2010; Klein et al., 2005; Mitnitski et al., 2001; Puts et al., 2005; Rockwood et al., 1999; Rolfson et al., 2006; Sündermann et al., 2011). The indicators used to quantify these various components were presented in Table 2.1, 2.2, 2.3 and 2.4.

Psychological domain

Cognitive function. Cognitive function was considered as a component of frailty in more than half (51%, 22/43) of the 43 identified studies. Cognitive frailty was mainly characterized by deficits in global cognitive function and was measured using cognitive screening instruments such as the Mini Mental State Examination (MMSE) (Amici et al., 2008; Avila-Funes et al., 2009; Cacciatore et al., 2005; Hubbard et al., 2009; Jones et al., 2004; Jung et al., 2014; Kim et al., 2014; Puts et al., 2005; Rockwood et al., 1999; Rothman et al., 2008), the Clock-Drawing Test (Rolfson et al., 2006), Mini-Cog measures (Robinson et al., 2013) or a series of cognitive tests (measuring language, executive function, spatial ability, and verbal and nonverbal memory) (Sarkisian et al., 2008). Additionally, six of the 43 studies quantified cognitive frailty using self-report of memory problems (Bielderman et al., 2013; Brehmer-Rinderer et al., 2013; de Vries et al., 2013; Gobbens, van Assen, et al., 2010; Kamaruzzaman et al., 2010; Strawbridge et al., 1998). Only three studies (Freiheit, 2010; García-García et al., 2014; Studenski et al., 2004) included indicators to reflect specific aspects of cognitive function, such as, neuromotor processing, verbal fluency, and executive function.

Emotional disorders. Over one third of the selected studies (14/43) used emotional disorders in their measures of frailty. Emotional disorders were mainly quantified by the presence of depressive symptoms and anxiety (Amici et al., 2008; Bielderman et al., 2013; Brehmer-Rinderer et al., 2013; de Vries et al., 2013; De Witte et al., 2013; Freiheit, 2010; Gobbens, van Assen, et al., 2010; Jones et al., 2004; Kamaruzzaman et al., 2010; Puts et al., 2005; Rolfson et al., 2006; Rothman et al., 2008). Other studies used coping/mastery (De Witte et al., 2013; Gobbens, van Assen, et al., 2010; Puts et al., 2005b), pessimism (Ravaglia et al., 2008), motivation (Jones et al., 2004), and fear of falling (Brehmer-Rinderer et al., 2013; Cacciatore et al., 2005) as indicators of frailty in the psychological domain.

Social/environmental domain

Only 10 of the 43 articles included frailty components of the social domain in their assessment of frailty. Components in the social domain included living alone (Freiheit, 2010; Gobbens, van Assen, et al., 2010), loneliness (Bielderman et al., 2013; de Vries et al., 2013; Gobbens, van Assen, et al., 2010), social support/resource as needed (Cacciatore et al., 2005; de Vries et al., 2013; De Witte et al., 2013; Gobbens, van Assen, et al., 2010; Jones et al., 2004; Rolfson et al., 2006), social network and social activities (Brehmer-Rinderer et al., 2013; de Vries et al., 2013; Tocchi et al., 2014). One study also included the environmental domain, which was assessed in terms of housing and neighborhood conditions (De Witte et al., 2013). Indicators for these social/environmental frailty components used self-report responses (Table 2.1, 2.2, 2.3 and 2.4).

Discussion

An overview of findings

In this literature review, 43 studies published between 1997 and 2014 were examined. These studies focused on measures of frailty and the components and corresponding indicators of frailty in the physical, psychological and social/environmental domains. Consistent with previous work (Bergman et al., 2007; Sternberg, Wershof Schwartz, Karunananthan, Bergman, & Mark Clarfield, 2011), this review found a lack of consensus regarding components used to characterize frailty. This is evident in the fact that 43 different measures were found. In addition, for each measure, the components of frailty varied within each domain. In the physical domain, the components varied considerably. The most commonly reported components were mobility and balance, nutrition, muscle weakness, and disability. In the psychological domain, cognitive function and emotional disorders, including depression and anxiety, were the most frequent components. Compared to the physical and psychological domains, which were noted in 33 of the papers, the social domain was discussed in only 10 papers. Because of this small number of published papers, synthesis of the components in the social domain was limited. Frailty components in the social domain included living alone, loneliness, lack of social support, network, and activities. These findings have important implications for the clinicians, who may be able to use these components to comprehensively identify the frail older adults from physical, psychological and social perspectives.

Critique of frailty measures

This review highlights considerable gaps in frailty measures within the current literature. One problem associated with frailty measures is the use of un-weighted scores. All but three (Carrière et al., 2005; Jung et al., 2014; Kamaruzzaman et al., 2010) of the 43 measures used un-weighted scores. For example, “mobility” and “loneliness” are equally weighted in the Tilburg

Frailty Indicator, giving these two components equal importance for predicting frailty-related adverse outcomes. However, because declines in mobility may lead to loneliness, mobility should perhaps be assigned greater weight than loneliness. In fact, one study (Rothman et al., 2008) reported the difference in importance of each frailty component for predicting adverse outcomes. According to the Precipitating Events Project, mobility was the strongest predictor for disability, long-term nursing home stay, and mortality, compared to other frailty components (Rothman et al., 2008). Another reason for weighting scores is that applying weighted components can improve the predictive power of a frailty measure (Kamaruzzaman et al., 2010; Romero-Ortuno, Walsh, Lawlor, & Kenny, 2010; Theou, Brothers, Mitnitski, & Rockwood, 2013). Kamaruzzaman et al. reported that the weighted Fraily Index (FI), using data from the British Women's Heart and Health Study (BWHHS), was a better independent predictor of 2.5-year mortality, hospitalization, and institutionalization than the traditional un-weighted Frailty Index (Hazard Ratios (HR) of 1.8 vs. 1.5 , 1.6 vs. 1.4, and 2.0 vs. 1.5 ($p<.001$) respectively). However, a limitation of weighted frailty components is that they rely on statistical methods that are not easy to calculate and use in clinical practice to screen frail older adults. Moreover, weights for each component are dependent on the study population and may not be generalizable to other populations. Given the varying importance of frailty components and the difficulty of generalizing, weighted frailty scores may be better when predicting frailty-related adverse outcomes in the population studies with large sample sizes, whereas the un-weighted frailty scores may be more feasible and usable in clinical work when screening individual frail older adults.

In addition to the issue of weighting, frailty components in the physical domain are in need of further clarification. The overlap with other concepts, such as, disability and comorbidity, confound the measure of frailty. This literature review found that approximately 40% of identified studies treated disability as a component of frailty and nearly 21% considered comorbidity a physical frailty component. However, it may be problematic to use disability and comorbidity as components of frailty measures. In fact, disability is a consequence of both frailty and comorbidity and comorbidity is an antecedent of frailty (Fried et al., 2001). Frailty measures combined with disability may increase measurement bias when assessing the vulnerability of this population. This is because disability itself is an important predictor for adverse outcomes, such as hospitalization and mortality (Davydow, Hough, Levine, Langa, & Iwashyna, 2013; Ponzetto et al., 2003; Sarria Cabrera, Gomes Dellaroza, Trelha, Cecilio, & Souza, 2012). More importantly, treating disability and comorbidity as frailty components may affect the interventions designed to prevent or mitigate frailty for these vulnerable older adults. Using frailty measures, which do not include disability and comorbidity as components, may identify frail older adults who are between robust and functioning disabled. For these older adults identified as frail, focused interventions are analogous to primary prevention, emphasizing health promotion and health education to foster a healthier lifestyle and reduce risk factors. However, if using frailty measures that include disability as a component, older adults will be identified as individuals who are functionally dependent. As such, the targeted interventions are secondary preventions that aim to control disease progression and prevent further deteriorations. It is reasonable to separate disability and comorbidity from frailty measures because studies (Fried et al., 2004; Fried et al., 2001) have shown that frailty, disability, and comorbidity are separate, but, overlapping entities that confer specific care needs and are associated with different prognoses in older adults.

Another important finding in this review is that over half of the identified articles consider cognitive function as an important component of frailty. Indeed, it is reasonable to include cognitive function in frailty measures as the common mechanisms of physical frailty and cognitive impairment (Robertson, Savva, & Kenny, 2013). In this review, cognitive impairment in the psychological domain of frailty was mainly determined by declines in global cognitive function (e.g. decreased MMSE). However, three frailty measures used specific aspects of cognitive function instead of global cognitive function (Freiheit, 2010; García-García et al., 2014; Studenski et al., 2004). For example, Freibeit et al. (2010) used executive function, tested by the Trail-Making Test Part B (TMTB), as an indicator to quantify cognitive function, and found that TMTB was a better predictor of both ADLs and frailty than the global measure (e.g. MMSE).

It may be more precise and sensitive to use the specific aspects of cognitive function to identify frailty rather than to use global cognitive function. For example, Park and Reuter-Lorenz (2009) showed processing speed performance, working memory, and long-term memory declined steeply with increasing age, while word knowledge performance was preserved over time. Therefore, using global cognitive indicators, rather than specific aspects of cognitive indicators, to identify frailty in older adults may not be able to detect early declines in cognitive function. Considering that only three frailty measures used specific aspects of cognitive function as an indicator, future studies are needed to compare the specific aspects of cognitive function with global cognitive functioning in frailty measures.

Whether frailty measures should be multi-domain or not is another controversial issue. In this study, only 14% of frailty measures (10/43) contained components associated with all three domains (physical, psychological and social). In fact, an ongoing debate is whether social factors are components of frailty or predictors of frailty (Gobbens, Luijkx, Wijnen-Sponselee, & Schols, 2010). Markle-Reid and Browne (2003) argued that frailty must be a multidimensional concept because the presence of frailty may result from conditions occurring within society and the environment as well as the biological and physiological conditions within the individuals. Similarly, Gobbens et al. stated that multidimensional frailty, including all three domains, reflects a holistic view of humanity. In contrast, Woo et al. (2005) claimed that social factors (e.g. socioeconomic factors, lifestyle, and social support) are the determinants of frailty.

Another debate of multidimensional frailty has centered on the added value of psychological and social components for predicting frailty-related adverse outcomes. Gobbens et al. (2013) found adding psychological and social frailty components improved the ability of frailty model to predict QOL in community-dwelling older adults. In contrast, Ament et al. (2014) reported that cognitive, psychological, and social frailty components failed to significantly account for additional variance in QOL and ADL/IADL after controlling for physical frailty components. Given that the added predictive power of psychological and social frailty has not yet been established, future studies are needed to validate the additional variance in frailty-related adverse outcomes explained by the addition of psychological and social frailty compared to physical frailty.

Limitations and Strength

One limitation of this literature review is the exclusion of the grey literature (e.g. dissertations, theses, and unpublished data), which may have omitted some frailty measures that are currently in development. Another limitation is that only studies written in English were included and those frailty measures in other language may have been omitted. However, a noted strength of this literature review, to the best of our knowledge, is that this is the first of its kind to describe the components of frailty in each physical, psychological and social domain along with its corresponding indicators.

Conclusion

This literature review provides a comprehensive overview of the components of frailty within three domains: physical, psychological and social. Although consensus on frailty measures remains elusive, this review describes the most commonly used frailty components and the corresponding indicators in contemporary publications. These findings can be used to guide the development of a theoretical framework of frailty in future studies. Clinicians can use these frailty components and their corresponding indicators to comprehensively identify frail older adults from physical, psychological and social perspectives to provide holistic care to meet the multidimensional healthcare needs of this vulnerable population. This literature review also raises concerns about current frailty measures. In particular, concerns are raised regarding the use of weighted scores in determining the level of frailty, the inclusion or exclusion of disabilities and comorbidities in the frailty measures, the use of specific aspects of cognitive function, and multidimensionality of frailty measures. Each of these concerns need to be clarified in future studies and should be taken into account when developing measures to identify frail older adults.

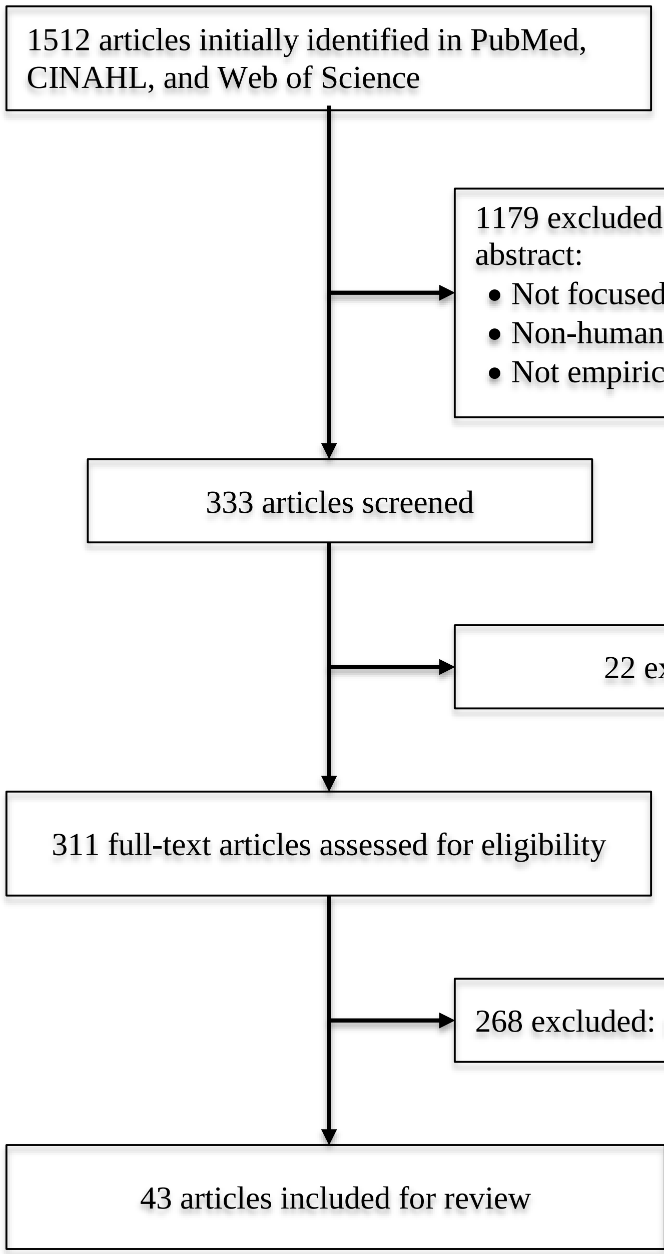


Figure 2.1. Search strategy for studies included in literature review

Table 2.1. Frailty components and indicators in the self-report and objective mixed measures.

Author/ Year	**Measure characteristics**	**Physical domain**		**Psychological domain**		**Social domain**	
		Component	**Indicator**	**Component**	**Indicator**	**Component**	**Indicator**
Avila-Fune et al. (2009)	Expanded Fried's frailty phenotype	Nutrition: Endurance: Mobility: Muscle weakness: Physical acidity:	Weight loss (self-reported unintentional weight loss >3kg or BMI<21kg/m2 Self-report exhaustion (2 items) Gait speed by 6-m walking test (lowest quintile) One self-report items of having Difficulty rising from a chair Self-report questions about daily leisure activities	Cognition:	MMSE		

Author/ Year	Measure characteristics	Physical domain		Psychological domain		Social domain	
		Component	**Indicator**	**Component**	**Indicator**	**Component**	**Indicator**
Binder et al. (2002)	Score: frail if >=2 indicators	Physical performance:	Modified physical performance tests: • Timed (50 feet floor walk • Putting on and removing a lab coat • Picking up a penny from the floor standing up 5 times from a chair • Lifting a 7-pound book to a shelf climbing one fight of stairs • Tandem balance tests • Climbing up and down 4 flights of stairs • Performing a 360 degree turn				
		Disability:	ADLs IADLs (≥2 IADLs or ≥1 ADLs)				
		Symptom and sign:	Achievement of a VO2 peak10-18 mL/kg•min				

Author/ Year	Measure characteristics	Physical domain		Psychological domain		Social domain	
		Component	**Indicator**	**Component**	**Indicator**	**Component**	**Indicator**
Carriere et al. (2005)	Score: weighted statistical equation	Mobility: Muscle strength: Nutrition: Muscle strength: Physical activity: Global health: Age: Education:	Gait speed (6 m walking, normal space) Chair tests BMI ($\geq$27.6 kg/m^2) Grip strength (<47kPa) Questions about physical exercise (<6.9 MET/week) Self-report global health Increasing age Lower education				
Chin A Paw et al. (1999)	Frail: Inactivity combined with weight loss	Physical activity: Nutrition:	Inactivity <210 min/week • Weight loss (5-yr loss >4 kg) • Low BMI (<23.5 kg/m^2) • Energy intake <7.6 MJ/day				

Author/ Year	Measure characteristics	Physical domain		Psychological domain		Social domain	
		Component	**Indicator**	**Component**	**Indicator**	**Component**	**Indicator**
Ensrud et al. (2008)	Study of Osteoporotic Fractures Index (SOF Index) Score: range 0-3 (robust,0; pre-frail, 1; Frail, >=2)	Nutrition: Muscle weakness: Endurance:	Weight loss (>=5% loss in 2 years) Chair test (inability to rise from chair 5 times without using arms) Reduced energy level (1 item from Geriatric Depression Scale).				
Freibeit et al. (2010)	Score: range 0-5	Balance: Nutrition:	Tandem test (holding a full tandem position <10s) BMI (<21 or >30 kg/m2)	Cognition: Emotional disorders:	Executive function tested by Trail-Making Test Part B Depression (15-item Geriatric Depression Scale)	Living alone	Self-report

Author/ Year	Measure characteristics	Physical domain		Psychological domain		Social domain	
		Component	**Indicator**	**Component**	**Indicator**	**Component**	**Indicator**
Fried et al. (2001)	Frailty phenotype Score: robust, 0 indicator; pre-frail, 1-2; frail, >=3.	Nutrition: Muscle weakness: Endurance: Mobility: Physical activity:	Unintentionally weight loss (>=10 lbs. unintentional loss in prior year) Grip strength (lowest 20%, stratified by gender) Self-report exhaustion (2 items from CES-D) Gait speed (walk 15 ft., lowest 20% stratified by gender) Low activity (kilocalories expended per week by the MLTA)				
García-García et al. (2014)	Frailty Trait Scale (FTS, 12 items) Score: each item 0-4, total score= (the sum of each items /total score possible by individual) ×100	Nutrition: Balance: Mobility: Muscle weakness: Endurance: Physical activity: Vascular system:	BMI Weight loss $\geq$4.5kg Waist Circumference Albumin Romberg test Gait speed (3 meters at normal gait, lowest quintile) Grip strength Knee extension strength Chair test (number of times standing up in 30s, lowest quintile) PASE, lowest quintile Brachial ankle index	Cognition:	Verbal fluency test		

Author/ Year	Measure characteristics	Physical domain		Psychological domain		Social domain	
		Component	**Indicator**	**Component**	**Indicator**	**Component**	**Indicator**
Hyde et al. (2010)	FRAIL scale Score: frail if >=3 indicators (self-report, move)	Endurance: Resistance: Mobility: Comorbidity: Nutrition:	Fatigue (items from SF-36) Difficulty climbing a flight of stairs (items from SF-36) Difficulty walking more than 100m (items from SF-36) $\geq$ 5 illnesses present (a list of 14 illnesses) Weight loss>=5% (from 4th year to 5th year)				
Hubbard et al. (2009)	Modified Frailty Score Score: fit (0 indicator), pre-frail (1-2 indicators), frail (3-5 indicators)	Nutrition: Muscle weakness: Mobility: Symptom/ Sign:	Weight loss (>5kg in preceding year) Grip strength ($\leq$16kg by dynamometer) Timed get-up-go ($\geq$17s) Decrease lung function FEV1<=30%	Cognition:	MMSE<24		
Jung et al. (2014)	Score: weighted score (0-1), >=0.35 frail	Mobility and balance: Disability: Nutrition:	SPPB ADLs IADLs Albumin	Cognition:	MMSE		

Author/ Year	Measure characteristics	Physical domain		Psychological domain		Social domain	
		Component	Indicator	Component	Indicator	Component	Indicator
Kim et al. (2014)	Base on CGA. Score: each indicator 0-2, the total score range 0-18, frail if scores >=5	Nutrition: Disability: Comorbidity:	Mini nutritional assessment Mid-arm Circumference Albumin ADLs IADLs Charlson comorbidity index Malignant disease Nursing Delirium Screening Scale	Cognition:	MMSE		
Robinson et al. (2013)	Score: non-frail, 0-1 indicator; pre-frail, 2-3; frail, >=4	Mobility: Nutrition: Disability: Comorbidity: Symptom/ Sign: Falls:	Timed up and go ($\geq$15s) Serum albumin<3.4g/dL ADLs (Katz score <=5) Charlson index (>=3) Anemia (hematocrit level<35%) One or more falls within 6 months	Cognition:	Mini-cog measures (<=3)		

Author/ Year	Measure characteristics	Physical domain		Psychological domain		Social domain	
		Component	**Indicator**	**Component**	**Indicator**	**Component**	**Indicator**
Sünderman n et al. (2011)	Comprehensive Assessment of Frailty (CAF) Score: range 1-35, not frail 1-10; moderately frail, 11-25; severely frail, >25	Mobility: Balance: Other physical performance: Muscle weakness: Endurance: Disability: Nutrition: Symptom/ Sign: Other:	Gait speed (4 meters walking test) Tandem balance test Get-up-and-down, pick up a pen from the floor, put on and remove a jacket Grip strength (by dynamometer) Self-reported exhaustion IADLs Serum albumin FEV_1 Rockwood's Clinical Frailty Scale				

Author/ Year	Measure characteristics	Physical domain		Psychological domain		Social domain	
		Component	Indicator	Component	Indicator	Component	Indicator
Kamaruzzaman et al. (2010)	British Frailty Index (35 items) Score: range 0-1, each indicator was assigned relative weights in its association with frailty	Disability: Sensory function: Symptoms/signs: Nutrition: Comorbidity:	8 items about physical activity (e.g. ability to household chores, walkout) 3 items about visual impairment 4 items about cardiac symptoms/disease 5 items about respiratory symptoms/disease BMI Waist hip ratio 7 items about conditions 3 items using physiological markers about hypertensive, postural hypotension and sinus tachycardia	Emotional disorders: Cognition:	2 items about depressive and anxious problems Memory problems		
Mitnitski et al. (2001)	Frailty Index (92 item version) Score: by counting the number of deficits divide the total number of deficits	Symptoms/ Signs Abnormal lab values Comorbidity Disability		Cognition: Emotional disorders:	Self-report memory problem Depressive and anxious symptoms		

Author/ Year	**Measure characteristics**	**Physical domain**		**Psychological domain**		**Social domain**	
		Component	**Indicator**	**Component**	**Indicator**	**Component**	**Indicator**
Puts et al. (2005)	Expanded Fried's frailty phenotype Score: range 0-9 (static frailty if 1-2 pre-frail;>=3 frail; dynamic frailty if decline from T1 to T2	Nutrition: Sensory function: Physical activity: Symptoms/ Signs:	BMI Weight loss Vision capacity Hearing capacity LASA physical activity questionnaire Lung function by peak expiratory flow Incontinence	Cognition: Emotional disorders:	MMSE Depression by CES-D Sense of mastery by short version Pearlin and Schooler Mastery scale		
Ravaglia et al. (2008)	Score: 0-2 presence, normal;>=3 presence, frailty with increasing risk of mortality	Physical activity: Sensory function: Nutrition: Disability: Mobility and balance: Comorbidity: Age: Gender:	Self-report <4 h/wk of moderate intensity activity Self-report blindness or deafness Calf circumference <31cm IADLs Tinetti gait and balance test (score ≤24) ≥3 medication use Age ≥80 Male	Emotional disorders:	Pessimism about one's health		

Author/ Year	Measure characteristics	Physical domain		Psychological domain		Social domain	
		Component	**Indicator**	**Component**	**Indicator**	**Component**	**Indicator**
Rothman et al. (2008)	Expanded Fried's frailty phenotype	Mobility: Physical activity: Nutrition: Endurance: Muscle weakness:	Gait speed (10 ft, fastest pace) Physical Activity Scale for the Elderly (men, <64; women, <52) Weight loss (≥10 pounds) Self-report exhaustion (2 items by CES-D) Grip strength	Cognition: Emotional disorders:	MMSE Depression by 11-item CES-D		
Sarkisian et al. (2008)	Expanded Fried's frailty phenotype	Nutrition: Muscle weakness: Endurance: Mobility: Physical activity: Lab tests: Symptoms/ signs:	Weight loss Grip strength Subjective weakness (1 item by the HSC) Self-report exhaustion (1 item from the HSC) Gait speed (10 ft walking, normal pace) Weighted energy expenditure by the YPAS IL-6 CRP Anorexia	Cognition:	Global cognitive function by a serials tests of language, executive function, special ability, and verbal and non-verbal memory		

Note: *ADL=activities of daily living; BMI=Body Mass Index; CES-D=Center for Epidemiologic Studies Depression Scale; CRP= C-reactive protein;FEV*$_1$*=volume exhaled during the first second of a forced expiratory maneuver started from the level of total lung capacity; HSC=Hopkins Symptom Checklist; IADL=instrumental activities of daily living; IL-6= Interleukin 6;Kpa=kilopascal; kg=kilogram*; *LASA physical activity=Longitudinal Aging Study Amsterdam Physical Activity Questionnaire; MJ=megajoule; MET=Metabolic Equivalent of Task;* MLTA=Minnesota Leisure Time Activity; *MMSE=Mini Mental State Examination;* PASE=Physical Activity Scale for the Elderly; SF-36=Short Form 36 Health Survey; *SPPB=Short Physical Performance Battery; YPAS=Yale Physical Activity Survey.*

Table 2.2. Frailty components and corresponding indicators in objective frailty measures

Author/ Year	**Measure characteristics**	**Physical domain**	
		Component	**Indicator**
Brown et al. (2000)	Score: 0-36, (32-36, not frail;25-31 mild frailty, 17-24 moderate frailty, <17 severe)	Physical performance:	(9 tests): • book lift; • put on and take off coat; • pick up penny; chair rise; • turn 360; • 50-ft walk; • one flight of stairs; • four flights of stairs; balance (Progressive Romberg test).
Gill et al. (2002)	Score: 1 indicator, moderately frail; 2 indicator, severely frail	Mobility: Muscle weakness:	Take ≥10s to perform a rapid-gait test (10ft) Chair test (inability to stand up from a seated position without using arms)
Klein et al. (2005)	Score: none (0 indicator), mild (1-2 indicators), moderate (3 indicators), severe (4-5 indicators)	Mobility: Symptom/Sign: Muscle strength: Sensory function:	Gait speed (highest quartile, stratified by gender) Peak expiratory flow rate (lowest quartile, stratified by gender) •Grip strength (lowest quartile, stratified by gender) •Chair test (inability to stand from sitting position without using arms in one try) Visual impairment (best-corrected visual acuity of 20/40 or poorer in the better eye)
Opasich et al. (2010)	Score: non-frail, BPOMA>19 and GUG <=10s; moderately frail, BPOMA<=19 and GUG >10s; Severely frail, BPOMA<=9 and GUG>10s	Mobility: Balance:	GUG BPOMA (static balance and dynamic balance)

Note: BPOMA= Balance performance oriented mobility assessment; *GUG=Get-up- and- Go test.*

Table 2.3. Frailty components and its indicators in self-report frailty measures

Author/ Year	**Measure characteristics**	**Physical domain**		**Psychological domain**		**Social domain**	
		Component	**Indicator**	**Component**	**Indicator**	**Component**	**Indicator**
Amici et al. (2008)	Marigliano-Cacciafesta polypathological scale (MCPS) Item:11 Score: 0-245 (25-49, medium-severe; 50-74 severe; >75 very severe	Comorbidity:	• Neurological disorders; • Cardiopathy; • Respiratory disorders; • Renal disorders; • Locomotive apparatus disorders; • Sensory deprivation; • Metabolism and nutritional state; • Peripheral vascular system; • Malignant cancerous disorders; • Gastroenteritis disorders.	Cognition:	Cognitive state and mood		
Johansen et al. (2014)	Based on Fried's Frailty phenotype Item: 5 Score:0-5, frail if scores>=3	Physical performance: Nutrition: Endurance: Physical activity:	$\leq$75 on the physical function scale of the SF-36 Self-report unintentional weight loss >=10 lb in previous year Exhaustion (2 items from CES-D) Kilocalories per week expended by the short version of the MLTAQ				

Author/ Year	Measure characteristics	Physical domain		Psychological domain		Social domain	
		Component	Indicator	Component	Indicator	Component	Indicator
Tocchi et al. (2014)	Frailty index for elders (FIFE) Item: 10 Score: not define	Disability: Health care use Nutrition: General health: Endurance:	3 items about difficulties in out of bed, bathing, and eat 2 items about hospitalization and ER 2 items about loss weight, and poor appetite 1 item about self-rate poor health 1 item about self-report tired			Social activities	self-report less social activities
de Vries et al. (2013)	Evaluative Frailty Index for Physical Activity (EFIP) Item: 50 Score: range 0-50	Disability: General health: Comorbidity:	Questions about physical functioning Self-report health Questions about chronic conditions	Cognition: Emotional disorder:	Memory problems Emotion like depressed, anxious, happy etc.	Social functioning:	Loneliness, social activities, social connections etc.
Bielderman et al. (2013)	Groningen Frailty Indicator (GFI) Item: 15 Score: range0-15	Mobility: Sensory function: Nutrition: Comorbidity: General health:	Difficulties in walking Vision problem Hearing problem Weight loss Taking 4 or more medications Self-rate physical fitness	Cognition: Emotional disorders:	Self-report memory problem Feeling depressed Feeling anxious	Loneliness	3 questions about feeling lonely

Author/ Year	Measure characteristics	Physical domain		Psychological domain		Social domain	
		Component	**Indicator**	**Component**	**Indicator**	**Component**	**Indicator**
De Witte et al. (2013)	Comprehensive Frailty Assessment Instrument (CFAI) Item: 35 Score: range 19-97	Disability:	Physical functioning about carrying shopping bags, walking, bending or lifting, and walkout (4 items)	Emotional disorders:	Feeling depressed, losing self-confidence, lacking coping skills pressed (5 items)	Loneliness: Social support: Social relation: Environment--al domain:	3 items 3 items 10 items housing conditions (5 items)
Brehmer-Rinderer et al. (2013)	Vienna Frailty Questionnaire (VFQ-ID-R) Item: 34 Score: not define	Mobility: Balance: Muscle weakness: General health: Symptom: Disability:	Self-report decrease Self-report decrease Decrease of strength in the arms and legs, and grip strength General health decline Falls ADLs IADLs	Cognition: Emotional disorder:	Memory problem Feeling abou nervousness, sadness, anger etc.	Social relatior	Less relations with work, friends, family

Author/ Year	Measure characteristics	Physical domain		Psychological domain		Social domain	
		Component	**Indicator**	**Component**	**Indicator**	**Component**	**Indicator**
Gobbens, van Assen, et al. (2010)	Tilburg Frailty Indicator (TFI) Item: 15 Score: range 0-15	Physical activity: Nutrition: Balance: Sensory function: Muscle weakness: Endurance:	Self-report general health Weight loss Difficulty in balance Difficulty in vision/hearing Decease of strength Self-report fatigue	Cognition: Emotional disorders:	Memory problem Depression Anxiety Coping	Social relation: Social support:	Living alone Loneliness Self-report enough social support
Kanauchi et al. (2008)	Using 2 questionnaires: HRCA; VES-13 Score: HRCA A component score> 1, or A component score=1 and B component >0, indicating frail; VES-13 score >=3 indicating frail. Frail if either HRCA or VES-13 indicating frail.	Disability:	• HRCA: A component: ▪ self-reported requirements for help in preparing meals, ▪ taking out the garbage, ▪ doing housework, ▪ walking up and down stairs, ▪ using a walker or cane, ▪ identifying the current year; B component: ▪ self-reported answers for leaving their residence, ▪ needing help in dressing, ▪ having health impediments. • VES-13: age, self-rated health, limitations in physical functions and functional disabilities				

Author/ Year	Measure characteristics	Physical domain		Psychological domain		Social domain	
		Component	**Indicator**	**Component**	**Indicator**	**Component**	**Indicator**
Rolfson et al. (2006)	Edmonton Frail Scale Item:11 Score: the sum of each item, range 0-17	Balance and mobility: Disability: Nutrition: Comorbidity: Symptoms/ signs: General health:	TUG Functional dependence Weight loss Medication use Continence Self-report general health	Cognition: Emotional disorders:	Clock draw test Mood disorders	Social support	
Cacciatore, et al. (2005)	Frailty Staging System (FSS) Score: range 0-7; class 1, 0 or 1 indicator; class 2, 2-3; class 3, 4-7	Disability: Mobility: Sensory function: Symptoms/ Signs:	ADLs Ability to do heavy housework Walk up and down stairs to the second floor and to walk half a mile Visual function Hearing Urinary continence	Cognition:	MMSE<24	Social support	
Jones et al. (2004)	Frailty Index-CGA (FI-CGA) Item: 10 Score: each domain is scored as 0=no problem, 1=minor problem, or 2=major problem; 0-7 mild; 7-13 moderate; >13 severe	Mobility Balance Disability: Nutrition Bowel function Bladder function	ADLs/IADLs	Cognition Mood and motivation		Social resources	

Author/ Year	Measure characteristics	Physical domain		Psychological domain		Social domain	
		Component	**Indicator**	**Component**	**Indicator**	**Component**	**Indicator**
Saliba et al. (2001)	Vulnerable elderly survey Item: 13 Score: frail if scores >=3	Age General health: Disability:	Self-rate health Physical function limitation ADLs/IADLs				
Rockwood et al. (1999)	Score: 0=independent; 1=incontinence only; 2= more than 1 assistance; 3=more than 2 assistance	Mobility: Disability: Symptoms/ Signs:	Difficulty in walking ADLs Continence	Cognition:	Self-report cognitive problems		
Strawbridge et al. (1998)	Score: each item is scored from 1 to 4 and subjects scoring a 3 or higher on at least one item in any domain were considered to have a problem with that domain. Frail if having problems in 2 or more domains.	Physical functioning: Nutritive functioning: Sensory functioning:	Balance, weakness in arms, weakness in legs, get dizzy or faint when stand up quickly) Loss of appetite, unexpected weight loss) Vision and hearing problems	Cognition:	Difficulty paying attention, trouble finding the right word, difficulty remembering things, forgetting where put something		

Author/ Year	Measure characteristics	Physical domain		Psychological domain		Social domain	
		Component	**Indicator**	**Component**	**Indicator**	**Component**	**Indicator**
Brody (1997)	Met the criteria in either 3	Nursing home services, supportive services, stay nursing home					

Note: *ADL=activities of daily living; IADL=instrumental activities of daily living; CES-D=Center for Epidemiologic Studies Depression Scale;; MLTAQ=Minnesota Leisure Time Activity Questionnaire; HRCA=Hebrew Rehabilitation Center for Aged vulnerability index; VES-13= Vulnerable Elders Survey-13 items*

Table 2.4. Characteristics of clinician/researcher subjective measures

Author/ Year	Measure characteristics
Gerdhem et al. (2003)	Subjective frailty score: a subjective evaluation of an individual's general health appearance within 15s from first sight, and transfer this into an arbitrary scale from 1-100 Score: 1=not frail at all to 100 very frail or aged
Rockwood et al. (2005)	CSHA Clinical Frailty Scale: based on subjective clinical judgment. Item:7 Score: 7 points from 1 very fit to 7 severely frail
Studenski et al. (2004)	Clinical Global Impression of Change in Physical Frailty (CGIC-PF): 1.mobility (walking, transfers, stairs, assistive device), 2.balance (falls, fear of falling, balance examination), 3.strength (grip, chair rise, manual muscle tests), 4.endurance (self-report of energy and fatigue), 5.nutrition (weight, albumin, cholesterol), and 6.neuromotor performance (speed of movement, attention, coordination). Based on clinical judgment, the amount of change from baseline to 6 months of follow-up: 1=worse to 7=marked improvement

Note: CSHA=Canadian Study on Health and Aging

Reference

Abellan van Kan, G., Rolland, Y., Bergman, H., Morley, J. E., Kritchevsky, S. B., & Vellas, B. (2008). The I.A.N.A Task Force on frailty assessment of older people in clinical practice. *The Journal of Nutrition Health and Aging, 12*(1), 29-37.

Ament, B., de Vugt, M.E., Verhey, F.R. J., & Kempen, G.. (2014). Are physically frail older persons more at risk of adverse outcomes if they also suffer from cognitive, social, and psychological frailty? *European Journal of Ageing, 11*(3), 213-219.

Amici, A., Baratta, A., Linguanti, A., Giudice, G., Servello, A., Scalise, C., . . . Cacciafesta, M. (2008). The Marigliano–Cacciafesta polypathological scale: A tool for assessing fragility. *Archives of Gerontology and Geriatrics, 46*(3), 327.

Avila-Funes, J. A., Amieva, H., Barberger-Gateau, P., Le Goff, M., Raoux, N., Ritchie, K., . . . Dartigues, J. F. (2009). Cognitive impairment improves the predictive validity of the phenotype of frailty for adverse health outcomes: the three-city study. *Journal of American Geriatric Society, 57*(3), 453-461. doi: 10.1111/j.1532-5415.2008.02136.x

Bergman, H., Ferrucci, L., Guralnik, J., Hogan, D. B., Hummel, S., Karunananthan, S., & Wolfson, C. (2007). Frailty: an emerging research and clinical paradigm--issues and controversies. *The Journals of Gerontology Series A: Biological Sciences and Medical Sciences, 62*(7), 731-737.

Bielderman, A., van der Schans, C. P., van Lieshout, M. R., de Greef, M. H., Boersma, F., Krijnen, W. P., & Steverink, N. (2013). Multidimensional structure of the Groningen Frailty Indicator in community-dwelling older people. *BMC Geriatrics, 13*, 86. doi: 10.1186/1471-2318-13-86

Binder, E. F., Schechtman, K.B., Ehsani, A.A., Steger-May, K., Brown, M.h, Sinacore, D. R., . . . Holloszy, J.O. (2002). Effects of Exercise Training on Frailty in Community-Dwelling Older Adults: Results of a Randomized, Controlled Trial. *Journal of the American Geriatrics Society, 50*(12), 1921.

Brehmer-Rinderer, B., Zeilinger, E. L., Radaljevic, A., & Weber, G. (2013). The Vienna Frailty Questionnaire for Persons with Intellectual Disabilities-Revised. *Research in Developmental Disabilities, 34*(6), 1958-1965.

Brody, Kathleen K. (1997). Evaluation of a self-report screening instrument to predict frailty outcomes in aging populations. *Gerontologist, 37*(2), 182.

Brody, K.K., Johnson, R.E., Ried, L. D., Carder, P. C., & Perrin, N. (2002). A Comparison of Two Methods for Identifying Frail Medicare-Aged Persons. *Journal of the American Geriatrics Society, 50*(3), 562.

Brown, M., Sinacore, D.R., Binder, E.F., & Kohrt, W. M. (2000). Physical and performance measures for the identification of mild to moderate frailty. *Journals of Gerontology - Series A Biological Sciences and Medical Sciences, 55*(6), M350.

Cacciatore, F., Abete, P., Mazzella, F., Viati, L., Della Morte, D., D'Ambrosio, D., . . . Rengo, F. (2005). Frailty predicts long-term mortality in elderly subjects with chronic heart failure. *European Journal of Clinical Investigation, 35*(12), 723.

Carrière, I., Colvez, A., Favier, F., Jeandel, C., & Blain, H. (2005). Hierarchical components of physical frailty predicted incidence of dependency in a cohort of elderly women. *Journal of Clinical Epidemiology, 58*(11), 1180.

Chin A Paw, M. J. M., Feskens, E. J. M., Dekker, J. M., Kromhout, D., & Schouten, E. G. (1999). How to select a frail elderly population? A comparison of three working definitions. *Journal of Clinical Epidemiology, 52*(11), 1015.

Davydow, D. S., Hough, C. L., Levine, D.A., Langa, K.M., & Iwashyna, T.J. (2013). Functional disability, cognitive impairment, and depression after hospitalization for pneumonia. *American Journal of Medicine, 126*(7), 615.

de Vries, N. M., Staal, J. B., Rikkert, Mgmo, & Nijhuis-van der Sanden, M. W. G. (2013). Evaluative Frailty Index for Physical Activity (EFIP): A Reliable and Valid Instrument to Measure Changes in Level of Frailty. *Physical Therapy, 93*(4), 551-561.

De Witte, N., Gobbens, R., De Donder, L., Dury, S., Buffel, T., Verté, D., & Schols, J. M. G. A. (2013). Validation of the Comprehensive Frailty Assessment Instrument against the Tilburg Frailty Indicator. *European Geriatric Medicine, 4*(4), 248.

Ensrud, K.E., Ewing, S. K., Taylor, B.C., Fink, H.A., Cawthon, P.M., Stone, K. L., . . . for the Study of Osteoporotic Fractures Research, Group. (2008). Comparison of 2 Frailty Indexes for Prediction of Falls, Disability, Fractures, and Death in Older Women. *Archives of Internal Medicine, 168*(4), 382.

Freiheit, E. A. (2010). Development of a frailty index for patients with coronary artery disease. *Journal of the American Geriatrics Society, 58*(8), 1526.

Fried, L. P., Ferrucci, L., Darer, J., Williamson, J. D., & Anderson, G. (2004). Untangling the concepts of disability, frailty, and comorbidity: implications for improved targeting and care. *The Journals of Gerontology Series A: Biological Sciences and Medical Sciences, 59*(3), 255-263.

Fried, L. P., Tangen, C. M., Walston, J., Newman, A. B., Hirsch, C., Gottdiener, J., . . . McBurnie, M. A. (2001). Frailty in older adults: evidence for a phenotype. *The Journals of Gerontology Series A: Biological Sciences and Medical Sciences, 56*(3), M146-156.

Fulop, T., Larbi, A., Witkowski, J. M., McElhaney, J., Loeb, M., Mitnitski, A., & Pawelec, G. (2010). Aging, frailty and age-related diseases. *Biogerontology, 11*(5), 547-563. doi: 10.1007/s10522-010-9287-2

García-García, F.J., Carcaillon, L., Fernandez-Tresguerres, J., Alfaro, A., Larrion, J. L., Castillo, C., & Rodriguez-Mañas, L. (2014). A new operational definition of frailty: the Frailty Trait Scale. *Journal of the American Medical Directors Association, 15*(5), 371.e377.

Gerdhem, P., Ringsberg, K. A. M., Magnusson, H., Obrant, K.J., & Åkesson, K. (2003). Bone Mass Cannot Be Predicted by Estimations of Frailty in Elderly Ambulatory Women. *Gerontology, 49*(3), 168.

Gill, T. M., Baker, D. I., Gottschalk, M., Peduzzi, P.N., Allore, H., & Byers, A. (2002). A Program to Prevent Functional Decline in Physically Frail, Elderly Persons Who Live at Home. *The New England Journal of Medicine, 347*(14), 1068.

Gill, T. M., Gahbauer, E. A., Allore, H.G., & Han, L. (2006). Transitions Between Frailty States Among Community-Living Older Persons. *Archives of Internal Medicine, 166*(4), 418.

Gobbens, R. J., Luijkx, K. G., Wijnen-Sponselee, M. T., & Schols, J. M. (2010). Towards an integral conceptual model of frailty. *The Journal of Nutrition, Health & Aging. , 14*(3), 175-181.

Gobbens, R. J., Luijkx, Katrien G., & van Assen, Marcel A. L. M. (2013). Explaining quality of life of older people in the Netherlands using a multidimensional assessment of frailty. *Quality of Life Research : An International Journal of Quality of Life Aspects of Treatment, Care and Rehabilitation, 22*(8), 2051-2061.

Gobbens, R. J., van Assen, M. A., Luijkx, K. G., Wijnen-Sponselee, M. T., & Schols, J. M. (2010). The Tilburg Frailty Indicator: psychometric properties. *Journal of the American Medical Directors Association, 11*(5), 344-355. doi: 10.1016/j.jamda.2009.11.003

Hogan, D.B., MacKnight, C., & Bergman, H. (2003). Models, definitions, and criteria of frailty. *Aging Clinical and Experimental Research, 15*(3 Suppl), 1.

Hubbard, R. E., O'Mahony, M. S., & Woodhouse, K.W. (2009). Characterising frailty in the clinical setting-a comparison of different approaches. *Age and Ageing, 38*(1), 115.

Hyde, Z., Flicker, L., Almeida, O.P., Hankey, G.J., McCaul, K. A., Chubb, S. A. P., & Yeap, B. (2010). Low Free Testosterone Predicts Frailty in Older Men: The Health in Men Study. *The Journal of Clinical Endocrinology & Metabolism, 95*(7), 3165.

Johansen, K. L., Dalrymple, L. S., Delgado, C., Kaysen, G. A., Kornak, J., Grimes, B., & Chertow, G. M. (2014). Association between body composition and frailty among prevalent hemodialysis patients: a US Renal Data System special study. *Journal of the American Society of Nephrology, 25*(2), 381-389. doi: 10.1681/asn.2013040431

Jones, D. M., Song, X., & Rockwood, K. (2004). Operationalizing a frailty index from a standardized comprehensive geriatric assessment. *Journal of American Geriatric Society, 52*(11), 1929-1933. doi: 10.1111/j.1532-5415.2004.52521.x

Jung, H.W., Kim, S.W., Ahn, S., Lim, J.Y., Han, J.W., Kim, T.H., . . . Kim, C.H. (2014). Prevalence and outcomes of frailty in Korean elderly population: comparisons of a multidimensional frailty index with two phenotype models. *PLoS One, 9*(2), e87958.

Kamaruzzaman, S., Ploubidis, G.B., Fletcher, A., & Ebrahim, S. (2010). A reliable measure of frailty for a community dwelling older population. *Health Quality Life Outcomes, 8*(1), 123.

Kanauchi, M., Kubo, A., Kanauchi, K., & Saito, Y. (2008). Frailty, health-related quality of life and mental well-being in older adults with cardiometabolic risk factors. *International Journal of Clinical Practice, 62*(9), 1447.

Kim, S.W., Han, H.S., Jung, H.W., Kim, K., Hwang, D.W., Kang, S.B., & Kim, C.H.. (2014). Multidimensional frailty score for the prediction of postoperative mortality risk. *Journal of American Medical Association Surgery, 149*(7), 633.

Kinsella, K., & Phillips, D.R. (2005). Global aging: The challenge of success. *Population Bulletin, 60*(1), 3.

Klein, B, Klein, R., Knudtson, M.D., & Lee, K.E. (2005). Frailty, morbidity and survival. *Archives of Gerontology and Geriatrics, 41*(2), 141.

Markle-Reid, M., & Browne, G. (2003). Conceptualizations of frailty in relation to older adults. *Journal of Advanced Nursing, 44*(1), 58-68.

Mitnitski, A. B., Mogilner, A. J., & Rockwood, K. (2001). Accumulation of deficits as a proxy measure of aging. *Scientific WorldJournal, 1*, 323-336. doi: 10.1100/tsw.2001.58

Morley, J. E., Vellas, B., van Kan, G. A., Anker, S.D., Bauer, J. M., Bernabei, R., . . . Walston, J. (2013). Frailty consensus: a call to action. *Journal of the American Medical Directors Association, 14*(6), 392.

Opasich, C., Patrignani, A., Mazza, A., Gualco, A., Cobelli, F., & Pinna, G. D. (2010). An elderly-centered, personalized, physiotherapy program early after cardiac surgery. *European Journal of Cardiovascular Prevention and Rehabilitation, 17*(5), 582.

Park, D. C., & Reuter-Lorenz, P. (2009). The adaptive brain: aging and neurocognitive scaffolding. *Annual Review Psychology, 60*, 173-196. doi: 10.1146/annurev.psych.59.103006.093656

Ponzetto, M., Zanocchi, M., Maero, B., Giona, E., Francisetti, F., Nicola, E., & Fabris, F. (2003). Post-hospitalization mortality in the elderly. *Archives of Gerontology and Geriatrics, 36*(1), 83.

Puts, M. T., Lips, P., & Deeg, D. J. (2005b). Static and dynamic measures of frailty predicted decline in performance-based and self-reported physical functioning. *Journal of Clinical Epidemiology, 58*(11), 1188.

Ravaglia, G., Forti, P., Lucicesare, A., Pisacane, N., Rietti, E., & Patterson, C. (2008). Development of an easy prognostic score for frailty outcomes in the aged. *Age and Ageing, 37*(2), 161.

Rizzoli, R., Reginster, J.Y., Arnal, J.F., Bautmans, I., Beaudart, C., Bischoff-Ferrari, H., . . . Bruyère, O. (2013). Quality of Life in Sarcopenia and Frailty. *Calcified Tissue International, 93*(2), 101.

Robertson, D. A., Savva, G.M., & Kenny, R.A. (2013). Frailty and cognitive impairment-A review of the evidence and causal mechanisms. *Ageing Research Reviews, 12*(4), 840.

Robinson, T. N., Wu, D. S., Pointer, L., Dunn, C. L., Cleveland, J. C., & Moss, M. (2013). Simple frailty score predicts postoperative complications across surgical specialties. *American Journal of Surgery, 206*(4), 544.

Rockwood, K., & Hubbard, R. (2004). Frailty and the geriatrician. *Age Ageing, 33*(5), 429-430. doi: 10.1093/ageing/afh153

Rockwood, K., Song, X., MacKnight, C., Bergman, H., Hogan, D. B., McDowell, I., & Mitnitski, A. (2005). A global clinical measure of fitness and frailty in elderly people. *Canadian Medical Association Journal, 173*(5), 489-495. doi: 10.1503/cmaj.050051

Rockwood, K., Stadnyk, K., MacKnight, C., McDowell, I., Hébert, R., & Hogan, D.B. (1999). A brief clinical instrument to classify frailty in elderly people. *The Lancet, 353*(9148), 205.

Rolfson, D. B., Majumdar, S. R., Tsuyuki, R. T., Tahir, A., & Rockwood, K. (2006). Validity and reliability of the Edmonton Frail Scale. *Age Ageing, 35*(5), 526-529. doi: 10.1093/ageing/afl041

Rolfson, D. B., Wilcock, G., Mitnitski, A., King, E., de Jager, C.A., Rockwood, K., . . . Searle, S.D. (2013). An assessment of neurocognitive speed in relation to frailty. *Age and Ageing, 42*(2), 191.

Romero-Ortuno, R., Walsh, C.D., Lawlor, B.A., & Kenny, R.A. (2010). A Frailty Instrument for primary care: Findings from the Survey of Health, Ageing and Retirement in Europe (SHARE). *BMC Geriatrics, 10*(1), 57.

Rothman, M. D., Leo-Summers, L., & Gill, T. M. (2008). Prognostic significance of potential frailty criteria. *Journal of the American Geriatrics Society, 56*(12), 2211-2116. doi: 10.1111/j.1532-5415.2008.02008.x

Saliba, D., Elliott, M., Rubenstein, L.Z., Solomon, D.H., Young, R.T., Kamberg, C. J., . . . Wenger, N.S. (2001). The Vulnerable Elders Survey: A Tool for Identifying Vulnerable Older People in the Community. *Journal of the American Geriatrics Society, 49*(12), 1691.

Sarria Cabrera, M.A., Gomes Dellaroza, M.S., Trelha, C.S., Cecilio, C.H., & de Souza, S.E. (2012). One-Year Follow-up of Non-institutionalized Dependent Older Adults: Mortality, Hospitalization, and Mobility. *Canadian Journal on Aging, 31*(3), 357.

Sarkisian, C.A., Gruenewald, T. L., John Boscardin, W., & Seeman, T.E. (2008). Preliminary evidence for subdimensions of geriatric frailty: the MacArthur study of successful aging. *Journal of the American Geriatrics Society, 56*(12), 2292-2297.

Singh-Manoux, A., Kivimaki, M., Glymour, M. M., Elbaz, A., Berr, C., Ebmeier, K.P., . . . Dugravot, A. (2012). Timing of onset of cognitive decline: Results from Whitehall II prospective cohort study. *BMJ (Online), 344*(7840), d7622.

Song, X., Mitnitski, A., & Rockwood, K. (2010). Prevalence and 10-year outcomes of frailty in older adults in relation to deficit accumulation. *Journal of American Geriatric Society, 58*(4), 681-687. doi: 10.1111/j.1532-5415.2010.02764.x

Sternberg, S. A., Wershof Schwartz, A., Karunananthan, S., Bergman, H., & Mark Clarfield, A. (2011). The identification of frailty: a systematic literature review. *Journal American Geriatric Society, 59*(11), 2129-2138. doi: 10.1111/j.1532-5415.2011.03597.x

Strawbridge, W. J., Shema, S. J., Balfour, J. L., Higby, H. R., & Kaplan, G. A. (1998). Antecedents of frailty over three decades in an older cohort. *The Journals of Gerontology Series B: Psychological Sciences and Social Sciences, 53*(1), S9-16.

Studenski, S., Hayes, R.P., Leibowitz, R.Q., Bode, R., Lavery, L., Walston, J., . . . Perera, S. (2004). Clinical Global Impression of Change in Physical Frailty: Development of a Measure Based on Clinical Judgment. *Journal of the American Geriatrics Society, 52*(9), 1560.

Sündermann, S., Dademasch, A., Praetorius, J., Kempfert, J., Dewey, T., Falk, V., . . . Walther, T.. (2011). Comprehensive assessment of frailty for elderly high-risk patients undergoing cardiac surgery. *European Journal of Cardio-Thoracic Surgery, 39*(1), 33.

Theou, O., Brothers, T. D., Mitnitski, A., & Rockwood, K. (2013). Operationalization of Frailty Using Eight Commonly Used Scales and Comparison of Their Ability to Predict All-Cause Mortality. *Journal of the American Geriatrics Society, 61*(9), 1537.

Tocchi, C., Dixon, J., Naylor, M., Jeon, S., & McCorkle, R. (2014). Development of a frailty measure for older adults: the frailty index for elders. *Journal of Nursing Measurement, 22*(2), 223.

Woo, J., Goggins, W., Sham, A., & Ho, S. C. (2005). Social determinants of frailty. *Gerontology, 51*(6), 402-408. doi: 10.1159/000088705

CHAPTER 3

Comparisons of Two Frailty Models in Older Adults and Frailty Levels between Older Adults with and Without Heart Failure

Abstract

Background: The two predominant conceptualizations of frailty are: Fried's physical frailty model and Gobbens' multidimensional frailty model. However, the added predictive power of a multidimensional frailty model over the physical frailty model remains unclear.

Aims: (1) To compare Fried's physical frailty model and Gobbens' multidimensional frailty model for their ability to predict basic and instrumental activities of daily living (ADL/IADL) disability and quality of life (QOL) in older adults; and (2) to compare the levels of frailty between older adults with HF and without HF, controlling for demographic covariates.

Data and design: A cross-sectional, secondary data anlaysis design was used to analyze 2006 wave data from the Health and Retirement Study.

Sample: A total of 5,027 older adults comprised the sample for frailty model comparison; 303 older adults with HF and 935 older adults without HF were used to compare the levels frailty.

Measures: Frailty was quantified according to both the Fried's model and Gobbens' model. Disability was measured by activities of daily living and instrumental activities of daily living tool. QOL was measured by the Satisfaction with Life Scale. Covariates included socio-demographics and number of chronic diseases.

Results: Compared to the Fried's physical frailty model, the use of psychological components in the Gobbens' model significantly increased the power to predict disability whereas the inclusion of social components did not. However, the psychological and social components of the Gobbens' model significantly increased the predictive value for QOL compared to the Fried's model. Additionally, older adults with HF had higher levels of frailty across all domains of frailty compared to older adults without HF.

Conclusion: This study supports the added predictive value of the psychological and social frailty components and that a multidimensional frailty model better predict disability and QOL than a purely physical frailty model.Older adults with HF were more likely to be frail in all three domain of physical, psychological and social compared to older adults without HF.

Key words: frailty, heart failure, disability, quality of life

Introduction

Frailty is a global health syndrome faced by many adults. It is a state of increased vulnerability and decreased reserve capacity (Morley et al., 2013). The prevalence of frailty rises dramatically as age increases, from only 3.2% in adults age 65-70 to 25.7% in adults age 85-90 (Fried et al., 2001). Its prevalence also varies considerably across countries. For example, in Taiwan the prevalence of frailty is 4% as measured by a modified Frailty Phenotype (Chen, Chen, Wu, & Lue, 2010) compared to 30% in the United as measured by an Index of Deficit Accumulation (Cigolle, Ofstedal, Tian, & Blaum, 2009). While this may reflect actual differences across countries, the wide range of prevalence rates of frailty may be due to the measures and models used to capture frailty.

Older adults with heart failure (HF) are particularly vulnerable to the development of frailty (Uchmanowicz, Loboz-Rudnicka, Szelag, Jankowska-Polanska, & Loboz-Grudzien, 2014), because of decreased physical capacity due to declines in skeletal muscle and body composition (Persinger et al., 2003; Slettaløkken et al., 2012). Coexisting frailty in older adults with HF ranges from 21% to 40% depending on frailty measures and models used (Boxer, Dauser, Walsh, Hager, & Kenny, 2008; Lupon et al., 2008; McNallan et al., 2013). The coexistence of frailty and HF increases older adults' risks for basic and instrumental activity of daily living (ADLs/IADLs) disability and diminishes their quality of life (QOL) (Buck & Riegel, 2011; Cacciatore, Abete, Mazzella, Viati, Della Morte, D'Ambrosio, et al., 2005; Khandelwal et al., 2012). Further, failure to identify frailty and consider its impact on the outcomes of older adults with HF may interfere with nurses' and health providers' abilities to provide effective health care targeted at delaying the onset of disability and improving QOL.

Although frailty is an important health problem in older adults, the issue of conceptualizing frailty remains unresolved. To date there have been two predominant conceptualizations of frailty. One is to define frailty according to a physical phenotype, as typified by Fried's Frailty Phenotype (Fried et al., 2001). Within this phenotype, frailty is characterized as a purely physical condition and quantified by the presence of at least three of the following five physical components: poor nutrition, slow walking speed, limited grip strength, low physical activity, and decreased endurance. A more recent conceptualization of frailty, from a broader perspective, defines frailty as a multidimensional syndrome that includes deficits in physical, psychological, and social domains. For example, the Gobbens' Integral Conceptual Model of Frailty (ICMF) (Gobbens, Luijkx, Wijnen-Sponselee, & Schols, 2010) is multidimensional and defines frailty as a dynamic state with losses in one or more of these three domains of human functioning. The physical components in Gobbens' models were expanded from Fried's model to include three additional components: impaired vision, poor hearing, and difficulties in balance. The psychological components in this model include cognitive impairment, depressive disorder, anxiety, and low coping skills, and the social components include poor social relations, lack of social support, and living alone.

Although conceptualizing frailty as a multidimensional syndrome is increasing (Malaguarnera, Vacante, Frazzetto, & Motta, 2013; Markle-Reid & Browne, 2003; Morley et al., 2013), findings about the predictive power of a multidimensional frailty model over a physical frailty model are inconsistent. For example, Gobbens et al. (2013) reported that adding psychological and social frailty components significantly improved the ability to predict QOL when compared to the use of physical frailty components alone. In contrast, Ament et al. (2014), in an examination of the ability of multidimensional frailty to predict IADL disability and QOL among physically frail older adults, found only physical frailty was a significant predictor for IADL disability. Psychological and social frailty failed to predict IADL disability and QOL.

Although frailty is a debilitating health problem in older adults, no consensus exists as to which frailty model most accurately identifies older adults at risk of adverse health outcomes. Models that can accurately identify older adults who are frail and likely to experience adverse health outcomes are needed for risk stratification and to support health care planning and delivery for nurses and other healthcare providers. Unfortunately, it remains unclear how much predictive power the psychological and social components add to that of the physical components in models of frailty (Ament, de Vugt, Verhey, & Kempen, 2014; Gobbens et al., 2013). Given the inconsistency in frailty models, it is difficult to determine the levels of frailty in older adults with HF. To address these inconsistencies and knowledge deficiency, the purposes of this study were: 1) to compare Fried's physical frailty model and Gobbens' multidimensional frailty model for their ability to predict ADLs/IADLs and QOL, and 2) to compare levels of frailty between older adults with HF and those without HF, controlling for demographic covariates.

Methods

Design and Data

This study used a cross-sectional, secondary data analysis design. The data used in this analysis were from the 2006 wave of the Health and Retirement study (HRS), a nationally representative longitudinal survey of adults aged 51 and older living in the United States. The HRS survey has been conducted every two years since 1992 and has collected information about health transitions in older adults. Starting from the 2006 wave, the HRS survey randomly selected one-half of the sample at each wave to participate in enhanced face-to-face interviews.

This enhanced interview included objective measures of physical performance (e.g., grip strength, balance tests, gait speed) and self-administered psycho-social questionnaires (e.g., social network, life satisfaction, loneliness).

This study was reviewed by the University of Michigan Health Behavior and Health Sciences Institutional Review Board (IRB). It was deemed to be a not regulated human research, because it used the HRS publicly available data and contained no unique identifiers and no sensitive data.

Sample

The sample consisted of respondents who participated in the HRS 2006 wave. Of the 18,469 respondents participating in the 2006 wave, 11,402 were age 65 years and older. Among the sample assigned to engage in enhanced face-to-face interviews, 224 resided in a nursing home, 459 were interviewed by proxy and 508 refused a face-to-face interview. As such, 8,379 remained eligible to complete the objective physical measures and the psychosocial questionnaires. Of which, 5,027 were at least age 65 and comprised the sample of this study (Figure 3.1).

Four questions in the HRS were used to identify self-reported HF. Participants were first asked, “Has a doctor ever told you that you had a heart attack, coronary heart disease, angina, congestive heart failure, or other heart problems?” If answered “yes” , they then responded to the following question “In the last two years, has a doctor told you that you have congestive heart failure?” Older adults were classified as having a HF diagnosis if they answered “yes”. Those who answered “no” were classified as not having HF. Participants were also asked, “Has a doctor ever told you that you have congestive heart failure?” If they answered “yes”, they were then asked, “In what year was your congestive heart failure first diagnosed?” Participants who reported with HF diagnosis at 2006 or before were identified as having self-reported HF. These questions jointly yielded a total of 303 older adults who self-reported diagnosed HF .

Older adults without heart failure comprised the comparison group. Older adults without HF were identified by: 1) no self-reported heart disease or heart failure; 2) no self-report other serious chronic conditions (chronic lung diseases, stroke, cancer in last two years, and arthritis); and 3) no psychiatric problems. However, older adults with the common comorbidities of aging (hypertension or diabetes) were included. As a result, 935 older adults without HF comprised the comparison group in this study.

Measures

Frailty. Frailty was measured using both the Fried's model (Fried et al., 2001) and the Gobbens' model (Gobbens, van Assen, Luijkx, Wijnen-Sponselee, & Schols, 2010). Using the Fried's model, frailty was measured using five physical components: poor nutrition, slow walking speed, limited grip strength, low physical activity, and decreased endurance. Using the Gobbens' model, frailty was quantified by eight physical components (the five aforementioned physical components plus impaired vision, poor hearing, and difficulties in balance), four psychological components (cognitive impairment, depressive disorder, anxiety, and low coping skill), and three social components (poor social relations, lack of social support, and living alone). The components of frailty and corresponding indicators were listed in Table 1.

Disability (ADLs/IADLs). Disability is defined as limitations in the ability to perform daily activities (ADLs and IADLs) that are essential to living an independent life (Pope & Tarlov, 1991). In this study, The ADL/IADL items were combined together in this study to measure the level of disability, in order to provide enhanced range and sensitivity of measurement (Spector & Fleishman, 1998). HRS respondents were asked if they had "any difficulty" (Yes/No) in 11

ADL/IADL tasks "because of physical, mental, emotional or memory problems". The ADL tasks included: 1) dressing, 2) eating, 3) using the toilet, 4) bathing and showering, 5) getting in and out of bed, and 6) walking across a room. The IADL tasks included: 1) preparing a hot meal, 2) shopping for groceries, 3) making telephone calls, 4) taking medication, and 5) managing money. Potential ADL/IADL scores range from 0 to 11 (number of items with reported difficulty) (Chan, Kasper, Brandt, & Pezzin, 2012). Higher scores indicate more ADL/IADL disability (Chan et al., 2012). For purposes of analyses, ADL/IADL disability was dichotomized into 0= "no ADL/IADL disability" and 1= "one or more ADL/IADL disability".

Quality of life (QOL). Quality of life refers to an individual's emotional or cognitive assessment of the congruence between his/her life expectations and achievements (Diener, Emmons, Larsen, & Griffin, 1985). Quality of life was measured using the Satisfaction with Life Scale (SWLS), a five-item scale used in HRS to measure QOL. The coefficient alpha of the SWLS was reported to be 0.87, with a two-month test-retest reliability coefficient of 0.82 (Pavot & Diener, 2009). The respondents of the HRS were asked how much they agreed or disagreed with statements such as "In most ways my life is close to ideal", using a 1-to-6 scale from 1=strongly disagree to 6=strongly agree. The total SWLS score is the average of the five items. Higher scores indicate greater QOL.

Covariates The covariates in this study included socio-demographic factors and the number of chronic conditions. The socio-demographic factors included age, gender, race, years of education, marital status, and annual household income. The number of chronic conditions was based on the presence of hypertension, diabetes, cancer, lung disease, stroke, arthritis, and psychiatric problems.

Data analysis

All analyses were conducted using Stata 13.0. Because the design of the HRS included oversampling of African Americans and Hispanics, as well as a clustered and stratified sample, these features were taken into account in the analysis. As such, the analyses in this study were weighted using the “svy” commands in Stata to adjust for the complex sample design of the HRS and the differential proportion of selection. Sample characteristics were described using descriptive statistics. List-wise deletion was used for missing data.

Objective 1: To select a frailty model based on its predictive ability for ADLs/IADLs and QOL

A series of regression models were conducted to test the ability of the two frailty models (Fried’s and Gobbens’) to predict ADL/IADL disability and QOL. Because the physical frailty indicators in Fried’s model overlap with physical frailty indicators in Gobbens’ model, the Wald test was used to evaluate the difference between models. This test is used when parameters in one model are nested within another model (Fox, 1997), as is the case with the Fried’s and Gobbens’ models. The null hypothesis of the Wald test is that a set of parameters is simultaneously equal to zero. If the test is able to reject the null hypothesis ($\alpha<.05$), this suggests that removing a set of variables from the model will substantially reduce the overall fit of that model and that set of variables result in a statistically significant improvement in the overall fit of the model.

Because ADL/IADL was dichotomized as a binary variable, a series of logistic regression models were conducted. In Model 1, after controlling for demographic characteristics (age, gender, years of education, race, marital status, annual household income, and number of chronic conditions), the predictors of ADL/IADL were Fried’s five physical frailty indicators (poor nutrition, slow walking speed, limited grip strength, low physical activity, and decreased endurance). After running Model 1, the Wald test was performed to test if these five frailty indicators significantly predicted the ADL/IDAL disability, controlling for demographic characteristics.

Model 2 included the predictors from Model 1 plus the three additional physical frailty indicators from the Gobbens' model (impaired vision, poor hearing, and difficulties in balance). After running Model 2, the Wald test was conducted to test the significance of the additional three physical indicators.

In Model 3, the predictors included the eight physical frailty indicators in Model 2, the covariates of demographics and four psychological frailty indicators of the Gobbens' model (cognitive impairment, depressive disorder, anxiety, and low coping skills. The Wald test was conducted to test the significance of the set of the four psychological frailty indicators.

In Model 4, the predictors included the eight physical frailty indicators of Model 2, the demographics covariates, and three social frailty indicators of the Gobbens' model (poor social relations, lack of social support, and living alone). After running this model, the Wald test was conducted to test the significance of the set of three social frailty indicators.

In Model 5, the predictors were the eight physical frailty indicators, the demographics covariates, and both four psychological frailty indicators and three social indicators. Wald tests were conducted to test the significance of a set of physical indicators, a set of four psychological indicators, and a set of three social indicators. If the set of four psychological indicators is not significant, it suggests that the set of four psychological indicators is redundant for predicting ADL/IADL when physical and social frailty indicators are already in the logistic model. If the Wald test shows the set of three social indicators is not significant, that suggests the set of three social indicators is redundant when physical and psychological frailty indicators are already in the model, and does not provide any added predictive power.

Similarly, for the continuous outcome of QOL, a series of five linear regression models were conducted to compare the predictive ability of the Fried's and the Gobbens' models. Wald tests were used to examine the significance of the set of predictors.

In order to show the discrimination of the final selected frailty model compared to Fried's physical frailty model, logistic regression models were used to examine receiver operating characteristic curves (ROC) for each outcome of ADL/IADL disability and QOL. The areas under the curve (AUC) generated from the final selected frailty model and Fried's physical model were calculated and compared (Cleves, 2002). Because QOL was a continuous variable in this study, the scores of QOL were then dichotomized by the median into two categories: "0=low QOL (lower than median)" and "1=high QOL (higher than median)". All analyses were controlled for demographic covariates.

Objective 2: To compare the levels of frailty between older adults with HF and older adults without HF

The frailty model (either Fried's or Gobbens') was selected based on the results of Objective 1. The mean of frailty scores was calculated to indicate the level of frailty, with higher scores indicating higher levels of frailty. The mean of frailty scores was calculated only when frailty indicators have no more than 25% missing data (at least 12 items non-missing). Linear regression models were performed with the dependent variable of frailty scores and independent variables of the presence of self-reported HF and demographic covariates (age, gender, years of education, race, marital status, annual household income, and number of chronic conditions).

Results

Sample characteristics

Among the total sample (n=5027), the mean age of older adults was 75 years and 57% of older adults were females. The average education level was high school (mean=12.33, SE=0.09). Nearly 90% of the sample population was Caucasian/White. Nearly 60% of older adults were married/partnered. Over 90% had at least one chronic condition (hypertension, diabetes, cancer, lung diseases, heart problems, stroke, arthritis, and psychiatric problems).

Older adults with HF were older, less educated and had a lower annual household income compared to those older adults without HF. They also were less likely to be married or partnered and were more likely to have three or more chronic conditions than older adults without HF. No significant differences were found in gender or race between older adults with HF and those without HF. The weighted sample population characteristics are shown in detail in Table 3.2.

Prevalence of frailty indicators

The proportion of each frailty indictor in the sample of general older adults (n=5027) was examined (Figure 3.2). The percentages of deficits in frailty components ranged from 6% (poor nutrition) to 43% (endurance). The three most common indicators of frailty were deficits in endurance, mobility and balance (43%, 40%, and 32% respectively). The three least common indicators of frailty were poor nutrition, depressive disorder and lack of social support (6%, 10%, and 11% respectively).

Comparison of Fried's and Gobbens' models on their predictive ability for ADLs/IADLs

A series of logistic regression models in the sample of all older adults were conducted to examine the ability of frailty indicators to predict ADL/IADL disability (Table 3.3). In order to use the same sample size in a series of regression models, the analyses only included older adults who completed all the frailty measures (n=3288). In Model 1, the result showed that four of the five indicators (physical inactivity, mobility, strength, and endurance) were significant predictors, after adjustment for demographic characteristics. The Wald test of the set of these five physical indicators in Fried's model was significant ($F [5,48]=48.22$, $p<.001$), indicating that these five indicators together significantly predicted the ADL/IADL disability.

In Model 2, the predictors were the five physical indicators of Fried's model plus three additional physical indicators based on Gobbens' model, after controlling for demographic covariates. Logistic regression results showed that all, but nutrition, were significant predictors for ADLs/IADLs. The p value associated with the Wald test of the 3 additional indicators was <.001, which indicates that adding these three physical indicators significantly increased the predictive power of the model from Fried's model to physical domains of Gobbens' model.

In Model 3, the four psychological frailty indicators were added to the physical indicators. Logistic regression analysis showed significant predictors of ADL/IADL disability were physical activity, mobility, strength, endurance, vision, cognition, depression, and anxiety. The p value associated with the Wald test of the four psychological indicators was <.001, meaning that adding these four psychological indicators significantly increase the predictive power for ADL/IADL disability over the physical frailty indicators alone.

In Model 4, the predictors were the three social frailty indicators as well as the eight physical indicators, after controlling for demographic covariates. The logistic regression analysis showed that the significant predictors for ADLs/IADLs were physical activity, mobility, strength, endurance, vision, balance, and social relations. The Wald test of the three social indicators was $p=.0002$. By adding these three social indicators significantly increased the ability to predict ADL/IADL disability compared to the physical frailty indicators alone.

In Model 5, the predictors were all eight physical indicators, four psychological indicators, and three social indicators, after controlling for demographic covariates. The results showed that the significant predictors for ADLs/IADLs were physical activity, mobility, strength, endurance, vision, cognition, depression, and anxiety. The p values associated with the Wald tests of five Fried's physical indicators, and additional three Gobbens' physical indicators both were <.001, indicating these physical indicators were important for the fit of the model. The Wald test of the set of four psychological frailty indicators was significant (F[4,49]=7.17, p=.0001), indicating that removing these four psychological indicators would reduce the predictive power of this model. The Wald test of the set of three social frailty indicators was non-significant (F[3,50]=1.42, p=.2479), which means that the three social frailty indicators did not significantly increase the power of the model to predict ADL/IADL disability compared to the physical and psychological frailty components in the model.

These five logistic regression models showed that the physical and psychological domains of the Gobbens' model better predicted ADL/IADL disability than Fried's model. The AUCs of physical and psychological domains of Gobbens' model and Fried's model was calculated and compared (Figure 3.3). The results showed that using both physical and psychological domains of Gobbens' model (AUC=0.8011) was able to better discriminate older adults who had difficulty to perform one or more ADL/IADL tasks compared to the Fried's model (AUC=0.7764) (p<.001).

Comparison of Fried's and Gobbens' models on their predictive ability for QOL

A series of linear regression models (n=3288) were conducted to compare the ability of frailty indicators to predict QOL in all older adults (Table 3.4). In Model 1, the linear regression results indicated physical activity and endurance were significant predictors for QOL, after controlling for demographic characteristics. The Wald test of the set of these five physical frailty indicators was significant (F[5,48]=20.01, p<.001), which means that these five physical indicators together were important for predicting QOL.

In Model 2, the results showed that the significant predictors for QOL were physical activity, endurance, and vision. The Wald test of the set of additional three physical indicators was significant (F[2,50]=5.02, p=.0041), indicating that adding these additional three physical indicators can increased the predictive power for QOL compared to the five physical indicators in Fried's model.

In Model 3, the linear regression analysis showed physical activity, endurance, depression, anxiety, and coping were the significant predictors for QOL. The Wald test of the set of four psychological frailty indicators was significant (F[4,49]=58.38, P<.001). This result means that adding these four psychological frailty indicators significantly increased the power of model to predict QOL compared to the physical frailty indicators alone.

In Model 4, the linear regression results showed the significant predictors for QOL were physical activity, endurance, vision, social relations, and social support. The p value associated with the Wald test of the set of three social frailty indicators was significant (F[3,50]=81.01, P<.001), indicating that adding the three social indicators increased the predictive power for QOL over the physical frailty indicators in the model.

In Model 5, the linear regression results showed the significant predicators for QOL were physical activity, endurance, depression, anxiety, coping, social relations, and social support. The Wald test of the set of five Fried's physical indicators was significant (F[5, 48]=6.27, p=.001), which indicates that these five physical indicators based on Fried's model were important for predicting QOL. However, the Wald test of the set of three addition physical indicators (impaired vision, poor hearing, and difficulty in balance) based on Gobbens' model was not significant

(F[3, 50]=2.47, p=.073), which indicates that removing these three physical indicators did not reduce the predictive power of the model when the other physical, psychological and social indicators were present. Additionally, the Wald test for the set of four psychological indicators (F[4,49]=21.61, p<.001) and the set of three social indicators (F[3,50]=41.14, P<.001) was significant, indicating that these psychological and social indicators significantly improved the predictive power of the model.

These five linear regression models showed that Gobbens' model which include all three domains (physical, psychological, and social) had better ability to predict QOL than the Fried's model. To further examine the discrimination of these two frailty models, QOL was dichotomized and logistic regression was conducted to calculate the AUCs of Gobbens' model and Fried's model. The results showed that Gobbens' model (AUC=0.7358) was able to better discriminate older adults who had high QOL than Fried's model (AUC=0.6786) (p<.001) (Figure 3.4).

Comparison of the levels of frailty between HF older adults and non-HF older adults

Based on the results of frailty model comparisons, frailty was then assessed by the three subscales: physical (eight indicators), psychological (four indicators) and social (three indicators). The mean scores of physical frailty, psychological frailty, and social frailty were created. The means of frailty scores were calculated only when frailty indicators had no more than 25% missing data (at least 6 in physical domain, 3 in psychological domain, and 3 in social domain, respectively, were non-missing). Among older adults with HF and without HF (n=1238), 120 (10%) had 25% missing data in physical domain, and 118 (10%) in psychological domain and 129 (11%) in social domain.

Bar graphs were used to display the levels of frailty in three domains between older adults with HF (n=303) and older adults without HF (n=935) (Figure 3.5). To test the impact of HF on levels of frailty, linear regression analyses were conducted (Table 3.5). The results showed that the older adults with HF had higher levels of physical frailty ($\beta=0.26$, $p<.001$), psychological frailty ($\beta=0.18$, $p<.001$), and social frailty ($\beta=0.11$, $p<.001$) compared to the older adults without HF. These relationships between HF and frailty subscales remained significant ($p<.001$), even after controlling for the demographic covariates.

Discussion

Findings of this study show that compared to the Fried's physical frailty model, the use of the psychological components in the Gobbens' model significantly increased the power to predict ADL/IADL disability. However, the inclusion of social components did not. For the outcome of QOL, adding the psychological and social components of the Gobbens' model significantly increased the predictive value compared to the Fried's model. However, the additional three physical components (impaired vision, poor hearing, and difficulties in balance) in the Gobbens' model did not predict QOL. These results support the view that a multidimensional frailty model is able to predict adverse health outcomes better than a purely physical frailty model. However, neither the Fried's model nor Gobbens' model was sufficiently robust to predict both ADLs/IADLs disability and QOL. For the different outcomes (ADLs/IADLs or QOL), the different subscales of frailty (physical, psychological, and social) had different predictive abilities. In fact, the findings in this study suggest the need to treat frailty as a multidimensional concept consisting of three subscales. This would facilitate a more accurate identification of older adults who are frail within each domain and a more precise evaluation of their adverse health outcomes risks. Given the multidimensional nature of frailty, which is found in this study, it is important to evaluate the effect of HF on frailty in physical, psychological, and social domains.

Another important finding of this study is that older adults with HF have higher levels of frailty across all three domains of frailty compared to older adults without HF. This suggests that a restricted focus to only frailty in the physical domain among older adults with HF is not sufficient. Older adults with HF may also suffer from frailty in psychological or social domains.

The abilities of frailty subscales to predict ADL/IADL and QOL

In the present study, the relationships between frailty and ADL/IADL disability were examined. Because difficulties in ADLs/IADLs are usually considered a physical-related outcome (Miller, Rejeski, Reboussin, Have, & Ettinger, 2000), it is expected that older adults with higher levels of physical frailty will have more difficulties in performing ADLs/IADLs. Results form this study found that physical frailty components were significant predictors for ADL/IADL disability, even after controlling for other frailty components and demographic covariates. These findings are consistent with other studies (Fried et al., 2001; Rothman, Leo-Summers, & Gill, 2008) that reported physical frailty increased the risk of ADL/IADL disability. However, in this study poor nutrition measured by weight loss and low BMI was not a significant predictor of ADL/IADL disability, which is inconsistent with Rothman et al.' (2008) findings. This may be attributed to the low prevalence rate of poor nutrition in the current study (only 6%), which may lead to insufficient statistical power; however, in the Rothman et al.' study, the prevalence rate of weight loss was approximately 20%.

In addition to the predictive ability of physical frailty, this study showed frailty in the psychological domain predicted ADL/IADL disability. A previous study conduced by Dodge et al. (2005) revealed, in both cross-sectional and longitudinal design, that older adults with cognitive impairment had higher risks of declines in ADL/IADL abilities compared with older adults with intact cognitive function. Previous studies have also shown that depressed older adults have a high risk of ADL/IADL disability compared to non-depressed older adults (Kivela & Pahkala, 2001; Penninx, Leveille, Ferrucci, van Eijk, & Guralnik, 1999). Consistent with these previous studies, the current study suggests that cognitive impairment and emotional disorders increased the risk for ADL/IADL disability. This study also showed an influence of social frailty on ADL/IADL disability when controlling for physical frailty. However, this relationship was diminished when psychological frailty components were added to the regression analysis. This may because psychological frailty moderates and attenuates the relationship between social frailty and functioning disability. For example, older adults with less social contact and social relations may develop the conditions of psychological frailty such as depression and anxiety. Taken together, the findings of the present study reveal that declines in functioning disability assessed by ADL/IADL disability are influenced not only by physical frailty, but also by psychological frailty.

The current study also demonstrates the association between frailty and deceases in QOL. In accordance with previous studies (Kanwar et al., 2013; Rizzoli et al., 2013), the findings in this study support the conclusion that older adults with higher levels of frailty in the physical domain also are at risk for decreased QOL. The current study also demonstrated that adding frailty components in the psychological and social domains significantly increased the model’s power to predict QOL compared to the use of a purely physical frailty model. This is consistent with Gobbens et al. (2013). However, this current study differs from Ament et al. (2014), which found no additional predictive ability of psychological and social frailty on predicting QOL in older adults who were already physically frail. This difference may be due to the use of single-item self-report measure of QOL by Ament et al, which could have negatively influenced the reliability of the measure. Unlike Ament et al., the current study used a well-established measure- Satisfaction with Life Scale (SWLS)- to assess the general QOL in older adults with better construct reliability.

Although neither the Gobbens' model nor the Fried's model is complete enough to predict both ADL/IADL disability and QOL, the findings in the present study support the conceptualization of frailty as multidimensional. Compared to a purely physical frailty model, this study showed a multidimensional frailty model can improve the predictive power of frailty measures and can better identify older adults who are at risk of adverse outcomes. Researchers have recently embraced the a multidimensional nature of frailty, acknowledging that frailty may result from conditions occurring in society and environment as well as the biological and physiological conditions within the individuals (Fulop et al., 2010; Gobbens, Luijkx, et al., 2010; Markle-Reid & Browne, 2003). Given the multidimensional perspective of frailty, the current study demonstrated that different domains of frailty captured predict different health outcome. For example, physical frailty and psychological frailty were important predicators of ADL/IADL disability whereas psychological and social frailty played an important role for evaluating the risk of deceases in QOL. Consistent with previous studies (Bielderman et al., 2013; Sarkisian, Gruenewald, John Boscardin, & Seeman, 2008), the current study provides support for the use of domains of frailty, instead of an overall single frailty score across domains, to improve the ability to predict health adverse outcomes in older adults.

The impact of HF on frailty in each domain

Older adults with HF in this study had higher levels of frailty in physical, psychological, and social domains compared to older adults without HF. This is consistent with other studies showing a strong association between HF and physical frailty (Cacciatore, Abete, Mazzella, Viati, Della Morte, D'Ambrosio, et al., 2005; McNallan et al., 2013). Older adults with HF may become frail through different pathways compared with older adults without HF. For example, studies have shown that older adults with HF are more likely to experience depression (Moudgil & Haddad, 2013) and cognitive impairment (Hajduk, Kiefe, Person, Gore, & Saczynski, 2013), suggesting that older adults with HF may become frail because of deficits in the psychological domain. However, previous studies mainly focused on the relationship between HF and physical frailty. To the best of the author's knowledge, no study has evaluated the impact of HF on psychological and social frailty. The findings in the current study provide empirical evidence linking HF and frailty in the psychological and social domain. These findings suggest interventions aimed at preventing frailty in older adults with HF should focus on psychological and social domains as well as the physical frailty domain.

Limitations and Strengths

This study had three limitations. First, this study used a cross-sectional design with a single time point that does not allow for an examination of changes of frailty over time or an evaluation of the time impact of HF-frailty interaction frailty. Second, the sample size for comparison of frailty level was 303 for older adults with HF and 935 for older adults without HF. This sample size was much smaller than the sample size for testing frailty model (n=5027), which may have reduced the power to detect the difference between the two groups. Third, the missing data rate of frailty components in this study was approximated 35% and there were a total of 3,288 respondents who completed all the frailty measures. When analyzing the missing data, it was found that the respondents with complete data were more likely to be younger ($t=9.37$, $P<.001$), female ($\chi2=31.67$, $p<.001$), Caucasian ($\chi2=139.29$, $p<.001$), less educated (t=-

13.16, $p<.001$), married ($\chi2=56.44$, $p<.001$) and more number of conditions ($t=8.88$, $p<.001$). It may be problematic to use imputation methods to address the missing data in this case, because the differences between respondents with complete data and those with incomplete data may cause the problems with the assumption of Missing Completely at Random (MCAR) and possibly Missing at Random (MAR) (Soley-Bori, 2013). To address this concern, list-wise deletion was used in this study to manage missing data. Although this method may increase the Type 2 error, the sample size in this study was sufficiently large (over 3000 of completed data) to overcome this problem.

This study also has several strengths. The data used in this study was based on a large, nationally representative survey. The frailty indicators were measured using objective physical performance measures and well-established psychological and social questionnaires from the HRS. To the best of the author's knowledge, this is the first study to compare the multidimensional frailty levels (physical, psychological, and social) between older adults with HF and without HF, and therefore will contribute to the literature in a substantive way to enhance our knowledge regarding frailty in older adults.

Conclusion

In conclusion, findings from this study support the importance of including the psychological and social domain frailty components and that a multidimensional frailty model has better power to predict ADL/IADL disability and QOL than a purely physical frailty model. The improvement of its predictive power may contribute to better identification of older adults at risk of disability and decreased quality of life. This study also demonstrates the strong relationships between HF and physical, psychological, and social frailty, which raises concerns for older adults with these two syndromes. These findings will be used to inform future interventions aimed at delaying the onset of frailty or addressing the frailty-related adverse health outcomes in older adults with HF.

Table 3.1. Measures of frailty

Component	Indicator using HRS data	Model
Physical domain		
Poor nutrition	≥10% weight loss in the previous two year, or a current BMI less than 18.5 kg/m^2	F&G
Slow walking speed	A usual-pace walking speed on a 2.5m course lower than gender- and height-stratified cut-points (Fried et al., 2001). • Men, height ≤173cm: speed ≤0.653 m/s • Men, height >173cm: speed ≤0.762m/s • Women, height ≤159cm: speed ≤0.653 m/s • Women, height>159cm: speed ≤0.762 m/s	F&G
Limited grip strength	Grip strength of dominant hand below gender- and BMI-stratified cut-points as used in the CHS (Fried et al., 2001) • Men, BMI≤24: ≤29kg • Men, BMI24.1-28: ≤30kg • Men, BMI>28: ≤32kg • Women, BMI≤23: ≤17kg • Women, BMI23.1-26: ≤17.3kg • Women, BMI26.1-29: ≤18kg • Women, BMI>29: ≤21kg	F&G
Low physical activity	The levels of physical activity were determined by the average frequency of mild (1-3MET), moderate (3-6MET), and vigorous physical (6-10 MET) activities weighted according to their intensity (Cigolle et al., 2009) Low physical activity was defined as the lowest quartile stratified by gender. • Men: ≤1.9; Women: ≤1.42	F&G
Decreased endurance	"Much of the time during the past week, you had a lot of energy" • Answered No	F&G
Impaired vision	" How good is your eyesight for seeing things at a distance?" " How good is your eyesight for seeing things up close?" • Answered pair or poor for either one of two questions.	G
Poor hearing	"Is your hearing excellent, very good, good, fair, or poor?" • Answered pair or poor	G
Difficulties in balance	Balance test: semi-tandem stance, full tandem stance, or side-by-side stance • Inability to hold the full-tandem stance position for 30 seconds (Guralnik et al., 1994).	G
Psychological domain		
Cognitive impairment	Cognitive function was assessed by four tests, including 10-word immediate and delayed recall tests of memory, a serial 7s subtraction test of working memory, and counting backwards to assess attention and processing speed. A composite score of these four tests ranged from 0 to 27. • A score of 11 or less was classified as cognitive impairment while a score of 12 to 27 was classified as normal cognitive function (Langa, Kabeto, & Weir, 2010).	G

Depressive disorder	Depression was assessed by the eight-item Center for Epidemiologic Studies Depression (CES-D) scale, which includes six negative items (depression, everything is an effort, sleep is restless, felt alone, felt sad, and could not get going) and two reverse-coded positive items (felt happy and enjoyed life). • Those with a CES-D score of 4 or higher were classified as having a depressive disorder (Lohman, Dumenci, & Mezuk, 2014).	G
Anxiety	Anxiety was assessed by the five-item Beck Anxiety Inventory, with response choices ranging from 1(never) to 4 (most of the time) (Brenes, Guralnik, Williamson, Fried, & Penninx, 2005). • The average of these five anxiety items was calculated, with a higher score indicating a higher level of anxiety. • The midpoint (2) was used as a cutoff point. • Anxiety was defined as an average score of 2 or higher in this study.	G
Low coping skills	Level of coping skill was assessed by the Constraints Index, a five-item scale ranging from 1=strongly disagree to 6=strongly agree (Lachman & Weaver, 1998). • An average of the Constraint Index items was calculated, and higher score indicated worse coping skill. • The midpoint (3) was used as a cutoff point in this study. • A cut-point of 3 or higher was used in this study to identify low coping skills.	G
Social domain		
Poor social relations	Social relations was used as a surrogate measure of loneliness based on the HRS data, which consisted of three items (felt lack companionship, felt left out, and felt isolated) ranging from 1=often to 3=hardly ever or never (Hughes, Waite, Hawkley, & Cacioppo, 2004). These three items were averaged. • A cut-point of 2 or below, which is the midpoint of the scale, was used to identify poor social relations.	G
Lack of social support	Social support was assessed by the 12-item Positive Social Support Index (social support from spouse/partner, children, family, and friends) (Clarke, Fisher, House, Simth, & Weir, 2008). • An average score, ranging from 1 to 4, was calculated, with a higher score indicating greater social support. • The midpoint of scale (2.5) was used as a cut-off point • Lack of social support was defined as an average score of 2.5 or below.	G
Living alone	The number of people living in the house. • Living alone: the number=1	G

Note: F=Fried's physical model; G=Gobbens' multidimensional model

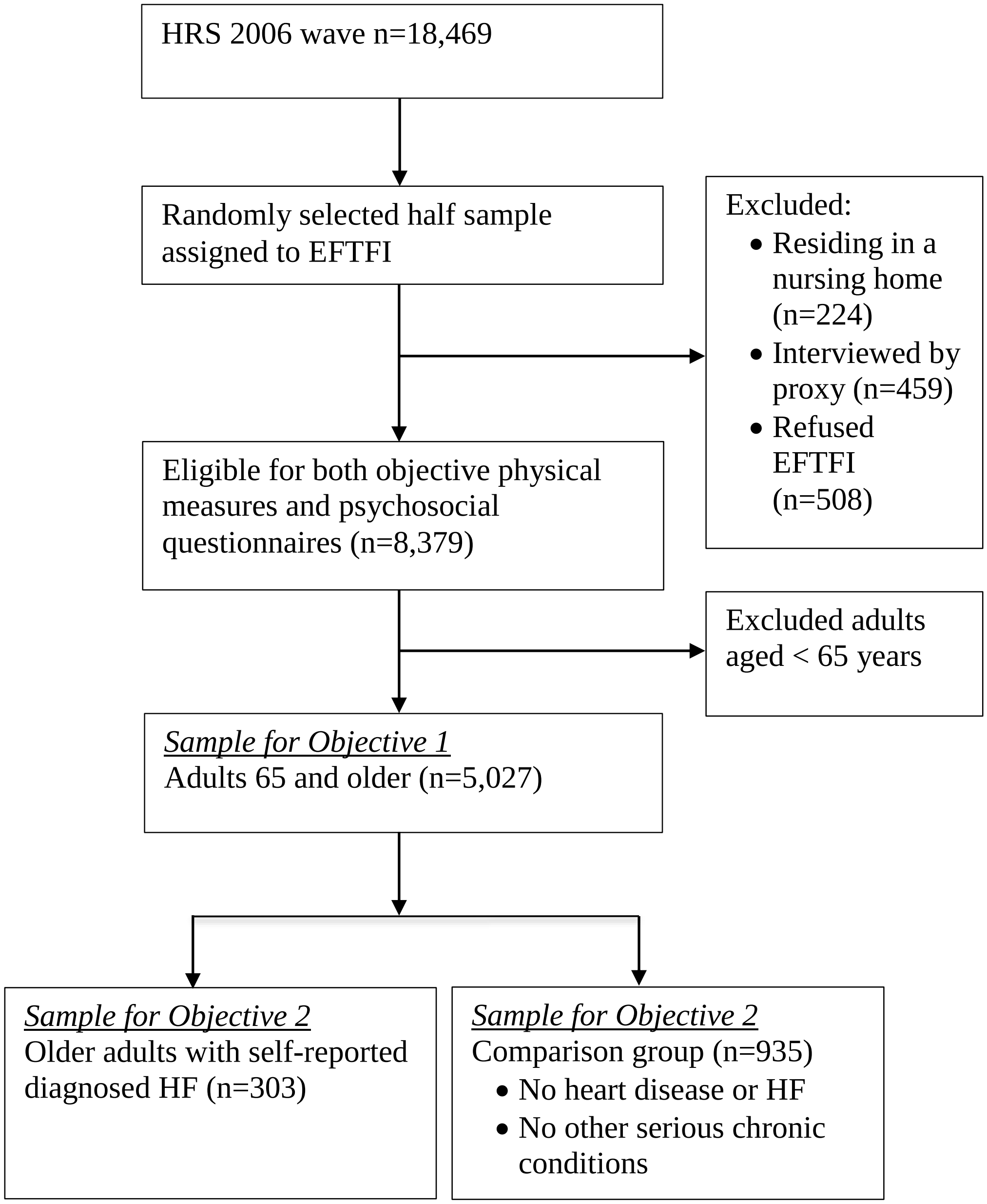


Figure 3.1: Flowchart for sample selection
Note: EFTFI=enhanced face-to-face interviews

Table 3.2. Sample characteristics: Weighted proportion and mean

Variable		General older adults (n=5027)	Non-HF (n=935)	HF (n=303)	
		Mean (SE)	*Mean (SE)*	*Mean (SE)*	*p value*
Age		74.93 (0.15)	73.49(.32)	76.52(.43)	<.001
Years of education		12.33 (0.09)	12.73 (.15)	11.90 (.20)	0.0013
Annual household income ($)		51969.11 (2168.78)	63689.78 (6271.65)	33939.65 (.2361.98)	<.001
		Proportion	*Proportion*	*Proportion*	*p value*
Gender	Male	0.4228	0.4722	0.4704	
	Female	0.5771	0.5278	0.5296	0.9573
Race	White/ Caucasian	0.8883	0.881	0.8909	
	Black /African American	0.0841	0.0789	0.0913	
	Other	0.0276	0.0401	0.0178	0.1335
Marital status	Married/ Partnered	0.5912	0.6401	0.5278	
	Separated/ Divorced/ Spouse absent	0.0921	0.09	0.1067	
	Widowed	0.29	0.2417	0.3536	
	Never married	0.0266	0.0282	0.0119	0.0014
Number of chronic conditions	None	0.0905	0.4784	0	
	One	0.2236	0.4298	0.0343	
	Two	0.2791	0.0918	0.0936	
	Three or more	0.4068	0	0.8721	<.001

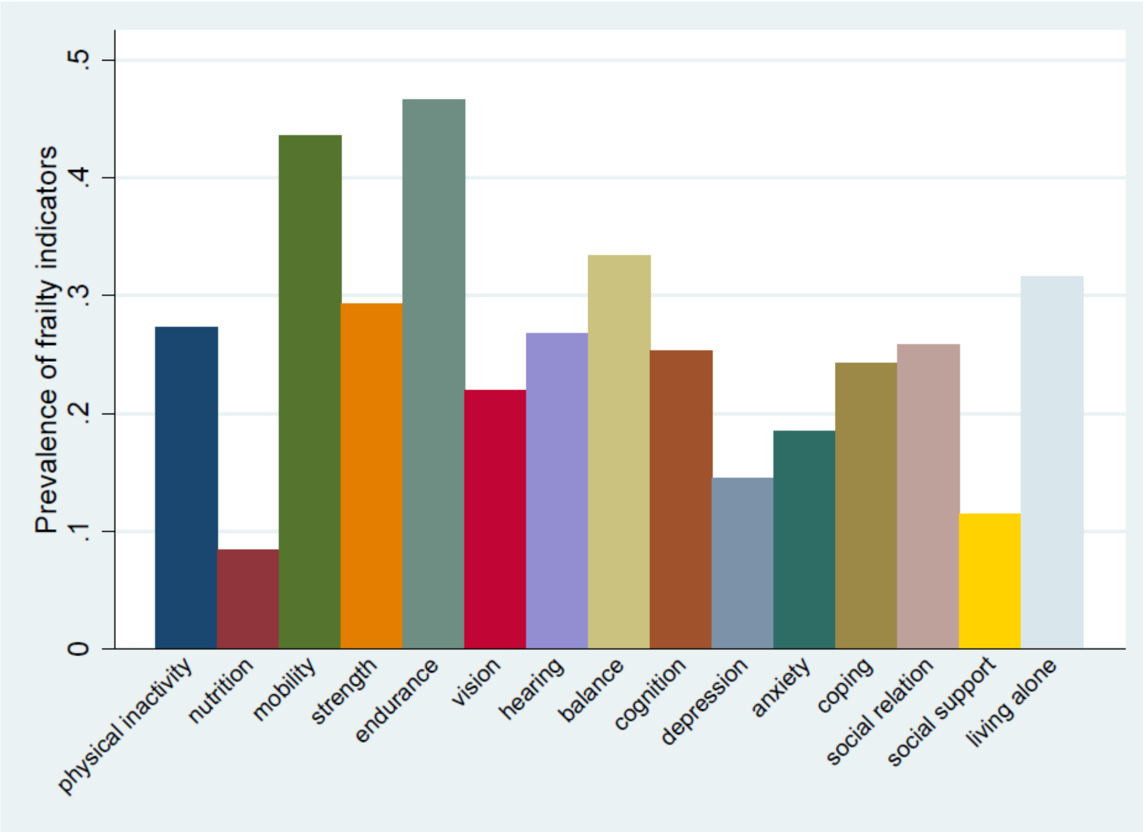


Figure 3.2. The weighted percentage of frailty indicators in the total sample population (n=5027)

Table 3.3. Logistic regression analyses on the prediction of ADLs/IADLs by frailty indicators, controlling for demographic covariates (n=3288)

	Predictor	Coefficient	S.E.	t	p
Model 1	Physical activity	0.73	0.11	6.71	<.001
	Nutrition	0.00	0.18	-0.01	0.990
	Mobility	0.58	0.10	5.72	<.001
	Strength	0.31	0.10	3.01	0.004
	Endurance	0.77	0.09	8.86	<.001
Model 2	Physical activity	0.65	0.11	5.77	<.001
	Nutrition	-0.01	0.19	-0.04	0.967
	Mobility	0.54	0.10	5.20	<.001
	Strength	0.38	0.11	3.42	0.001
	Endurance	0.73	0.10	7.67	<.001
	Vision	0.48	0.12	3.87	<.001
	Hearing	0.28	0.14	2.07	0.044
	Balance	0.28	0.13	2.10	0.040
Model 3	Physical activity	0.59	0.14	4.30	<.001
	Nutrition	0.08	0.21	0.37	0.713
	Mobility	0.51	0.12	4.24	<.001
	Strength	0.44	0.10	4.34	<.001
	Endurance	0.62	0.10	6.21	<.001
	Vision	0.51	0.13	4.02	<.001
	Hearing	0.26	0.15	1.74	0.088
	Balance	0.24	0.14	1.65	0.105
	Cognition	0.32	0.14	2.37	0.021
	Depression	0.49	0.13	3.83	<.001
	Anxiety	0.37	0.14	2.73	0.009
	Coping	0.23	0.12	1.92	0.061
Model 4	Physical activity	0.61	0.12	4.91	<.001
	Nutrition	0.05	0.19	0.28	0.781
	Mobility	0.51	0.11	4.65	<.001
	Strength	0.39	0.11	3.70	0.001
	Endurance	0.66	0.10	6.65	<.001
	Vision	0.49	0.12	4.02	<.001
	Hearing	0.26	0.14	1.82	0.074
	Balance	0.32	0.14	2.27	0.027
	Social relations	0.37	0.11	3.39	0.001
	Social support	0.16	0.16	1.02	0.313
	Living alone	0.10	0.15	0.69	0.493
Model 5	Physical activity	0.57	0.14	4.15	<.001
	Nutrition	0.10	0.20	0.49	0.628
	Mobility	0.51	0.12	4.18	<.001
	Strength	0.43	0.10	4.26	<.001

Endurance	0.61	0.10	6.12	<.001
Vision	0.50	0.13	3.88	<.001
Hearing	0.25	0.15	1.69	0.097
Balance	0.24	0.15	1.63	0.109
Cognition	0.32	0.14	2.31	0.025
Depression	0.46	0.14	3.38	0.001
Anxiety	0.34	0.14	2.45	0.018
Coping	0.21	0.14	1.54	0.129
Social relations	0.16	0.13	1.20	0.237
Social support	0.12	0.17	0.67	0.503
Living alone	0.14	0.15	0.98	0.330

Note: All 5 models controlled the demographic covariates (age, gender, years of education, race, marital status, household income) and number of chronic conditions.

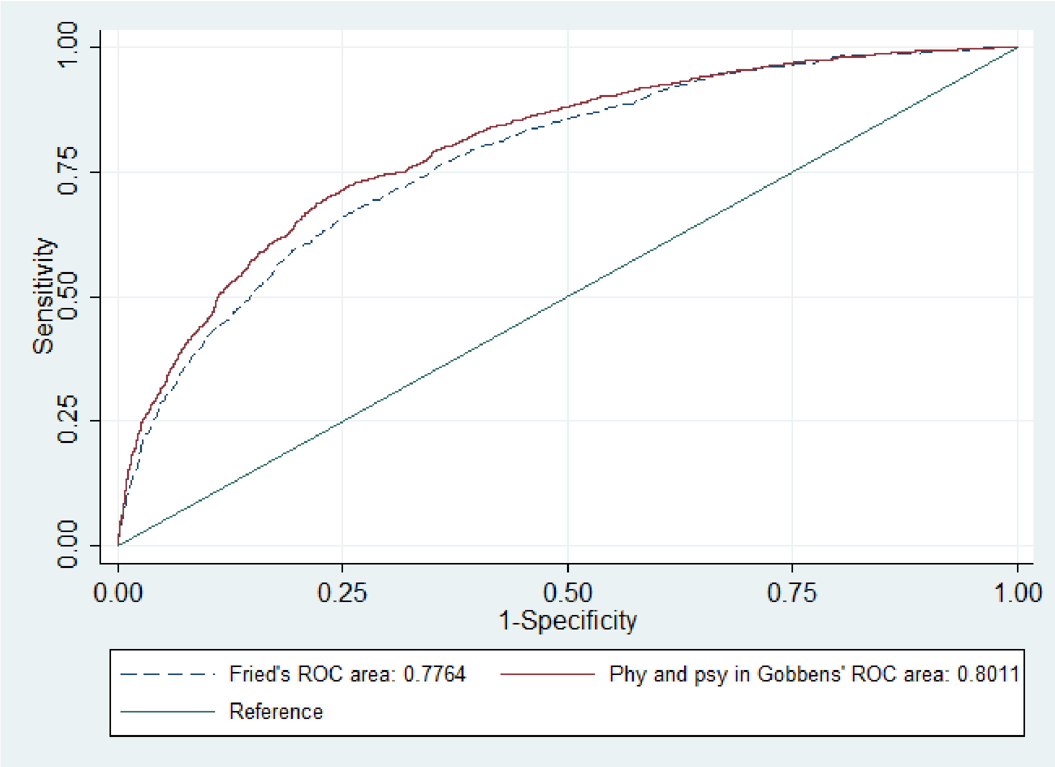


Figure 3.3. A comparison of AUC for ADL/IADL disability between Fried's physical model and Gobbens' physical and psychological domains (p<.001)

Note: ROC=0.7764 for the Fried model; ROC=0.8011 for physical and psychological domains from the Gobbens model

Table 3.4. Linear regression analyses on the prediction of QOL by frailty indicators controlling for the demographic covariates (n=3288)

	Predictor	Coefficient	S.E.	t	p
Model 1	Physical activity	-0.19	0.05	-3.77	<.001
	Nutrition	0.0003	0.11	0.00	0.998
	Mobility	-0.08	0.04	-1.96	0.055
	Strength	0.02	0.05	0.47	0.642
	Endurance	-0.38	0.04	-8.44	<.001
Model 2	Physical activity	-0.20	0.05	-3.72	<.001
	Nutrition	0.00	0.12	0.02	0.980
	Mobility	-0.08	0.04	-1.75	0.086
	Strength	0.04	0.05	0.75	0.456
	Endurance	-0.34	0.04	-7.57	<.001
	Vision	-0.17	0.06	-2.99	0.004
	Hearing	-0.07	0.05	-1.46	0.150
	Balance	-0.04	0.05	-0.81	0.421
Model 3	Physical activity	-0.15	0.06	-2.63	0.011
	Nutrition	-0.03	0.10	-0.25	0.801
	Mobility	-0.05	0.04	-1.14	0.260
	Strength	0.03	0.04	0.60	0.554
	Endurance	-0.23	0.04	-5.33	<.001
	Vision	-0.11	0.05	-2.00	0.051
	Hearing	-0.09	0.05	-1.86	0.068
	Balance	-0.01	0.05	-0.29	0.774
	Cognition	0.03	0.06	0.41	0.681
	Depression	-0.59	0.08	-7.70	<.001
	Anxiety	-0.37	0.06	-5.87	<.001
	Coping	-0.42	0.05	-8.48	<.001
Model 4	Physical activity	-0.13	0.05	-2.61	0.012
	Nutrition	-0.02	0.10	-0.15	0.882
	Mobility	-0.07	0.04	-1.78	0.080
	Strength	0.03	0.05	0.53	0.597
	Endurance	-0.26	0.05	-5.50	<.001
	Vision	-0.11	0.05	-2.23	0.030
	Hearing	-0.06	0.05	-1.37	0.176
	Balance	-0.05	0.05	-1.01	0.317
	Social relations	-0.63	0.05	-12.58	<.001
	Social support	-0.57	0.07	-7.76	<.001
	Living alone	0.06	0.09	0.67	0.509
Model 5	Physical activity	-0.10	0.05	-2.01	0.049
	Nutrition	-0.05	0.09	-0.50	0.617
	Mobility	-0.05	0.04	-1.24	0.221
	Strength	0.02	0.05	0.50	0.622

Endurance	-0.20	0.05	-4.40	<.001
Vision	-0.07	0.05	-1.45	0.153
Hearing	-0.08	0.05	-1.76	0.085
Balance	-0.03	0.04	-0.70	0.490
Cognition	0.05	0.06	0.80	0.430
Depression	-0.43	0.08	-5.45	<.001
Anxiety	-0.29	0.06	-4.53	<.001
Coping	-0.29	0.05	-5.61	<.001
Social relations	-0.50	0.05	-9.62	<.001
Social support	-0.49	0.07	-6.60	<.001
Living alone	0.05	0.08	0.58	0.564

Note: All 5 models controlled the demographic covariates (age, gender, years of education, race, marital status, household income) and number of chronic conditions.

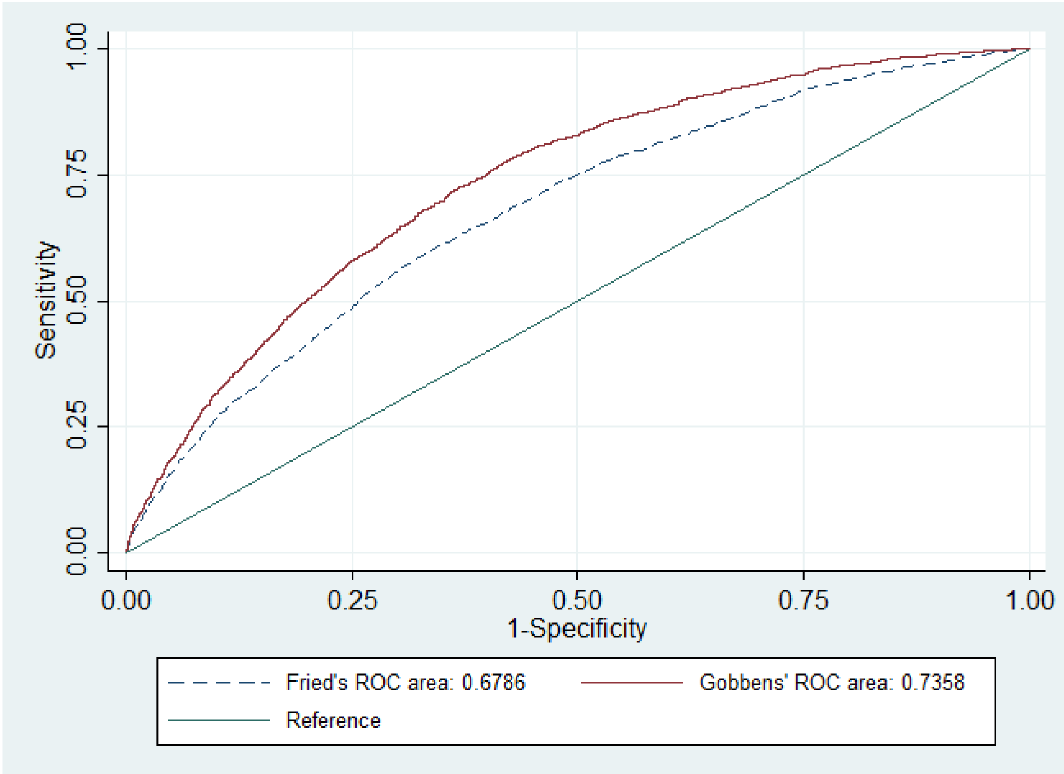


Figure 3.4. A comparison of AUC for QOL between Fried's model and Gobbens' model (p<.001)

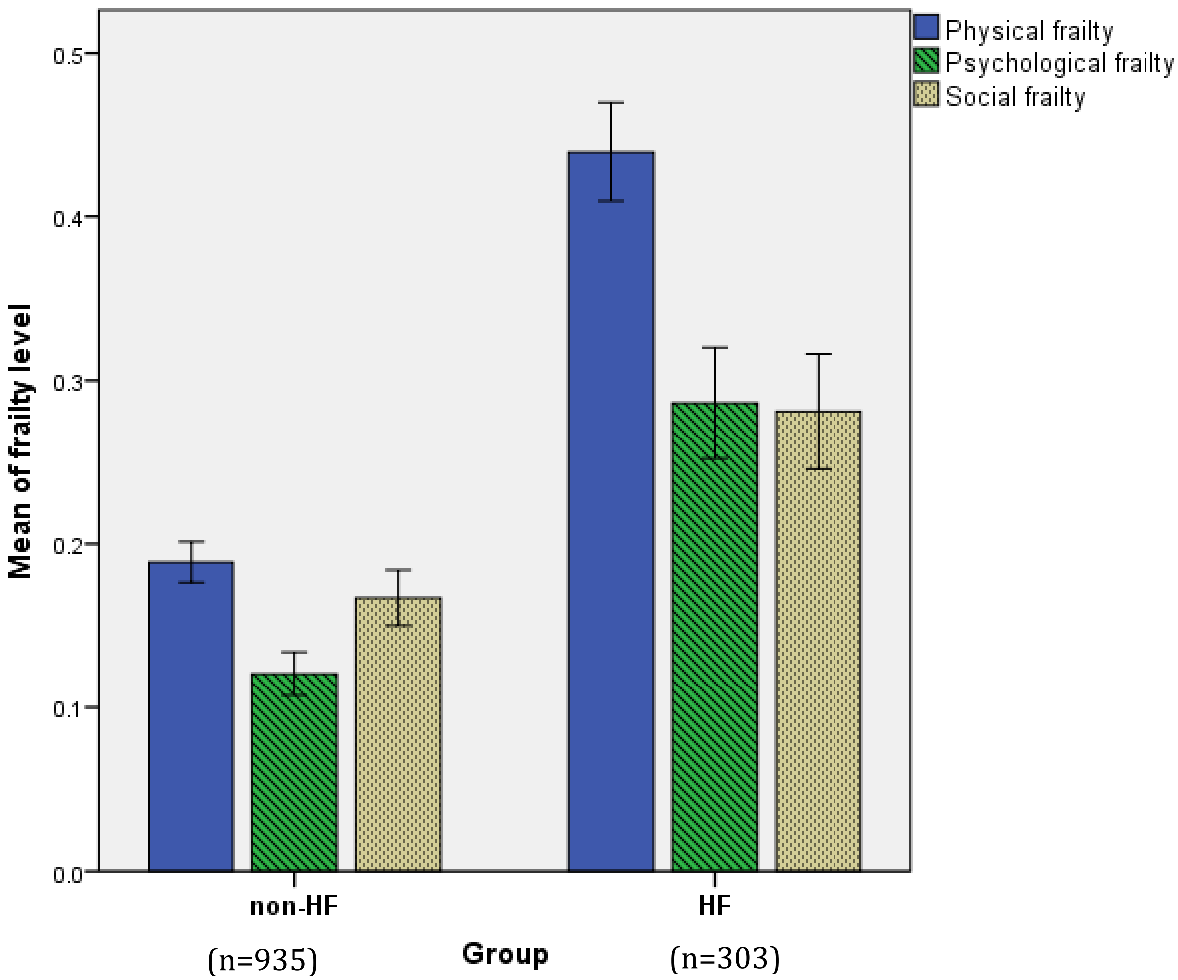


Figure 3.5. Bar graph to show frailty levels in three domains: a comparison between HF (n=303) and non-HF (n=935)

Note: bar line represent 95% confidence interval

Table 3.5. Linear regression analyses to compare the levels of frailty influenced by heart failure.

Predicator: Heart failure	Outcomes		
	Physical frailty (n=1118)	Psychological frailty (n=1120)	Social frailty (n=1109)
	Coefficient (Std. E)		
Model 1	.26 (.02) *	.18 (.02) *	.11 (.02) *
Model 2	.21 (.02) *	.14 (.02) *	.07 (.02) *

Note: Model 1 had only heart failure as the predicator; Model 2 was adjusted for the demographic covariates (age, gender, years of education, race, marital status, and annual household income); *, p<.001

References

Ament, B. L., de Vugt, M.E., Verhey, F.R. J., & Kempen, G.I. (2014). Are physically frail older persons more at risk of adverse outcomes if they also suffer from cognitive, social, and psychological frailty? *European Journal of Ageing, 11*(3), 213-219.

Bielderman, A., van der Schans, C. P., van Lieshout, M. R., de Greef, M. H., Boersma, F., Krijnen, W. P., & Steverink, N. (2013). Multidimensional structure of the Groningen Frailty Indicator in community-dwelling older people. *BMC Geriatrics, 13,* 86. doi: 10.1186/1471-2318-13-86

Boxer, R. S., Dauser, D. A., Walsh, S. J., Hager, W. D., & Kenny, A. M. (2008). The association between vitamin D and inflammation with the 6-minute walk and frailty in patients with heart failure. *The Journal of the American Geriatrics Society, 56*(3), 454-461. doi: 10.1111/j.1532-5415.2007.01601.x

Brenes, G. A., Guralnik, J. M., Williamson, J., Fried, L. P., & Penninx, B. W. (2005). Correlates of anxiety symptoms in physically disabled older women. *American Journal of Geriatric Psychiatry, 13*(1), 15-22. doi: 10.1176/appi.ajgp.13.1.15

Buck, H. G., & Riegel, B. (2011). The impact of frailty on health related quality of life in heart failure. *European Journal of Cardiovascular Nursing, 10*(3), 159-166. doi: 10.1016/j.ejcnurse.2010.06.001

Cacciatore, F., Abete, P., Mazzella, F., Viati, L., Della Morte, D., D'Ambrosio, D., . . . Rengo, F. (2005). Frailty predicts long-term mortality in elderly subjects with chronic heart failure. *European Journal of Clinical Investigation, 35*(12), 723.

Chan, K.S., Kasper, J.D., Brandt, J., & Pezzin, L.E. (2012). Measurement equivalence in ADL and IADL difficulty across international surveys of aging: findings from the HRS, SHARE, and ELSA. *The Journals of Gerontology. Series B, Psychological sciences and social sciences, 67*(1), 121.

Chen, C.Y., Chen, L., Wu, S., & Lue, B.. (2010). The prevalence of subjective frailty and factors associated with frailty in Taiwan. *Archives of Gerontology and Geriatrics, 50,* S43.

Cigolle, C. T., Ofstedal, M. B., Tian, Z. Y., & Blaum, C. S. (2009). Comparing Models of Frailty: The Health and Retirement Study. *Journal of the American Geriatrics Society, 57*(5), 830.

Clarke, P., Fisher, G., House, J., Simth, J., & Weir, D. (2008). Guide to Content of the HRS Psychosocial Leave-Behind Participant Lifestyle Questionnaires: 2004 &2006. Retrieved from http://hrsonline.isr.umich.edu/sitedocs/userg/HRS2006LBQscale.pdf.

Cleves, M. (2002). From the help desk: Comparing areas under receiver operating characteristic curves from two or more probit or logit models. *The Stata Journal, 2*(3), 301-313.

Diener, E., Emmons, R. A., Larsen, R. J., & Griffin, S. (1985). The Satisfaction With Life Scale. *Journal of Personality Assessment, 49*(1), 71-75.

Dodge, H. H., Kadowaki, T., Hayakawa, T., Yamakawa, M., Sekikawa, A., & Ueshima, H. (2005). Cognitive impairment as a strong predictor of incident disability in specific ADL-IADL tasks among community-dwelling elders: the Azuchi Study. *Gerontologist, 45*(2), 222-230.

Fox, J.(1997). *Applied regression analysis, linear models, and related methods.* Thousand Oaks, CA: Sage Publications.

Fried, L. P., Tangen, C. M., Walston, J., Newman, A. B., Hirsch, C., Gottdiener, J., . . . McBurnie, M. A. (2001). Frailty in older adults: evidence for a phenotype. *Journal of Gerontology Series A: Biological Sciences and Medical Sciences, 56*(3), M146-156.

Fulop, T., Larbi, A., Witkowski, J. M., McElhaney, J., Loeb, M., Mitnitski, A., & Pawelec, G. (2010). Aging, frailty and age-related diseases. *Biogerontology, 11*(5), 547-563. doi: 10.1007/s10522-010-9287-2

Gobbens, R. J., Luijkx, K. G., Wijnen-Sponselee, M. T., & Schols, J. M. (2010). Towards an integral conceptual model of frailty. *The Journal of Nutrition, Health & Aging. , 14*(3), 175-181.

Gobbens, R. J., Luijkx, Katrien G., & van Assen, Marcel A. L. M. (2013). Explaining quality of life of older people in the Netherlands using a multidimensional assessment of frailty. *Quality of Life Research : An International Journal of Quality of Life Aspects of Treatment, Care and Rehabilitation, 22*(8), 2051-2061.

Gobbens, R. J., van Assen, M. A., Luijkx, K. G., Wijnen-Sponselee, M. T., & Schols, J. M. (2010). The Tilburg Frailty Indicator: psychometric properties. *Journal of the American Medical Directors Association, 11*(5), 344-355. doi: 10.1016/j.jamda.2009.11.003

Guralnik, J. M., Simonsick, E. M., Ferrucci, L., Glynn, R. J., Berkman, L. F., Blazer, D. G., . . . Wallace, R. B. (1994). A short physical performance battery assessing lower extremity function: association with self-reported disability and prediction of mortality and nursing home admission. *Journal of Gerontology, 49*(2), M85-94.

Hajduk, A. M., Kiefe, C. I., Person, S.D., Gore, J.G., & Saczynski, J.S. (2013). Cognitive change in heart failure: a systematic review. *Circulation. Cardiovascular quality and outcomes, 6*(4), 451.

Hughes, M. E., Waite, L. J., Hawkley, L. C., & Cacioppo, J. T. (2004). A Short Scale for Measuring Loneliness in Large Surveys: Results From Two Population-Based Studies. *Research on Aging, 26*(6), 655-672. doi: 10.1177/0164027504268574

Kanwar, A., Singh, M., Lennon, R., Ghanta, K., McNallan, S. M., & Roger, V. L. (2013). Frailty and health-related quality of life among residents of long-term care facilities. *Journal of Aging and Health, 25*(5), 792-802. doi: 10.1177/0898264313493003

Khandelwal, D., Goel, A., Kumar, U., Gulati, V., Narang, R., & Dey, A. B. (2012). Frailty is associated with longer hospital stay and increased mortality in hospitalized older patients. *The Journal of Nutrition Health and Aging, 16*(8), 732-735. doi: 10.1007/s12603-012-0369-5

Kivela, S. L., & Pahkala, K. (2001). Depressive disorder as a predictor of physical disability in old age. *Journal of American Geriatric Society, 49*(3), 290-296.

Lachman, M. E., & Weaver, S. L. (1998). The sense of control as a moderator of social class differences in health and well-being. *Journal of Personality and Social Psychology, 74*(3), 763-773.

Langa, K.M., Kabeto, M ., & Weir, D. (2010). Report on race and cognitive impairment using HRS in, 2010 Alzheimer's disease facts and figures. Retrieved from http://www.alz.org/documents_custom/report_alzfactsfigures2010.pdf.

Lohman, M., Dumenci, L., & Mezuk, B. (2014). Sex differences in the construct overlap of frailty and depression: evidence from the Health and Retirement Study. *Journal of American Geriatric Society, 62*(3), 500-505. doi: 10.1111/jgs.12689

Lupon, J., Gonzalez B Fau - Santaeugenia, Sebastian, Santaeugenia S Fau - Altimir, Salvador, Altimir S Fau - Urrutia, Agustin, Urrutia A Fau - Mas, Dolores, Mas D Fau - Diez, Crisanto, . . . Valle, V.(2008). Prognostic implication of frailty and depressive symptoms in an outpatient population with heart failure. *Revista Española de Cardiología (English version), 61(8):835-42.*

Malaguarnera, M., Vacante, M., Frazzetto, P.M., & Motta, M. (2013). What is the frailty in elderly? Value and significance of the multidimensional assessments. *Archives of Gerontology and Geriatrics, 56*(1), 23-26.

Markle-Reid, M., & Browne, G. (2003). Conceptualizations of frailty in relation to older adults. *Journal of Advanced Nursing, 44*(1), 58-68.

McNallan, S. M., Chamberlain, A. M., Gerber, Y., Singh, M., Kane, R. L., Weston, S. A., . . . Roger, V. L. (2013). Measuring frailty in heart failure: a community perspective. *American Heart Journal, 166*(4), 768-774. doi: 10.1016/j.ahj.2013.07.008

Miller, M.E., Rejeski, J., Reboussin, B.A., Have, T.R., & Ettinger, W.H. (2000). Physical Activity, Functional Limitations, and Disability in Older Adults. *Journal of the American Geriatrics Society, 48*(10), 1264-1272.

Morley, J. E., Vellas, B., van Kan, A., Anker, S.D., Bauer, J.M., Bernabei, R., . . . Walston, J. (2013). Frailty consensus: a call to action. *Journal of the American Medical Directors Association, 14*(6), 392.

Moudgil, R., & Haddad, H. (2013). Depression in heart failure. *Current Opinion in Cardiology, 28*(2), 249.

Pavot, W., & Diener, E. (2009). *Review of the Satisfaction with Life Scale*.

Penninx, B. W., Leveille, S., Ferrucci, L., van Eijk, J. T., & Guralnik, J. M. (1999). Exploring the effect of depression on physical disability: longitudinal evidence from the established populations for epidemiologic studies of the elderly. *American Journal of Public Health, 89*(9), 1346-1352.

Persinger, R., Janssen-Heininger, Y., Wing, S., Matthews, D., LeWinter, M., & Toth, M. (2003). Effect of heart failure on the regulation of skeletal muscle protein synthesis, breakdown, and apoptosis. *American Journal of Physiology - Endocrinology And Metabolism, 284*(5), E1001-1008.

Pope, A., & Tarlov, A.R. (1991). *Disability in America: Toward a national agenda for prevention*. Washington, D.C: National Academy Press.

Rizzoli, R., Reginster, J.Y., Arnal, J.F., Bautmans, I., Beaudart, C., Bischoff-Ferrari, H., . . . Bruyère, O. (2013). Quality of Life in Sarcopenia and Frailty. *Calcified Tissue International, 93*(2), 101.

Rothman, M. D., Leo-Summers, L., & Gill, T. M. (2008). Prognostic significance of potential frailty criteria. *Journal of the American Geriatrics Society, 56*(12), 2211-2116. doi: 10.1111/j.1532-5415.2008.02008.x

Sarkisian, C.A., Gruenewald, T.L., John Boscardin, W., & Seeman, T.E. (2008). Preliminary evidence for subdimensions of geriatric frailty: the MacArthur study of successful aging. *Journal of the American Geriatrics Society, 56*(12), 2292-2297.

Slettaløkken, G., Rehn, T. A., Munkvik, M., Rud, B., Sökjer-Petersen, M., Lunde, P. K., . . . Hallén, J. (2012). Preserved metabolic reserve capacity in skeletal muscle of post-infarction heart failure patients. *Scandinavian journal of medicine & science in sports, 22*(2), 199-206.

Spector, W. D., & Fleishman, J. A. (1998). Combining activities of daily living with instrumental activities of daily living to measure functional disability. *The journals of gerontology. Series B, Psychological Sciences and Social Sciences, 53*(1), S46-57.

Soley-Bori, M. (2013). Dealing with missing data: Key assumptions and methods for applied analysis. Retrieved from http://www.bu.edu/sph/files/2014/05/Marina-tech-report.pdf

Uchmanowicz, I., Loboz-Rudnicka, M., Szelag, P., Jankowska-Polanska, B., & Loboz-Grudzien, K. (2014). Frailty in Heart Failure. *Current Heart Failure Reports*. doi: 10.1007/s11897-014-0198-4

CHAPTER 4

The Impact of Multidimensional Frailty on Disability and Quality of Life in Older Adults with Heart Failure

Abstract

Background: Frailty is a prevalent syndrome in older adults with heart failure (HF), that has recently been viewed as a multidimensional syndrome, including deficits in physical, psychological, and social domains. However, few studies have examined the relationships between HF and multidimensional frailty over time.

Aims: 1) to examine the frailty levels and changes (physical, psychological and social domains) between older adults with HF and without HF over time; 2) to assess the impact of HF and each frailty domain on functional disability and QOL over time; 3) to investigate the mediation effect of frailty domains; and 4) to examine the influence of individual characteristics on frailty levels and its changes in each domain among older adults with HF.

Data and Design: This study used longitudinal data from the Health and Retirement Study at two time-points from two cohorts in baseline (2006/2008) and 4 years later (2010/2012).

Sample: The sample consisted of two groups: older adults with HF (n=630) and older adults without HF (n=1671).

Measures: Frailty was quantified in three domains: physical, psychological, and social. ADL/IADL Disability and QOL were measured using well-established instruments. Individual characteristics included demographics, number of chronic conditions, lifestyle behaviors, and experience of life events.

Results: Older adults with HF had higher levels of frailty across all three domains (physical, psychological, and social) compared to older adults without HF. All three frailty domains and HF were associated with increased risk of ADL/IADL disability and decreased QOL over time. The relationship between HF and outcomes (ADL/IADL disability and QOL) were mediated by the frailty domains. However, different domains of frailty were influenced by different individual characteristics.

Conclusions: Multidimensional frailty is prevalent in older adult with HF and is highly associated with risks of disability and deceased QOL. More studies are needed to develop individual-tailored interventions aimed at preventing frailty and improving health outcomes in older adults with HF.

Key words: frailty, heart failure, disability, quality of life

Introduction

Heart failure (HF) is a debilitating chronic condition that increases the risk of functional disability (Wong, Chaudhry, Desai, & Krumholz, 2011) and diminishes quality of life (QOL) (Heo, Moser, Lennie, Zambroski, & Chung, 2007). It is a critical public health issue, with an estimated prevalence of 5.7 million in the United States (Mozaffarian et al., 2015). With increasing age, frailty often occurs among older adults with HF: its prevalence ranges from 21% to 40%, depending on study population and frailty measures used (Boxer, Shah, & Kenny, 2014; Lupon et al., 2008; McNallan et al., 2013).

As an evolving concept, many researchers have recently adopted a multidimensional view of frailty, acknowledging that frailty includes not only the physical domain, but also the psychological and social domains (Bergman et al., 2007; Gobbens, Luijkx, Wijnen-Sponselee, & Schols, 2010; Markle-Reid & Browne, 2003). However, existing studies have primarily focused on physical frailty and HF (Cacciatore et al., 2005; Khan et al., 2013; McNallan et al., 2013). Few studies have examined the relation between HF and frailty in psychological and social domains. To the best of the author's knowledge, the present study is the first to examine the changes in frailty across these three domains (physical, psychological, and social) over time among older adults with HF. Given the view that frailty is a multidimensional concept, the current focus on a single physical domain limits our theoretical and practical knowledge of frailty. In addition, an examination of dynamic changes in frailty among older adults with HF is essential to develop interventions that address their holistic frailty health needs.

Studies have demonstrated that demographics, comorbidity, lifestyle factors and life events are associated with risk of frailty in older adults. For instance, adults who are age 65 or older age, female, African American, less educated, and of low socioeconomic status and have one or more comorbidity are more likely to be frail compared to older adults who do not have these characteristics (Etman, Burdorf, Van der Cammen, Mackenbach, & Van Lenthe, 2012; Fried et al., 2001; Mitnitski, Mogilner, & Rockwood, 2001; Puts, Lips, & Deeg, 2005; Strawbridge, Shema, Balfour, Higby, & Kaplan, 1998). Lifestyle behaviors (e.g. smoking and heavy drinking) and life trauma experiences (e.g. death loved one, serious illness, traffic accident) are associated with a high risk of developing frailty (Gobbens, van Assen, Luijkx, Wijnen-Sponselee, & Schols, 2010; Strawbridge et al., 1998; Woods et al., 2005). However, the influence of these factors on frailty across the three frailty domains (physical, psychological, and social) remains unclear among older adults with HF.

Functional disability and decreased QOL are adverse health outcomes experienced by older adults with HF (Boxer et al., 2014; Buck & Riegel, 2011; Cacciatore et al., 2005). Functional disability is commonly defined as difficulties in performing activities of daily living (ADL) and/or instrumental activities of daily living (IADL) (Pope & Tarlov, 1991). ADL/IADL functions are essential for older adults to live independently and engage in self-care. Older adults with HF are more likely to have difficulties in ADL/IADL, which is associated with increased risks for hospitalization, nursing home stay and mortality (Dunlay et al., 2015; Gure, Kabeto, Blaum, & Langa, 2008).

QOL is another important health outcome in older adults with HF. It has been defined as an individual’s emotional or cognitive assessment of the congruence between his/her life expectations and achievements (Diener, Emmons, Larsen, & Griffin, 1985). As a subjective evaluation, QOL is related to many aspects of one’s life (e.g. the physical, psychological, cultural and social) (Harper et al., 1998). Decreased QOL is not only an important health outcome in itself, but it is also a predictor of hospital readmission and mortality for older adults with HF (Mejhert, Kahan, Persson, & Edner, 2006). Despite the importance of ability to perform ADL/IADL and QOL among older adults with HF, the relationships among HF, multidimensional frailty, and ADL/IADL disability and decreased QOL remain unclear.

To address these knowledge gaps about multidimensional frailty in older adults with HF, the goals of this study are: 1) to examine the frailty levels and its changes (physical, psychological and social domains) between older adults with HF and older adults without HF over time (from 2006/2008 to 2010/2012); 2) to assess the impact of HF and each frailty domain on functional disability and quality of life (QOL) over time; 3) to investigate the mediation effect of each frailty domain; and 4) to examine the influence of individual characteristics on frailty levels and its changes in each domain among older adults with HF. The framework of this study is presented in Figure 1.

Methods

Design and Data

This study used longitudinal data from the biennial Health and Retirement Study (HRS) 2006-2012 waves. The HRS survey is a nationally representative longitudinal study, which collects information about the health transitions in older adults aged 51 and older living in the United States. The HRS is currently the foremost database to assess health disparities in the United States. It contains long-running panel data of physical health, affective and cognitive functioning, and health risk behaviors [1992-present] (Hayward, 2002), which will be used to measure frailty in older adults and address the research questions in this study. Starting with the 2006 wave, a random one-half of the sample at each wave has been selected to participate in an enhanced face-to-face (EFTF) interview, which includes objective measures of physical performance and self-administered psycho-social questionnaires. A random one half of the 2006 sample was selected to EFTF interview, and the other half was selected for EFTF interview in 2008. In 2010, the first half was again interviewed, and in 2012 the second half was interviewed a second time. In other words, the HRS collected physical measures and psychosocial measures every four years for each respondent. Data from EFTF interviews were used in this study in order to quantify multidimensional frailty. In this study, the data, used to quantify frailty, were collected at two time-points for two different cohorts: baseline (2006/2008) and 4 years later (2010/2012).

Sample

The sample in this study consisted of two groups: 1) older adults with HF and 2) older adults without HF. Older adults with HF and older adults without HF were included if they were 65 years of age or older at baseline and participated in both physical measures and psychological questionnaires in the EFTF interviews. Excluded were older adults currently residing in a nursing home, interviewed by proxy (e.g. a family member), and older adults who refused an EFTF interview.

Older adults with HF were identified using questions in the HRS. In the first approach, the older adults were asked whether a doctor told them that they had congestive heart failure in the last two years. If older adults answered “yes”, they were classified as having self-reported diagnosed HF. In the second approach, older adults were asked whether a doctor ever told them that they had congestive heart failure and in what year their congestive heart failure was first diagnosed. Older adults who answered having a diagnosis of HF at 2006/2008 and before were classified as having self-reported HF. By these two approaches, a total of 630 older adults with HF were identified at baseline.

The older adults without HF were identified by following criteria: 1) no self-reported heart disease or HF; 2) no other serious chronic conditions (chronic lung diseases, stroke, cancer diagnosed in last two years, and arthritis); and 3) no psychiatric problems. Older adults with common comorbidities of hypertension or diabetes were eligible for this study. The comparison group was older adults without HF in order to exclude the confounding effect of other serious chronic conditions. This resulted in a total of 1671 older adults without HF identified at baseline.

Measures

Frailty. Frailty is conceptualized as having three domains: physical, psychological, and social. These frailty domains were quantified using the data from the HRS survey. Physical frailty included eight components: poor nutrition, slow walking speed, limited grip strength, low physical activity, decreased endurance, impaired vision, poor hearing, and difficulties in balance. Psychological frailty included four components: cognitive impairment, depressive disorder, anxiety, and low coping skills. Social frailty included three components: poor social relations, lack of social support, and living alone. Each component yielded a dichotomous score of "0=no deficit" or "1=deficit". The frailty scores in each domain were then calculated by averaging the scores from all components in each domain. Higher scores indicated higher levels of frailty. The frailty components in each domain are listed below.

Physical frailty. Using the HRS data, poor nutrition was defined as a ≥10% weight loss in the previous year, or a current BMI less than 18.5 kg/m2. Slow walking speed was defined as a usual-pace walking speed on a 2.5m track lower than gender- and height-stratified cut-points, as established in the Cardiovascular Health Study (CHS) (Fried et al., 2001). Limited grip strength was defined as having dominant hand grip strength below gender- and BMI-stratified cut-points as used in the CHS (Fried et al., 2001). The levels of physical activity were determined by the average frequency of mild, moderate, and vigorous physical activities weighted according to their intensity (Cigolle, Ofstedal, Tian, & Blaum, 2009). Low physical activity was defined as the lowest quartile stratified by gender. Decreased endurance was determined by a self-reported question about having a lot of energy much of the time during the past week. Impaired vision was defined as having self-reported fair/poor distance or near vision. Poor hearing referred to self-reported fair or poor hearing. Difficulties in balance referred to an inability to hold the full-tandem stance position for 30 seconds (Guralnik et al., 1994).

Psychological frailty. Cognitive function was assessed by the following tests in the HRS: a 10-word immediate and delayed recall tests of memory, a serial 7s subtraction test of working memory, and counting backwards to assess attention and processing speed. A composite score of these four tests ranged from 0 to 27. A score of 11 or less was classified as cognitive impairment, while a score of 12 to 27 was classified as normal cognitive function (Langa, Kabeto, & Weir, 2010). Depression was assessed using the eight-item Center for Epidemiologic Studies Depression (CES-D) scale, which includes six negative items (depression, everything is an effort, sleep is restless, felt alone, felt sad, and could not get going) and two reverse-coded positive items (felt happy and enjoyed life). Older adults with a CES-D score of 4 or higher were classified as having a depressive disorder (Lohman, Dumenci, & Mezuk, 2014). Anxiety was assessed using the five-item Beck Anxiety Inventory, with responses ranging from 1(never) to 4 (most of the time) (Brenes, Guralnik, Williamson, Fried, & Penninx, 2005). The average of these five anxiety items was calculated. A higher score indicates a higher level of anxiety. Anxiety was defined as an average score of 2 (midpoint) or higher in this study. Levels of coping skill was assessed using the Constraints Index, a five-item scale ranging from 1=strongly disagree to 6=strongly agree (Lachman & Weaver, 1998). An average of the Constraint Index items was calculated. Higher score indicates worse coping skill. A cut-point of 3 (midpoint) or higher was used in the current study to identify low coping skills.

Social frailty. Using measures from the HRS, social relations was used as a surrogate measure of loneliness based on the HRS data, which consisted of three items (felt lack of companionship, felt left out, and felt isolated) ranging from 1=often to 3=hardly ever or never (Hughes, Waite, Hawkley, & Cacioppo, 2004). These three items were averaged and a cut-point of 2 (midpoint) or below was used to identify poor social relations. Social support was assessed using the 12-item Positive Social Support Index (social support from spouse/partner, children, family, and friends) (Clarke, Fisher, House, Simth, & Weir, 2008). An average score, ranging from 1 to 4, was calculated. A higher score indicates greater social support. In this study, lack of social support was defined as an average score of 2.5 (midpoint) or below. Living alone was determined by one question in the HRS which asked about the number of people living in the house.

Functional disability. Functional disability was assessed by the difficulties in performing ADL/IADL tasks (Pope & Tarlov, 1991). In the HRS survey, ADL/IADL included 11 tasks: six ADL tasks (dressing, eating, using the toilet, bathing and showering, getting in and out of bed, and walking across a room); and five IADL tasks (preparing a hot meal, shopping for groceries, making telephone calls, taking medication, and managing money). Each task yielded a dichotomized score of "0=no difficulty" or "1=having difficulty or need assistance". For purposes of this study, the total score of ADL/IADL disability was dichotomized into 0= "no ADL/IADL disability" and 1= "one or more ADL/IADL disability".

Quality of life. QOL was measured using the Satisfaction with Life Scale (SWLS). The SWLS is a five-item Likert-type scale. Using the SWLS, the HRS respondents were asked how much they agree or disagree with statements such as “In most ways my life is close to ideal” by choosing one of six possible options (from 1=strongly disagree to 6=strongly agree). The total SWLS score was the average of the five items ranging from 1 to 6, with higher scores indicating greater QOL. The coefficient alpha of the SWLS was reported to be 0.87, with a two-month test-retest reliability coefficient of 0.82 (Pavot & Diener, 2009).

Individual characteristics. Individual characteristics in this study included demographic characteristics, number of chronic diseases, lifestyle factors, and major life events. Demographic characteristics included age, gender, race, years of education, marital status, and annual household income. The number of chronic conditions was determined based on the presence of hypertension, diabetes, cancer, lung disease, stroke, arthritis, and psychiatric problems.

Lifestyle factors included smoking and drinking. Smoking was measured by two questions within the HRS asking if older adults had ever smoked cigarettes or smoked cigarettes now. The answers were classified into three categories: 0=never smoker; 1=past smoker; and 2=current smoker. Drinking problem was evaluated by two questions. The respondents were first asked if they ever drink any alcoholic beverages such as beer, wine, or liquor. If they answered “yes”, they were then asked “In the last three months, on the days you drink, about how many drinks do you have?” Based on the answers from these two questions, drinking behavior was classified into three categories: 0=no problem (never have used alcohol, or less 2 drinks per day for males/ less one drink per day for females); 1=moderate drinking (>2 but <5 drinks per day for males, or >1 but <5per day for females); and 2=heavy drinking (>5 drinks per day) (Mezuk, Bohnert, Ratliff, & Zivin, 2011).

Life events were measured using a 7-item checklist of lifetime traumas (Krause, Shaw, & Cairney, 2004), which includes having a child who die, being in a major fire or disaster, firing a weapon in combat, having spouse or partner addicted to drugs, being a victim of physical attack, having a life threatening illness, and having a spouse or child having life threatening illness. Life events were be coded as “1=yes” if participants reported any one of these seven lifetime traumas in the checklist, and coded as “0=no” if respondents did not report any of these lifetime traumas.

Data analyses

Descriptive statistics were used to describe the individual characteristics of older adults at baseline with HF and without HF. Continuous variables were described using means and standard deviations and categorical variables were described using frequencies and percentages. The differences in individual characteristics between older adult with HF and without HF at baseline were also examined. Independent t-tests were used for continuous variables and chi-square test was used for categorical variables.

In order to compare the levels of frailty and their changes over the 4-year period between older adults with and without HF, generalized estimating equation (GEE) models were used in this study. GEE models are a method for fitting population-averaged models, which are used for the analysis of data collected in longitudinal, nested, or repeated measures designs (Ballinger, 2004; Liu, Dixon, Qiu, Tian, & McCorkle, 2009). To compare the levels of frailty, GEE models were conducted with the outcomes of physical frailty, psychological frailty, and social frailty respectively and with the predictor of groups (HF group and non-HF group) controlling for demographics (age, gender, years of education, race, marital status, and annual household income) and cohort effect. In order to test whether groups had similar change between baseline and year 4 for frailty outcome measures, GEE models also included 2-way interaction between time points and groups. These models were estimated using an unstructured correlation structure with categorical time points. Statistical significance was set at α<.05 (two-tailed).

To estimate the influence of HF and frailty domains on health outcomes (ADL/IADL and QOL), two GEE models were separately conducted with HF and three frailty domains as predictors, and with ADL/IADL and QOL as dependent variables respectively. The models also included time and interaction terms between time and HF to assess whether there were difference in health outcomes between baseline and year four, and whether the association between HF and health outcomes was different between baseline and year four. Both these two GEE models controlled for demographics and cohort effect. The GEE model for the continuous dependent variable of QOL used the Gaussian distribution with the identity link function while the GEE for the binary dependent variable of ADL/IADL used the binomial distribution with the logit link function.

In order to test the mediation effect of frailty domains, the nonparametric bootstrap, in which the raw data were sampled 5000 times with replacement to create bootstrap samples, was used (Shrout & Bolger, 2002). For each of the bootstrap samples, four GEE models were conducted. Of those four, three GEE models used the potential mediators (physical, psychological, and social frailty) as the dependent variable and provided the relevant regression coefficients for the effect of HF on the potential mediators (the a paths); and the fourth GEE model used QOL or ADL/IADL as the dependent variables with HF and three potential mediators as predictors (the b paths). These four GEE models provided the three separate “a” paths (e.g. HF-> physical frailty) and the three “b” paths from mediator to dependent variable (e.g. physical frailty -> QOL). Then, three product terms of a and b corresponding to the three indirect paths (e.g. HF -> physical frailty -> QOL) were created. The three product terms corresponding to the indirect path were saved and this procedure was repeated 5000 times to estimate the bias-corrected percentile confidence interval (bca CI) of the six products (three for QOL and three for ADL/IADL). The mediation effect is considered significant if these confidence intervals do not include zero (Hayes, 2013; MacKinnon, 2008). Each of the GEE models had age, gender, years of education, race, marital status, annual household income, cohort effect and time point as covariates, used participant as the clustering variable given that each participant provided data at two different times, and assumed an autoregressive (AR-1) correlated error process to account for the dependency in the data due to time. The GEE models for QOL used the Gaussian distribution with the identity link function and the GEE models for ADL/IADL used the binomial distribution with the logit link function.

Lastly, to test the impact of individual characteristics among older adults with HF, GEE models were conducted using only the sub-sample of older adults with HF. Three GEE models were performed with the three frailty domains as outcomes. The predictors of these three models were demographic characteristics, the number of chronic conditions, lifestyle factors, life event factors, time point and cohort effect. In order to test whether the association between individual characteristic and outcomes was different over the 4 years period, the initial models also included the interactions between individual characteristics and time points. Wald χ^2 statistics were used to assess the significance of the interaction terms in the models. If the interactions were not significant, they were removed as predictors and the models were refitted for parsimony.

Results

Sample characteristics

A total of 2301 HRS respondents (630 older adults with HF; 1671 older adults without HF) at baseline (2006/2008) were included in this study. Older adults with HF were significantly older than those without HF (76 vs. 73.2; $p<.001$), and had fewer years of formal education (Mean=11.89) compared to older adults without HF (Mean=12.46) ($t=3.78$; $p=.0002$). Additionally, older adults with HF were more likely to be non-married (divorced, widowed, and never married), have household annual income less than $20,000, be past smoker, have no drinking problem, and have negative life events experience compared to older adults without HF. Older adults with HF had more chronic conditions than older adults without HF ($p<.001$). There were no differences in gender and race between older adults with and without HF. Demographic characteristic with the sample of older adult with HF (n=630) and without HF (n=1671) are shown in details in Table 4.1.

Comparisons of frailty levels and changes between HF and non-HF

The impact of HF on physical frailty, psychological frailty, and social frailty were examined (Table 4.2, 4.3, and 4.4, and Figure 4.2). Overall, compared to healthy older adults, older adult with HF had significantly higher levels of physical ($\beta=0.21$, $p<.001$), psychological ($\beta=0.14$, $<.001$) and social frailty ($\beta=0.04$, $p<.001$). However, across these three GEE models, the interaction of time and group was non-significant, indicating changes in physical, psychological, and social frailty between baseline and year 4 did not differ between older adults with HF and older adults without HF.

Impact of HF and frailty on health outcomes over 4-year period

The impact of HF and frailty across three domains over a 4-year period on ADL/IADL disability and QOL was examined using the sample of both older adults with HF and without HF (Table 4.5 and Table 4.6). The GEE results showed all three domains of frailty (physical, psychological, and social) significantly increased the likelihood of ADL/IADL disability, after controlling for demographic covariates (Table 4.5). Older adults with physical frailty score equal to one were approximately fifty-three times more likely to have difficulty in one or more ADL/IADL compared to older adults with score of physical frailty equal to zero (Odds Ratio [OR]=53.59, p<.001). Older adults with HF were nearly three times more likely to have difficulties in performing ADL/IADL (OR=2.74, p<.001) compared to older adults without HF. Older adults at time 2 (2010 or 2012) were nearly 1.5 times more likely to have ADL/IADL disability than older adults at time 1 (2006 or 2008) (OR=1.43, P=.004). However, the interactive effect between HF and time was not significant (OR=0.82, p=.344), indicating the association between HF and ADL/IADL disability did not change over 4-year time period.

The physical (β= -1.06, p<.001), psychological (β=-1.04, p<.001), and social frailty (β =-1.08, p<.001) were significantly associated with decreased QOL, after controlling for demographic covariates (Table 4.6). Additionally, older adults with HF had lower level of QOL than older adults without HF (β=-0.24, p=.001). All older adults at time 2 had higher level of QOL than older adults at time 1 (β=0.32, p<.001). No interaction between HF and time point was found (β=-0.17, p=.064). However, a cohort effect was noted on QOL (β=0.47, p<.001), indicating that older adults in Cohort 2 (2008/2010) had higher level of QOL than older adults in Cohort 1 (2006/2012).

Mediation of frailty on the relationship between HF and health outcomes

The results of GEE models using bootstrap showed a significant mediation effect for physical (bias-corrected percentile confidence interval (bcaCI) [0.664, 0.0950]), psychological (bca CI [0.159, 0.302]), and social frailty (bca CI [0.0002, 0.0573]) on the relationship between HF and ADL/IADL disability, although the mediated effect through social frailty was very small. Significant mediation effects were also observed for decreased QOL for all three domains of frailty: physical frailty (bca CI [-0.275, -0.161]), psychological frailty (bca CI [-0.1638, -0.0917]), and social frailty (bca CI [-0.0701, -0.0145]) (Table 4.7).

The impact of individual characteristics on frailty in older adults with HF

Using the sub-sample of older adults with HF, the impact of individual characteristics on three domains of frailty in older adults with HF was examined (Table 4.8, 4.9, and 4.10). For frailty in physical domain, time (β=0.05, $p<.001$) was a significant predictor among older adults with HF, indicating that older adults with HF became more physically frail over time from baseline to year 4 (Table 4.8). Older adults with HF who were older than 70 years, female, educated < 12 years, widowed and who had more chronic conditions had increased levels of physical frailty compared to older adults with HF who did not have these characteristics. Compared to those who report not drinking alcohol, moderate drinking was associated with lower level of physical frailty (β=-0.06, p=.016). No interactions between time and individual characteristics were found and there was no difference between two cohorts.

Psychological frailty. GEE model showed that age, education, race, household income, and experience of life events were significant predictors of psychological frailty (Table 4.9). Compared to older adults with HF aged 65-70 years, older adults with HF who were 76-80 years, and 86 years and older had higher levels of frailty in psychological domain. Similarly, older adults with HF who were better educated (12 years and greater), and had higher household income ($20,000 or more) had lower levels of psychological frailty than older adults with HF who did not. Older adults with HF who were African Americans, had more number of chronic conditions, and experienced negative life events had higher level of frailty in psychological domain (Table 4.9).

Social frailty. GEE results showed marital status and household income were the only two significant predictor for social frailty in older adults with HF (Table 4.10). Compared to older HF adults who were married or partnered, those who were divorced (β=0.28, p<.001), widowed (β==0.24, p<.001), or never married (β=0.33, p<.001) reported higher levels of social frailty. Also, compared to older adults with HF who had annual household income less than $20,000, those having household income greater than $50,000 had lower level of frailty in social domain (β=-0.12, p<.001).

Discussions

This study found that older adults with HF had higher levels of frailty in the all three frailty domains (physical, psychological and social) at baseline and four years later compared to older adults without HF. However, unexpectedly, the interactions between HF and time were not significant, indicating changes in frailty (physical, psychological and social domains) between baseline and year four were not statistically different between older adults with and without HF. This study also found that HF and frailty across all three domains predicted the risks of functional disability and decreased QOL over four years period, and frailty in physical, psychological, and social domains mediated the relationship between HF and both functional disability and QOL. Another important finding is that different domains of frailty in older adults with HF are influenced by different individual characteristics. This finding suggests that there is heterogeneity in the risks of each frailty domain among older adults with HF.

Comparisons of frailty levels and changes between HF and non-HF

Findings from this study are consistent with previous studies reporting older adults with HF had high risk of physical frailty (Cacciatore et al., 2005; McNallan et al., 2013). This study showed that HF was associated with higher levels of psychological and social frailty. It provides the empirical evidence to support the view that older adults with HF are frail in more than just the physical domain. In order to decrease risk of disability and improve QOL in older adults with HF, nursing research should develop and test interventions focusing on all three domains of frailty.

No significant interactive effect of HF and time points on frailty domain were found, which was inconsistent with the hypothesis of this dissertation (Chapter 1). It was assumed that older adults with HF would have as steeper rate of frailty change across the four years period, because of the somatic and mental burdens related to HF (Hajduk, Kiefe, Person, Gore, & Saczynski, 2013; Moudgil & Haddad, 2013; Persinger et al., 2003). However, as seen in Figure 2, the slopes of physical, psychological, and social frailty were not statistically different for older adults with HF and older adults without HF. There are two possible reasons. First, the sample in this study consisted of the older adults living in the community. It is possible that older adults with HF who have increasing frailty levels may have resided in nursing homes or even died during the 4 years period and did not participate in the HRS. Second, older adults who live in the community may have social support from family and neighbors that may be protective factors for increased frailty levels. These may be attributed to the similarity in the rate of frailty changes between older adults with HF and older adults without HF in this study.

Relationships among HF, frailty and health-related outcomes

This study examined the relationship among HF, frailty, and health-related outcomes of ADL/IADL and QOL. Consistent with previous studies (Boxer et al., 2014; Buck & Riegel, 2011; Cacciatore et al., 2005; Wong et al., 2011), this study also found that HF and frailty in the physical domain predicted the ADL/IADL disability and decreased QOL. In addition, this study showed that frailty in the psychological and social domains increased the risk of ADL/IADL disability and decreased QOL. By examining the mediation effect of the three frailty domains, this study showed that older adults with HF experienced difficulties in performing ADL/IADL and a diminished QOL indirectly through frailty across all three domains. To the best of the author's knowledge, this is the first study to test the mediation effect of frailty in older adults with HF. These findings provide the empirical evidence to support the relationships between frailty and health-related outcomes among older adults with HF. These results also extend the frailty literature and provide a testable framework to investigate frailty in older adults with HF. It also suggests that nurses and other clinicians can provide multifaceted interventions to prevent frailty or delay its onset to decrease the ADL/IADL disability and improve QOL in older adults with HF. Frailty is not an inevitable process of aging and can be prevented or treated (Ahmed, 2007). Existing studies found that muscle strengthening exercises (Binder et al., 2002; Wolf et al., 1996) and nutritional strategies (Ahmed, 2007) reduced frailty in the physical domain. An interdisciplinary multifaceted treatment program reduced the proportion of physical frailty by nearly 15% (Cameron et al., 2013). More interventions regarding with multidimensional frailty are needed to be developed and tested in further studies.

The impact of individual characteristics on frailty across three domains

This study found that in older adults with HF, age, gender, education level, number of chronic conditions, marital status, and moderate drinking behavior affected the levels of physical frailty. These findings are consistent with previous studies reporting increasing age, female gender, and low education level were associated with increased physical frailty in older adults (Etman et al., 2012; Fried et al., 2001; Strawbridge et al., 1998). Additionally, in accordance with previous studies (Fried et al., 2001; Woods et al., 2005), this study also found the number of chronic conditions was significantly associated with increased level of physical frailty among older adults with HF. The influence of comorbidity on physical frailty may be attributed to the shared risk factors for these chronic illnesses and frailty (Fulop et al., 2010). This study found that older adults with HF who drink moderately had lower levels of physical frailty compared to non-drinkers. Considering the association between moderate drinking and a reduced risk of heart disease (Mezuk et al., 2011), moderate drinking may also be a protective factor for physical frailty in older adults with HF. Additional research is needed in this area.

This study also examined the individual characteristics that influenced frailty in the psychological domain. These findings are consistent with previous studies that reported higher education levels and higher socioeconomic status (SES) are protective factors for cognitive function and emotion (Hendrie et al.), which are two components of psychological frailty. These findings suggest that older HF adults with low SES are more vulnerable to be psychological frailty. Nurses and health providers should assess HF adults living in lower SES communities or rural area for frailty in the psychological domain. This study also found that older adults who experienced negative life events had higher level of psychological frailty. This may be due to the negative long-term effects of negative life-threatening events on individuals' emotional health and quality of life (Schneider et al., 2012).

In the social domain, marital status was the main individual characteristics associated with the levels of frailty. Based on the theory of Socio-emotional Selectivity, as people age, they tend to engage more in close social relations because of the perceived limited lifetime (Carstensen, Isaacowitz, & Charles, 1999). This may explain why marital status is so important to social frailty. This finding suggests the importance of spouse/partner effect in older adults with HF (Chung et al., 2009). Strategies to reinforce existing social networks or build new social networks may be helpful for older adults with HF who are not married or who are at risk for social frailty.

This study found individual characteristics were not associated with the changes in physical, psychological or social frailty over time among older adults with HF. One reason may be that the changes in frailty domains were not noted t between baseline and year 4 (e.g. no statistically significantly change in psychological and social frailty over 4 year period in this study).

Strengths and Limitations

This study has three strengths. A noted strength of this study is its use of a longitudinal design to examine frailty among older adults with HF across all three domains (physical, psychological and social) and its impact on ADL/IADL disability and QOL. The findings of this study contribute to the frailty literature from a multidimensional perspective. Second, this study used the data from the HRS a nationally representative survey that is the foremost database to assess health disparities in the United States (Hayward, 2002). Another strength is that using data from two different cohorts (2006/2010, and 2008/2012) increases the sample size and allows for controlling the cohort effect in the analyses.

This study also has a number of limitations. First, the HRS does not include data about the severity of HF (e.g. New York Heart Association Functional Classification) or information about specific HF drug therapies and adherence. These may be important factors influencing the levels of frailty and be confounders for the risks of health outcomes in older adults with HF. Second, the data in this longitudinal study were collected at only two time points with a 4-year interval. It may have been insufficient to detect the significant changes in frailty (Rockwood, Song, & Mitnitski, 2011) and to measure the trajectory of frailty over time among older adults with HF. Third, the HRS data only included community-dwelling older adults. The most vulnerable older adults may not reside in the community or have died during the study period and therefore not represented in the sample. This may result in underestimating the levels of frailty and rates of frailty changes among older adults with HF. Last, the HRS data on HF were self-reported and it may be that HF was under-reported (Gure et al., 2012).

Conclusions

Frailty is a critical geriatric syndrome that is highly prevalent among older adults with HF. Frailty and HF often coexist in older adults with HF, adversely impacting health-related outcomes such as ADL/IADL ability and QOL. Moreover, frailty is a multidimensional condition. Standard health care usually focuses on physical domain alone. More studies are needed to develop the individual-tailored interventions aimed at preventing or delaying the onset of multidimensional frailty in order to improve health adverse outcomes in older adults with HF.

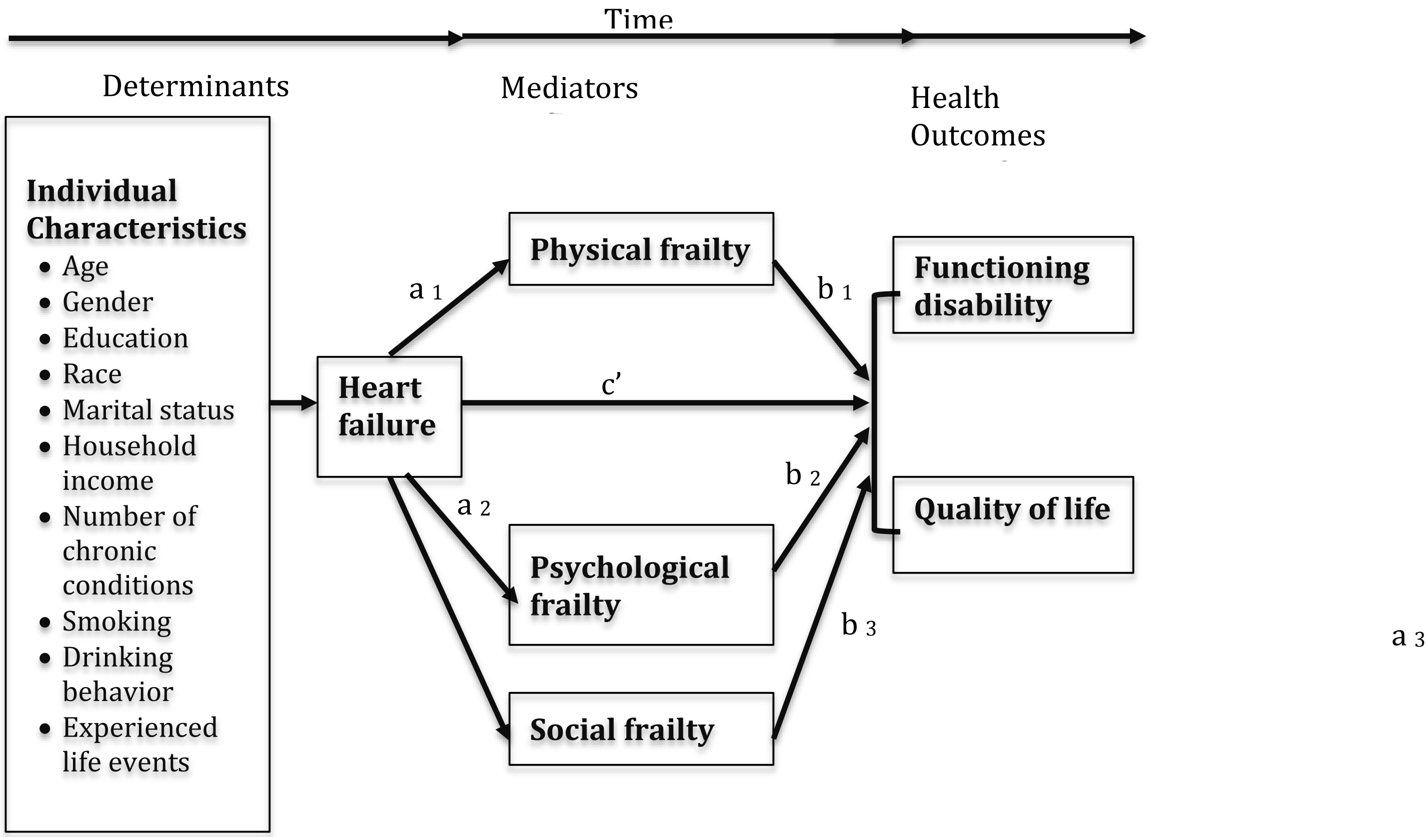


Figure 4.1. Theoretical framework

Note: a1, a2, a3 =effect of HF on physical, psychological, and social frailty respectively; b1, b2, b3=direct effects of physical, psychological, and social frailty on disability or quality of life; c'=direct effect of HF on disability or quality of life.

Table 4.1. Characteristics among older adults with HF and without HF at baseline (n=2301)

	Non-HF (n=1671)	HF (n=630)	
	Mean (SD)	*Mean (SD)*	*t (p)*
Age	73.2 (6.8)	76(7.3)	-8.50 (<.001)
Years of education	12.46 (3.40)	11.89 (2.91)	3.78(.0002)
	n (%)	*n (%)*	χ^2 *(p)*
Gender			0.07(.785)
Male	801(47.94)	306(48.47)	
Female	870 (52.06)	324(51.43)	
Race			3.55(.170)
Caucasian	1371 (82.05)	536(85.08)	
African American	224 (13.41)	74(11.75)	
Other	76 (4.55)	20(3.17)	
Marital Status			32.41(<.001)
Married	1079(64.57)	333(52.86)	
Divorced	169(10.11)	73(11.59)	
Widowed	382(22.86)	212(33.65)	
Never married	41(2.45)	12(1.90)	
Number of chronic conditions			1.5 $^{e+03}$(<.001)
None	747(44.70)	0	
One	748(44.76)	16(2.54)	
Two or more	176(10.53)	614(97.46)	
Annual household income			59.92(<.001)
<$20,000	407(24.36)	238(37.78)	
$20,000-$50,000	669(40.04)	259(41.11)	
≥$50,000	595(35.61)	133(21.11)	
Smoking			50.09(<.001)
Never smoker	798(48.19)	204(32.54)	
Past smoker	678(40.94)	355(56.62)	
Current smoker	180(10.87)	68(10.85)	
Drinking behavior			33.05(<.001)
No drinking problem	798(68.91)	419(82.32)	
Moderate drinking	338(29.19)	87(17.09)	
Heavy drinking	22(1.90)	3(0.59)	
Life event			109.38(<.001)
None	805(48.17)	150 (24.13)	
Yes	886(51.83)	481 (75.87)	

Table 4.2. GEE results about the impact of HF on frailty in physical domain over four years period (n=2165*).

Predictor	Coefficient	S.E	z	p
Time	0.05	0.00	9.44	<.001
Group				
Heart failure	0.21	0.01	20.26	<.001
Healthy older adults (R)				
Time* group	0.01	0.01	0.60	0.546
Age	0.01	0.00	18.59	<.001
Female	0.01	0.01	1.80	0.072
Years of education	-0.01	0.00	-9.52	<.001
Race				
Caucasian (R)				
African American	0.02	0.01	1.61	0.107
Other	0.00	0.02	0.18	0.854
Marital status				
Married (R)				
Divorced	0.04	0.01	2.73	0.006
Widowed	0.01	0.01	1.46	0.143
Never married	0.04	0.02	1.83	0.068
Household income	-6.02 $^{e-08}$	4.37 $^{e-08}$	-1.38	0.169
Cohort	0.004	0.01	-0.63	0.526

*Note: * the sample using in this analyses because of the missing data*

Table 4.3. GEE results about the impact of HF on frailty in psychological domain over four years period (n=2135*)

Predictor	Coefficient	S.E	z	p
Time	0.04	0.01	7.13	<.001
Group				
Heart failure	0.14	0.01	10.80	<.001
Healthy older adults (R)				
Time* group	-0.02	0.02	-1.04	0.298
Age	0.01	0.001	9.21	<.001
Female	0.01	0.01	0.96	0.338
Years of education	-0.02	0.001	-13.16	<.001
Race				
Caucasian (R)				
African American	0.08	0.01	5.98	<.001
Other	0.08	0.03	2.90	0.004
Marital status				
Married (R)				
Divorced	0.03	0.02	1.78	0.075
Widowed	0.03	0.01	2.44	0.015
Never married	0.08	0.03	2.57	0.01
Household income	-5.02^{e-08}	2.65^{e-08}	-1.89	0.058
Cohort	-0.13	0.06	-2.23	0.03

*Note: * the sample using in this analyses because of the missing data*

Table 4.4. GEE results about the impact of HF on frailty in social domain over four years period (n=2121*).

Predictor	Coefficient	S.E	z	p
Time	0.01	0.01	1.61	0.106
Group				
Heart failure	0.04	0.01	3.76	<.001
Healthy older adults (R)				
Time* group	0.03	0.02	1.80	0.072
Age	0.00	0.001	2.04	0.042
Female	-0.01	0.01	-1.57	0.116
Years of education	-0.002	0.001	-1.48	0.139
Race				
Caucasian (R)				
African American	-0.02	0.01	-1.54	0.122
Other	-0.03	0.02	-1.23	0.219
Marital status				
Married (R)				
Divorced	0.28	0.02	16.98	<.001
Widowed	0.26	0.01	21.14	<.001
Never married	0.30	0.04	8.05	<.001
Household income	-3.24^{e-08}	2.58^{e-08}	-1.26	0.209
Cohort	-0.01	0.01	-0.84	0.40

*Note: * the sample using in this analyses because of the missing data*

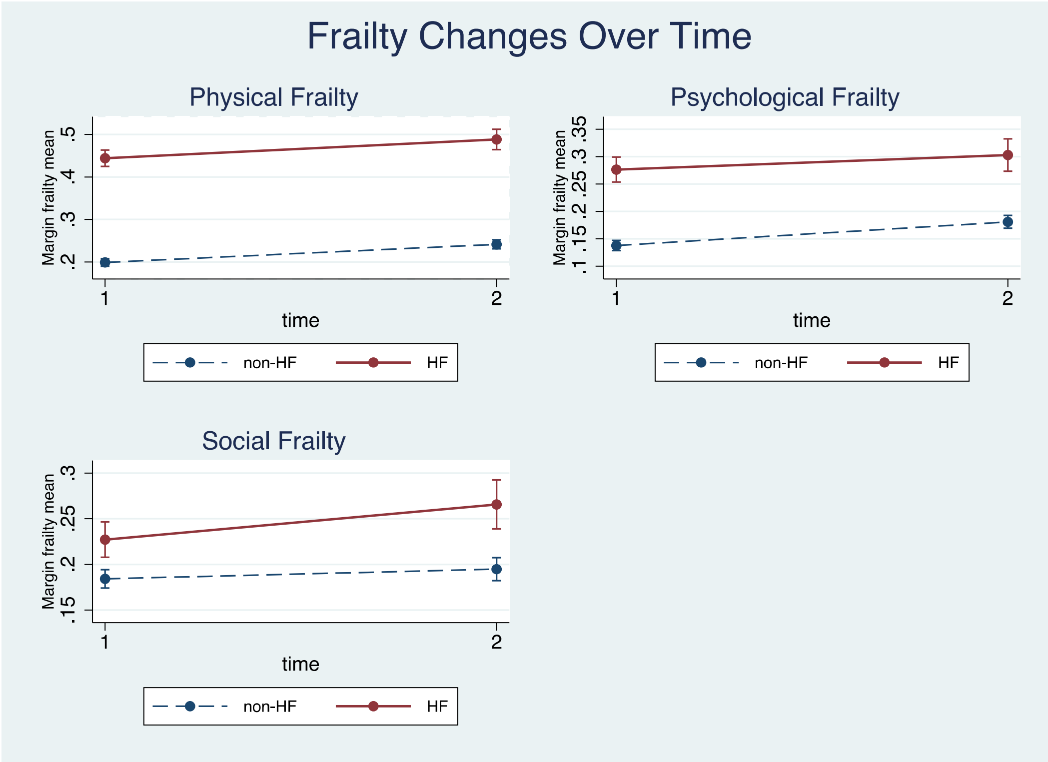


Figure 4.2. Changes in frailty in physical, psychological, and social domains over 4 years period between HF group and non-HF group

Table 4.5. GEE results about the influence of frailty and HF in ADLs/IADLs over four years period (n=1994*).

	Odds Ratio	S.E	z	p
Physical frailty	53.59	16.89	12.63	<.001
Psychological frailty	6.07	1.51	7.25	<.001
Social frailty	1.72	0.41	2.26	0.024
Time	1.43	0.18	2.84	0.004
Group:				
Heart failure	2.74	0.43	6.50	<.001
Healthy older adults (R)				
Time* Group	0.82	0.17	-0.95	0.344
Age	1.02	0.01	1.73	0.083
Female	1.03	0.13	0.20	0.842
Years of education	0.98	0.02	-1.07	0.283
Race:				
White (R)				
Black	1.05	0.19	0.27	0.791
Other	1.71	0.22	-1.09	0.272
Marital status				
Married (R)				
Divorced	0.68	0.14	-1.86	0.063
Widowed	0.91	0.14	-0.63	0.528
Never married	1.36	0.52	0.81	0.418
Household income ($)	1.00	1.28^{e-06}	-0.92	0.359
Cohort	0.93	0.11	-0.60	0.545

*Note: * the sample using in this analyses because of the missing data*

Table 4.6. GEE results about the influence of frailty in QOL over four years period (n=1973*)

	Coefficient	S.E	z	p
Physical frailty	-1.06	0.13	-7.85	<.001
Psychological frailty	-1.04	0.12	-8.41	<.001
Social frailty	-1.08	0.11	-9.50	<.001
Time	0.32	0.04	7.44	<.001
Group:				
Heart failure	-0.24	0.07	-3.43	0.001
Healthy older adults (R)				
Time* Group	-0.17	0.09	-1.85	0.064
Age	0.03	0.004	7.11	<.001
Female	0.12	0.05	2.31	0.021
Years of education	0.01	0.01	1.35	0.178
Race:				
White (R)				
Black	-0.14	0.09	-1.60	0.111
Other	0.01	0.14	0.05	0.961
Marital status				
Married (R)				
Divorced	-0.06	0.09	-0.69	0.488
Widowed	0.01	0.07	0.18	0.858
Never married	0.23	0.21	1.08	0.279
Household income	1.81^{e-07}	1.37^{e-07}	1.31	0.189
Cohort	0.47	0.05	9.35	<.001

*Note: * the sample using in this analyses because of the missing data*

Table 4.7. Results of GEE models using the bootstrap to examine mediation effect of frailty domains on the relationship between HF and health outcomes.

Outcomes	Mediator	a path		b path		ab product
		β (SE)	z (p)	β (SE)	z (p)	[95% CI]
ADL/ IADL (n=1994)	Physical frailty	0.21 (0.01)	20.82 (p<.001)	3.99 (0.32)	12.62 (<.001)	[0.664, 0.0950]
	Psychological frailty	0.13 (0.01)	10.24 (p<001)	1.82 (0.25)	7.31 (<.001)	[0.159, 0.302]
	Social frailty	0.05 (0.01)	4.61 (p<.001)	0.53 (0.24)	2.22 (.027)	[0.0002, 0.0573]
QOL (n=1973)	Physical frailty	0.21 (0.01)	20.96 (<.001)	-1.06 (0.14)	-7.87 (<.001)	[-0.275, -0.161]
	Psychological frailty	0.13 (0.01)	10.29 (<.001)	-1.03 (0.12)	-8.33 (<.001)	[-0.1638, -0.0917]
	Social frailty	0.05 (0.01)	4.62 (<.001)	-1.09 (0.11)	-9.53 (<.001)	[-0.0701, -0.0145]

Note: *a path=effect of HF on mediators; b path=direct effects of mediators on outcome; ab product =indirect effect of HF on outcome through proposed mediators (product of a and b coefficients estimates); all analyses controlling for age, gender, years of education, race, marital status, annual household income, cohort, and time point.*

Table 4.8. GEE results about the impact of individual characteristics on physical frailty among older adults with HF (n=463*)

	Coefficients	Std. E	z	p
Time	0.05	0.01	3.54	<.001
Age				
65-70 years (R)				
71-75 years	0.08	0.02	3.45	0.001
76-80 years	0.11	0.02	4.55	<.001
81-85 years	0.21	0.03	6.67	<.001
86 and older	0.23	0.03	6.82	<.001
Female	0.07	0.02	3.02	0.003
Education				
Less than 12 years (R)				
12 years and greater	-0.05	0.02	-2.34	0.019
Race				
Caucasian (R)				
African American	0.03	0.03	0.88	0.381
Other	0.02	0.05	0.49	0.621
Marital status				
Married (R)				
Divorced	0.00	0.03	0.07	0.941
Widowed	-0.05	0.02	-2.08	0.037
Never married	-0.07	0.06	-1.23	0.217
Household income				
<$ 20,000 (R)				
$20,000-$50,000	-0.02	0.02	-1.09	0.275
>$50,000	-0.06	0.03	-1.92	0.055
Number of chronic conditions	0.04	0.01	5.98	<.001
Smoking				
Never smoker(R)				
Past smoker	0.03	0.02	1.63	0.104
Current smoker	0.06	0.04	1.72	0.085
Drinking behavior				
No drinking problem (R)				
Moderate drinking	-0.06	0.03	-2.41	0.016
Heavy drinking	0.02	0.03	0.65	0.519
Life events				
No (R)				
Yes	0.01	0.02	0.27	0.784
Cohort	-0.02	0.02	-1.29	0.197

*Note: * the entire sample size for older adults with HF was 630, but the sample using in this analyses was 463because of the missing data*

Table 4.9. GEE results about the impact of individual characteristics on psychological frailty among older adults with HF (n=462*)

	Coefficients	Std. E	z	p
Time	0.01	0.02	0.89	0.372
Age				
65-70 years (R)				
71-75 years	0.03	0.03	0.83	0.409
76-80 years	0.07	0.03	2.14	0.032
81-85 years	0.06	0.04	1.51	0.132
86 and older	0.18	0.04	4.17	<.001
Female	0.05	0.03	1.65	0.1
Education				
Less than 12 years (R)				
12 years and greater	-0.06	0.03	-2.14	0.033
Race				
Caucasian (R)				
African American	0.09	0.04	2.47	0.014
Other	0.02	0.08	0.21	0.831
Marital status				
Married (R)				
Divorced	-0.06	0.05	-1.23	0.217
Widowed	-0.05	0.03	-1.44	0.15
Never married	-0.02	0.10	-0.24	0.809
Household income				
<$ 20,000 (R)				
$20,000-$50,000	-0.10	0.03	-3.27	0.001
>$50,000	-0.21	0.04	-5.62	<.001
Number of chronic conditions	0.04	0.01	4.09	<.001
Smoking				
Never smoker (R)				
Past smoker	0.01	0.03	0.26	0.795
Current smoker	0.03	0.05	0.75	0.453
Drinking behavior				
No drinking problem (R)				
Moderate drinking	0.00	0.03	0.13	0.899
Heavy drinking	0.24	0.20	1.20	0.232
Life events				
No (R)				
Yes	0.07	0.03	2.16	0.031
Cohort	-0.01	0.02	-0.28	0.781

*Note: * the entire sample size for older adults with HF was 630, but the sample using in this analyses was 462because of the missing data*

Table 4.10. GEE results about the impact of individual characteristics on social frailty among older adults with HF (n=463*)

	Coefficients	Std. E	z	p
Time	0.02	0.02	1.14	0.253
Age				
65-70 years (R)				
71-75 years	-0.02	0.03	-0.73	0.463
76-80 years	-0.03	0.03	-1.17	0.241
81-85 years	-0.01	0.04	-0.21	0.836
86 and older	0.01	0.04	0.28	0.780
Female	-0.02	0.03	-0.81	0.417
Education				
Less than 12 years (R)				
12 years and greater	0.02	0.02	0.84	0.400
Race				
Caucasian (R)				
African American	-0.06	0.03	-1.63	0.104
Other	0.01	0.06	0.16	0.875
Marital status				
Married (R)				
Divorced	0.28	0.04	7.17	<.001
Widowed	0.24	0.03	8.42	<.001
Never married	0.33	0.07	4.90	<.001
Household income				
<$ 20,000 (R)				
$20,000-$50,000	-0.04	0.03	-1.56	0.118
>$50,000	-0.12	0.03	-3.79	<.001
Number of chronic conditions	0.01	0.01	1.86	0.063
Smoking				
Never smoker (R)				
Past smoker	-0.02	0.02	-1.00	0.315
Current smoker	0.00	0.04	-0.11	0.91
Drinking behavior				
No drinking problem (R)				
Moderate drinking	0.00	0.03	0.13	0.894
Heavy drinking	-0.05	0.09	-0.50	0.619
Life events				
No (R)				
Yes	0.01	0.03	0.52	0.606
Cohort	-0.03	0.02	-1.66	0.097

*Note: * the entire sample size for older adults with HF was 630, but the sample using in this analyses was 463because of the missing data*

Reference

Ahmed, N. (2007). Frailty: an emerging geriatric syndrome. *American Journal of Medicine, 120*(9), 748-753.

Ballinger, G.A. (2004). Using Generalized Estimating Equations for Longitudinal Data Analysis. *Organizational Research Methods, 7*(2), 127-150.

Bergman, H., Ferrucci, L., Guralnik, J., Hogan, D. B., Hummel, S., Karunananthan, S., & Wolfson, C. (2007). Frailty: an emerging research and clinical paradigm--issues and controversies. *The Journals of Gerontology Series A: Biological Sciences and Medical Sciences, 62*(7), 731-737.

Binder, E. F., Schechtman, K. B., Ehsani, A. A., Steger-May, K., Brown, M., Sinacore, D. R., . . . Holloszy, J. O. (2002). Effects of exercise training on frailty in community-dwelling older adults: results of a randomized, controlled trial. *Jouranl of American Geriatric Society, 50*(12), 1921-1928.

Boxer, R.S., Shah, K.B., & Kenny, A.M. (2014). Frailty and prognosis in advanced heart failure. *Current Opinion in Supportive and Palliative Care, 8*(1), 25.

Brenes, G. A., Guralnik, J. M., Williamson, J., Fried, L. P., & Penninx, B. W. (2005). Correlates of anxiety symptoms in physically disabled older women. *American Journal of Geriatric Psychiatry, 13*(1), 15-22. doi: 10.1176/appi.ajgp.13.1.15

Buck, H. G., & Riegel, B. (2011). The impact of frailty on health related quality of life in heart failure. *European Journal of Cardiovascular Nursing, 10*(3), 159-166. doi: 10.1016/j.ejcnurse.2010.06.001

Cacciatore, F., Abete, P., Mazzella, F., Viati, L., Della Morte, D., D'Ambrosio, D., . . . Rengo, F. (2005). Frailty predicts long-term mortality in elderly subjects with chronic heart failure. *European Journal of Clinical Investigation, 35*(12), 723.

Cameron, I. D., Fairhall, N., Langron, C., Lockwood, K., Monaghan, N., Aggar, C., . . . Kurrle, S. E. (2013). A multifactorial interdisciplinary intervention reduces frailty in older people: randomized trial. *BMC Medine, 11*, 65. doi: 10.1186/1741-7015-11-65

Carstensen, L.L., Isaacowitz, D.M., & Charles, S.T. (1999). Taking Time Seriously. *American Psychologist, 54*(3), 165-181.

Chung, M. L., Lennie, T. A., Riegel, B., Wu, J. R., Dekker, R. L., & Moser, D. K. (2009). Marital status is an Independent Predictor of Event-Free Survival of Patients with Heart Failure. *American Journal of Critical Care, 18*(6), 562.

Cigolle, C. T., Ofstedal, M. B., Tian, Z. Y., & Blaum, C. S. (2009). Comparing Models of Frailty: The Health and Retirement Study. *Journal of the American Geriatrics Society, 57*(5), 830.

Clarke, P., Fisher, G., House, J., Simth, J., & Weir, D. (2008). Guide to Content of the HRS Psychosocial Leave-Behind Participant Lifestyle Questionnaires: 2004 &2006. Retrieved from http://hrsonline.isr.umich.edu/sitedocs/userg/HRS2006LBQscale.pdf.

Diener, E., Emmons, R. A., Larsen, R. J., & Griffin, S. (1985). The Satisfaction With Life Scale. *Journal of Personality Assessment, 49*(1), 71-75.

Dunlay, S. M., Manemann, S. M., Chamberlain, A. M., Cheville, A. L., Jiang, R., Weston, S. A., & Roger, V. L. (2015). Activities of daily living and outcomes in heart failure. *Circulation: Heart Failure, 8*(2), 261-267. doi: 10.1161/circheartfailure.114.001542

Etman, A., Burdorf, A., Van der Cammen, T., Mackenbach, J.P., & Van Lenthe, F.J. (2012). Socio-demographic determinants of worsening in frailty among community-dwelling older people in 11 European countries. *Journal of Epidemiology and Community Health, 66*(12), 1116-1121.

Fried, L. P., Tangen, C. M., Walston, J., Newman, A. B., Hirsch, C., Gottdiener, J., . . . McBurnie, M. A. (2001). Frailty in older adults: evidence for a phenotype. *Journal of Gerontology Series A: Biological Sciences and Medical Sciences, 56*(3), M146-156.

Fulop, T., Larbi, A., Witkowski, J. M., McElhaney, J., Loeb, M., Mitnitski, A., & Pawelec, G. (2010). Aging, frailty and age-related diseases. *Biogerontology, 11*(5), 547-563. doi: 10.1007/s10522-010-9287-2

Gobbens, R. J., Luijkx, K. G., Wijnen-Sponselee, M. T., & Schols, J. M. (2010). Towards an integral conceptual model of frailty. *The Journal of Nutrition, Health & Aging. , 14*(3), 175-181.

Gobbens, R. J., van Assen, M. A., Luijkx, K. G., Wijnen-Sponselee, M. T., & Schols, J. M. (2010). Determinants of Frailty. *Journal of the American Medical Directors Association, 11*(5), 356-364.

Guralnik, J. M., Simonsick, E. M., Ferrucci, L., Glynn, R. J., Berkman, L. F., Blazer, D. G., . . . Wallace, R. B. (1994). A short physical performance battery assessing lower extremity function: association with self-reported disability and prediction of mortality and nursing home admission. *Journal of Gerontology, 49*(2), M85-94.

Gure, T. R., Blaum, Caroline S., Giordani, Bruno, Koelling, Todd M., Galecki, Andrzej, Pressler, Susan J., . . . Langa, Kenneth M. (2012). The Prevalence of Cognitive Impairment in Older Adults with Heart Failure. *Journal of the American Geriatrics Society, 60*(9), 1724-1729. doi: 10.1111/j.1532-5415.2012.04097.x

Gure, T. R., Kabeto, M. U., Blaum, C. S., & Langa, K. M. (2008). Degree of disability and patterns of caregiving among older Americans with congestive heart failure. *The Journal of General Internal Medicine, 23*(1), 70-76. doi: 10.1007/s11606-007-0456-1

Hajduk, A.M., Kiefe, C.I., Person, S.D., Gore, J.G., & Saczynski, J.S. (2013). Cognitive change in heart failure: a systematic review. *Circulation. Cardiovascular Quality and Outcomes, 6*(4), 451.

Harper, A., Power, M., Orley, J., Herrman, H., Schofield, H., Murphy, B., . . . Sartorius, N. (1998). Development of the World Health Organization WHOQOL-BREF Quality of Life Assessment. *Psychological Medicine, 28*(3), 551-558.

Hayes, A. F. (2013). *Introduction to mediation, moderation, and conditional process analysis: a regression-based approach*. New York: The Guilford Press.

Hayward, M.D. (2002). Using the Health and Retirement Survey to Investigate Health Disparities. http://hrsonline.isr.umich.edu/sitedocs/dmc/hrs_healthdisparities_hayward.pdf

Hendrie, H. C., Albert Ms Fau - Butters, Meryl A., Butters Ma Fau - Gao, Sujuan, Gao S Fau - Knopman, David S., Knopman Ds Fau - Launer, Lenore J., Launer Lj Fau - Yaffe, Kristine, . . . Wagster, M. V. The NIH Cognitive and Emotional Health Project. Report of the Critical Evaluation Study Committee. (1552-5279 (Electronic)).

Heo, S., Moser, D. K., Lennie, T. A., Zambroski, C. H., & Chung, M. L. (2007). A comparison of health-related quality of life between older adults with heart failure and healthy older adults. *Heart & Lung, 36*(1), 16-24. doi: 10.1016/j.hrtlng.2006.06.003

Hughes, M. E., Waite, L. J., Hawkley, L. C., & Cacioppo, J. T. (2004). A Short Scale for Measuring Loneliness in Large Surveys: Results From Two Population-Based Studies. *Research on Aging, 26*(6), 655-672. doi: 10.1177/0164027504268574

Khan, H., Kalogeropoulos, A. P., Georgiopoulou, V. V., Newman, A. B., Harris, T. B., Rodondi, N., . . . Butler, J. (2013). Frailty and risk for heart failure in older adults: the health, aging, and body composition study. *American Heart Journal, 166*(5), 887-894. doi: 10.1016/j.ahj.2013.07.032

Krause, N., Shaw, B.A., & Cairney, J. (2004). A Descriptive Epidemiology of Lifetime Trauma and the Physical Health Status of Older Adults. *Psychology and Aging, 19*(4), 637-648.

Lachman, M. E., & Weaver, S. L. (1998). The sense of control as a moderator of social class differences in health and well-being. *Journal of Personality and Social Psychology, 74*(3), 763-773.

Langa, K.M., Kabeto, M ., & Weir, D. (2010). Report on race and cognitive impairment using HRS in, 2010 Alzheimer's disease facts and figures. Retrieved from http://www.alz.org/documents_custom/report_alzfactsfigures2010.pdf.

Liu, S., Dixon, J., Qiu, G., Tian, Y., & McCorkle, R. (2009). Using Generalized Estimating Equations to Analyze Longitudinal Data in Nursing Research. *Western Journal of Nursing Research, 31*(7), 948-964.

Lohman, M., Dumenci, L., & Mezuk, B. (2014). Sex differences in the construct overlap of frailty and depression: evidence from the Health and Retirement Study. *Journal of American Geriatric Society*, *62*(3), 500-505. doi: 10.1111/jgs.12689

Lupon, J., Gonzalez, B., Santaeugenia, S., Altimir, S., Urrutia, A., Mas, D., . . . Valle, V. (2008). Prognostic implication of frailty and depressive symptoms in an outpatient population with heart failure. *REVISTA ESPANOLA DE CARDIOLOGIA, 61*(8), 835.

MacKinnon, D.P. (2008). *Introduction to statistical mediation analysis*. Mahwah, NJ: Lawrence Erlbaum, Inc.

Markle-Reid, M., & Browne, G. (2003). Conceptualizations of frailty in relation to older adults. *Journal of Advanced Nursing, 44*(1), 58-68.

McNallan, S. M., Chamberlain, A. M., Gerber, Y., Singh, M., Kane, R. L., Weston, S. A., . . . Roger, V. L. (2013). Measuring frailty in heart failure: a community perspective. *American Heart Journal, 166*(4), 768-774. doi: 10.1016/j.ahj.2013.07.008

Mejhert, M., Kahan, T., Persson, H., & Edner, M. (2006). Predicting readmissions and cardiovascular events in heart failure patients. *International Journal of Cardiology, 109*(1), 108-113.

Mezuk, B., Bohnert, A., Ratliff, S., & Zivin, K. (2011). Job Strain, Depressive Symptoms, and Drinking Behavior Among Older Adults: Results From the Health and Retirement Study. *The Journals of Gerontology Series B: Psychological Sciences and Social Sciences, 66B*(4), 426-434. doi: 10.1093/geronb/gbr021

Mitnitski, A. B., Mogilner, A. J., & Rockwood, K. (2001). Accumulation of deficits as a proxy measure of aging. *Scientific World Journal, 1*, 323-336. doi: 10.1100/tsw.2001.58

Moudgil, R., & Haddad, H. (2013). Depression in heart failure. *Current opinion in cardiology, 28*(2), 249.

Mozaffarian, D., Benjamin, E. J., Go, A. S., Arnett, D.K., Blaha, M.J., Cushman, M., . . . Turner, M.B. (2015). Heart Disease and Stroke Statistics—2015 Update: A Report From the American Heart Association. *Circulation, 131*(4), e29.

Pavot, W., & Diener, Ed. (2009). *Review of the Satisfaction with Life Scale*.

Persinger, R., Janssen-Heininger, Y., Wing, S., Matthews, D., LeWinter, M., & Toth, M. (2003). Effect of heart failure on the regulation of skeletal muscle protein synthesis, breakdown, and apoptosis. *American Journal of Physiology - Endocrinology And Metabolism, 284*(5), E1001-1008.

Pope, A. M., & Tarlov, Alvin R. (1991). *Disability in America: Toward a national agenda for prevention*. Washington, D.C: National Academy Press.

Puts, M. T., Lips, P., & Deeg, D. J. (2005). Sex differences in the risk of frailty for mortality independent of disability and chronic diseases. *Journal of the American Geriatrics Society, 53*(1), 40-47. doi: 10.1111/j.1532-5415.2005.53008.x

Rockwood, K., Song, X., & Mitnitski, A. (2011). Changes in relative fitness and frailty across the adult lifespan: evidence from the Canadian National Population Health Survey. *CMAJ : Canadian Medical Association Journal, 183*(8), E487-E494. doi: 10.1503/cmaj.101271

Schneider, J.C., Trinh, N.T., Selleck, E., Fregni, F., Salles, S.S., Ryan, C.M., & Stein, J. (2012). The Long-Term Impact of Physical and Emotional Trauma: The Station Nightclub Fire. *PLoS One, 7*(10), e47339. doi: 10.1371/journal.pone.0047339

Shrout, P. E., & Bolger, N. (2002). Mediation in experimental and nonexperimental studies: new procedures and recommendations. *Psychological Methods, 7(4):422-45*

Strawbridge, W. J., Shema, S. J., Balfour, J. L., Higby, H. R., & Kaplan, G. A. (1998). Antecedents of frailty over three decades in an older cohort. *The Journals of Gerontology Series B: Psychological Sciences and Social Sciences, 53*(1), S9-16.

Wolf, S. L., Barnhart, H. X., Kutner, N. G., McNeely, E., Coogler, C., & Xu, T. (1996). Reducing frailty and falls in older persons: an investigation of Tai Chi and computerized balance training. Atlanta FICSIT Group. Frailty and Injuries: Cooperative Studies of Intervention Techniques. *Journal of American Geriatric Society, 44*(5), 489-497.

Wong, C. Y., Chaudhry, S. I., Desai, M. M., & Krumholz, H. M. (2011). Trends in comorbidity, disability, and polypharmacy in heart failure. *The American journal of medicine, 124*(2), 136-143. doi: 10.1016/j.amjmed.2010.08.017

Woods, N. F., LaCroix, A. Z., Gray, S. L., Aragaki, A., Cochrane, B. B., Brunner, R. L., . . . Newman, A. B. (2005). Frailty: emergence and consequences in women aged 65 and older in the Women's Health Initiative Observational Study. *The Journal of the American Geriatrics Society, 53*(8), 1321-1330. doi: 10.1111/j.1532-5415.2005.53405.x

Chapter 5

Summary and Conclusions

The purpose of this dissertation was to examine frailty in older adults with HF. To this end, it described the frailty components and corresponding indicators in existing frailty measures and also critiqued existing frailty measures. In addition, a comparison of the prediction of ADL/IADL disability and quality of life (QOL) by the Fried's model and the Gobbens' model was conducted. Using this data, a cross-sectional comparison of frailty levels across three domains (physical, psychological, and social) between older adults with HF and older adults without HF was conducted. Furthermore, a longitudinal comparison of frailty levels and its changes across three domains between older adults with HF and without HF was performed. Next, the impact of HF and three frailty domains on disability and QOL over 4-year time period was longitudinally assessed. The mediation effect of three frailty domains in the relationship between HF and disability and QOL was also investigated. Finally, the influence of individual characteristics on frailty levels among older adults with HF was examined.

Summary of Dissertation Findings

Chapter 2 was an integrative literature review on the published measures of frailty (1997-2014). A total of 43 different frailty measures were identified, including the components and corresponding indicators of frailty in three domains (physical, psychological, and social). Across the three domains, the most frequently reported components of frailty were mobility and balance, nutrition, and cognitive function. The components and corresponding indicators of frailty varied considerably and only 10 of 43 frailty measures include the components across all three domains. Additionally, four specific concerns were identified: 1) the use of weighted frailty scores in determining the level of frailty; 2) the inclusion or exclusion of disabilities and comorbidities in the frailty measures; 3) the use of specific aspects of cognitive function in frailty measures; and 4) the multidimensionality of frailty measures. The findings from this literature review revealed the inconsistency in frailty components, which has implications for researchers and clinicians who study and deliver care to older adults at risk for frailty.

Chapter 3 begins with a comparison of two current predominant frailty models (Fried's physical frailty model and Gobbens' multidimensional frailty model) for their ability to predict ADL/IADL disability and QOL in Chapter 3. Compared to the Fried's physical frailty model, the inclusion of psychological components from the Gobbens' model significantly increased the power to predict ADL/IADL disability; and psychological and social components in the Gobbens' model significantly increased the ability to predict QOL. These findings support a multidimensional frailty model as better able to predict adverse health outcomes than a purely physical frailty model. These findings also suggest that for these different outcomes, each subscale of frailty (physical, psychological, and social) has different predictive abilities. These findings underscore the frailty should be measured as a multidimensional concept consisting of three domains rather than a one-dimensional concept with a single overall score. Chapter 3 also compares three domains of frailty among older adults with and without HF, using cross-sectional analysis. Results showed older adults with HF have higher levels of frailty across all three domains (physical, psychological, and social) compared to older adults without HF.

Chapter 4 was a longitudinal comparison of frailty levels between older adults with and without HF. In accordance with findings in Chapter 3, it found that older adults with HF had higher levels of frailty in all physical, psychological, and social domains across a 4-year period. Expanding beyond the previous literature, the result from this dissertation show older adults with HF are frail in more than just the physical domain. In Chapter 4, it also examined the relationships among HF, frailty and outcomes of ADL/IADL disability, and QOL. The findings revealed that HF and three frailty domains over time predicted the risks of ADL/IADL disability and decreased QOL. By investigating the mediation effect of frailty domains, this study revealed that older adults with HF experience ADL/IADL disability and decreased QOL through physical, psychological, and social frailty. To the author's knowledge, this is the first study to investigate the mediation effect of frailty in older adults with HF. Finally, in Chapter 4, the factors influencing the frailty levels were examined among older adults with HF. The study found that different domains of frailty in older adults with HF were influenced by different individual characteristics. Older age, being female, being less educated, having a greater number of chronic conditions, and widowed marital status were associated with higher level of physical frailty, whereas moderate drinking behaviors was associated to lower levels of frailty. Additionally, older HF adults who had low educated level (<12 years), were African-American, had low household income (annual <$20,000), and had experienced negative life events had higher levels of psychological frailty. However, marital status and household income level were the only two individual characteristics related to social frailty.

Strengths

This dissertation has four strengths. It used a rigorous research approach to examine the conceptual framework of frailty. It began with a comparison of frailty models using a sample of general older adults from the HRS. Subsequently, comparative analysis was conducted between two groups of older adults with and without HF using both a cross-sectional and a longitudinal design. Finally, individual differences in frailty were examined among older adults with HF.

Second, this study included both cross-sectional and longitudinal analyses to examine frailty levels in older adults with HF. Extending beyond a single moment in time, this study was able to show that levels of physical, psychological, and social frailty among older adults with HF were sequentially higher over a period of 4-year time compared to older adults without HF.

Third strength of this study was the use of objectives measures for frailty in the physical domain and the use of valid frailty measures in the psychological and social domains.

Last, by examining the mediation effects of the three frailty domains in the relationship between HF and adverse health outcomes (disability and decreased QOL), this study enhances understanding of these relationships and provides potential pathways for future interventions to prevent disability and improve QOL among older adults with HF.

Limitations

This dissertation has a number of limitations. First, this study is a secondary data analysis design using data from the Health and Retirement Study (HRS). The HRS data has not contained specific information about the severity of HF (i.e. NYHA functional classification), specific drug therapies, or medication adherence associated with HF. This information may have influenced the frailty levels and their changes in older adults with HF. Second, the data contained approximately 35% of missing data in frailty components, which reduce the sample size and may have reduced statistical efficiency (Pearson, 2006). Third, although a longitudinal design was used in the Chapter 4, the data for frailty measures were collected at only two time points (2006/2008-2010/2012) with a 4-year interval. These two time points may be insufficient to detect the significant changes in frailty (Rockwood, Song, & Mitnitski, 2011) and for investigating the trajectory of frailty over time among older adults with HF.

Implications for Nursing Science

This dissertation is consistent with the nursing meta-paradigm , consisting of four elements: human, health, nursing, and environments (Thorne et al., 1998). The studies in this dissertation are consistent with this nursing meta-paradigm. Frailty is an important health issue affecting older adults that is influenced by physical and psycho-social environmental factors. ADL/IADL disability and QOL are outcomes sensitive to nursing intervention. The results of this research contribute to nursing science by shedding light on the relationships between HF and frailty domains in older adults and the roles of individual characteristics in these relationships. Findings from this dissertation advance the understanding of the impact of frailty domains on ADL/IADL disability and QOL and also provide a specific theoretical framework for interventions designed to delay the onset of frailty or mitigate frailty-related adverse health outcomes.

The foci of nursing science also include the holistic health of humans. The results of this dissertation study support the view of multidimensional frailty. Given that frailty is a multi-domain syndrome, nurses should use an interdisciplinary approach, collaborating with physicians, physical therapists, psychologists, and social workers, to deliver holistic health care to older adults that addresses the physical, psychological, and social domains of frailty.

Implications for Nursing Practice

As the aging population is growing, the geriatric syndrome--frailty--will affect more individuals in the United States and elsewhere. Frailty is related to the increased likelihood of ADL/IADL disability and decreased QOL. In order to prevent disability and improve QOL in older adults with HF, nurses need to assess frailty using reliable tools to detect patients at risk for adverse outcomes. Nurses are in an excellent position to assess patients for signs of frailty. Nurses also should evaluate not only physical symptoms, but also psychological and social. Guiding by these assessments, nurses will be well position to lead an interdisciplinary team of physicians, psychologists, neurologists, and social workers to provide holistic care for older adults at risk of frailty.

Directions for Future Study

The findings in this dissertation provide directions for future study. First, more research is needed to clarify the frailty measures in each domain of physical, psychological, and social. Although this study suggests that a frailty measure purely focusing on the physical domain is insufficient to identify older adults at risk of adverse health outcomes, the exact frailty measures in psychological and social domains remains elusive and warrants future study.

Second, frailty co-exists with many chronic conditions (e.g. diabetes, COPD, renal diseases). Using the frailty conceptual framework established in this study, future studies are needed to investigate the frailty syndrome in older adults with other chronic conditions.

Third, this study has examined the determinants of three frailty domains, including demographic characteristics, lifestyle behavior, and the experience of life events. Although this examination has shed light on the individual difference in frailty levels among older adults with HF, more research is needed to explore the biological etiology of frailty. Studies have shown that inflammation biomarkers (e.g. CRP, IL-6) (Sarkisian, Gruenewald, John Boscardin, & Seeman, 2008) and some genetic factors (e.g. ApoE4) (Buchman et al., 2009) are associated with the aging process and may relate to the development of frailty. Future study is needed to evaluate these biomarkers in order to enhance the understandings in the pathways to develop frailty in older adults.

Fourth, the findings in this study suggest that the risks for disability and decreased QOL could be reduced by managing the levels of frailty in older adults with HF. To date, the preventive strategies and treatments for frailty remain unclear. Few studies have suggested that nutritional intervention (Ahmed, Mandel, & Fain, 2007) and exercising program (Binder et al., 2002; Wolf et al., 1996) may prevent and/or reduce frailty. The effects of these interventions need to be investigated and established in future studies.

Conclusions

In conclusion, frailty is a critical geriatric syndrome in older adults, especially in those with HF. It is more than just physical syndrome and it also include psychological and social domains. Older adults with HF have higher levels of frailty across all three domains compared to older adults without HF. Additionally, as frailty mediates the effect of HF on disability and decreased QOL, it may be possible to prevent disability and improve QOL through tailored interventions aimed at reducing frailty levels or delaying its onset. Additional study is needed.

References

Ahmed, N., Mandel, R., & Fain, M. J. (2007). Frailty: an emerging geriatric syndrome. *American Journal of Medicine, 120*(9), 748-753. doi: 10.1016/j.amjmed.2006.10.018

Binder, E. F., Schechtman, K. B., Ehsani, A. A., Steger-May, K., Brown, M., Sinacore, D. R., . . . Holloszy, J. O. (2002). Effects of exercise training on frailty in community-dwelling older adults: results of a randomized, controlled trial. *Journal of American Geriatric Society, 50*(12), 1921-1928.

Buchman, A. S., Boyle, P. A., Wilson, R. S., Beck, T. L., Kelly, J. F., & Bennett, D. A. (2009). Apolipoprotein E e4 Allele is Associated with More Rapid Motor Decline in Older Persons. *Alzheimer Disease and Associated Disorders, 23*(1), 63-69.

Pearson, R. (2006). The problem of disguised missing data. *ACM SIGKDD Explorations Newsletter*, *8*(1), 83-92.

Rockwood, K., Song, X., & Mitnitski, A. (2011). Changes in relative fitness and frailty across the adult lifespan: evidence from the Canadian National Population Health Survey. *CMAJ : Canadian Medical Association Journal*, *183*(8), E487-E494. doi: 10.1503/cmaj.101271

Sarkisian, C.A., Gruenewald, T. L., John Boscardin, W., & Seeman, T.E. (2008). Preliminary evidence for subdimensions of geriatric frailty: the MacArthur study of successful aging. *Journal of the American Geriatrics Society*, *56*(12), 2292-2297.

Thorne, S., Canam, C., Dahinten, S., Hall, W., Henderson, A., & Reimer Kirkham, S. (1998). Nursing's metaparadigm concepts: Disimpacting the debates. *Journal of Advanced Nursing, 27*(6), 1257-1268.

Wolf, S. L., Barnhart, H. X., Kutner, N. G., McNeely, E., Coogler, C., & Xu, T. (1996). Reducing frailty and falls in older persons: an investigation of Tai Chi and computerized balance training. Atlanta FICSIT Group. Frailty and Injuries: Cooperative Studies of Intervention Techniques. *Journal American Geriatric Society, 44*(5), 489-497.