October 2021

Examining a Fatigue Management Model That Identifies Risk Factors and Consequences of Fatigue in Older Individuals

Maral Torossian

University of Massachusetts Amherst

Examining a Fatigue Management Model That Identifies Risk Factors and Consequences of Fatigue in Older Individuals

A Dissertation Presented

By

MARAL TOROSSIAN

Submitted to the Graduate School of the
University of Massachusetts Amherst in partial fulfillment
of the requirements for the degree of

DOCTOR OF PHILOSOPHY

September 2021

College of Nursing

Examining a Fatigue Management Model that Identifies Risk Factors and Consequences of Fatigue in Older Individuals

A Dissertation Presented by

MARAL TOROSSIAN

Approved as to style and content by:

____
Cynthia Jacelon, Chair

____
Joohyun Chung, Member

____
Sara Mamo, Member

____
Allison Vorderstrasse, Dean
College of Nursing

DEDICATION

I would like to dedicate this dissertation to my wonderful family. To my parents, Raffi and Zevart, who sacrificed so much so that I can be where I am today. They were my biggest support system, and those who motivated me to keep going every time I was about to give up. It is impossible to put into words how much appreciate what you have done for me. I hope I did make you proud, and I promise to try my best to do so every day.

I also dedicate this to my relatives in the United States, Maral, Harout, Bedig, and Vera for their incredible support, and for opening their doors to me when I needed that. They are the reason I was able to thrive in a foreign country, and I will always be grateful for that. Last but not least, I dedicate this dissertation to my fiancé, Brandon, who has been impatiently waiting for this moment. I cannot express how grateful I am for all the support, love, appreciation, motivation he has provided me with, and for always doing everything in his power to make me happy.

ACKNOWLEDGMENTS

I am forever grateful for my PhD program advisor, Dr. Cynthia Jacelon, for her consistent support throughout my journey in the PhD program. Not only has she constantly guided me on academic and career-related decisions, but has also gone above and beyond in ensuring my emotional well-being given the challenges as an international student. She has been an incredible mentor, advisor, supporter, motivator, and a second mother to me.

I also want to express my gratitude to Dr. Joohyun Chung for her patience and guidance throughout my dissertation work a committee member, Dr. Sara Mamo for her helpful feedback as my outside member. I also want to thank all College of Nursing faculty individually for all their hard work, and for inspiring me every day to become a better nurse scientist. A very special thanks to Dr. Jessica Pearlman, who contributed so much in the statistical decisions. Her support, guidance, and time dedicated to me despite her competing priorities are priceless.

ABSTRACT

EXAMINING A FATIGUE MANAGEMENT MODEL THAT IDENTIFIES RISK FACTORS AND CONSEQUENCES OF FATIGUE IN OLDER INDIVIDUALS

SEPTEMBER 2021

MARAL TOROSSIAN, B.S., LEBANESE AMERICAN UNIVERSITY

M.S., UNIVERSITY OF MASSACHUSETTS AMHERST

Ph.D., UNIVERSITY OF MASSACHUSETTS AMHERST

Directed by: Professor Cynthia Jacelon

Fatigue is experienced by 40-74% of older individuals living with a chronic disease. Despite advances in scientific knowledge around risk factors and consequences associated with fatigue, a comprehensive model that can serve as a guide for healthcare providers caring for older individuals with fatigue is lacking. Thus, the purpose of this study was to examine a fatigue model based on the Theory of Unpleasant Symptoms (TUS). The model included psychological, physiological, and situational risk factors of fatigue, as well as fatigue outcomes, such as physical, social, and cognitive performances, perceived health, and quality of life (QOL). This was a secondary data analysis of the "Patient-Reported Outcomes Measurement Information System Profiles – Health Utilities Index" dataset. Multiple regression analysis and path analyses were used to examine the association between fatigue and the above-mentioned variables. Findings suggested that number of comorbidities, pain, sleep, depression, anxiety, education, and sensory impairment (SI) were significant predictors of fatigue. In their turn, higher fatigue scores predicted lower physical, social, and cognitive performance, as well as worse perceived health and QOL. Additionally, fatigue outcomes mediated the relationship between

fatigue and QOL. Health care providers of older individuals with fatigue should closely monitor and manage the physiological, psychological, and situational risk factors of fatigue, which would, in turn, improve these individuals' performance on all three levels, perceived health, as well as their QOL. Future research should be directed towards exploring other risk factors of fatigue, examining feedback loops depicted in the TUS, identifying whether neurodegenerative diseases moderate the relationship between CP and QOL, and identifying variables that mediate the relationship between certain risk factors and fatigue.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

CHAPTER 1

INTRODUCTION

Background

Fatigue is experienced by 40-74% of older individuals living with a chronic disease (Menting et al., 2018). Fatigue is defined as an overwhelming sense of decreased capacity for activity, physical or mental, due to an imbalance in the availability, utilization, or restoration of resources (Aaronson et al., 1999), and is attributed to disease-specific, psychological, or cognitive factors (Goedendorp et al., 2014). Fatigue is described as an unpleasant, troublesome, and a burdensome symptom, contributing to irritability, poor motivation, attention, memory, and a decline in social and physical function (Menting et al., 2018; Ream & Richardson, 1996).

Although individuals in all age groups experience fatigue, fatigue is of particular interest in older individuals (Torossian & Jacelon, 2020). First, fatigue is common in older adults following hospitalization. As many as 77% of patients above the age of 70 reported fatigue upon hospital admission, and were three times more likely than those without fatigue at admission to retain this symptom three months following discharge (van Seben et al., 2019). Second, fatigue can be one of the early signs of abnormal aging, and is a self-reported indicator of frailty (Avlund, 2010). Third, fatigue is an independent predictor of mortality; for example, older individuals with hematological malignancies who experienced higher levels of fatigue had significantly worse prognosis, and a shortened overall survival, compared to those with lower levels of fatigue (Hofer et al., 2018). In addition, when fatigue coexists with other chronic conditions, it becomes more debilitating and limiting. Yet, fatigue is often viewed as a normal part of the aging

Paragraphs 1,2, and 3 in Chapter 1 are fully or partially retrieved from Torossian, M., & Jacelon, C. (2020). Chronic illness and fatigue in older individuals: A systematic review. *Rehabilitation Nursing*. doi:10.1097/RNJ.0000000000000278 process, rather than a manifestation of an underlying condition. Thus, advancing the understanding of factors related to fatigue, and exploring fatigue management strategies may help control some aspects of frailty, reduce the odds of symptom persistence post hospital discharge, and improve the quality of life of older individuals.

Currently, there is increased research interest in the area of chronic disease symptom management, including fatigue. Many researchers have addressed fatigue in terms of its triggers, consequences, management strategies, and older individuals' perceptions of fatigue. However, clinicians still face challenges understanding the risk factors for fatigue, and the extent to which it affects health outcomes. Study findings either pertain to a single chronic disease, or to the relationship between fatigue and one or two risk factors, or consequences. The narrow scope of this research limits the applicability of findings. To date, there has not been a comprehensive examination of risk factors and consequences of fatigue in a single study. Risk factors for fatigue are interdependent, and co-influence fatigue levels and fatigue outcomes experienced by older individuals. Thus, examination of the extent to which risk factors predict fatigue, singly and in combination, and the degree to which fatigue affects outcomes would provide an understanding of where to direct intervention efforts, and the outcomes used to measure intervention effectiveness.

Purpose

The purpose of this study was to provide a broader understanding of the extent to which select risk factors contribute to the experience of fatigue, and the impact fatigue has on identified patient outcomes. Fatigue has been shown to be associated with a number of physiological, psychological, and situational risk factors. Physiologic factors associated with fatigue identified from existing literature include, but are not limited to, age (Lin et al., 2015; Silva et al., 2011), gender (Salter et al., 2019), number of comorbidities (Hardy & Studenski, 2010; Horne et al., 2019; Lin et al., 2015), sleep-related impairment, sleep disturbance (Barak et al., 2020; Hawker et al., 2010), and pain (Overcash et al., 2018). Psychological factors associated with fatigue include depression and anxiety (Karakurt & Ünsal, 2013), while situational factors include lifestyle and personal variables, such as marital status (Jing et al., 2015; Lin et al., 2015), education (Jing et al., 2015; Karakurt & Ünsal, 2013; Kessing et al., 2015; Lin et al., 2015; Muszalik et al., 2016), social support (Kwag et al., 2011), and physical activity (Tolstrup Larsen et al., 2018; Nicklas et al., 2016). Fatigue, according to existing literature, has consequences on performance-based outcomes. These include older individual's physical, social, and cognitive performances, perceived health, quality of life, and longevity (Banerjee et al., 2020; Bhalla et al., 2014; Hofer et al., 2018; Li et al., 2018; Plach et al., 2006; Stephen, 2008).

Despite advances in scientific knowledge around risk factors and consequences associated with fatigue, a comprehensive model that could serve as a guide for healthcare providers caring for older individuals with fatigue is lacking. Thus, the purpose of this study was to present a fatigue model inclusive of the common risk factors and consequences, which would help explain the associations among variables. This comprehensive model would also expose the proportion of unexplained variance in fatigue scores, which would be the first step towards exploring previously unexamined predictors of fatigue in future studies.

Research Questions

This study was guided by the following research questions:

1) To what extent do each of the physiological (age, gender, number of comorbidities, pain, sleep), psychological (depression, anxiety), and situational (race, marital status, education, hospitalization, sensory impairment) factors predict fatigue in older individuals?
2) To what extent does fatigue influence older individuals' physical performance, social performance, cognitive performance, perceived health, and quality of life?
3) Do the above-mentioned fatigue consequences (physical performance, social performance, cognitive performance, perceived health) mediate the relationship between fatigue and QOL?
4) Does gender moderate the relationship between number of comorbidities and fatigue?

Definitions

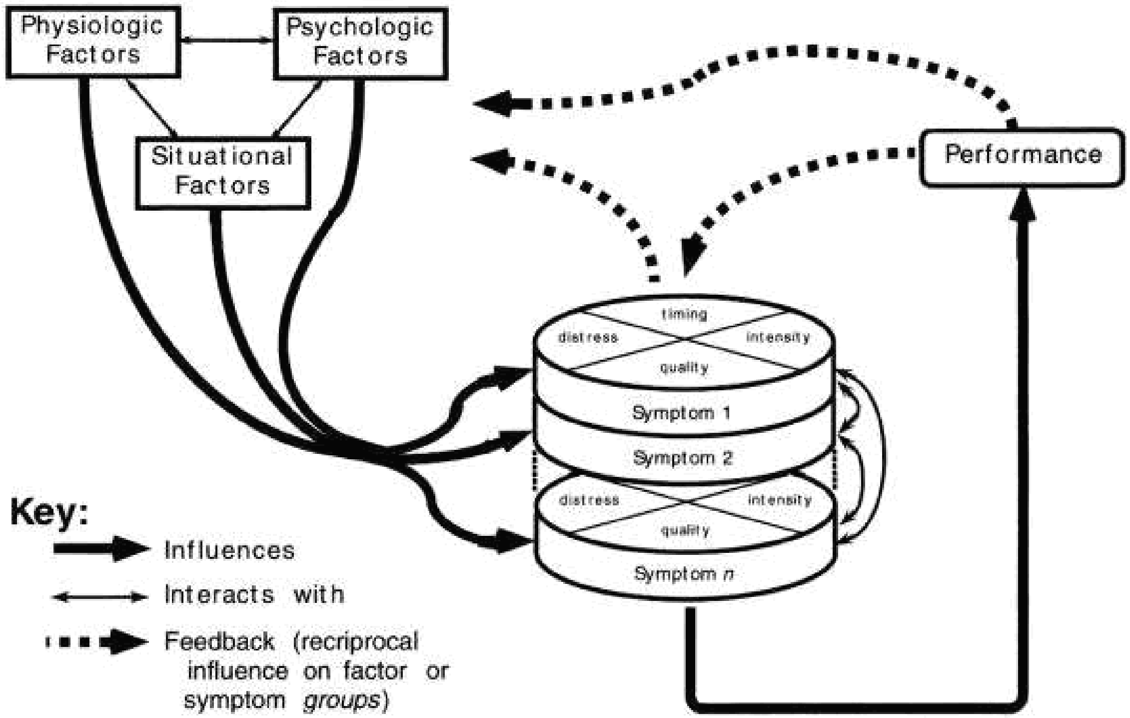
- Fatigue is an unpleasant feeling of exhaustion experienced with or without physical symptoms. It is characterized by a decreased capacity in accomplishing physical or mental activities due to an imbalance in the availability, utilization, and restoration of resources, secondary to physical or psychological factors (Aaronson et al., 1999; Goedendorp et al., 2014).
- Physiological factors are defined as variables that relate to the activities or functions of cells, tissues, and organs of the human body, and to the physical and chemical processes involved in these functions (Merriam-Webster, n.d.)
- Psychological factors are defined as variables that pertain to an individual's emotions, mood, affect, feelings, and mental state (Lenz et al., 1997), that affect one's behavior.

- Situational factors are defined as aspects of one's social and physical surrounding that can influence an individual's experience of symptoms (fatigue) (Lenz et al., 1997)
- Comorbidities are defined as one or more long-term or chronic health-related conditions that are present simultaneously in an individual.
- Sleep disturbance is defined as a phenomenon which results in the alteration of one's subjective and objective sleep measures (Richards et al., 2019)
- Sleep-related impairment is defined as any disruption in the integrity of physical, emotional, or social performance as a result of inadequate or inefficient sleep.
- Quality of life is defined as a subjective evaluation of positive and negative aspects of life (Centers for Disease Control and Prevention [CDC], 2020), including physical, social, emotional, and financial aspects.
- Physical performance is defined as the ability to carry out basic actions that allow an individual to perform more complex tasks that are essential for self-care, maintenance of social roles, and independence (Painter et al., 1999).
- Social performance is defined as one's ability to carry out social roles, which constitute a set of behaviors and attitudes expected of an individual, based on one's position, or on a particular function that they perform in a social context (American Psychological Association [APA], n.d.).
- Cognitive performance is defined as an individual's conscious intellectual activity (Merriam-Webster, n.d.) that includes comprehending, reasoning, remembering, and concentrating.

Conceptual Framework

The middle-range Theory of Unpleasant Symptoms (TUS) provides a framework that depicts the relationship between the experienced symptom, the factors influencing it, and the alteration in one's performance as a result of the symptom (Lenz et al., 1997). The theory was first introduced in 1995, and revised in 1997. In TUS, "symptoms" are defined as the subjective perceptions of threats to health by the individual, and indicators of change in normal function (Lenz et al., 1997). Symptoms experienced by individuals are characterized by intensity (severity/strength), timing (frequency, duration), distress (degree of perceived bother from the experience of symptom), and quality (what the symptom feels like to an individual) (Lenz et al., 1997). In TUS, influencing factors refer to a set of physiological (function of bodily systems), psychological (mental state, mood), and situational (marital status, social support) factors that are assumed to be interrelated, and influence each other. Lastly, performance, which is the outcome of the experienced symptom, is conceptualized as functional (physical, social, and work-related) and cognitive (concentration, problem-solving) activities. (Lenz et al., 1997) (Figure 1).

Figure 1. 1: ***A Diagram Representing the Paths in the Theory of Unpleasant Symptoms***



Lenz, E. R., Pugh, L. C., Milligan, R. A., Gift, A., & Suppe, F. (1997). The middle-range theory of unpleasant symptoms: an update. *ANS. Advances in Nursing Science*, *19*(3), 14–27. https://doi.org/10.1097/00012272-199703000-00003

The TUS was developed with the assumption that symptoms share similar attributes and characteristics, and thus a theory on symptom experience can guide the management of more than one symptom. This theory has been used as a framework in studies examining fatigue in the post-partum period (Milligan et al., 1996), symptom experience in breast cancer patients (Kim et al., 2014), including pain, fatigue, sleep disturbance, and anxiety (Schreier et al., 2019). In this study, TUS guided the development of the proposed model. The model aimed to examine the relationship between a number of influencing factors, fatigue, and fatigue-related patient outcomes in older individuals with chronic diseases.

Methodology Overview

In this study, a large existing data set, “Patient-Reported Outcomes Measurement Information System Profiles – Health Utilities Index”, was used to explore the relationships among variables using structural equation modeling (SEM). This dataset was collected from an internet panel managed by “Opinion 4 Good” (OP4G), a philanthropic, online research panel, and was funded as a supplement to PROMIS statistical center. The dataset includes measures of the Health Utility Index, PROMIS Global items, and other PROMIS measures that assess fatigue, physical activity, pain, sleep, ability to participate in social roles and activities, emotional distress (anxiety, anger, depression), and cognition from 3000 subjects (Cella, 2016) (see Chapter Three for an in-depth description of these variables).

To analyze the data “PROMIS Profiles -HUI” dataset, structural equation modelling (SEM) consisting of only path analyses was carried out. SEM is a causal inference method in which the researcher specifies the directionality of the relationship between variables, whereby variables are regressed on, or hypothesized to be predicted by other variables. In SEM, a set of a priori, theory-based hypotheses are required, upon which the fit of the model is tested, using a confirmatory approach. If statistical results do not show a good fit, the model can be respecified to improve fit based on certain statistical parameters and theoretical underpinnings (Kline, 2015). SEM also depicts the beta coefficient of all paths depicted in a given model. SEM includes two types of variables: observed, and latent. Observed variables are constructs that can be easily quantified or observed, such as age, marital status, and annual income. The relationship between observed variables is examined through path analyses. Latent variables, on the other hand, cannot be observed, but can be quantified through their indicators (e.g., stress can be quantified through measurement of cortisol levels). Measurement models rather than path analyses are used to examine the relationship among latent variables in SEM. In this study, only observed variables (path analyses) will be conducted.

TUS guided the choice of variables as either risk factors (independent variables), or consequences (dependent variables) of fatigue for the proposed model. Risk factors were categorized into physiological, psychological, and situational, as suggested by Lenz et al. (1997). Physiological risk factors examined included age, gender, number of comorbidities, sleep, and pain. Psychological variables included depression and anxiety, while situational factors included race, educational level, marital status, frequency of hospitalization in the past 12 months, and sensory (hearing and vision) impairment (SI). The reason why SI was categorized as a situational factor is because it is the subjective perception of SI rather than the physiological changes that become bothersome and burdensome to the individual. Lastly, outcomes hypothesized to be influenced by fatigue included physical, social, and cognitive performances, perceived health, and quality of life.

Significance of Inquiry

Fatigue has been extensively studied over the recent two decades. These examinations have advanced the scientific knowledge of a number of risk factors of fatigue (Alhanbali et al., 2017; Hornsby et al., 2016; Loh et al., 2018), and the extent to which each of these factors contribute to the experience of fatigue. Based on these findings, a number of fatigue management interventions have been developed to help minimize the experience and burden of fatigue, and improve individuals' quality of life. Similarly, researchers have investigated outcomes associated with fatigue (Banerjee et al., 2020; Salter et al., 2019). Despite these advances in knowledge, findings have been limited in generalizability, due to their focus on one particular chronic disease, or a few variables. A study examining the predictive power of multiple significant risk factors simultaneously through SEM modeling, in more than one chronic disease, is lacking.

The simultaneous examination of regression coefficients of fatigue risk factors would account for the covariance among these factors, and reveal a more accurate predictive power of each of the risk factors in relation to fatigue. This, in turn, would provide a clearer representation of the way in which all influencing factors, combined, impact the experience of fatigue in older individuals with chronic conditions. This is significant, as resources, screening practices, and early fatigue management interventions can then be directed towards risk factors that strongly predict fatigue. Additionally, this strategy would identify the percentage of additional risk factors that need to be explored in future studies, to help screen, prevent, or control fatigue more efficiently.

Furthermore, the correlation coefficients between fatigue and multiple outcomes while accounting for a number of covariates (see Chapter 3) would identify the circumstances under which fatigue should be screened for as a potential risk factor. Lastly, the SEM modeling would also highlight the mediating effect of fatigue consequences on the relationship between fatigue and quality of life, so that significant mediators can be incorporated into interventions targeted at improving the quality of life of older individuals experiencing fatigue.

CHAPTER 2

REVIEW OF THE LITERATURE

Introduction

Fatigue is a symptom experienced by individuals in different age groups and populations, which makes it a topic of interest for a vast number of researchers. A number of studies have sought to identify its causes, in order to develop effective interventions for fatigue management. However, much of the knowledge regarding the risk factors of fatigue have pertained to working age groups, and thus are not applicable to the population of older adults. For example, workload, types of shifts, years of work, and other work-related factors have been identified as fatigue-related risk factors in a number of studies (Lu et al., 2017; McElroy et al., 2020); Murray et al., 2019). However, according to the U.S. Bureau of Labor Statistics (2017), individuals above the age of 65 spend two-thirds of their time participating in household and leisure activities, including watching TV, relaxing, and reading. Thus, in order to explore risk factors of fatigue in older adults, choosing age- and lifestyle-relevant fatigue predictors is key.

Although all age groups can experience fatigue, its burden varies significantly between age groups. Fatigue becomes more burdensome and debilitating in older adults above the age of 60 compared to younger individuals and children. This is partly due to the coexistence of a number of chronic illnesses in this population, with common underlying processes, such as inflammation (Hardy & Studenski, 2010), making it one of the most prevalent symptoms reported in older individuals (van Seben et al., 2019). Fatigue is also associated with poorer prognosis, and higher odds of mortality in this population (Hofer et al., 2018). Throughout the literature, a number of physiological, psychological, and situational risk factors have been examined, and their association with fatigue levels in older individuals has been established. Similarly, outcomes ranging from physical performance, to functional and cognitive activities have been investigated, and have been shown to be impacted by fatigue levels experienced by older adults. The purpose of this literature review was to examine the commonly reported risk factors and consequences of fatigue in older individuals.

The Theory of Unpleasant Symptoms (TUS) was the theoretical framework that guided the literature review. TUS is a middle-range theory developed by Lenz et al. (1997), with the aim of guiding research and practice in the management of one or more symptoms. The theory depicts three levels of influencing factors (physiological, psychological, situational) that influence the experience of a symptom in terms of duration, quality, intensity, and distress. The experience of the symptom, in its turn, impacts performance on the functional (physical and social), and cognitive levels.

The first category of influencing factors are physiological variables related to the biological processes that maintain or disrupt a normal body function, including nutrition, existence of a pathology, energy levels, trauma, etc. Psychological influencers constitute the second category of influencing factors, and are variables related to one’s state of mind, mood, and affective reaction to a disease or illness, such as depression, and anxiety. Lastly, situational influencers are variables related to an individual’s physical and social environment, such as place of residence, educational background, social network, and support. In TUS, the three levels of influencing factors are inter-related, and impact the experience of symptoms (Lenz et al., 1997). In this theory, an individual can experience one or more symptoms simultaneously, and each symptom is characterized by its duration, intensity, quality, and distress, the latter reflecting the extent to which an individual is bothered by the symptom. According to Lenz et al. (1997), two individuals can experience a symptom at the same intensity, or duration, but experience a different level of distress, depending on their individual interpretation of the experience of symptom. This aspect is also the one that impacts an individual's quality of life most.

The four dimensions of a symptom, in their turn, affect the individual's functional and cognitive performance. Functional performance is operationalized as an individual's physical and social function. That is, the extent to which one is able to carry out activities of daily living, fulfill work- and role-related tasks, and to participate in social interactions. Cognitive performance is operationalized as one's ability to carry out cognitive tasks, such as problem-solving, thinking, reasoning, and concentrating. Finally, according to TUS, there exists a feedback loop, or a reciprocal relationship between the symptom itself and its influencing factors, between performance and symptom experience, and between performance and influencing factors. That is, a decline in daily activity as a result of any symptom, can in turn, deteriorate one's physiological well-being (influencing factor), further worsening the symptom experience (Lenz et al., 1997).

To explore the extent to which TUS was used as a framework in studies examining fatigue in older individuals, a search was conducted in PubMed and CINAHL. The keywords used were "Theory of unpleasant symptoms" AND "fatigue" AND "older adults OR older individuals OR seniors OR geriatrics OR elderly", and no year restrictions were applied. Results showed that TUS has been widely used in a number of chronic diseases, including breast cancer, kidney disease, heart disease, and lung disease, and has been examined in relation to one or more symptoms simultaneously.

TUS has guided the examination of the prevalence of, and the correlation between a number of symptoms in several studies. Almutary et al. (2017) examined a cluster of symptoms such as fatigue, restless legs, fluid volume, sexual drive, and others, commonly reported in chronic kidney disease (CKD). In another study, Reishtein (2005) investigated dyspnea, sleep difficulty, and fatigue in relation to functional performance in individuals with chronic obstructive pulmonary disease (COPD). In individuals with rheumatoid arthritis (RA), the cluster of symptoms consisted of pain, fatigue, and depression (Oh et al., 2018). In a fourth study, symptoms examined included fatigue and insomnia (Redeker et al., 2000). Lastly, Schreier et al. (2019) examined the correlation between pain, fatigue, anxiety, and sleep disturbance. In the latter study, only pain was examined for intensity or interference. Other symptom characteristics such as duration or distress were not examined for fatigue, sleep disturbance, and anxiety.

The way in which influencing factors were operationalized varied across studies. Physiological factors were operationalized as disease stage, number of comorbidities (Almutary et al., 2017), medications, (Eckhardt et al., 2014), age, gender, sleep (McCann & Boore, 2000), immune system function (Kim et al., 2014), and laboratory data, including absolute neutrophil count, hemoglobin and/or albumin levels (Kim et al., 2015; Liu, 2006). Psychological influencing factors were operationalized as one or more of the following: psychological distress (Almutary et al., 2017), depression/anxiety (Eckhardt et al., 2014; Kim et al., 2014; Kim et al., 2015; Liu, 2006; McCann & Boore, 2000; Redeker et al., 2000), fighting spirit (Kim et al., 2015), mood, and stress (Oh et al., 2004). Lastly, situational factors were operationalized as gender (Almutary et al., 2017; Liu, 2006), age (Liu, 2006), sleep quality (Oh et al., 2004), educational level, income or employment

(Eckhardt et al., 2014; Liu, 2006), family/social support (Kim et al., 2014; Kim et al., 2015; So et al., 2013), marital status (McCann & Boore, 2000), and religion (Liu, 2006).

Obviously, the categorization of age, gender, and sleep was not consistent across studies. In some studies, these were considered physiological factors (McCann & Boore, 2000), while in others, they were examined as situational factors (Almutary et al., 2017; Liu et al., Oh et al., 2004). Furthermore, unlike other researchers, Kim et al. (2015) did not categorize sociodemographic (age, religion, education) and clinical factors (stage and type of cancer) into situational or physiological factors. Instead, these factors were examined separately in relation to fatigue.

Some studies examined the extent to which influencing factors influence the different dimensions of symptom experience, while others examined the influence of a symptom(s) on outcomes, or investigated both influencing factors and outcomes in relation to the symptom(s). In the study by Reishtein (2005), the relationship between a cluster of symptoms (dyspnea, sleep difficulty, fatigue) and functional performance was examined. In the study by Oh et al. (2018) involving subjects with rheumatoid arthritis (RA), TUS was modified such that the outcome was quality of life (QOL), and not performance (Oh et al., 2018). This was also true in three other studies involving women with breast cancer (Hsu & Tu, 2014; Kim et al., 2015; So et al., 2013), and coronary heart disease (Eckhardt et al., 2014), where the outcome of interest was QOL. In the study by Hsu and Tu (2014), functional ability, a performance-based outcome in TUS, was found to be a mediator between fatigue and QOL.

To sum up, TUS has been used as a conceptual framework to examine the association between fatigue, either alone or with co-existing symptoms, and different influencing factors highlighted in TUS. Fatigue outcomes examined included performance, mainly functional, and/or quality of life. Cognitive performance was not included as one of the outcomes in any of the above-mentioned studies. In addition, the focus was on one particular chronic disease, and not all aspects of the theory were examined. That is, most studies either examined influencing factors, or outcomes in relation to the symptom. In this review, influencing factors and performance-based outcomes of all levels (physical, functional, cognitive) were examined in relation to fatigue, with no focus on any particular chronic disease.

Methods

The concepts of TUS guided the search strategy which aimed to explore "influencing factors" and consequences related to "performance" or any other outcome. PubMed, CINAHL, Web of Science, and Psych Info were searched using the following search strategy: "fatigue" AND "risk factors OR influencing factors OR predictors OR correlates OR antecedents OR causes OR outcomes OR impact OR consequences" AND "older individuals OR older adults OR seniors OR geriatrics OR elderly". Additional articles were identified through snowball sampling. Research studies were limited to those published in the last 10 years, and in English language. Despite fatigue being one of the attributes of frailty, studies examining "frailty" correlates were excluded, as findings could not be directly linked to fatigue. Similarly, articles were excluded if they examined "fatigability", which is beyond the scope of this review. Articles satisfying the eligibility criteria from the first strategy were grouped and organized into a matrix (Garrard, 2017) as either physiological, psychological, or situational risk factors. Consequences of fatigue were grouped into performance-based outcomes highlighted in TUS, which included physical, functional, and cognitive levels. Additional non-performance-based outcomes such as quality of life and perceived health, which were not part of TUS, are also presented.

Evidence Related to Physiological Risk Factors

Physiological factors refer to variables related to the biological processes that occur at the cellular or system level in individuals, in order to maintain proper body function. In this literature review, physiological factors included age, number of comorbidities, gender, sleep, and pain. Findings on these variables were grouped, and presented below.

Age was negatively and weakly correlated (r = -.02, $p < 0.05$) with fatigue in male and female older adults with Multiple Sclerosis (MS) (Salter et al., 2019), as well as in cancer survivors (Bevilacqua et al., 2018), indicating that older individuals experience less fatigue. However, in individuals who had experienced a myocardial infarction, those reporting fatigue were significantly older than those without fatigue (Crane et al., 2016). This was also supported in another study involving women, whereby those above the age of 75 were almost five times more likely to experience fatigue (OR = 4.81) than their younger counterparts (Jing et al., 2015). However, researchers in another study on women with breast cancer women reported a non-linear association between age and fatigue, whereby women in the 61-70 age group had the highest fatigue scores compared to younger, or older women (Muszalik et al., 2016).

Number of comorbidities was another variable examined in multiple studies. There was a significant difference in number of comorbidities between fatigued and non-fatigued individuals in two studies (Horne et al., 2019; Lin et al., 2015). Number of comorbidities was also positively correlated with fatigue ($r_S = .18$, $p < 0.05$) (Silva et al., 2011), and was a significant predictor of fatigue (Kim & Son, 2019). Lastly, in a study including women exclusively, this positive association between number of comorbidities and fatigue was also supported. Women with breast cancer who had one comorbidity had 1.83 times higher risk of fatigue compared to those with no comorbidities, and this risk was threefold with two or more chronic diseases (Jing et al., 2015).

Regarding gender-fatigue association, being female was a significant predictor of higher fatigue scores in individuals with MS (Salter et al., 2019), cancer survivors (Bevilacqua et al., 2018), and older individuals in general (Chou, 2013; Soyuer & Şenol, 2011). In another study, it was evident that gender moderated the relationship between number of comorbidities and fatigue. Self-reported comorbidities explained 9% of the variance in fatigue scores in females, but was not a significant predictor in males (Horne et al., 2019).

In what relates to sleep, there was a positive correlation between sleep and fatigue. In two studies comparing fatigued and non-fatigued individuals, sleep disorders were significantly more prevalent in individuals in the former group (Hawker et al., 2010; Loh et al., 2018). Sleep was also found to be significant predictor of fatigue in older adults generally (Barak et al., 2020), and those with diabetes (Kim & Son, 2019). Lastly, a two-month improvement in sleep predicted a long-term decline in fatigue levels in individuals with arthritis (Vitiello et al., 2014).

Pain intensity was another biophysiological factor significantly associated with fatigue. Findings of all studies aligned in terms of the significant positive association between fatigue and pain. This was supported in community dwelling older adults

(Crowe et al., 2017), individuals with disabilities above the age of 65 ($r = .44$, $p < 0.01$) (Teshale et al., 2019), Multiple Sclerosis (Salter et al., 2019), Rheumatoid Arthritis (Oh et al., 2018), and in older women with breast cancer ($r = .58$, $p < 0.001$) (Overcash et al., 2018; Schreier et al., 2019).

Based on the evidence, it can be inferred that age, gender, and number of comorbidities are risk factors for fatigue, as the opposite cannot be true due to temporal precedence of these variables to fatigue. However, it is important to note that the association between fatigue and the other two variables, sleep and pain, does not infer causality. None of the studies examining this association was a randomized control trial, which implies that the relationship between fatigue and these two variables can be bi-directional.

Evidence Related to Psychological Risk Factors

Findings across multiple studies were consistent in terms of the relationship between fatigue and psychological variables. Depression and anxiety were significantly correlated with fatigue scores in four studies (Chou, 2013; Karakurt & Ünsal, 2013; Overcash et al., 2018; Silva et al., 2011). Similarly, comparing fatigue scores across different levels of depression and anxiety separately, individuals with moderate or severe depression or anxiety had significantly higher fatigue scores compared to the low anxiety/depression group (Crane et al., 2016; Polikandrioti et al., 2018; Salter et al., 2019; Soyuer & Şenol, 2011). Depression was also found to be a significant predictor of worse fatigue in two studies (Barak et al., 2020; Kim & Son, 2019), despite a low predictive power ($R^2 = .002$ & $B = 0.19$ respectively). Note that, in the study by Barak et al. (2020), depression was not a significant predictor of fatigue when examined simultaneously with sleep as a risk factor of fatigue.

Despite the strengths in the latter study which included a large sample size, proportionate representation of males and females, and transparency about the proportion of missing data, there were a number of limitations that were not explicitly acknowledged. The presence of underlying sleep disorders, the use of sleep medications, stress, caffeine intake, and other sleep-related factors were not accounted for when examining the relationship between sleep and fatigue. Similarly, covariates that could have influenced depression-fatigue association, like social support, physical activity, depression medications, and others were not examined. Also, only the frequency of sleep problems was analyzed, without a clear definition of what constituted sleep problems.

Another limitation was the unidimensional assessment of the variables of interest. Fatigue, the dependent variable, was measured in terms of severity only, despite fatigue being a multidimensional concept (frequency, quality, duration). Similarly, sleep problems were measured in terms of frequency, while depression in terms of whether or not there was a primary diagnosis of depression or not. Lastly, sample characteristics such as educational level, race/ethnicity, and number of comorbidities were not included, which would have contributed to the generalizability of findings. Sample characteristics presented included age, gender, and marital status. Note that, these characteristics were not included in the analyses to account for their covariance, which could have significantly influenced study findings. These limitations represent a threat to the internal and external validity of findings, and thus should be accounted for when interpreting study findings.

Evidence Related to Situational Risk Factors

Situational factors are personal and lifestyle factors that influence fatigue levels experienced by older individuals. Situational factors identified in the literature included education, economic status, race/ethnicity, marital status, medication use, hospital admission rate, and physical activity. Education status was correlated with fatigue in all, but one study. Five studies showed that individuals with higher levels of education had significantly lower fatigue levels (Jing et al., 2015; Karakurt & Ünsal, 2013; Kessing et al., 2015; Lin et al., 2015; Muszalik et al., 2016), which did not hold true in the study by Karakoc and Yurtsever (2010). Economic status was positively associated with fatigue scores: employed individuals, or those in a "very good" economic status, had significantly less fatigue compared to those who were unemployed (Kessing et al., 2015), or to those in "good", or "difficult" economic standing (Muszalik et al., 2016). Race and ethnicity were included as covariates in studies in which fatigue was a dependent variable (Franklin & Harrel, 2013; Lin et al., 2013), suggesting that there is a correlation between race and fatigue. However, Bevilacqua et al (2018) found no association between race, ethnicity and fatigue, contrary to the results of the study by Chou (2013), whereby non-Whites were more likely to report chronic fatigue than Whites.

Strengths of the study by Chou (2013) included the large sample size, the weighting of data to represent the population of older adults in England, assessment of collinearity among fatigue correlates, and accounting for the covariance of age, gender, race/ethnicity, and education in the logistic regression analyses. However, the study had a number of limitations, some of which were acknowledged by the researcher, such as cross-sectional nature of data which cannot establish causality, the use of self-reports for medical conditions, and the low response rate of 57%.

Limitations not explicitly stated in the latter study included the exclusion of all participants with any missing data, without examining whether key variables such as depression level, anxiety, and suicidal attempts were significantly different between respondents and non-respondents. Doing so would have minimized bias in findings, and informed whether the sample is representative of this population. In addition, there was a risk for social desirability bias, specifically in the question related to suicidal attempts, which has been extensively documented in the literature (Friedman et al., 2004; Linehan & Nielsen, 1983; van de Mortel, 2008). Additionally, internal consistency of the data in the included sample was not measured, and thus data around the reliability of the used measures in this sample was lacking. Covariates like social support, counseling, financial status, and others that could have mediated the relationship between mental disorders and fatigue were not examined. Lastly, the researcher concluded that chronic fatigue was more prevalent in non-whites compared to whites, when findings reflected a higher proportion of white older individuals (94%) in the group with chronic fatigue compared to non-whites (5.1%), which rendered findings confusing.

Findings on marital status varied greatly. Two studies involving older men and women showed no significant difference in fatigue scores between married, widowed, single, or divorced individuals (Bevilacqua et al., 2018; Horne et al., 2019). The study by Karakurt and Ünsal (2013) supported these findings, with the exception that in their study, widowed individuals experienced worse fatigue. This was contrary to findings of another study in which married older individuals experienced significantly higher fatigue than unmarried ones (Mollaoglu et al., 2011). Lastly, two studies involving either men or women exclusively showed that single men and single women have higher odds of fatigue (*OR* = 1.94 and *OR* = 1.42, respectively) compared to their married counterparts (Jing et al., 2015; Lin et al., 2015).

Sensory impairment (SI), including hearing and vision, was another risk factor of fatigue. Despite being linked to physiological factors, SI was categorized as a situational factor in this review, as the burden of SI is manifested in a social context. Unlike other chronic conditions which independently impact the individual's experience of symptoms, the repercussions of hearing problems are dependent upon social interactions, and hence its classification as a situational factor. Alhanbali et al. (2017) found that individuals with HI, who were aged between 55 and 85, reported significantly higher fatigue levels compared to those without HI. In another study, individuals with HI experienced severe fatigue more frequently than the expected normative data (Hornsby & Kipp, 2016). This might be, in part, due to the significant increase in listening effort these individuals exert when interacting with others, compared to those with normal hearing. This was supported in the study by Alhanbali et al. (2017), where listening effort was significantly correlated with fatigue scores. In another study, hearing handicap - a measure of the impact of HI on the emotional and social adjustment of older individuals – was significantly associated with general, emotional, physical, and mental fatigue (Hornsby & Kipp, 2016). Note that, in the same study by Hornsby and Kipp (2016), the degree of HI per se was not significantly associated with fatigue. In what relates to vision impairment, results of one study have shown that there is a positive association between visual symptoms and fatigue (Berthold Lindstedt et al., 2019). However, evidence supporting this relationship remains limited.

Other situational factor included frequency of hospitalization and medication use. In a study, admission rates were significantly higher in older individuals experiencing fatigue and weakness (55%), as compared to controls (36.4%) (Bhalla et al., 2014). Regarding medications, diuretics, nitrates, and psychotropic medications were associated with worse fatigue scores (general and exertional), while exertional fatigue scores were better in individuals taking beta-blockers. Other medications such as ACE inhibitors, statins, aspirin, and calcium antagonists did not significantly impact fatigue scores (Kessing et al., 2015).

A number of studies investigated the influence of physical activity (PA) or exercise on fatigue. A study examining the correlation between PA and fatigue cross-sectionally and longitudinally found a significant correlation, at baseline and at the 18-month follow-up between PA (measured in steps/day) and fatigue ($r = .19$, $p < 0.05$ – higher scores indicating less fatigue) (Nicklas et al., 2016). Similarly, other studies supported the correlation between PA and perceived fatigue ($r_S = -.38$, $p < 0.01$) (Silva et al., 2011), and total fatigue scores (Kwag et al., 2011; Lin et al., 2015). PA was shown to be a predictor of lower fatigue scores in older individuals, with a regression coefficient $\beta = -.52$, $p < 0.01$ (Kwag et al., 2011).

Note that, none of the studies was a randomized control trial. Hence, the relationship between fatigue and physical activity can be bi-directional. The former variable was shown to impact fatigue levels significantly, but the opposite can also be true. It can be argued that older individuals experiencing fatigue would eventually increase their periods of rest, decrease their PA, and withdraw from social activities. This is an important consideration, as these variables could potentially be positively influenced by proper fatigue management.

Consequences of Fatigue

In alignment with the Theory of Unpleasant Symptoms (TUS), fatigue consequences were grouped into performance-based outcomes, consisting of functional performance (physical and social), and cognitive performance. Regarding physical performance, findings of a study showed that fatigue scores were negatively correlated with activities of daily living (ADL) ($r = .45$) (Karakurt & Ünsal, 2013), as well as functional independence (Soyuer & Şenol, 2011). In older women with breast cancer, fatigue significantly predicted functional decline from baseline to 12 months post-chemotherapy, and a slower recovery to baseline function levels (Hurria et al., 2019).

From a social performance standpoint, fatigue correlated positively with physical and social disability ($r = .45$, $p < 0.001$), with a moderate effect size (Mollaoglu et al., 2011). Researchers in two studies found a significant negative correlation between social support (informational, security, emotional, and perceived) and fatigue ($-.78 < r < -.65$, $p < 0.001$) (Karakoc & Yurtsever, 2010; Kwag et al., 2011). In another study, individuals with MS who had worse fatigue scores experienced a decline in their ability to participate in social roles and activities (Salter et al., 2019), which also influenced their satisfaction with their social ability. Lastly, in a study by Franklin and Harrel (2013), fatigue predicted 3% of the variance in satisfaction with social ability, with a regression coefficient of $\beta = -.18$, $p < 0.05$.

In what relates to cognitive performance, findings of a study involving cognitively intact older adults showed a negative association between fatigue and cognitive abilities, including memory, reasoning, speed of processing, and every day problem-solving (Lin et al., 2013). Similarly, in another study, higher fatigue levels predicted lower attention/processing scores, in addition to executive function, and psychomotor speed, with small to moderate effect sizes (Banerjee et al., 2020). However, in the latter study, fatigue levels did not predict memory, learning, and language domains. In another study, fatigue was not significantly correlated with Mini-Cog scores either, which is a brief measure of cognitive impairment (Overcash et al., 2018).

In addition to the performance-based outcomes of fatigue based on the Theory of Unpleasant Symptoms (TUS), consequences of fatigue included perceived health, and quality of life (QOL). Higher fatigue levels predicted higher health impairment ($\beta = .43$, $p < 0.01$), and was associated with lower levels or perceived health in community-dwelling older women (Silva et al., 2011). In addition, in older individuals with myeloproliferative neoplasms, those experiencing higher fatigue had a significantly lower quality of life (Tolstrup Larsen et al., 2018). Similarly, in the study by Schmidt et al. (2018), fatigue was one of the most significant predictors of QOL ($\beta = -.22$, $p < 0.05$). Another predictor of QOL was social performance (Schmidt et al., 2018), which was also shown to be an outcome of fatigue in other studies (see above).

In addition to these outcomes, TUS highlights a relationship between the experienced symptom, fatigue, and its influencing factors, whereby the former impacts its influencing factors through a feedback loop. This is supported by the fact that evidence regarding the association, and not the causality, between certain risk factors and fatigue has been supported in the literature. Also, despite being examined as risk factors, some of these variables have also been examined as consequences of fatigue. For example, in the study by Franklin and Harrel (2013), higher fatigue scores predicted higher depression ($\beta = .43$, $p < 0.01$), and significantly increased odds of poor sleep (*OR* = 1.57) (Overcash et al., 2018). Hence, it can be argued that risk factors or predictors such as physical activity, hospital admission rate, depression, pain, and sleep not only influence fatigue, but are also impacted by this symptom.

Fatigue impacts older individuals on multiple levels, including physical function, ability to fulfill social roles, as well as cognitive function. In addition, it negatively influences one's perception of health, and quality of life. Hence, preventing or managing fatigue effectively is key for the prevention of these undesirable consequences that significantly impact older individuals' state of mind and body.

Summary

This review highlighted the influencers of fatigue, its outcomes, and presented an overview of the use of the Theory of Unpleasant Symptoms (TUS) in different populations and research areas. The influence of a number of risk factors on fatigue was supported. Physiological influencing factors included age, number of comorbidities, gender, sleep, and pain, although findings on age-fatigue association did not align. There was consensus in findings in what relates to psychological factors, whereby depression and anxiety were shown to be significant predictors of fatigue in all studies. Lastly, findings were in alignment on situational risk factors like education, economic status, sensory impairment (SI), medication use, rate of hospital admission, and physical activity, but not on race/ethnicity and marital status.

TUS-based consequences related to fatigue included performance outcomes on physical, social, and cognitive levels. Physical performance was operationalized as the ability to perform daily activities and functional independence, while social performance as a decline in ability to perform social roles and activities, as well as satisfaction with social roles. Findings on physical and social performance outcomes were in alignment, unlike that of cognitive performance. In the case of the latter, some studies found a positive association between fatigue and memory, which did not hold true in other studies. Lastly, other consequences of fatigue that do not reflect performance per se were also examined in relation to fatigue, and included perceived health and QOL. As discussed above, some influencing factors of fatigue can also be regarded as fatigue outcomes. This is important, as it further builds on the significance of proper fatigue management, which would help minimize the burden of multiple outcomes associated with the experience of fatigue.

Studies using TUS as a theoretical framework have focused on one particular population, which limits generalizability. As mentioned earlier, fatigue is a manifestation of underlying physiological processes that are common in multiple chronic conditions. Hence, examining fatigue correlates in more than one chronic disease is plausible. This is further supported by the fact that findings on risk factors and consequences of fatigue were in alignment, despite being examined separately in different chronic conditions.

In addition, researchers using TUS in more than one study had modified the outcome of interest to represent psychological or subjective outcomes like depression or quality of life, rather than objective performance measures presented in the theory. One study showed that functional performance, one of the outcomes in TUS, was a mediator between fatigue and QOL. However, the mediating role of the other TUS outcomes (cognitive performance, social performance) were not examined as potential mediators. The inclusion of QOL as an additional outcome is plausible based on the findings of this literature review as well, as not all consequences of fatigue were performance-based. However, rather than the substitution of performance with QOL, its addition to TUS would help identify and treat fatigue outcomes associated with QOL. For example, in one study, social performance was found to be an outcome of fatigue, and a risk factor for a poor QOL. Thus, examining the mediating role of all performance-based outcomes (physical, functional, cognitive), and perceived health ratings on QOL would be valuable in enhancing the QOL of older individuals experiencing fatigue.

Another gap identified in this review was the examination of some, but not all, parts of the theory. Some studies focused on influencing factors alone, without examining the consequences associated with fatigue (Liu et al., 2006; Reishtein, 2005). In other cases, fatigue consequence was modified to QOL, with focus on only one particular risk factor (So et al., 2013), or with a focus on QOL alone, without examination of risk factors (Oh et al., 2018). Thus, a comprehensive model investigating all risk factors and performance outcomes of fatigue highlighted in TUS, without a focus on one particular chronic disease, is lacking. If examined, this would help direct the attention of healthcare providers, family members, and carers to more than one risk factor, significantly increasing chances of successful prevention and management of fatigue in older adults with different chronic diseases, in addition to the disease-specific triggers that vary among older individuals. Also, identifying the extent to which fatigue influences performance and subjective outcomes would inform care providers about situations in which screening for fatigue would be recommended.

Therefore, the proposed research study will help fill in these gaps through the following. First, all influencing factors (physiological, psychological, situational) will be examined in relation to fatigue in older individuals, without a focus on a chronic disease in particular. This simultaneous examination would account for the covariance between different predictors of fatigue which were not included in previous studies, and help identify the proportion of variance explained by the included risk factors, and provide a sense of the unexplored variables for future research considerations. Second, variables around which findings did not align (age, race/ethnicity, marital status) will be included, which would help clarify the ambiguity around the association between fatigue and these variables. Third, the strength of the relationship between fatigue and all performance outcomes (physiological, functional, and cognitive), in addition to perceived health and quality of life will be examined. Third, the mediating role of all outcomes on the relationship between fatigue and quality of life will be examined. Accordingly, interventions can be directed to improve outcomes that strongly predict QOL, which would improve QOL of older individuals.

CHAPTER 3

METHODS

Introduction

Evidence from the previous chapter highlighted gaps and inconsistencies in findings, upon which research questions and hypotheses were identified for further investigation. In this chapter, the research questions and hypotheses guided the study, and the statistical methods used for examining the hypotheses are presented. In addition, since a secondary data source was used to answer the research questions, an overview of the secondary analysis method, and a detailed description of the dataset is presented.

Research Design

A non-experimental, quantitative, cross-sectional exploratory study design was utilized through secondary data analysis (SDA), using the Patient-Reported Outcomes Measurement Information System-Health Utilities Index (PROMIS-HUI, Version 1.1) (Cella, 2017). In SDA, the researcher analyzes an existing dataset for a purpose other than that for which data was collected in the first place. SDA has become firmly embedded in nursing research as a means to move the nursing profession forward, improve patient care, health care delivery, and health policy (O'Connor, 2020).

Data Source

This is a publicly available dataset that consists of 150 items on socio-demographic data, comorbidities, PROMIS global form, PROMIS profile measures on seven domains, consisting of emotional distress (ED), fatigue, physical function, pain, sleep, social participation, and cognition, in addition to the HUI. PROMIS profiles domains were administered in a random manner, but the instruments within each domain, as well as the items in the HUI were administered in a fixed order. However, items within individual PROMIS profile instruments were administered in a random order (See Table 3.1).

Table 3. 1: ***Instruments used in PROMIS-HUI Dataset.***

Domain	Instrument	Item
	Socio-demographic and clinical questions	12
	PROMIS Global Health	10
Emotional Distress	PROMIS ED-Anxiety	8
	PROMIS ED-Depression	8
	PROMIS ED-Anger	8
Fatigue	PROMIS Fatigue (Experience)	8
	PROMIS Fatigue (Impact)	8
Physical Function	PROMIS Physical Function (v1.1)	18
Pain	PROMIS Pain Intensity	3
	PROMIS Pain Interference	9
Sleep	Sleep Disturbance	8
	Sleep-related Impairment	8
Social	PROMIS Ability to Participate in Social Roles and Activities (v2.0)	8
	PROMIS Satisfaction with Social Roles and Activities (v2.0)	8
Cognition	PROMIS Cognitive Function	8
	PROMIS Cognitive Function-Abilities	8
	Health Utilities Index (HUI)	17
	Total	157

Study Sample

Recruitment

Participants in this study were recruited from an online internet survey company, "Opinions 4 Good" (Op4G). This platform maintains a panel of 152,000 respondents of different demographic backgrounds that is readily available for researchers (Opinions 4 Good, 2020). For PROMIS-HUI, respondents were selected such that they were representative of the 2010 U.S. Census, despite analysis later showed that the selected sample was sicker than the general U.S. population (Hays et al., 2016). Eligibility criteria included being 18 years of age or older, English-speaking, part of the U.S. general population, and enrolled in the Op4G panel. To recruit participants, an email was sent to members of the panel notifying them of a new survey opportunity. Interested participants filled out a consent form, followed by a survey consisting of nearly 150 items, and were compensated with an incentive provided by Op4G, which did not exceed 10 USD. The study was approved by the appropriate Institutional Review Board, the details of which were not explicitly mentioned.

Demographics

The original sample in the dataset consisted of n = 3000 respondents, 1458 (48.6%) of which were males, and 729/3000 (24.3%) were individuals above the age of 60. Only 16.6% of respondents were of Hispanic/Latino ethnic backgrounds, 16.6% were black race, 9.3% were Asian, 1.6 % were American Indian, Alaska Native, Native Hawaiian or other Pacific Islanders, while the remaining 2.6% were of other/mixed races. In terms of geographic location, the majority (37%) were from the South, the minority was from the Northeast (18%), while the rest were from the West (33%) and the Midwest (20%). Only 14% of participants had less than a high school degree, while the rest varied between having a high school degree (31%), vocational program/ associate/technical degree (28%), or a college/advanced degree (27%). Of the chronic diseases/health history reported, hypertension was the most common (34%), followed by Rheumatoid Arthritis (RA) (20%), and rest of chronic diseases varied between asthma, migraines, diabetes, angina, cancer, lung, heart, liver, and/or kidney disease (Hays et al., 2016). For this study, only individuals above the age of 60 were included, as all the research questions pertained to fatigue in older individuals.

Study Measures

The independent variables hypothesized expected to influence fatigue included physiological, psychological, and situational factors. Fatigue, a multidimensional symptom, was also hypothesized to predict performance outcomes, perceived health, and quality of life (QOL). The operational definition of these variables, and the corresponding items that measure them are presented in the Table 3.2. (Refer to Ch.1 for theoretical definitions).

Table 3. 2: ***Operational Definitions/Items Measuring Variables in this study***

	Domain	Variable	Type	Operational Definition (no. of items)
Influencers	Physiological	Age	Interval/ratio	Age in years
		Gender	Nominal	Male/female
		No. of comorbidities	Interval/ratio	Total number of reported chronic diseases (high blood pressure, chest pain, coronary artery disease, heart failure, heart attack, stroke, liver disease, kidney disease, arthritis, headaches/migraines, asthma, lung disease, diabetes, cancer, depression, anxiety, alcohol/drug problem, sleep disorder, HIV, spinal cord injury, multiple sclerosis)
		Pain	Interval/ratio	PROMIS pain intensity (3) PROMIS pain interference (9)
		Sleep	Interval/ratio	Sleep disturbance (8) Sleep-related impairment (8)
	Psychological	Depression Anxiety	Interval/ratio Interval/ratio	PROMIS ED-Depression (8) PROMIS ED-Anxiety (8)
	Situational	Race	Nominal	White Black or African-American Asian American Indian or Alaska Native Native Hawaiian or Pacific Islander Other
		Marital Status	Nominal	Never married Married

				Previously married (separated, widowed, divorced) In a committed relationship
		Education	Nominal	Below high school High school/GED Some college/technical degree College degree Advanced degree
		Hospitalization	Interval/ratio	Frequency of hospital stay in the past 12 months (1)
		Sensory impairment	Interval/ratio	<u>Hearing</u> Able to hear what was said in a group conversation with at least three other people (1) Able to hear what was said in a conversation with one other person in a quiet room (1) <u>Vision</u> Able to see well enough to read a newspaper (1) Able to see well enough to recognize a friend on the other side of the street (1)
Symptom	Fatigue		Interval/ratio	PROMIS fatigue experience (8) PROMIS fatigue impact (8)
Outcomes	Performance	Functional performance	Interval/ratio	<u>Physical</u> PROMIS physical function (18) <u>Social</u> PROMIS ability to participate in social roles and activities (8) PROMIS satisfaction with social roles and activities (8)
		Cognitive performance	Interval/ratio	PROMIS cognitive function (8) PROMIS cognitive function-abilities (8)
	Perceived health		Interval/ratio	Overall physical health (1) Overall mental health (1)
	Quality of life		Interval/ratio	Poor, fair, good, very good, excellent

Race, marital status, educational level, as well as gender (physiological factor) were nominal level variables. All others were either interval/ratio level variables, or ordinal level variables treated as continuous.

Non-PROMIS continuous measures included age, number of comorbidities, hospitalization, sensory impairment (SI), perceived health, and QOL. Age was based on a self-report of the number of years lived, while number of comorbidities was based on the presence (1) or the absence (0) of the listed chronic diseases. Hospitalization was operationalized as self-reports of the frequency of hospital stay in the last 12 months. SI was based on the score of four items reflecting vision impairment (2 items) and hearing impairment (2 items). Scores for SI ranged between 0 and 4, higher scores reflecting a higher level of SI. Perceived health was based on the score of two items that assess subjective ratings of physical and mental health. Each of these items was based on a 5-point Likert scale, resulted in a summative score ranging from 0 to 10. Lastly, QOL was based on one item only, the response to which ranges from "poor" to "excellent". This variable was treated as a continuous variable. (Table 3.2).

All remaining variables were measured using PROMIS measures. These are based on 5-point Likert scales, whereby higher scoring reflects more of the measured concept. In some cases, higher scores reflect a desirable outcome (physical function, social participation), while in others, and undesirable outcome (fatigue, pain). PROMIS measures are publicly available, and can be accessed at Intro to PROMIS (healthmeasures.net).

Fatigue

A total of 16 items were selected from PROMIS item bank - v.1.0 – fatigue, which included eight items on fatigue impact (FATIMP3, FATIMP16, FATIMP21, FATIMP30, FATIMP33, FATIMP39, AN3), and eight items on fatigue experience (FATEXP18, FATEXP20, FATEXP35, FATEXP40, FATEXP41, HI7, HI12). Response options included were "not at all" (1), "A little bit" (2), "Somewhat" (3), "Quite a bit" (4), "Very much" (5). The reliability and construct validity of PROMIS-fatigue short forms have been supported in individuals with heart failure, chronic obstructive pulmonary disease, back pain, arthritis, depression, and cancer (Cella et al., 2016; Flynn et al., 2015). The total score of these 16 items, combined, was used as the operational definition of fatigue in this study.

Pain

PROMIS short form v1.0 - pain intensity 3a, and nine items from the PROMIS item bank v1.1 - pain interference were used to measure pain in this PROMIS-HUI dataset. The selected nine items included PAININ3, PAININ8, PAININ9, PAININ10, PAININ11, PAININ14, PAININ22, PAININ31, and PAININ34. Research has supported the validity of the interference short form, comprised of 12 items (Broderick et al., 2013), but not that of the select items. In this study, pain was operationalized as the sum of scores of pain intensity and pain interference.

Sleep

This variable was operationalized as the sum of scores from sleep disturbance and sleep-related impairment items selected from their respective item banks. Items selected from sleep disturbance item bank for the original study included SLEEP20, SLEEP44, SLEEP67, SLEEP90, SLEEP108, SLEEP109, SLEEP115, SLEEP116. The other eight items from the item bank for sleep-related impairment included SLEEP6, SLEEP7, SLEEP10, SLEEP25, SLEEP27, SLEEP29, SLEEP30, and SLEEP33. The reliability and validity of sleep disturbance and sleep-related impairment item banks has been supported in individuals with different health conditions, with and without sleep problems (Yu et al., 2011).

Depression

Although depression and anxiety are indicators of emotional distress, each was included separately rather than as a total score of emotional distress. The reason for this is because depression has been extensively examined as a correlate of fatigue, both as a risk factor and as an outcome. Thus, one of the aims of this study was to examine the association between fatigue and depression particularly, excluding other domains of emotional distress. In this study, depression was operationalized as the sum of scores of the eight items selected from PROMIS item bank v.1.0 Emotional Distress – Depression, which included EDDEP04, EDDEP05, EDDEP06, EDDEP17, EDDEP22, EDDEP29, EDDEP36, and EDDEP41. PROMIS Depression item bank questions, and these selected eight items particularly, have demonstrated a high internal consistency, and adequate factor loadings (Nolte et al., 2019), which supports their reliability as depression measures.

Anxiety

This is another variable that constitutes PROMIS emotional distress. In this study, anxiety was operationalized as the total score obtained from responses to eight items selected from PROMIS emotional distress v.1.0 Emotional Distress – Anxiety item bank, including EDANX01, EDANX05, EDANX30, EDANX40, EDANX41, EDANX46, EDANX53, and EDANX54. PROMIS Anxiety short form has shown to be a reliable tool for the measurement of anxiety in older individuals of different ethnic groups (Teresi et al., 2016).

Social Performance

This construct was operationalized as the sum of scores on eight items selected from PROMIS ability to participate in social roles and activities (SRA) v.2.0 item bank, and eight items from PROMIS satisfaction with SRA v2.0 item bank. Ability to participate in SRA included SRPPER11CaPS, SRPPER14r1, SRPPER15CaPS, SRPPER18CaPS, SRPPER23CaPS, SRPPER26CaPS, SRPPER28r1, and SRPPER46CaPS. Satisfaction with SRA was measured by the following eight items: SRPSAT06r1, SRPSAT09r1, SRPSAT33r1, SRPSAT33CaPS, SRPSAT34r1, SRPSAT45CaPS, SRPSAT46CaPS, and SRPSAT49r1. Both item banks have shown to have good internal consistency in individuals with rheumatoid arthritis when administered in computer adaptive testing (Bartlett et al., 2015).

Physical performance

This was operationalized as the total sum of scores on 18 items selected from PROMIS v2.0 item bank - Physical function. These items included PFA16r1, PFA17, PFA29r1, PFA38, PFA44, PFA53, PFA54, PFB21r1, PFB33, PFA10, PFA11, PFA15, PFA21, PFA23, PFB9, PFB10, PFB24, and PFB42. The psychometric properties of PROMIS Physical Function item bank have been supported in a number of studies (Crins et al., 2018; Oude Voshaar et al., 2015).

Cognitive performance

This was operationalized as the total sum of scores on 16 items, eight of which were on cognitive function, and the rest were on cognitive function-abilities. The questions were chosen from PROMIS item bank - Cognitive Function v2.0, and PROMIS item bank – Cognitive Function-abilities v2.0 respectively. Questions from the latter item bank included PC10r, PC39r, PC1r, PC42r, PC36r, PC2r, PC8r, and PC26r, and those from the former question bank included PCCaPS12r, PC6r, PCCaPS3r, PC47_2r, PC43_2r, PC45_2r, PC44_2r, and PCCaPS22r. The reliability of PROMIS Cognition short form, which includes some of these items, has been supported (Fieo et al., 2016; Saffer et al., 2014).

Data Analysis Plan

A number of statistical analysis techniques were utilized to answer the research questions in this study, using Stata IC (2019, Version 16). Significance was set at $\alpha = .05$, and power was calculated after determining the final sample size (exclusion of individuals below the age of 60). Research questions examined in this study, and the statistical procedures conducted to answer each of the questions, are presented below.

Research Question 1

To what extent do each of the physiological (age, gender, number of comorbidities, pain, sleep), psychological (depression, anxiety), and situational (race, marital status, education, hospitalization, sensory impairment) factors predict fatigue in older individuals?

To answer this research question, multiple linear regression was used. All risk factors were entered simultaneously into the regression model as independent variables, and fatigue was entered as the dependent variable (see path model below). The beta coefficient of each of the variables were evaluated, as well as the R^2, which is a measure of the percentage of explained variance in fatigue by the risk factors included in the model 1.

Model 1

Age, gender, number of comorbidities, pain, sleep, depression, anxiety, marital status, education, sensory impairment, race, hospitalization → fatigue

Research Questions 2&3

To what extent does fatigue influence functional performance (physical and social), cognitive performance, perceived health, and quality of life (QOL)? Do the above-mentioned consequences of fatigue (i.e., physical performance, social performance, cognitive function and perceived health) mediate the effect of fatigue on QOL?

For research questions 2 & 4, path analysis was used to examine the consequences of fatigue, and the mediating effects of fatigue outcomes on the relationship between fatigue and QOL. Path analysis is a special case of structural equation models (SEM), and the two terms are used interchangeably in the literature. SEM involves the evaluation of path models, and may also include measurement models. Path models are those depicting the relationship between observed variables, while measurement models involve the evaluation of latent (unobserved) variables through their indicators (observed variables), using confirmatory factor analysis (CFA) (Lei & Wu, 2007). In this study, only path analyses were used, as all variables were observed, and not latent.

SEM represents an extension of general linear models (GLM), including regression, and ANOVA, which takes a confirmatory approach to test proposed hypothesis (Lei & Wu, 2007). SEM has a number of advantages over GLM questions. First, in the former, variables are not categorized as independent or dependent, as a variable can be examined both as an independent or a dependent variable in different equations of the model (Baron & Kenny, 1986). Second, SEM allows the examination of multiple mediators at once, which was the case of the proposed model in this study, rather than having to combine the results of multiple equations to assess for mediation (Gunzler et al., 2013). Third, SEM allows for the examination of the suggested model fit

(Gunzler et al., 2013), according to which relationships between variables can be modified, if needed, for a better model fit.

To answer research questions that address consequences of fatigue and mediating effects of these outcomes on QOL, path analyses was conducted in two models (model 2 and model 3).

Model 2

1) Fatigue → physical performance, social performance, cognitive performance, perceived health
2) Fatigue, physical performance, social performance, cognitive performance, perceived health → QOL

The resultant beta coefficients of the variables of interest and their significance were evaluated, which revealed both direct and indirect effects (mediation). In addition, the overall model fit was evaluated using Chi-square test (X^2), the comparative fit index (CFI), the Tucker–Lewis index (TLI), the root mean squared error of approximation (RMSEA), and the standardized root mean squared residual (SRMR). In model 3, paths evaluated in models 1 and 2 were combined, with the aim of examining the net impact of fatigue on its outcomes, and of the impact of outcomes on QOL, while controlling for all the risk factors previously examined.

Model 3

1) Age, gender, number of comorbidities, pain, sleep, depression, anxiety, marital status, education, sensory impairment, race, hospitalization → fatigue
2) Fatigue → physical performance, social performance, cognitive performance, perceived health

3) Fatigue, physical performance, social performance, cognitive performance, perceived health → QOL
4) Age, gender, number of comorbidities, pain, sleep, depression, anxiety, marital status, education, sensory impairment, race, hospitalization → physical performance, social performance, cognitive performance, perceived health, QOL

Similar to the model 2, beta coefficients and fit indices of model were be evaluated, and compared to those in model 2. The resultant differences in these coefficients were interpreted as being a result of the impact of all the covariates added to the final model. In other words, this model revealed a more accurate estimation of outcomes and mediation effects, and the acceptance or the rejection of their respective hypotheses. Figure 3.1 depicts the paths examined in this study (paths between covariates are excluded for simplicity).

Research Question 4

Does gender moderate the relationship between the number of comorbidities and fatigue?

For this research question, two-way Analysis of variance (ANOVA) was conducted, as both independent variables are nominal level measures. The outcome variable was fatigue, while number of comorbidities and gender were entered as independent variables. The number of comorbidities was dichotomized into “high” – more than two comorbidities – and “low” – less than two comorbidities. The effect of this moderation, if significant, was to be examined using eta squared (η^2).

Literature findings showed that being a female was a significant predictor of fatigue. However, only one study investigated the moderating role of gender on the relationship between the number of comorbidities and fatigue. The aim of this question was to further investigate the moderating role of gender, to support/refute previous findings.

Limitations

Secondary data analysis (SDA) has a number of advantages, for which researchers have been utilizing it as a methodology to answer different research questions. These include overcoming the challenge of recruiting populations that are hard to access, especially in times of a global pandemic, such as COVID-19, during which primary data collection would be targeted to research studies aimed at managing the pandemic. Other benefits of SDA include minimizing or avoiding respondent burden in over-researched groups, enhancing researcher objectivity, and saving time and cost (O'Connor, 2020). However, SDA has its limitations that need to be acknowledged. First, since data was collected for other purposes, some variables that would be important to answer the secondary research question can be missing (Cheng & Phillips, 2014). Second, the de-identification of respondent data, such as zip codes, occupation, and income could result in the elimination of important covariates that might have influenced findings. Third, the researcher analyzing the secondary data would not be aware of the specific nuances at the time of data collection, which can sometimes influence the way data is interpreted (Cheng & Phillips, 2014). Lastly, important information about data can be missed due to improper or lengthy documentation. The latter problem can be minimized by succinct documentation of data by the data collection team, and an in-depth examination of all relevant documentation by the user (Cheng & Phillips, 2014).

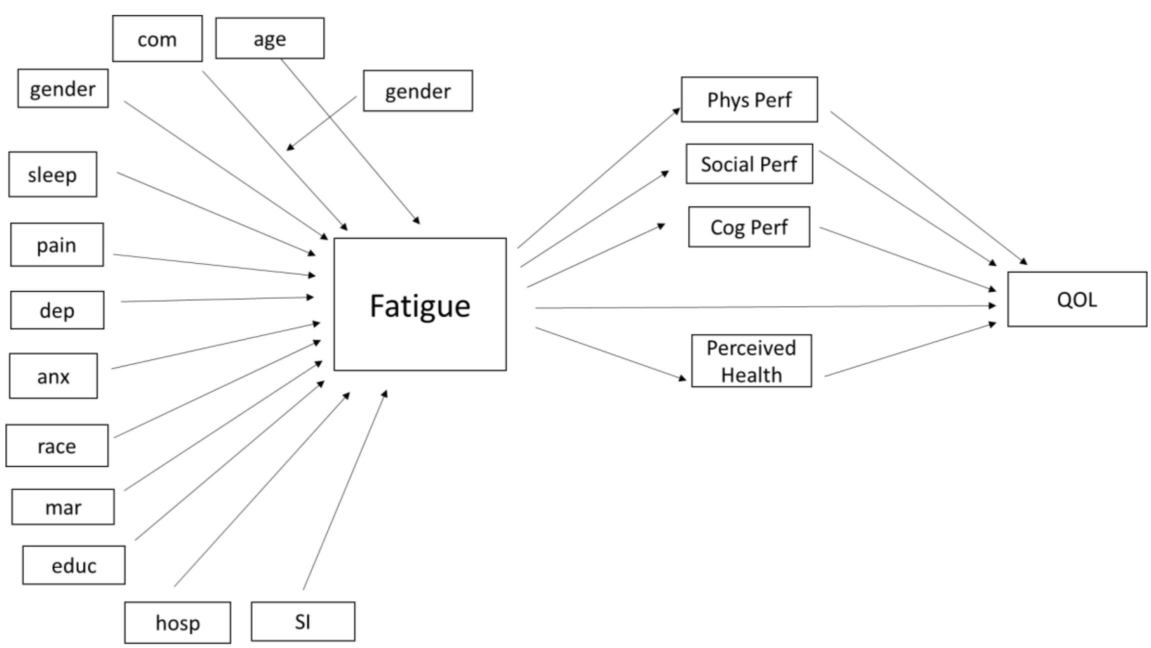
In what relates to the utilized data source, strengths of PROMIS-HUI dataset included a large sample size (N=3000), a proportionate representation of the U.S population based on 2010 U.S. Census, no specific inclusion or exclusion criteria (chronic diseases), which made findings generalizable to older individuals with different chronic diseases, and the use of reliable, valid items to measure various concepts. However, it was not clear whether items from various item banks were chosen randomly, and why short forms, the reliability and validity of which has been supported, were not chosen instead. Another limitation was the lack of data on the response rate, and a comparison between characteristics of respondents and non-respondents to examine for risk of non-response bias (Lindner et al., 2001).

In addition to SDA-related limitations, this research study had a number of limitations that should be acknowledged. First, the examined paths in this model do not infer causality, and thus results should be interpreted with this consideration in mind. Second, gender was a binary variable, a considerable limitation which hinders transferability of findings to non-binary older adults. Also, as highlighted in Chapter 2, medication use, physical activity, social support, and others have been examined as predictors of fatigue. However, this dataset did not include any data on these variables. Hence, these risk factors were excluded from this study. Third, this was a one-time survey, and thus test-retest reliability could not be examined. Fourth, although the sample was chosen such that it reflects the U.S Census Bureau 2010, there was still a risk of self-selection bias. Fifth, some variables of interest (QOL, hospitalization rate, perceived health) were operationalized as the score on one or two items, which limited their reliability. Lastly, the theory of unpleasant symptoms (TUS) depicts another level of relationship in which the symptom itself impacts its influencing factor through a feedback loop (refer to Chapter 1 for a diagram of TUS), and fatigue outcomes, in their turn, impact fatigue and the influencing factors. Based on the suggested feedback loops, fatigue, in its turn, would impact pain, sleep, depression, sensory impairment, and anxiety. In addition, fatigue outcomes would impact the experience of fatigue. These relationships were beyond the scope of this study, and thus were not examined.

Methods Summary

In this chapter, the research questions examined, the dataset used, the variables included, and the operationalization of the variables were presented. In addition, the data analysis utilized to answer each research question, and the limitations of the suggested methodology were presented and discussed. Results of the statistical analyses highlighted here are presented in Chapter 4, Results.

Figure 3. 1: *Diagram Representing the Proposed Fatigue Model*



Com: co-morbidities; dep: depression; anx: anxiety; mar: marital status; educ: education; hosp: hospitalization; SI: sensory impairment

CHAPTER 4

RESULTS

The purpose of this research study was to address four aims, based on the Theory of Unpleasant Symptoms (TUS), through secondary data analysis (SDA). The first aim was to identify the physiological, psychological, and situational risk factors of fatigue in older individuals with chronic diseases. Physiological factors identified in the literature included age, number of comorbidities, gender, pain, and sleep. Psychological factors included depression and anxiety, while situational factors included race, educational background, marital status, number of hospitalizations, and sensory impairment (SI), which included hearing and vision impairments.

The second aim was to examine effect of fatigue on cognitive, physical, and social performances, as well as perceived health, while the third aim was to investigate whether any of these outcome variables/consequences mediated the relationship between fatigue and quality of life (QOL). Lastly, the fourth aim was to examine whether gender moderates the relationship between number of comorbidities and fatigue.

In this chapter, data was examined for meeting assumptions of different statistical tests, after which various statistical analyses including Pearson's correlation, ANOVA, t-tests, multiple linear regression, and path analyses were conducted to answer the four research questions in this study. The tabular and graphical representations of the examined assumptions, as well the results obtained from statistical analyses, are presented below.

IRB Approval and Acquisition of Data

The institutional review board (IRB) at the University of Massachusetts determined that this project does not involve intervention or interaction with individuals, or does not use identifiable private information [45 CFR 46.102(f)(1), (2)]. Thus, no additional review was needed. The memorandum provided by the IRB to the researcher is included in Appendix A.

Dataset Preparation

PROMIS-HUI dataset was examined for missing data points. Descriptive analyses showed that missing data were not systematic, and do not represent a threat to the internal validity of study findings. Data for 20 participants were deleted due to inaccurate data entry (unrealistic numbers). Of the remaining sample of n=2980, those below the age of 60, and two participants who had missing data points for “quality of life” were excluded, rendering the final sample size n = 725. All statistical procedures in this study were carried out using Stata IC (2019, Version 16).

Assumptions Checking

Path analysis is based on a series of linear regressions. Accordingly, all assumptions of linear regression were tested to ensure that the appropriate tests are used, and that reported data is accurate and valid (Verma & Abdel-Salam, 2019). The tested assumptions included normality of residuals of outcome variables, homoscedasticity, linearity, and absence of multicollinearity. In this study, the outcome variables were fatigue, physical performance, social performance, cognitive performance, perceived health, and QOL. Although the latter two were treated as continuous, they will not be tested for these assumptions due to their narrow range which makes assumption-checking not very informative.

Assumption of Normality

According to the central limit theorem (CLT), when the sample size is large enough (n > 30), the random selection of samples from that given sample yields a normal distribution, even if the distribution of variables in the original sample was skewed (Verma & Abdel-Salam, 2019). In this case, a sample size of n = 727 renders the parametric tests robust to violations of this assumption. Despite that, normality of residuals was examined. Shapiro-Wilk test was conducted, in addition to a visual presentation (histogram) of the distribution of the six outcome variables.

To meet the assumption of normality, the p-value of the Shapiro-Wilk test should be more than 0.05 (failing to reject the null hypothesis that the distribution of the residual is normal). In this case, all p-values, except for that of QOL and perceived health, were < 0.05, indicating that the distributions of the residuals of these variables were not normal (Table 4.1). In addition to Shapiro-Wilk test, Quantile-Quantile (Q-Q) plots were used to visualize the extent to which the distributions of the residuals of different variables in this sample deviate from normality. A Q-Q plot is commonly used to decide whether a univariate sample of a given size comes from a specified distribution (Das & Resnick, 2008), by comparing it to the specified theoretical distribution (straight line). The examination of the visual outputs (Q-Q plots) of the residuals of all six dependent variables (DVs) highlighted that these were only slight deviations from normality.

Table 4. 1: ***Shapiro-Wilk Tests for Normality of Residuals of Outcome Variables (n = 725)***

Variables	W	P
Fatigue	0.98	< .001
Physical performance	0.99	< .001

Social performance	0.99	< .001
Cognitive performance	1.00	.02
Perceived health	1.00	.07
Quality of life	1.00	.55

Despite the results of Shapiro-Wilk tests for normality which showed that four out of six DVs were not normal, it was determined that there were no serious deviations from normality. In addition, the large sample size would make the tests robust to violations of normality. Hence, it was deemed safe to assume that the assumption of normality was met.

Assumption of Homoscedasticity

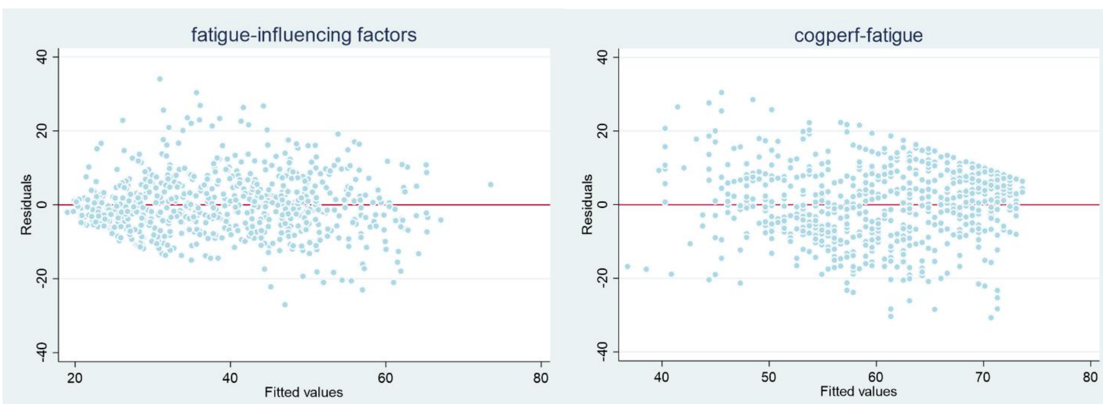
This assumption requires that the residuals of above-mentioned outcome variables exhibit a similar variance across different levels of the independent variable (IV). To test this assumption, Breusch-Pagan/Cook-Weisberg test for heteroskedasticity was conducted (Table 4.2), in addition to "fitted vs residual" graphs of the six outcome (dependent) variables. In this study, fatigue was both the IV and the DV, depending on the part of the model being examined.

Table 4. 2: Breusch-Pagan / Cook-Weisberg Test for Heteroskedasticity of Outcome Variables (n = 725)

Outcome variable	X^2	P-value
Fatigue	23.84	< .001
Physical performance	33.89	< .001
Social performance	0.84	.36
Cognitive performance	12.73	< .001
Perceived health	14.25	< .001
Quality of life	0.99	.32

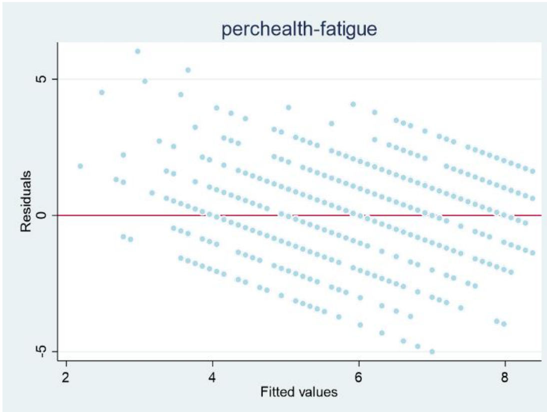
In the first part of the model, fatigue was the dependent (outcome) variable, while age, number of comorbidities, pain, sleep, depression, anxiety, number of hospitalizations, and sensory impairment were the continuous IVs. Thus, for this model, the assumption of homoscedasticity for the outcome variable fatigue was examined in relation to all these IVs, entered into the regression equation simultaneously. The fitted vs residual plot of the fatigue as the outcome variable is presented in Figure 4.1 (1st graph on the left). For all other parts of the model, fatigue was the IV, while physical performance, social performance, cognitive performance, perceived health, and QOL were the dependent (outcome) variables respectively. The “fitted vs residuals” plots of each of these outcome variables are also presented in Figure 4.3.2.

Figure 4. 1: ***Fitted vs Residual Plots of Outcome Variables and Their Predictors***

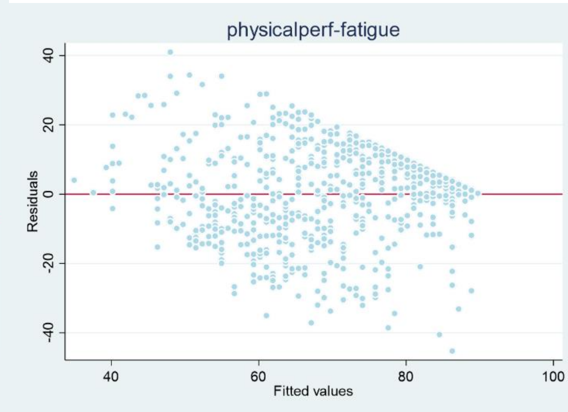


DV: Fatigue
IV: age gender number of comorbidities, pain, sleep, depression, anxiety, race, education, marital status, number of hospitalizations, sensory impairment

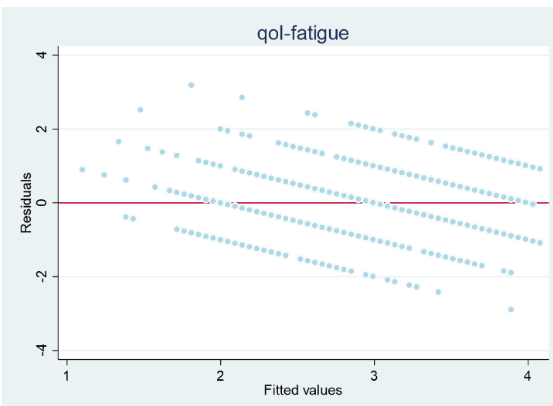
DV: cognitive performance
IV: fatigue



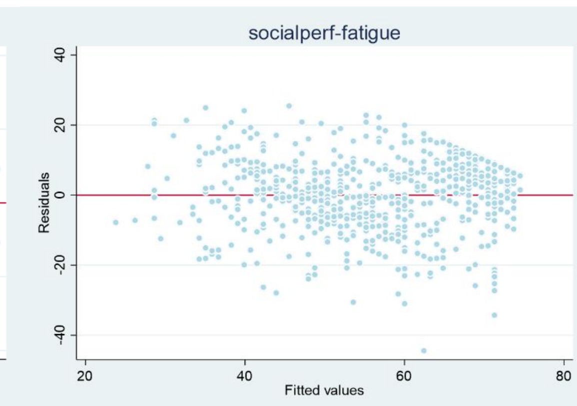
DV: perceived health
IV: fatigue



DV: physical performance
IV: fatigue



DV: quality of life
IV: fatigue



DV: social performance
IV: fatigue

The graphs of the two variables “perceived health” and “quality of life” looked different in that they did not form a horizontal line around the line y = 0. This might be because of their narrow range (1-10 and 1-5, respectively), and having only one IV (fatigue) to predict their respective scores. The tests revealed that residuals of fatigue, physical performance, cognitive performance, and perceived health were heteroskedastic, while those of the remaining two variables were homoscedastic. The visual representations also confirmed the tests (Figure 4.1).

Homoscedasticity is important for accuracy of findings. Significant violations to this assumption impact the accuracy of statistical estimates, and increases chances of Type I error. That is, rejecting a true null hypothesis, by finding a significant relationship when between two variables, when in reality, the relationship is insignificant. Luckily, there are a number of ways to overcome the problem of heteroscedasticity, one being the use the "robust" option when conducting the regression and path analyses. This option was chosen in this study to enhance accuracy of findings.

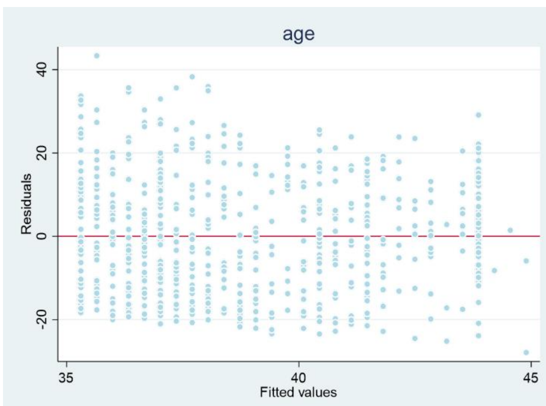
Assumption of Linearity

For this assumption to be met, the relationship between the IV and DV should be linear (Osborne & Waters, 2002; Verma & Abdel-Salam, 2019). That is, for every increase (or decrease) in x, y increases (or decreases). To test the assumption of linearity, residual vs fitted plots of all outcome variables were produced. To meet this assumption, the scatterplots of the residuals of the DV should depict a linear pattern rather than a curvilinear one (Osborn & Waters, 2002). Regression analysis cannot be conducted unless the assumption of linearity is met.

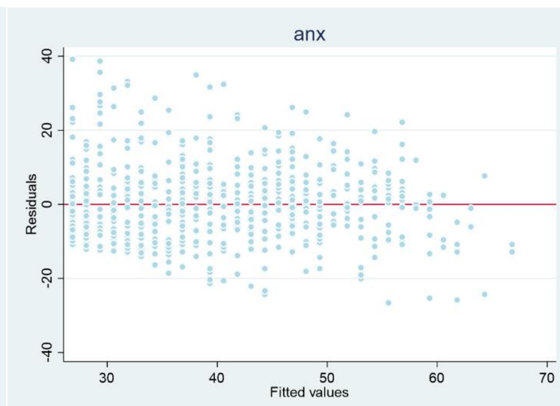
The linearity between the outcome variables physical performance, social performance, cognitive performance, quality of life, and fatigue was examined in the scatterplots in Figure 4.1. The graphs showed that the residuals "bounce" randomly around the line $y = 0$. That is, the scatterplots do not depict a "U" shaped pattern of the residuals, which would implicate a non-linear relationship. Therefore, the relationship between the respective dependent (outcome) variables and fatigue (as an IV) was linear.

In what pertains to the relationship between fatigue as a DV, and its eight continuous predictors (depression, pain, sleep, number of comorbidities, anxiety, age, hospitalization, and sensory impairment), the graphs of the respective bivariate relationships are presented in Figure 4.2. Based on the scatterplots, the relationship between fatigue and its predictors, except for number of hospitalizations, was linear. The scatterplot for number of hospitalizations showed that the relationship between this variable and fatigue is not linear, nor homoscedastic. For that, number of hospitalizations was dichotomized into two categories: individuals hospitalized twice or less in the past 12 months, and those hospitalized more than twice in the past 12 months. The cut-off level 2 was based on the average rate of hospitalization per community-dwelling older adult (Gjesten et al., 2018).

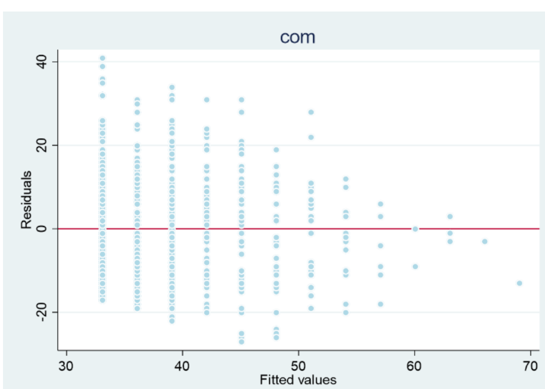
Figure 4. 2: ***Residual vs Fitted Plot of Fatigue and its Six Individual Predictors Respectively***



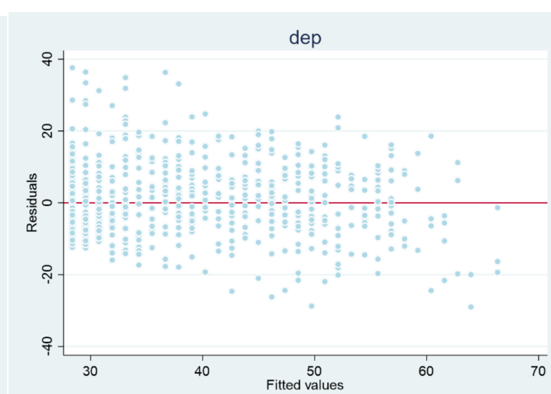
Age



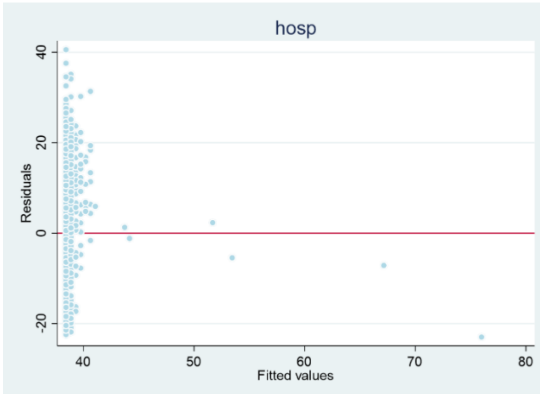
Anxiety



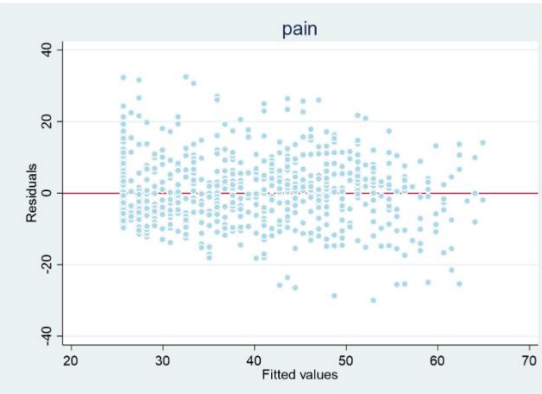
Number of comorbidities



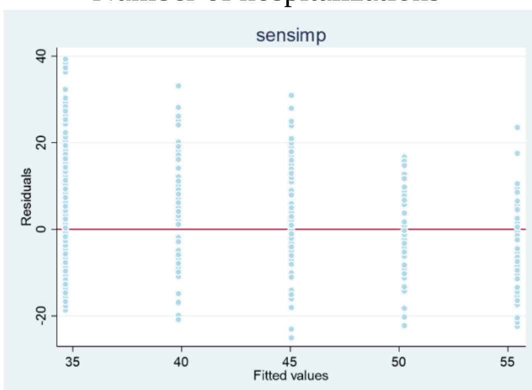
Depression



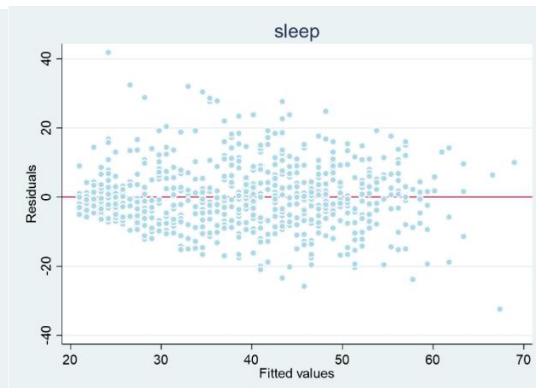
Number of hospitalizations



Pain



Sensory Impairment



Sleep

Absence of Multicollinearity

This assumption pertains to the concept of independence between the independent variables. That is, the correlation between the independent variables should be low. Multicollinearity is examined by the “tolerance” test and variance inflation factor (VIF), the latter being the reciprocal of tolerance. Higher tolerance values suggest lower multicollinearity, and are hence desirable. On the other hand, VIF values closer to one (absence of collinearity) are desired.

In this study, a cut-off level of 0.1 was chosen for tolerance levels, as suggested by Kuhn and Johnson (2013), which is the equivalent of VIF = 10. In the first model in which fatigue was the outcome variable, all tolerance and VIF levels of continuous IVs were acceptable, indicating low multicollinearity among them (Table 4.3). In the case of the second model in which QOL was the outcome variable, multicollinearity was examined among the four IVs, including perceived health, physical performance, social performance, and cognitive performance, the results of which are presented in Table 4.4. Similar to the previous model, there was no evidence of multicollinearity among independent variables.

Table 4. 3: ***Tolerance and VIF of Predictors of Fatigue (n = 725)***

Dependent variable: Fatigue		
Independent variable	Tolerance	VIF
Age	0.81	1.24
Number of comorbidities	0.75	1.33
Pain	0.40	2.48
Sleep	0.35	2.84
Depression	0.28	3.62
Anxiety	0.27	3.70
Sensory impairment	0.61	1.65

Table 4. 4: ***Tolerance and VIF of Predictors of QOL (n = 725)***

Dependent variable: QOL		
Independent variable	Tolerance	VIF
Physical performance	0.41	2.46
Social performance	0.46	2.17
Cognitive performance	0.51	1.94
Perceived health	0.47	2.12

Based on the findings of the tests pertaining to all four assumptions, it was determined that residuals of DVs are normally distributed, and the relationship between the IVs and DVs is linear, except for that between fatigue and number of hospitalizations. This variable was positively skewed, and thus was dichotomized to avoid inaccuracy in findings. Data also showed that there was no multicollinearity between IVs, and that residuals of cognitive performance and social performance were homoscedastic. Regarding fatigue, physical performance, and perceived health, the distribution of their residuals was heteroscedastic. For this reason, the "robust" option for different statistical tests was used wherever needed, to account for this heteroscedasticity.

Results

Sample Characteristics

Of the total sample size (n = 725), the majority of participants were white (n = 440, 60.69%), and about half were female (n = 400, 55.17%). The average age was 70.18, with an age range of 60-88. The majority of participants had either a technical/associate's degree, or a college degree (n = 304; 41.76%), and were married (n = 453,62.48%). Participants had an average of 2-3 comorbidities, and the majority (n = 481, 66.34%) had not been admitted to the hospital in the past 12 months (Table 4.5).

Table 4. 5: ***Sociodemographic Characteristics of Study Sample (n = 725)***

Variable	Mean (SD)
Age	70.18(7.92)
Number of comorbidities	2.90(2.12)
Frequency of hospitalization (last 12 months)	0.84(4.41)
	Frequency (%)
Gender	
Male	325(44.83)
Female	400(55.17)
Race	
White	440(60.69)
Black	183(25.24)
Asian	93(12.83)
American Indian/Hawaiian/ Pacific Islander/Other	9(1.25)
Education	
Less than high school	237(32.55)
High school or GED	187(25.69)
Technical degree/Associate's degree	144(19.78)
College degree (BA/BS)	160(21.98)
Marital status	
Never married	74(10.21)
Married	453(62.48)
In a committed relationship	32(4.41)
Separated	7(0.97)
Divorced	88(12.14)
Widowed	71(9.79)

In terms of descriptive statistics of study variables, participants had mild pain with a mean of 27.38 (PROMIS range: 12-60), and moderate levels of sleep problems (M = 39.09; PROMIS range: 16-80) and fatigue (M = 38.32; PROMIS range: 16-80). Regarding the psychological variables, participants reported low levels of depression and anxiety on average. Most participants had no visual or hearing impairments (Table 4.6). In what relates to fatigue outcomes, most participants in this study had above average physical, social, and cognitive performance levels, and "good" perceived health and quality of life on a spectrum ranging from "poor" to "excellent".

Table 4. 6: ***Descriptive Statistics of Study Variables (n = 725)***

Variable	Mean (SD)	Range [possible range]
Pain	27.38(12.34)	12-58 [12-60]
Sleep	38.29(13.40)	18-74 [16-80]
Fatigue	38.79(14.13)	16-76[16-80]
Depression	16.78(8.15)	8-40 [8-40]
Anxiety	17.57(7.75)	8-40[8-40]
Sensory impairment	0.80(1.25)	0-4 [0-4]
Physical performance	69.92(18.02)	26-90[18-90]
Social performance	56.15(15.27)	16-80[16-80]
Cognitive performance	60.29(13.02)	20-80[16-80]
Perceived health	6.14(2.16)	2-10[2-10]
Quality of life	3.00(1.15)	1-5[1-5]

Statistical Analysis

A number of statistical procedures were conducted to answer the four research questions of this study using Stata IC (2019, Version 16.1). Alpha values for all tests were set at $\alpha = 0.05$, and power was calculated for each research question separately. The tests conducted and their respective results pertaining to all four research questions are presented below. Cronbach's alpha for all continuous variables was also calculated, and findings showed that instruments used in this sample were very reliable (Table 4.7). That is, all Cronbach's alpha coefficients were greater than 0.7.

Table 4. 7: ***Internal Consistency Reliability (Cronbach's alpha) Measures of Study Variables***

Instrument	Cronbach's alpha	Number of items
Fatigue	.95	16
Pain	.96	12
Sleep	.94	16
Depression	.95	8
Anxiety	.94	8
Sensory impairment	.79	4
Physical performance	.97	18
Social performance	.95	16
Cognitive performance	.92	16
Perceived health	.80	2
Quality of life	N/A	1 item

N/A: not applicable

Research question 1**:** To what extent do each of the physiological (age, gender, number of comorbidities, pain, sleep), psychological (depression, anxiety), and situational (race, marital status, education, hospitalization, sensory impairment (SI)) factors predict fatigue in older individuals?

To answer this research question, Pearson's product-moment correlation was conducted to examine the association between fatigue (DV), and the hypothesized continuous IVs (Table 4.8). Based on the findings, all IVs were significantly correlated with fatigue, and thus were entered into multiple linear regression.

Table 4. 8: ***Correlation Matrix of Study Variables***

	Fatigue	Age	Com	Pain	Sleep	Dep	Anx	SI
Fatigue	1.00							
Age	.19*	1.00						
Com	.45*	.23*	1.00					
Pain	.74*	.26*	.45*	1.00				
Sleep	.76*	.23*	.43*	.72*	1.00			
Dep	.68*	.24*	.41*	.67*	.71*	1.00		
Anx	.68*	.27*	.42*	.67*	.73*	.83*	1.00	
SI	.46*	.42*	.34*	.50*	.49*	.50*	.49*	1.00

Com: number of comorbidities; dep: depression; anx: anxiety; dep: depression, hosp: number of hospitalizations, SI: sensory impairment

$* p < 0.05$

In what relates to categorical variables, including gender, number of hospitalizations, education, marital status, and race, t-tests, Kruskal Wallis, Wilcoxon-Mann-Whitney, and ANOVA were conducted. Prior to conducting t-tests and ANOVA, data was checked for homogeneity of variance. This assumption was met for variables “race” and “marital status”, and thus one-way ANOVA was conducted. In the case of education, this assumption was violated, and thus Kruskal Wallis test, the non-parametric version of ANOVA was conducted. For dichotomous variables, the assumption of equality of variance was met for gender, and a t-test was conducted. However, for the dichotomized variable “number of hospitalizations” (less than two admissions vs three or more hospital admissions), this assumption was violated, and thus Wilcoxon-Mann-Whitney test was conducted.

Based on findings, fatigue levels were significantly different between white, black, and other races ($F = 61.42$, $p < .001$). Post hoc analyses showed that there were significant differences in fatigue levels between white and black ($p < .001$), as well as white and other races ($p < .001$), but no significant differences between black and other races ($p = 1.00$). Additionally, Kruskal Wallis test results ($X^2 = 159.69$, $p < .001$) suggested that fatigue levels were significantly different between groups of education indicating that. Similarly, based on Mann-Whitney test, levels of fatigue varied significantly between individuals who were hospitalized twice or less in the past 12 months, as compared to those hospitalized three times or more ($z = -5.30$, $p < .001$). In addition, males reported higher levels of fatigue than females ($t = 2.62$, $p < .01$). On the other hand, fatigue levels were not significantly different between individuals with different marital statuses ($F = 1.40$, $p = .24$).

To sum up, all variables, except for marital status, were significantly associated with fatigue. Hence, all significant variables were simultaneously entered into multiple linear regression, using "robust" option to account for heteroscedasticity of some variables (discussed above). The results of the regression are presented in Table 4.9.

Table 4. 9: ***Multiple Linear Regression of Outcome Variable Fatigue (n = 725)***

	β	Unstandardized Beta (SE)	t	p-value
Age	-.02	-0.03(.05)	-0.66	.509
Gender (1=male; 2=female)	-.01	-0.18(.64)	-0.28	.778
No. of comorbidities	.07	0.46(.17)	2.75	.006
Pain	.33	0.37(.05)	7.57	< .001
Sleep	.34	0.36(.04)	8.42	< .001
Depression	.12	0.21(.08)	2.59	.010
Anxiety	.10	0.19(.08)	2.23	.026
Race (reference: white)				
Black	-.04	-1.39(1.07)	-1.30	.195
Other races	-.02	-0.75(1.10)	-0.68	.498
Education (reference: less than High school)				
High school/GED	.04	1.26(1.28)	0.99	.324
Technical degree/Associate's degree	.08	2.80(1.45)	1.93	.054
College degree	.00	0.02(1.39)	0.01	.991
Hospitalization (in last 12 months) 0: ≤ 2/year 1: ≥ 3/year	.02	1.28(1.23)	1.04	.298
Sensory impairment	.04	0.49(.34)	1.43	.153
Constant	-	8.01(3.96)	2.02	.043
F (14, 710) = 136.23, p < .001				
R^2= 0.69				

Findings from the simultaneous entry of all significant risk factors of fatigue into multiple linear regression showed that some of the physiological factors, and both psychological factors were significant predictors of fatigue. Number of comorbidities (*B* = 0.46, *p* = .006), pain (*B* = 0.37, *p* < .001), sleep (*B* = 0.36, p < .001), depression (*B* = 0.21, *p* = .010), and anxiety (*B* = 0.19, *p* = .026) remained significant predictors of fatigue after adding all variables simultaneously, whereby individuals experiencing more pain, sleep problems, depression, and anxiety experienced significantly higher levels of fatigue.

On the other hand, age (*B* = -0.03, *p* = .509), gender (*B* = -0.18, *p* = .778), having been hospitalized less or more than twice/year (*B* = 1.28, *p* = .298), or having more SI (*B* = 0.49, *p* = .153) did not significantly predict fatigue levels. In addition, compared to being White, being Black (*B* = -1.39, *p* = .195), or belonging to any other race (*B* = -0.75, *p* = .498) were not risk factors for higher fatigue scores. Lastly, not having completed high school was not a significant risk factor for higher fatigue levels, as fatigue scores did not significantly vary between the former group and those who had completed high school/GED (*B* = 1.26, *p* = .234), or those who had achieved a technical (B=2.80, p=0.054) or a college degree (*B* = 0.02, *p* = .991). In other words, none of the situational factors remained significant when other variables were accounted for.

Overall, the effect size of this model was moderate. Variables entered into the regression accounted for 69% of the variance of fatigue scores. The model showed that none of the situational factors were significant, but both depression and anxiety (psychological factors), as well as higher number of comorbidities, pain, and sleep problems, were significant predictors of fatigue (Figure 4.4.1). The power achieved in this model was 1, due to the large sample size.

To better understand the relationship between fatigue and some of the independent variables that were insignificant, “education”, “sensory impairment”, and “age” were categorized differently, and re-entered into the regression equation. Age was dichotomized in two different ways. First, age was categorized into two groups, based on findings from a research study that differentiated between “older” and “oldest old” individuals (Paraschakis et al., 2012). The first group, “older adults”, included individuals in the 60-74 age range, and the other group, the “oldest old”, included those above the age of 75. The other categorizations were based on the cut-off level of 85, according to the cut-off levels supported by other researchers (Zizza et al., 2009). Lastly, age was categorized into three groups, including “youngest old” (60-74), “middle old” (75-84), and “oldest old” (≥ 85) (Lee et al., 2018), which was also deemed an insignificant predictor of fatigue. In all three cases, multiple regression analyses including the different categorizations of this variable showed that being in either category was not a significant predictor of fatigue.

In terms of education, the mean fatigue scores were calculated for each of the educational groups, and “High school/GED” and “Technical degree/Associate’s degree” were combined after establishing similar fatigue means in these two groups. Hence, education was categorized into three categories: “No high school”, “High school/GED/Technical or Associate’s Degree”, and “College Degree”. Lastly, sensory impairment (SI) was examined for the frequency of each of the obtained responses, based on which it was categorized into “No SI” and “At least one SI”, so that each group had an adequate sample size. The results of the regression with the modified categorization of education and SI are presented below (Table 4.10).

Table 4. 10: ***Multiple Regression Equation of Outcome Fatigue (n = 725)***

	Unstandardized Beta (SE)	β	t	p
Age	-0.04(0.05)	-.02	-0.82	.414
Gender (1=male; 2=female)	0.08(0.64)	.00	0.12	.905
No. of comorbidities	0.49(0.16)	.07	2.95	.003
Pain	0.37(0.05)	.32	7.57	< .001

Sleep	0.35(0.04)	.33	8.20	< .001
Depression	0.20(0.08)	.11	2.44	.015
Anxiety	0.20(0.08)	.11	2.34	.020
Race (White)	1		.	.
Black	-1.52(1.07)	-.05	-1.43	.154
Other	-0.82(1.11)	-.02	-0.74	.457
Education (Reference: College Degree)				
No high school	0.02(1.39)	.00	0.01	.991
High school/GED/Technical/Associate's	1.93(0.72)	.07	2.69	.007
Hospitalization (in last 12 months) 0: ≤ 2/year 1: ≥ 3/year	1.26(1.25)	.02	1.01	.314
Sensory impairment 0: no sensory impairment 1: one or more sensory impairment	2.04(0.83)	.07	2.45	.015
Constant	8.30(3.21)		2.59	.010
F (13, 711) = 149.69, p < .001				
R^2 = .69				

Findings of this modified regression analysis slightly shifted the regression coefficients and significance levels of the all the IVs. The most significant change was that of the modified variables, SI and education. Results showed that having one or more SI was a significant predictor of fatigue, whereby older individuals in this group reported fatigue levels twice that of individuals with no SI. Also, in reference to older adults with a college degree, having a high school, technical, or an associate's degree was a significant risk factor for higher fatigue scores. Interestingly, having no high school degree was not a predictor of fatigue.

Research questions 2&3**:** To what extent does fatigue influence functional performance, cognitive performance (CP), perceived health, and QOL? Do the above-mentioned consequences of fatigue (i.e., physical performance (PP), social performance (SP), cognitive function and perceived health) mediate the effect of fatigue on QOL?

To answer this research question, path analysis was conducted in two steps using "robust" option to account for heteroscedasticity. In the first path analysis, fatigue was set to be the IV, while physical, social, and cognitive performances, as well as perceived health, were set to be the outcome (dependent) variables and the mediators to the relationship between fatigue and QOL. In the second step, the same model was maintained, but all the risk factors of fatigue that were examined in research question 1 were added, and were set to impact fatigue, physical, social, and cognitive performances, as well as perceived health and quality of life. The aim of this second step was to examine the impact of fatigue on performance-based outcomes, perceived health, and QOL, net of the impact of the variables (covariates) examined in research question 1. Then, beta coefficients obtained from these two path analyses were examined for differences, to identify the effect of variables of interest net of the impact of other covariates (age, gender, number of comorbidities, etc.).

The findings of the first path analyses are displayed in Tables 4.11. The presented results regarding the direct effect of fatigue on the outcomes of interest showed that fatigue was a significant predictor of poorer physical ($B = -0.87$, $p < .001$), social ($B = -0.80$, $p < .001$), and cognitive performance ($B = -0.58$, $p < .001$), as well as poorer perceived health ($B = -0.10$, $p < .001$). Higher scores of these outcome variables, with the exception of cognitive performance, were shown to be significant predictors of a better QOL. Surprisingly, a better cognitive performance was a predictor of a poorer QOL ($B = -0.01$, $p < .014$). In addition, fatigue was not directly associated with QOL ($B = 0.00$, $p > .705$). The effects of all performance-based outcome variables on QOL were generally weak, but that of perceived health was moderate.

The indirect effect of fatigue on QOL was calculated to examine whether fatigue outcomes mediate the relationship between the fatigue and QOL. The results showed that the indirect path was significant (*B* = -0.05, *p* < .001), suggesting the presence of a mediating effect. Individual paths for mediators were not examined, since all mediators were significantly correlated, and examining them separately would not have been very informative.

Coefficients of both directs and indirect effects of fatigue on PP, SP, CP and perceived health decreased in magnitude when physical, psychological, and situational covariates were entered into the equation (Figure 4.4.1), but all significant paths in path 1 remained significant. As for the model fit, the coefficient of determination was .65, meaning that the IVs in the model explained 65% of the variance of the DVs, while that of path 2 was .92. Chi squared statistic, root mean square error of approximation (RMSEA), Tucker-Lewis Index (TLI), and comparative fit index (CFI) all showed perfect fit, because both models were saturated.

Table 4. 11: ***Direct and Indirect Effects of Fatigue on Outcome Variables and QOL (n = 725)***

	β(SE)	B(SE)	Z	P>|z|
Path Analysis Step 1				
<u>*Direct effects*</u>				
Physical performance				
Fatigue	-.68(.02)	-0.87(.03)	-27.19	< .001
Social performance				
Fatigue	-.75(.02)	-0.80 (.03)	-28.72	< .001
Cognitive performance				
Fatigue	-.64(.02)	-0.58(.03)	-21.40	< .001
Perceived health				
Fatigue	-.64(.02)	-0.10 (.00)	-22.04	< .001
Quality of life				
Physical performance	.09(.03)	0.01(.00)	2.64	.008
Social performance	.14(.03)	0.01(.00)	4.40	< .001

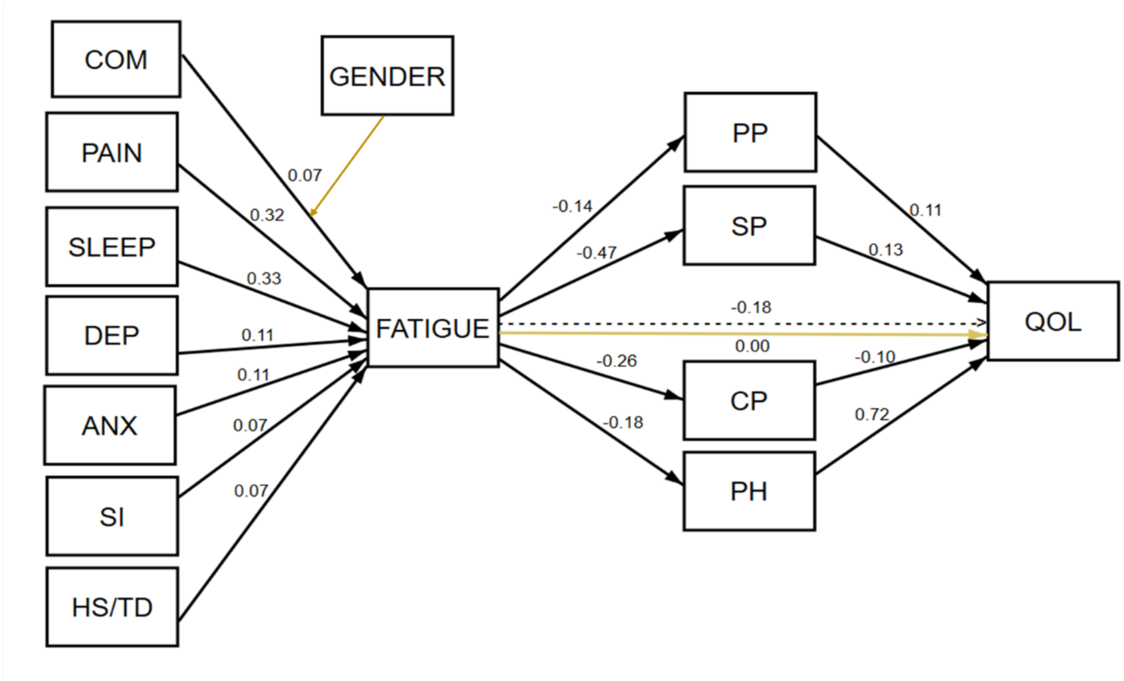
Cognitive performance	-.07(.03)	-0.01(.00)	-2.46	.014
Perceived health	.74(.03)	0.39(.02)	22.81	< .001
Fatigue	.01(.28)	0.00(.00)	0.38	.705
Indirect effects				
Quality of life				
Fatigue	-.59	-0.05(.00)	-15.31	< .001
CD = 0.650				
Path Analysis Step 2	β(SE)	B(SE)	Z	P>|z|
Direct effects				
Physical performance				
Fatigue	-.14(.04)	-0.18(.05)	-3.87	<.001
Social performance				
Fatigue	-.47(.05)	-0.51(.06)	-8.99	< .001
Cognitive performance				
Fatigue	-.26(.05)	-0.24(.05)	-5.32	< .001
Perceived health				
Fatigue	-.18(.05)	-0.03(.01)	-3.81	< .001
Quality of life				
Physical performance	.11(.05)	0.01(.00)	2.24	.025
Social performance	.13(.04)	0.01(.00)	3.50	< .001
Cognitive performance	-.09(.03)	-0.01(.00)	-2.69	.007
Perceived health	.72(.03)	0.39(.02)	20.85	< .001
Fatigue	.01(.04)	0.00(.00)	0.14	.888
Indirect effects				
Fatigue	-.18	-0.01(.00)	-4.40	< .001
CD = .921				

CD: Coefficient of determination

The results from the statistical analyses of research questions 2 and 3 showed that fatigue was a significant predictor of poorer physical, social, and cognitive performance, as well as poorer perceived health, with effect sizes ranging from -0.14 to -0.47. These outcome variables, in their turn, mediated the relationship between fatigue and QOL. This held true even after covariates like age, gender, number of comorbidities, race, and others were accounted for. Outcomes of fatigue, such as PP (B = 0.01, p < .01), SP (B = 0.01, p < .001), and perceived health (B = 0.39, p < .001) were positively correlated with QOL. Lastly, CP was negatively correlated with QOL (B = -0.01, p < .007), indicating that better cognitive performance was associated with a poorer quality of life (Figure

4.3). However, it is noteworthy mentioning that the relationship between fatigue outcomes, with the exception of perceived health, and QOL was very weak.

Figure 4. 3: ***Path Model of Significant Predictors and Outcomes of Fatigue***



COM: number of comorbidities; DEP: depression; ANX: anxiety; SI: sensory impairment; HS/TD: high school (or GED)/technical degree (or associate's degree) PP: physical performance; SP: social performance; CP: cognitive performance; PH: perceived healthl; QOL: quality of life

→ insignificant path; ---> indirect effect

In order to better understand the unexpected negative association between CP and QOL, additional analyses were conducted. Pairwise correlation between QOL, the DV, and its predictors (PP, SP, CP and perceived health). Results showed that the associations between all IVs/predictors and QOL were significant, and were positive, including that of cognitive performance (Table 4.12).

Table 4. 12: ***Pairwise Correlations between QOL and its Predictors (n = 725)***

Variables	1	2	3	4	5
Physical performance (1)	1.00				
Social performance (2)	.67*	1.00			

Cognitive performance (3)	.61*	.63*	1.00		
Perceived health (4)	.69*	.59*	.59*	1.00	
Quality of life (5)	.64*	.58*	.50*	.83*	1.00

*$p < 0.05$

In addition to examining pairwise correlations between variables, SP, CP, and perceived health were divided according to their domains, which, in turn, were entered into a regression equation. That is, SP was divided into "social ability" and "social satisfaction", CP was divided into "cognitive function" and "cognitive function-abilities", while perceived health was divided into "perceived physical health" and "perceived physical health". Physical performance was entered as one domain. The purpose of this segregation was to better explain which domain more significantly predicted QOL. The results of the regression are presented in Table 4.13.

Table 4. 13: ***Regression Analysis of QOL and its Predictors (n = 725)***

	B	Unstandardized beta (SE)	t	p
Fatigue	.00	0.00(.00)	.12	.905
Physical performance	.11	0.01(.00)	2.77	.006
Social ability	-.00	-0.00(.01)	-.10	.918
Social satisfaction	.09	0.01(.00)	2.99	.003
Cognitive ability	-.02	-0.00(.00)	-.79	.430
Cognitive function	.00	0.00(.01)	.03	.974
Physical health	.59	0.06(.04)	15.98	.000
Mental health	.23	0.21(.03)	6.57	.000
Constant	-	.31	-.56	0.575
F (8,716), $p < .001$				
$R^2 = .73$				

Findings from the regression analyses suggested that both cognitive ability (B = -0.00, p = .430), and cognitive function (B = 0.00, p = .974) did not significantly predict fatigue, with beta coefficients of zero in both cases. Better social satisfaction (B = 0.01, p = .003), but not social ability (B = -0.00, p = .918), significantly predicted better QOL. The relationship between physical performance and QOL was weak, but significant (B =

0.01, $p < 0.01$). Lastly, the relationship between mental health and QOL was weak ($B = 0.21$, $p < .001$), but that of physical health was moderate ($B = 0.60$, $p < .001$).

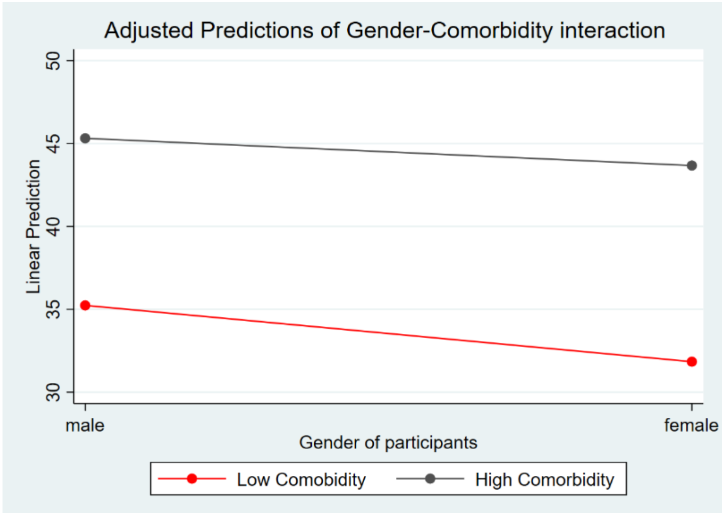
Research Question 4. Does gender mediate the relationship between number of comorbidities and fatigue?

To answer this question, two-way Analysis of Variance (ANOVA) was conducted, whereby gender (male/female) and comorbidity group (two or less/three or more) were the two factors, and fatigue was the DV. The partial sum of squares for each for the factors was calculated, as well the interaction effect between both factors. The results showed that number of comorbidities ($F = 129.06$, $p < .001$) and gender (F=6.83, p<0.001) significantly predicted fatigue (without covariates accounted for in multiple regression analysis discussed above). However, the interaction between comorbidities and gender was not significant ($F = 0.83$, $p = .364$), indicating that gender does not moderate the relationship between comorbidities and fatigue. The results obtained are presented in Table 4.14 and Figure 4.4.

Table 4. 14: ***Two-way ANOVA of Outcome Variable Fatigue (n = 725)***

Source	Partial SS	Df	MS	F	Prob>F
Model	23555.95	3	7851.98	47.56	< .001
Comorbidities (High/low)	21306.90	1	21306.90	129.06	< .001
Gender (male/female)	1127.25	1	1127.25	6.83	.010
Gender#com	136.38	1	136.38	0.83	.364
Residual	119032.72	721	165.09		
Total	142588.67	724	196.95		
Root MSE = 12.8489					
R^2= .17					
Adjusted R^2 = .16					

Figure 4. 4: ***Margins Plot of Number of Comorbidities and Gender***



Summary of Findings

In this chapter, assumptions such as linearity, homoscedasticity, normality, and absence of multicollinearity were examined, to enhance reliability of findings. Statistical tests including multiple linear regression, path analyses, Pearson correlation, analysis of variance (ANOVA), and some non-parametric tests were conducted to answer four research questions in this study. Findings from the analyses presented above can be summarized as follows. First, higher number of comorbidities, pain, sleep problems, depression, anxiety, education, and SI are significant risk factors of fatigue, while age, gender, race, marital status, and number of hospitalizations in the past 12 months, are not. Second, higher levels of fatigue predict poorer performance on the physical, social, and cognitive levels, as well as a poorer perceived health. In addition, the relationship between fatigue and QOL is mediated by these four outcome variables. Note that, out of the above-mentioned fatigue outcomes, perceived health was the strongest predictor of QOL. Lastly, results showed that gender does not moderate the relationship between number of comorbidities and fatigue. These findings are represented in Figure 4.3.

CHAPTER 5

DISCUSSION

The aim of this research study was to answer four research questions around fatigue in older individuals with chronic diseases, using the Theory of Unpleasant Symptoms (TUS) as a theoretical framework. The first aim was to identify the physiological, psychological, and situational risk factors of fatigue, and another aim was to examine whether gender moderates the relationship between number of comorbidities and fatigue. The two other questions pertained to outcomes of fatigue, and whether these outcomes moderated the relationship between fatigue and quality of life (QOL).

Risk factors of Fatigue, and Gender as a Moderator

Physiological factors examined in this study included age, gender, number of comorbidities, pain, and sleep. Of these, number of comorbidities, pain, and sleep were significant predictors of fatigue, while age and gender were not. Psychological factors examined in this study included depression and anxiety, both of which were shown to be significant risk factors of fatigue. The last category of risk factors included situational factors, which consisted of educational background, marital status, race, number of hospitalizations in the past 12 months, and sensory impairment (SI) (hearing and vision). Both SI and education were significant predictors of higher fatigue levels. Bivariate analyses showed that older individuals with no high school degree had the highest (worst) fatigue scores compared to those with a high school/technical/associate's degree, and to those with a college degree, the latter group having the lowest fatigue scores. However, when accounting for other covariates, only having a high school/technical/associate's degree, compared to a college degree, was a significant predictor of fatigue. Lastly, findings did not support the hypothesis that gender moderates the relationship between number of comorbidities and fatigue.

Fatigue and Health Outcomes, and the Mediating Role of These Outcomes

Path analyses revealed that fatigue was negatively correlated with physical, social, and cognitive performances, as well as perceived health. In their turn, physical and social performance, were positively and weakly associated with QOL, whereas perceived health was positively and strongly associated with QOL. On the other hand, the association between cognitive performance and QOL was negative, but almost negligible, similar to the other two performance-based outcomes. Lastly, findings suggested that these outcomes mediated the relationship between fatigue and QOL. These findings suggest that the majority of non-modifiable risk factors such as age, gender, and race, marital status, are not significant predictors of fatigue, whereas modifiable risk factors, such as pain, sleep, depression, and anxiety are.

Findings in the literature

Physiological and Psychological Factors

Findings pertaining to age-fatigue association in the literature were not in alignment. In a study involving older adults in Brazil, individuals above the age of 80 experienced more frailty, fatigue being a constituent of frailty, compared to those in the 60-79 age range (Duarte et al., 2019). Contrary to this finding, a number of studies highlighted a negative association between fatigue and age in samples with mean ages of 36.9 (Pouraboli et al., 2019), or 44.27 (Dolan & Kudrna, 2013), or an age range of 25-74 (Engberg et al., 2017). However, no studies examining this association in the United States among older individuals exclusively were found. These findings might suggest that older adults experience less fatigue compared to young adults, but this association becomes insignificant either when examining fatigue amongst older adults only, or when accounting for covariates simultaneously, which was not the case in the above-mentioned studies. In addition, sociodemographic factors might moderate the relationship between age and fatigue, which would explain the contrasting finding in one of the studies (Duarte et al., 2019).

In what relates to the other physiological risk factors, findings pertaining to gender-fatigue association were inconclusive. Findings in some studies supported the insignificant association between gender and fatigue (Lee et al., 2020; Pouraboli et al., 2019). However, in other studies, females reported significantly higher fatigue compared to males (Alekseeva et al., 2018; Engberg et al., 2017; Junghaenel et al., 2011). The significance of sleep and pain as risk factors of fatigue was supported in a number of studies (Alekseeva et al., 2018; Katz, 2017; Pope, 2020; Vassend et al., 2018). Lastly, the fifth physiological variable examined in this study, number of comorbidities, was found to be a significant risk factor of fatigue, which was supported in other studies as well (Duarte et al., 2019; Fiest et al., 2016). In what relates to the psychological factors, findings pertaining to both depression and anxiety were supported by other studies identified in the literature, whereby both these factors significantly predicted fatigue (Alekseeva et al., 2018; Carneiro et al., 2017; Vassend et al., 2018).

Situational Factors

The last category of hypothesized influencing factors of fatigue in this study was “situational factors”, which included race, education, marital status, number of hospitalizations, and SI. In this study, race was not a significant risk factor of fatigue.

Findings pertaining to race were supported in two other studies (Shakoor et al., 2017; Yazici et al., 2007). Also, researchers in a systematic review concluded that although African-Americans and Native Americans are at higher odds of chronic fatigue, ethnic differences alone would not explain the higher odds in this group (Dinos et al., 2009). Thus, it might be that the exclusion of a number of covariates in the studies included in the review is what led to the higher odds of fatigue in this ethnic minority.

The positive influence of educational attainment on fatigue was supported in the literature (Engberg et al., 2017; Junghaenel et al., 2011), which was not the case in this study. On the educational level, results in this study showed that having a “high school/technical/associate’s degree”, but not “no high school” degree, predicted higher fatigue scores compared to having a college degree. It is noteworthy mentioning that findings in this study also showed lower fatigue levels in groups with higher educational attainment, but this was insignificant after covariates were accounted for. The exclusion of a number of covariates, besides the inclusion of other age groups in both of the research studies might explain the discrepancy in findings. On the other hand, marital status was not a significant predictor of fatigue in this study even in bivariate analyses, and hence was excluded from multiple regression analyses. This finding was supported by some studies (Bevilacqua et al., 2018; Horne et al., 2019), and refuted by others (Jing et al., 2015; Lin et al., 2015).

In this study, having one or more SI was a significant predictor of fatigue. This was also supported in the literature, whereby studies revealed that individuals with visual, hearing, or dual SIs experience a higher severity of fatigue, and are at higher odds of fatigue (Hornsby et al., 2016; Schakel et al., 2019; Yamada et al., 2014). Lastly, number of hospitalizations was hypothesized to be a significant risk factor of fatigue, but this hypothesis was not supported. Researchers in other studies examined the opposite direction of this relationship, whereby fatigue was hypothesized to be a significant risk factor for a higher frequency of hospitalization. This hypothesis was supported (Heo et al., 2016; Paddison et al., 2013), whereby individuals with fatigue had more frequent, and higher odds of hospitalizations compared to those with no fatigue. The hypothesis of hospitalization preceding or predicting higher fatigue, as examined in this study, might also be true. However, having only 5.79% of the sample in the "≥ 2 hospitalizations in the past 12 months" might have been insufficient to detect significant differences between this group and those who had up to one hospitalization/year.

Association Between Fatigue and Health Outcomes

In terms of fatigue outcomes, findings in this study suggested that fatigue negatively impacted all three levels of performance (physical, social, cognitive), with the strongest relationship being with the social component, followed by cognitive performance (CP), the weakest relationship being with physical performance (PP). The weak relationship with PP might be related to the fact that only 12.69% of participants had below average PP. The relationship between fatigue and PP has been supported in a number of studies (Murphy et al., 2021; Norberg et al., 2010; Soares et al., 2015; Veldhuijzen van Zanten et al., 2021). In terms of fatigue-CP relationship, researchers in a study concluded that improvement in fatigue led to improvements in subjective cognitive function, but had no impact on objective cognitive function (Kinsinger et al., 2010), while findings of other studies have supported the influence of fatigue on objective cognitive performance as well (Busichio et al., 2004). In this study, the significant inverse relationship between fatigue and CP was based on subjective reports of CP only. Lastly, a study revealed that cognitive domains mainly impacted by fatigue included attention, memory, and reaction time, but not fine motor speed, reasoning, vocabulary, and global functioning (Cockshell & Mathias, 2010).

At the social performance (SP) level, studies supported the negative relationship between fatigue and SP identified in this study, with the former accounting for 48% of the variance in SP in one of the studies (Murphy et al., 2021; Salter et al., 2019; Smith et al., 2016; Veldhuijzen van Zanten et al., 2021). Lastly, the negative association between fatigue and perceived health has also been supported in the literature, whereby higher fatigue levels contributed to worse subjective health perceptions in young men and older adults (Flensner et al., 2008; Lekander et al., 2013; Veldhuijzen van Zanten et al., 2021).

All these fatigue outcomes, in their turn, were shown to significantly predict quality of life (QOL), but the association between each of PP, SP, and CP with QOL was very weak. The positive association between each of PP and perceived health, and QOL has been supported in the literature (de Oliveira et al., 2021; Holbein et al., 2019; Yoo et al., 2020). In addition, one of the studies revealed the mediating role of perceived health in the relationship between physical activity and QOL (Holbein et al., 2019) which would explain the weak association between PP and QOL in the current study. Similarly, studies supported the positive association between SP and QOL (Lestari et al., 2021; van Hees et al., 2020), especially that of in-person interactions (Lee et al., 2016). Lastly, in this study, there was a weak negative association between CP and QOL, contrary to findings of some studies, in which better cognitive function predicted either a better overall QOL (Park et al., 2018; Pascal de Raykeer et al., 2019; Sanborn et al., 2018), or some, but not all, aspects of QOL (Lašaitė et al., 2019). However, in two studies involving individuals with mild cognitive impairment (MCI), cognitive function was not significantly associated with QOL (Chuang et al., 2016; Hsiao et al., 2016).

The unexpected weak negative association between CP and QOL in this study can be attributed to the fact that QOL was based on responses to a single item, which does not accurately represent the multifaceted aspects of QOL. Another reason for this negative association could be due to the absence of data regarding the presence of neurodegenerative diseases, such as MCI or Alzheimer's disease, in which case better cognitive performance would be related to worse QOL (Chuang et al., 2016; Hsiao et al., 2016; Stites et al., 2017). Lastly, the association between fatigue and QOL was supported in other studies in the literature (Abrahams et al., 2018; Fan et al., 2020), which was not the case in this study. The lack of a significant association between these two variables can be explained by the inclusion of mediators, such as PP, SP, CP, and perceived health, which would have rendered findings pertaining to fatigue and QOL insignificant.

In this study, SP, CP, and perceived health consisted of two domains each. Post-hoc analyses were conducted whereby each domain was entered as a separate variable in the regression equation for QOL. This entry rendered CP insignificant, and suggested that social satisfaction, not social ability, predicted QOL. In addition, perceived physical health was a stronger predictor of QOL than that of perceived mental health.

As mentioned above, the significant association between QOL and PP, SP, and CP respectively in this study was almost negligible, and statistical significance in this case might be due to a large sample size alone rather than an actual clinical significance. This is further supported by the fact that CP was insignificant in the post-hoc analysis described above. It can be that perceived health mediates the relationship between all three performance outcomes (physical, social, cognitive) and QOL, which makes the association between these outcomes and QOL very weak.

Implications for Practice

Findings in this study can be summed up as follows. First, risk factors of fatigue in older individuals with various chronic diseases include number of comorbidities, pain, sleep, depression, anxiety, having a high school/technical/associate’s degree compared to a college degree, and having one or more SI. The inclusion of all hypothesized risk factors simultaneously rendered other variables, including gender, age, race, number of hospitalizations, marital status insignificant, contrary to findings obtained in pairwise correlations. Most variables which remained significant are modifiable, which supports the need for interventions targeting these risk factors. Multiple interventions that tackle different risk factors have been developed, and supported for their effectiveness. For example, cognitive behavioral therapy, mindfulness, sleep hygiene training, and others have been found to improve sleep (MacLeod et al., 2018; Wennberg et al., 2013), and the application of cold and/or hot packs, relaxation breathing techniques have been shown to effectively minimize pain (Fouladbakhsh et al., 2011). Meanwhile, the use of personal assistive robots (Chen et al., 2020), problem solving therapy (Enguidanos et al., 2011), and interpersonal psychotherapy (Bransford & Choi, 2012) have been shown to help with depression.

The above-mentioned interventions highlight how existing interventions target one outcome of interest, and are non-holistic, which warrants further investigations around holistic interventions that target multiple symptoms simultaneously, in order to maximize their effectiveness, and the use of resources. For instance, a study presented promising findings regarding yoga therapy in the management of depression, pain, and sleep, with high participant adherence rates (Cartwright et al., 2020). More studies on similar interventions are needed to make the implementation of such interventions feasible, and maintain high adherence and compliance rates.

In addition, given the prevalence of hearing, vision, and dual SI in older individuals (Elliott et al., 2015; Roets-Merken et al., 2014), consistent vision and hearing screening protocols for older individuals should be implemented in the community and nursing homes. In a study, researchers reported that less than half of the nursing home staff used hearing and vision screening tools to detect SI in residents (Andrusjak et al., 2021). Also, they identified a lack of routine assessments for SI, and of access to vision and hearing assistive devices (Andrusjak et al., 2021). There are a number of SI screening tools, including the Severe Dual Sensory Loss screening tool (Roets-Merken et al., 2014), which are reliable, valid, inexpensive, and easy-to-administer, and can be used by nurses and staff to detect SI in older individuals in nursing homes. Interestingly, in a study, subjective perceptions of hearing loss, rather than objective measures of hearing impairment, predicted fatigue scores (Hornsby & Kipp, 2016). That is, the social and emotional consequences of hearing loss, rather than the degree of hearing loss per se, was a significant predictor of worse fatigue (Hornsby & Kipp, 2016), which supports the inclusion of SI as a situational rather than a physiological factor in this study. This association further supports the potential role of hearing aids and other hearing rehabilitation strategies in mitigating the influence of perceived hearing loss on fatigue, even in the presence of an objective hearing loss.

In what relates to outcomes of fatigue which were shown to mediate the relationship between fatigue and QOL, it is important to screen for risk factors of poor perceived health, including risk of falls, ability to perform activities of daily living (ADL), sleep, and familiar support (Silva et al., 2017). In addition, older individuals should be aware of, and have access to physical activity programs, as physical activity is significantly associated with PP (van Lummel et al., 2015). Not only would this help improve QOL based on the findings of this study, but also cognitive function (Pereira et al., 2019). Besides, such programs or activities create a medium for social participation amongst individuals in this age group, and help combat social isolation (Crozier et al., 2020).

Findings of study are of value to older individuals experiencing fatigue, their family members, healthcare providers, and researchers interested in improving the management of fatigue and the improvement of QOL of older individuals. These findings highlight the importance of screening older individuals for the identified risk factors of fatigue, including pain, sleep, number of comorbidities, depression, anxiety, and SI, and implementing interventions that promote PP, SP, and perceived health. Proper identification and management of these risk factors can be an effective strategy to minimize levels of fatigue, improve PP, SP, and perceived health, and enhance QOL.

Recommendations for Future Research

Future research should examine a number of associations which were not examined in this study. First, IVs included in this study explained 69% of variance in fatigue scores, which suggests that researchers should aim for exploring other variables associated with fatigue, or adding ones that have been already examined as risk factors of fatigue (physical activity, social support) (Karakoc & Yurtsever, 2010; Kwag et al., 2011; Lin et al., 2015; Nicklas et al., 2016; Salter et al., 2019). Second, CP was negatively correlated with QOL, which warrants further investigation on the moderating role of neurodegenerative diseases, such as dementia, in the association between CP and QOL. In addition, the feedback loops depicted in the TUS were not investigated in this study. That is, examining the extent to which fatigue, in its turn, influences its predictors (sleep, pain, depression), and the extent to which PP, CP, and SP influence fatigue and its predictors. Establishing the direction of the relationship among these variables is crucial in planning for interventions targeted not only at fatigue management, but also other symptoms, including pain, sleep, depression, and anxiety.

Pairwise correlations in this study showed that all hypothesized risk factors of fatigue, except for marital status, were significantly correlated with fatigue. However, these associations were insignificant when other variables were accounted for. Hence, it would be useful to identify variables that mediate the relationship between risk factors, such as race, education, number of hospitalizations, age, gender, and fatigue. Future research efforts should also be directed towards examining the feasibility of multi-component interventions targeted at managing/minimizing risk factors of fatigue, improving physical, social, and cognitive performances, as well as perceived health in older individuals.

Strengths and Limitations of This Study

These findings should be viewed in lieu of this study's limitations, which are discussed here. First, this was a secondary data analysis, in which participants were recruited from an online panel. This renders the researcher unaware of the circumstances in which participants responded to questionnaires, besides the self-selection bias involved in this recruitment strategy. Also, a number of variables, including social support, physical activity, medications, and income, which have been shown to influence fatigue levels, were not included in the dataset. Third, there was no documentation on the response rate, or a comparison between characteristics of respondents and non-respondents, which increases self-selection bias. Fourth, the cross-sectional nature of this research study makes it impossible to conduct test-retest reliability to further validate findings. Furthermore, the basis on which researchers in the initial study chose particular items from the various item banks is not clear. Other limitations included the way in which some variables were operationalized in this study, and the homogeneity of the sample in some characteristics. For example, QOL was operationalized as the response to a single question asking participants to rate their QOL, which hinders the reliability of findings around predictors of QOL. Regarding homogeneity, the majority of the sample was white, and had been hospitalized less than once in the past 12 months, which could have made it less likely to find significant associations between these two variables and fatigue. Lastly, path analysis does not infer causality, the establishment of which calls for randomized control trials.

The strengths of this study lie in its large sample size, and the high power achieved, both of which enhance reliability and validity of findings. Also, participants were recruited from different parts of the US, which enhances generalizability. The significance of this research lies in the inclusion of 12 independent variables simultaneously, which had not been previously done, to account for their covariance. Also, the examination of outcomes of fatigue as mediators in the relationship between fatigue and QOL using the TUS helps plan multi-factorial interventions to improve QOL. Lastly, all relationships depicted in the TUS, except for feedback loops, were examined in this study, which provides a better understanding of the interplay between different variables associated with fatigue. It is noteworthy mentioning that the IVs which were entered into the multiple regression equation for fatigue were also included in the equations on outcomes of fatigue. Hence, the beta coefficients obtained represent the net impact of fatigue on PP, SP, CP, and QOL.

Summary of Findings

To conclude, TUS was used as a theoretical framework in this study to examine risk factors and outcomes of fatigue. Number of comorbidities, pain, sleep, depression, anxiety, educational background, and SI were found to be significant predictors of fatigue. In its turn, higher fatigue predicted lower PP, SP, CP, and perceived health (strongest relationship), but did not have a direct association with QOL. The relationship between fatigue and QOL was mediated by the above-mentioned outcomes of fatigue. These findings are of value to healthcare providers of older individuals experiencing fatigue, and of older individuals themselves. Findings suggest that fatigue management interventions should include pain, sleep, SI, depression, and anxiety management strategies. Also, QOL can be enhanced by better fatigue management, in addition to strategies that enhance an individual’s PP, SP, and perceived health. Future research should be directed towards exploring other risk factors of fatigue, examining feedback loops depicted in the TUS, identifying whether neurodegenerative diseases moderate the relationship between CP and QOL, and identifying variables that mediate the relationship between certain risk factors and fatigue.

APPENDIX

UNIVERSITY OF MASSACHUSETTS INSTITUTIONAL REVIEW BOARD

UMassAmherst

Human Research Protection Office

Mass Venture Center
100 Venture Way,
Suite 116
Hadley,
MA 01035
Telephone: 413-545-3428

Memorandum – Not Human Subjects Research Determination

Date: January 14, 2021

To: Maral Torossian, College of Nursing

Project Title: *Examining a Fatigue Management Model that Identifies Risk Factors and Consequences of Fatigue in Older Individuals*

HRPO Determination Number: 21-08

The Human Research Protection Office (HRPO) has evaluated the above named project and has made the following determination based on the information provided to our office:

☐ The proposed project does not involve research that obtains information about living individuals [45 CFR 46.102(f)].

☒ The proposed project does not involve intervention or interaction with individuals OR does not use identifiable private information [45 CFR 46.102(f)(1), (2)].

☐ The proposed project does not meet the definition of human subject research under federal regulations [45 CFR 46.102(d)].

<u>Submission of an Application to UMass Amherst IRB is not required.</u>

Note: This determination applies only to the activities described in the submission. If there are changes to the activities described in this submission, please submit a new determination form to the HRPO prior to initiating any changes. ***Researchers should NOT include contact information for the UMass Amherst IRB on any project materials.***

A project determined as "Not Human Subjects Research," must still be conducted ethically. The UMass Amherst HRPO strongly expects project personnel to:

- treat participants with respect at all times
- ensure project participation is voluntary and confidentiality is maintained (when applicable)
- minimize any risks associated with participation in the project
- conduct the project in compliance with all applicable federal, state, and local regulations as well as UMass Amherst Policies and procedures which may include obtaining approval of your activities from other institutions or entities.

Please do not hesitate to call us at 413-545-3428 or email humansubjects@ora.umass.edu if you have any questions.

Iris L. Jenkins, Assistant Director
Human Research Protection Office

REFERENCES

Aaronson, L. S., Teel, C. S., Cassmeyer, V., Neuberger, G. B., Pallikkathayil, L., Pierce, J., . . . Wingate, A. (1999). Defining and measuring fatigue. *The Journal of Nursing Scholarship*, *31*(1), 45-50.

Abrahams, H. J. G., Gielissen, M. F. M., Verhagen, C. A. H. H. V. M, & Knoop, H. (2018b). The relationship of fatigue in breast cancer survivors with quality of life and factors to address in psychological interventions: A systematic review. *Clinical Psychology Review, 63*, 1-11. https://10.1016/j.cpr.2018.05.004

Alekseeva, T. M., Gavrilov, Y. V., Kreis, O. A., Valko, P. O., Weber, K. P., & Valko, Y. (2018). Fatigue in patients with myasthenia gravis. *Journal of Neurology, 265*(10), 2312-2321. https://10.1007/s00415-018-8995-4

Alhanbali, S., Dawes, P., Lloyd, S., & Munro, K. J. (2017). Self-reported listening-related effort and fatigue in hearing-impaired adults. *Ear and hearing*, *38*(1), e39–e48. https://doi.org/10.1097/AUD.0000000000000361

Almutary, H., Douglas, C., & Bonner, A. (2017). Towards a symptom cluster model in chronic kidney disease: A structural equation approach. *Journal of Advanced Nursing, 73*(10), 2450-2461. https://10.1111/jan.13303

American Psychological Association (n.d.). *APA dictionary of psychology.* Retrieved from https://dictionary.apa.org/social-role

Andrusjak, W., Barbosa, A., & Mountain, G. (2021). Hearing and vision care provided to older people residing in care homes: A cross-sectional survey of care home staff. *BMC Geriatrics, 21*(1), 1-13. https://10.1186/s12877-020-01959-0

Avlund, K. (2010). Fatigue in older adults: An early indicator of the aging process? *Aging Clinical and Experimental Research, 22*(2), 100-115. doi:10.1007/BF03324782

Banerjee, N., Slugh, M., Kaur, S., Sun-Suslow, N., McInerney, K. F., Sun, X., & Levin, B. E. (2020). Neuropsychological correlates of subjective fatigue in non-demented older adults and the moderating effect of physical activity. *Aging, Neuropsychology, and Cognition, 27*(2), 254-269. https://10.1080/13825585.2019.1606889

Barak, Y., Leitch, S., Greco, P., & Glue, P. P. (2020). Fatigue, sleep and depression: An exploratory interRAI study of older adults. *Psychiatry Research*, *284*(112772), 1-3. https://10.1016/j.psychres.2020.112772

Baron, R. M., & Kenny, D. A. (1986). The moderator-mediator variable distinction in social psychological research: Conceptual, strategic, and statistical considerations. *Journal of Personality and Social Psychology, 51*(6), 1173-1182. https://10.1037//0022-3514.51.6.1173

Bartlett, S. J., Orbai, A., Duncan, T., DeLeon, E., Ruffing, V., Clegg-Smith, K., & Bingham, C. O. (2015). Reliability and validity of selected PROMIS measures in people with rheumatoid arthritis. *PloS One, 10*(9), e0138543. https://10.1371/journal.pone.0138543

Berthold Lindstedt, M., Johansson, J., Ygge, J., & Borg, K. (2019). Vision-related symptoms after acquired brain injury and the association with mental fatigue, anxiety and depression. *Journal of Rehabilitation Medicine, 51*(7), 499-505. https://10.2340/16501977-2570

Bevilacqua, L. A., Dulak, D., Schofield, E., Starr, T. D., Nelson, C. J., Roth, A. J., Holland, J. C., & Alici, Y. (2018). Prevalence and predictors of depression, pain, and fatigue in older- versus younger-adult cancer survivors. *Psycho-Oncology (Chichester, England), 27*(3), 900-907. https://10.1002/pon.4605

Bhalla, M. C., Wilber, Scott T., Stiffler, Kirk A., Ondrejka, J. E., & Gerson, L. W. (2014). Weakness and fatigue in older ED patients in the united states. *American Journal of Emergency Medicine, 32*(11), 1395-1398. https://10.1016/j.ajem.2014.08.027

Bransford, C. L., & Choi, S. (2012). Using interpersonal psychotherapy to reduce depression among home-bound elders. *Best Practices in Mental Health, 8*(1), 1-15.

Broderick, J. E., Schneider, S., Junghaenel, D. U., Schwartz, J. E., & Stone, A. A. (2013). Validity and reliability of patient-reported outcomes measurement information system (PROMIS) instruments in osteoarthritis. *Arthritis Care & Research (2010), 65*(10), 1625-n/a. https://10.1002/acr.22025

Busichio, K., Tiersky, L. A., Deluca, J., & Natelson, B. H. (2004). Neuropsychological deficits in patients with chronic fatigue syndrome. *Journal of the International Neuropsychological Society, 10*(2), 278-285. https://10.1017/S1355617704102178

Carneiro, C., Chaves, M., Verardino, G., Frade, A. P., Coscarelli, P. G., Bianchi, W. A., Ramos-E-Silva, M., & Carneiro, S. (2017). Evaluation of fatigue and its correlation with quality of life index, anxiety symptoms, depression and activity of disease in patients with psoriatic arthritis. *Clinical, Cosmetic and Investigational Dermatology, 10*, 155-163. https://10.2147/CCID.S124886

Cartwright, T., Cahill, M., & Sadana, V. (2020). A mixed methods evaluation of an individualised yoga therapy intervention for rheumatoid arthritis: Pilot study. *Complementary Therapies in Medicine, 50*, 1-7. https://10.1016/j.ctim.2020.102339

Cella, D. (2017). *PROMIS Profiles-HUI data* (Version 1.1) [Data set]. Harvard Dataverse. https://dataverse.harvard.edu/dataset.xhtml?persistentId=doi:10.7910/DVN/P7UKWR

Cella, D., Lai, J., Jensen, S. E., Christodoulou, C., Junghaenel, D. U., Reeve, B. B., & Stone, A. A. (2016). PROMIS fatigue item bank had clinical validity across diverse chronic conditions. *Journal of Clinical Epidemiology, 73,* 128-134. https://10.1016/j.jclinepi.2015.08.037

Centers for Disease Control and Prevention (2018, October 31). *Health related quality of life (HRQOL).* https://www.cdc.gov/hrqol/concept.htm

Chen, S., Moyle, W., Jones, C., & Petsky, H. (2020). A social robot intervention on depression, loneliness, and quality of life for taiwanese older adults in long-term care. *International Psychogeriatrics, 32*(8), 981-991. https://10.1017/S1041610220000459

Cheng, H. G., & Phillips, M. R. (2014). Secondary analysis of existing data: Opportunities and implementation. *Shanghai Jingshen Yixue, 26*(6), 371-375. https://10.11919/j.issn.1002-0829.214171

Chou, K. (2013). Chronic fatigue and affective disorders in older adults: Evidence from the 2007 british national psychiatric morbidity survey. *Journal of Affective Disorders*, *145*(3), 331-335. https://10.1016/j.jad.2012.08.012

Chuang, S. P., Wu, J. Y. W., Wang, C. S., & Pan, L. H. (2016). Cognitive function, depressive symptoms, function level, and quality of life in mild dementia and amnestic-mild cognitive impairment. *Journal of Medical Sciences*, *36*(1), 14-21. https://10.4103/1011-4564.177171

Cockshell, S. J., & Mathias, J. L. (2010). Cognitive functioning in chronic fatigue syndrome: A meta-analysis. *Psychological Medicine*, *40*(8), 1253-1267. https://10.1017/S0033291709992054

Crane, P. B., Efird, J. T., & Abel, W. M. (2016). Fatigue in older adults post myocardial infarction. *Frontiers in Public Health*, *4*, 55. https://10.3389/fpubh.2016.00055

Crins, M., van der Wees, P. J., Klausch, T., van Dulmen, S. A., Roorda, L. D., & Terwee, C. B. (2018). Psychometric properties of the PROMIS Physical Function item bank in patients receiving physical therapy. *PloS one*, *13*(2), e0192187. https://doi.org/10.1371/journal.pone.0192187

Crowe, M., Jordan, J., Gillon, D., McCall, C., Frampton, C., & Jamieson, H. (2017). The prevalence of pain and its relationship to falls, fatigue, and depression in a cohort of older people living in the community. *Journal of Advanced Nursing*, *73*(11), 2642–2651. https://doi.org/10.1111/jan.13328

Crozier, A., Porcellato, L., Buckley, B. J. R., & Watson, P. M. (2020). Facilitators and challenges in delivering a peer-support physical activity intervention for older adults: A qualitative study with multiple stakeholders. *BMC Public Health*, *20*(1), 1904. https://10.1186/s12889-020-09990-x

Das, B., & Resnick, S. I. (2008). QQ plots, random sets and data from a heavy tailed distribution. *Stochastic Models, 24*(1), 103-132. https://10.1080/15326340701828308

de Oliveira, L.F.S., Wanderley, R. L., de Medeiros, M.M.D., de Figueredo, O.M.C., Pinheiro, M. A., Rodrigues Garcia, R.C.M., Almeida, L.D.F.D., & Cavalcanti, Y. W. (2021). Health-related quality of life of institutionalized older adults: Influence of physical, nutritional and self-perceived health status. *Archives of Gerontology and Geriatrics*, *92*, 1-6. https://10.1016/j.archger.2020.104278

Dinos, S., Khoshaba, B., Ashby, D., White, P. D., Nazroo, J., Wessely, S., & Bhui, K. S. (2009). A systematic review of chronic fatigue, its syndromes and ethnicity: Prevalence, severity, co-morbidity and coping. *International Journal of Epidemiology*, *38*(6), 1554-1570. https://10.1093/ije/dyp147

Dolan, P., & Kudrna, L. (2013). More years, less yawns: Fresh evidence on tiredness by age and other factors. *The Journals of Gerontology: Series B*, *70*(4), 576-580. https://10.1093/geronb/gbt118

Duarte, Y. A. O., Nunes, D. P., Andrade, F. B., Corona, L. P., Brito, T. R. P., Santos, J. L. F. D, & Lebrão, M. L. (2019). Frailty in older adults in the city of São Paulo: Prevalence and associated factors. *Revista Brasileira De Epidemiologia*, *21Suppl 02*(Suppl 02), 1-16. https://10.1590/1980-549720180021.supl.2

Eckhardt, A. L., DeVon, H. A., Piano, M. R., Ryan, C. J., & Zerwic, J. J. (2014). Fatigue in the presence of coronary heart disease. *Nursing Research (New York), 63*(2), 83-93. https://10.1097/nnr.0000000000000019

Elliott, A. F., McGwin, G., Jr., Kline, L. B., & Owsley, C. (2015). Vision impairment among older adults residing in subsidized housing communities. *The Gerontologist, 55*(Suppl_1), S108-S117. https://10.1093/geront/gnv028

Engberg, I., Segerstedt, J., Waller, G., Wennberg, P., & Eliasson, M. (2017). Fatigue in the general population- associations to age, sex, socioeconomic status, physical activity, sitting time and self-rated health: The northern sweden MONICA study 2014. *BMC Public Health, 17*(1). https://10.1186/s12889-017-4623-y

Fan, X., Xing, C., Yang, L., Wang, J., & Feng, L. (2020). Fatigue, self-efficacy and psychiatric symptoms influence the quality of life in patients with myasthenia gravis in tianjin, china. *Journal of Clinical Neuroscience: Official Journal of the Neurosurgical Society of Australasia, 79*, 84-89. https://10.1016/j.jocn.2020.06.023

Fieo, R., Ocepek-Welikson, K., Kleinman, M., Eimicke, J. P., Crane, P. K., Cella, D., & Teresi, J. A. (2016). Measurement equivalence of the patient reported outcomes measurement information system ® (PROMIS ®) applied cognition - general concerns, short forms in ethnically diverse groups. *Psychological Test and Assessment Modeling, 58*(2), 255-307. https://www.ncbi.nlm.nih.gov/pubmed/28523238

Fiest, K. M., Fisk, J. D., Patten, S. B., Tremlett, H., Wolfson, C., Warren, S., McKay, K. A., Berrigan, L. I., & Marrie, R. A. (2016). Fatigue and comorbidities in multiple sclerosis. *International Journal of MS Care, 18*(2), 96-104. https://10.7224/1537-2073.2015-070

Flensner, G., Ek, A., Landtblom, A., & Söderhamn, O. (2008). Fatigue in relation to perceived health: People with multiple sclerosis compared with people in the general population. *Scandinavian Journal of Caring Sciences, 22*(3), 391-400. https://10.1111/j.1471-6712.2007.00542.x

Flynn, K. E., Dew, M. A., Lin, L., Fawzy, M., Graham, F. L., Hahn, E. A., Hays, R. D., Kormos, R. L., Liu, H., McNulty, M., & Weinfurt, K. P. (2015). Reliability and construct validity of PROMIS® measures for patients with heart failure who undergo heart transplant. *Quality of Life Research: An International Journal of Quality of Life Aspects of Treatment, Care and Rehabilitation*, *24*(11), 2591–2599. https://doi.org/10.1007/s11136-015-1010-y

Fouladbakhsh, J. M., Szczesny, S., Jenuwine, E. S., & Vallerand, A. H. (2011). Nondrug therapies for pain management among rural older adults. *Pain Management Nursing, 12*(2), 70-81. https://10.1016/j.pmn.2010.08.005

Franklin, A. L., & Harrell, T. H. (2013). Impact of fatigue on psychological outcomes in adults living with rheumatoid arthritis. *Nursing Research, 62*(3), 203–209. https://doi.org/10.1097/NNR.0b013e318283fcb3

Friedman, A. S., Terras, A., Zhu, W., & McCallum, J. (2004). Depression, negative self-image, and suicidal attempts as effects of substance use and substance dependence. *Journal of Addictive Diseases, 23*(4), 55–71. https://doi.org/10.1300/J069v23n04_05

Gjesten, M. T., Bronnick, K., & Testad, I. (2018). Characteristics and predictors for hospitalizations of home-dwelling older persons receiving community care: A cohort study from norway. *BMC Geriatrics, 18*(1), 1-9. https://10.1186/s12877-018-0887-z

Goedendorp, M. M., Tack, C. J., Steggink, E., Bloot, L., Bazelmans, E., & Knoop, H. (2014). Chronic fatigue in type 1 diabetes: Highly prevalent but not explained by hyperglycemia or glucose variability. *Diabetes Care, 37*(1), 73-80. doi:10.2337/dc13-0515

Green, K. (2017, May). Data on display senior shift: Activities change as we age. *U.S. Bureau of Labor Statistics.* https://www.bls.gov/careeroutlook/2017/data-on-display/mobile/older-americans.htm

Gunzler, D., Chen, T., Wu, P., & Zhang, H. (2013). Introduction to mediation analysis with structural equation modeling. *Shanghai Jingshen Yixue, 25*(6), 390-394. https://10.3969/j.issn.1002-0829.2013.06.009

Hardy, S. E., & Studenski, S. A. (2010). Qualities of fatigue and associated chronic conditions among older adults. *Journal of Pain & Symptom Management, 39*(6), 1033-1042. doi:10.1016/j.jpainsymman.2009.09.026

Hawker, G. A., French, M. R., Waugh, E. J., Gignac, M. a. M., Cheung, C., & Murray, B. J. (2010). The multidimensionality of sleep quality and its relationship to fatigue in older adults with painful osteoarthritis. *Osteoarthritis and Cartilage, 18*(11), 1365-1371. doi:10.1016/j.joca.2010.08.002

Hays, R. D., Revicki, D. A., Feeny, D., Fayers, P., Spritzer, K. L., & Cella, D. (2016). Using linear equating to map PROMIS(®) global health items and the PROMIS-

29 v2.0 profile measure to the Health Utilities Index mark 3. *PharmacoEconomics*, *34*(10), 1015–1022. https://doi.org/10.1007/s40273-016-0408-x

Heo, S., McSweeney, J., Tsai, P., & Ounpraseuth, S. (2016). Differing effects of fatigue and depression on hospitalizations in men and women with heart failure. *American Journal of Critical Care, 25*(6), 526-534. https://10.4037/ajcc2016909

Hofer, F., Koinig, K. A., Nagl, L., Borjan, B., & Stauder, R. (2018). Fatigue at baseline is associated with geriatric impairments and represents an adverse prognostic factor in older patients with a hematological malignancy. *Annals of Hematology*, *97*(11), 2235-2243. doi:10.1007/s00277-018-3420-8

Holbein, C. E., Veldtman, G. R., Moons, P., Kovacs, A. H., Luyckx, K., Apers, S., Chidambarathanu, S., Soufi, A., Eriksen, K., Jackson, J. L., Enomoto, J., Fernandes, S. M., Johansson, B., Alday, L., Dellborg, M., Berghammer, M., Menahem, S., Caruana, M., Kutty, S., . . . Cedars, A. (2019). Perceived health mediates effects of physical activity on quality of life in patients with a fontan circulation. *The American Journal of Cardiology*, *124*(1), 144-150. https://10.1016/j.amjcard.2019.03.039

Horne, C. E., Johnson, S., & Crane, P. B. (2019). Comparing comorbidity measures and fatigue post myocardial infarction. *Applied Nursing Research*, *45*, 1-5. doi:10.1016/j.apnr.2018.11.004

Hornsby, B. W. Y., & Kipp, A. M. (2016). Subjective ratings of fatigue and vigor in adults with hearing loss are driven by perceived hearing difficulties not degree of hearing loss. *Ear and Hearing, 37*(1), e1-e10. https://10.1097/aud.0000000000000203

Hornsby, B. W. Y., Naylor, G., & Bess, F. H. (2016). A taxonomy of fatigue concepts and their relation to hearing loss. *Ear and Hearing, 37*(Suppl 1), 136S-144S. https://10.1097/AUD.0000000000000289

Hsiao, H., Li, S., Yang, Y., Lin, L. L., Lin, S., & Wang, J. (2016). Cognitive function and quality of life in community-dwelling seniors with mild cognitive impairment in taiwan. *Community Mental Health Journal, 52*(4), 493-498. https://10.1007/s10597-016-9993-6

Hsu, M., & Tu, C. (2014). Improving quality-of-life outcomes for patients with cancer through mediating effects of depressive symptoms and functional status: A three-path mediation model. *Journal of Clinical Nursing, 23*(17-18), 2461-2472. https://10.1111/jocn.12399

Hurria, A., Soto-Perez-de-Celis, E., Allred, J. B., Cohen, H. J., Arsenyan, A., Ballman, K., Le-Rademacher, J., Jatoi, A., Filo, J., Mandelblatt, J., Lafky, J. M., Kimmick, G., Klepin, H. D., Freedman, R. A., Burstein, H., Gralow, J., Wolff, A. C., Magrinat, G., Barginear, M., & Muss, H. (2019). Functional decline and resilience in older women receiving adjuvant chemotherapy for breast cancer. *Journal of the American Geriatrics Society*, *67*(5), 920–927. https://doi.org/10.1111/jgs.15493

Jing, M., Wang, J., Lin, W., Lei, Y., & Wang, P. (2015). A community-based cross-sectional study of fatigue in middle-aged and elderly women. *Journal of Psychosomatic Research*, *79*(4), 288-294. doi:10.1016/j.jpsychores.2015.05.009

Junghaenel, D. U., Christodoulou, C., Lai, J., & Stone, A. A. (2011). Demographic correlates of fatigue in the US general population: Results from the patient-reported outcomes measurement information system (PROMIS) initiative. *Journal of Psychosomatic Research*, *71*(3), 117-123. https://10.1016/j.jpsychores.2011.04.007

Karakoc, T., & Yurtsever, S. (2010). Relationship between social support and fatigue in geriatric patients receiving outpatient chemotherapy. *European Journal of Oncology Nursing*, *14*(1), 61-67. doi:10.1016/j.ejon.2009.07.001

Karakurt, P., & Ünsal, A. (2013). Fatigue, anxiety and depression levels, activities of daily living of patients with chronic obstructive pulmonary disease. *International Journal of Nursing Practice*, *19*(2), 221-231. doi:10.1111/ijn.12055

Katz, P. (2017). Causes and consequences of fatigue in rheumatoid arthritis. *Current Opinion in Rheumatology, 29*(3), 269-276. https://10.1097/BOR.0000000000000376

Kessing, D., Denollet, J., Widdershoven, J., & Kupper, N. (2015). Fatigue and self-care in patients with chronic heart failure. *European Journal of Cardiovascular Nursing, 15*(5), 337-344. doi:10.1177/1474515115575834

Kim, H., Kim, S., Lee, H., & Oh, S. (2014). Factors affecting symptom experiences of breast cancer patients: Based on the theory of unpleasant symptoms. *Asian Oncology Nursing, 14*(1), 7-14

Kim, H. S., Oh, E. G., Lee, H., Kim, S. H., & Kim, H. K. (2015). Predictors of symptom experience in Korean patients with cancer undergoing chemotherapy. *European Journal of Oncology Nursing, 19*(6), 644-653. https://10.1016/j.ejon.2015.04.003

Kim, H., & Son, H. (2019). Fatigue-related factors for community-dwelling older adults with diabetes: A theory-guided multi-dimensional approach using the dynamic biopsychosocial model. *International Journal of Environmental Research and Public Health, 16*(22), 4502. https://10.3390/ijerph16224502

Kinsinger, S. W., Lattie, E., & Mohr, D. C. (2010). Relationship between depression, fatigue, subjective cognitive impairment, and objective neuropsychological functioning in patients with multiple sclerosis. *Neuropsychology, 24*(5), 573-580. https://10.1037/a0019222

Kline, R.B. (2015). Coming of age. In T.D. Little (Eds.), *Principles and practice of structural equation modeling* (pp. 7-24). The Guilford Press

Kuhn, M. & Johnson, K. (2013). *Applied predictive modeling*. Springer

Kwag, K. H., Martin, P., Russell, D., Franke, W., & Kohut, M. (2011). The impact of perceived stress, social support, and home-based physical activity on mental health among older adults. *International Journal of Aging & Human Development*, *72*(2), 137-154. https://10.2190/ag.72.2.c

Lašaitė, L., Krikščiūnienė, R., Žilaitienė, B., & Verkauskienė, R. (2019). Emotional state, cognitive functioning and quality of life of adult women with turner syndrome in Lithuania. *Growth Hormone & IGF Research, 45*, 37-42. https://10.1016/j.ghir.2019.03.001

Lee, A. R., Wolf, R., Contento, I., Verdeli, H., & Green, P. H. R. (2016). Coeliac disease: The association between quality of life and social support network participation. *Journal of Human Nutrition and Dietetics, 29*(3), 383-390. https://10.1111/jhn.12319

Lee, H. J., Pok, L. S. L., Ng, C. M., Yahya, F., Sockalingam, S., Tee, Y. C., & Raja, J. (2020). Fatigue and associated factors in a multi-ethnic cohort of rheumatoid arthritis patients. *International Journal of Rheumatic Diseases, 23*(8), 1088-1093. https://10.1111/1756-185X.13897

Lee, S. B., Oh, J. H., Park, J. H., Choi, S. P., & Wee, J. H. (2018). Differences in youngest-old, middle-old, and oldest-old patients who visit the emergency department. *Clinical and Experimental Emergency Medicine*, *5*(4), 249-255. https://10.15441/ceem.17.261

Lei, P.W., & Wu, Q. (2007). Introduction to structural equation modeling: Issues and practical considerations. *Educational Measurement: Issues and Practice, 26*(3), 33–43. https://doi.org/10.1111/j.1745-3992.2007.00099.x

Lekander, M., Andreasson, A. N., Kecklund, G., Ekman, R., Ingre, M., Akerstedt, T., & Axelsson, J. (2013). Subjective health perception in healthy young men changes in response to experimentally restricted sleep and subsequent recovery sleep. *Brain Behavior and Immunity, 34,* 43. https://doi.org/10.1016/j.bbi.2013.06.005

Lenz, E. R., Pugh, L. C., Milligan, R. A., Gift, A., & Suppe, F. (1997). The middle-range theory of unpleasant symptoms: an update. *ANS. Advances in Nursing Science, 19*(3), 14–27. https://doi.org/10.1097/00012272-199703000-00003

Lestari, S. K., de Luna, X., Eriksson, M., Malmberg, G., & Ng, N. (2021). A longitudinal study on social support, social participation, and older europeans' quality of life. *SSM - Population Health, 13,* 1-12. https://10.1016/j.ssmph.2021.100747

Li, C., Stanaway, F. F., Lin, J., & Chang, H. (2018). Frailty and health care use among community-dwelling older adults with diabetes: A population-based study. *Clinical Interventions in Aging, 13,* 2295-2300. https://10.2147/cia.s183681

Lin, F., Chen, D. G., Vance, D. E., Ball, K. K., & Mapstone, M. (2013). Longitudinal relationships between subjective fatigue, cognitive function, and everyday functioning in old age. *International Psychogeriatrics*, *25*(2), 275–285. https://doi.org/10.1017/S1041610212001718

Lin, W., Jing, M. J., Tang, J., Wang, J. J., Zhang, H. S., Yuan, L. X., & Wang, P. X. (2015). Factors associated with fatigue among men aged 45 and older: A cross-sectional study. *International Journal of Environmental Research and Public Health*, *12*(9), 10897-10909. https://doi.org/10.3390/ijerph120910897

Linehan, M. M., & Nielsen, S. L. (1983). Social desirability: Its relevance to the measurement of hopelessness and suicidal behavior. *Journal of Consulting and Clinical Psychology, 51*(1), 141-143. https://10.1037//0022-006X.51.1.141

Liu, H. E. (2006). Fatigue and associated factors in hemodialysis patients in Taiwan. *Research in Nursing & Health, 29*(1), 40-50. https://10.1002/nur.20109

Loh, K. P., Zittel, J., Kadambi, S., Pandya, C., Xu, H., Flannery, M., Magnuson, A., Bautista, J., McHugh, C., Mustian, K., Dale, W., Duberstein, P., & Mohile, S. G. (2018). Elucidating the associations between sleep disturbance and depression, fatigue, and pain in older adults with cancer. *Journal of Geriatric Oncology, 9*(5), 464-468. https://10.1016/j.jgo.2018.02.006

Lu, L., Megahed, F. M., Sesek, R. F., & Cavuoto, L. A. (2017). A survey of the prevalence of fatigue, its precursors and individual coping mechanisms among U.S. manufacturing workers. *Applied Ergonomics, 65*, 139-151. https://10.1016/j.apergo.2017.06.004

MacLeod, S., Musich, S., Kraemer, S., & Wicker, E. (1980). Practical non-pharmacological intervention approaches for sleep problems among older adults. *Geriatric Nursing, 39*(5), 506-512. https://doi.org/10.1016/j.gerinurse.2018.02.002

McCann, K., & Boore, J. R. P. (2000). Fatigue in persons with renal failure who require maintenance haemodialysis. *Journal of Advanced Nursing, 32*(5), 1132-1142. https://10.1046/j.1365-2648.2000.01584.x

McElroy, S. F., Olney, A., Hunt, C., & Glennon, C. (2020). Shift work and hospital employees: A descriptive multi-site study. *International Journal of Nursing Studies,* , 103746. https://10.1016/j.ijnurstu.2020.103746

Menting, J., Tack, C. J., Bleijenberg, G., Donders, R., Droogleever Fortuyn, H. A., Fransen, J., Goedendorp, M. M., Kalkman, J. S., Strik-Albers, R., van Alfen, N., van der Werf, S. P., Voermans, N. C., van Engelen, B. G., & Knoop, H. (2018). Is fatigue a disease-specific or generic symptom in chronic medical conditions? *Health Psychology, 37*(6), 530–543. https://doi.org/10.1037/hea0000598

Merriam-Webster (n.d.). *Cognitive.* Retrieved from https://dictionary.apa.org/social-role

Merriam-Webster (n.d.). *Physiological.* Retrieved from https://www.merriam-webster.com/dictionary/physiological

Milligan, R. A., Flenniken, P. M., & Pugh, L. C. (1996). Positioning intervention to minimize fatigue in breastfeeding women. *Applied Nursing Research*, *9*(2), 67-70. https://10.1016/S0897-1897(96)80435-6

Mollaoglu, M., Fertelli, T. K., & Tuncay, F. Ö. (2011). Fatigue and disability in elderly patients with chronic obstructive pulmonary disease (COPD). *Archives of Gerontology and Geriatrics, 53*(2), 93. https://10.1016/j.archger.2010.07.001

Murphy, S. L., Kratz, A. L., Whibley, D., Poole, J. L., & Khanna, D. (2021). Fatigue and its association with social participation, functioning, and quality of life in systemic sclerosis. *Arthritis Care & Research, 73*(3), 415-422. https://10.1002/acr.24122

Murray, K. E., Buul, A., Aden, R., Cavanaugh, A. M., Kidane, L., Hussein, M., Eastman, A., & Checkoway, H. (2019). Occupational health risks and intervention strategies for US taxi drivers. *Health Promotion International, 34*(2), 323-332. https://10.1093/heapro/dax082

Muszalik, M., Kołucka-Pluta, M., Kędziora-Kornatowska, K., & Robaczewska, J. (2016). Quality of life of women with breast cancer undergoing radiotherapy using the functional assessment of chronic illness therapy-fatigue questionnaire. *Clinical Interventions in Aging, 11*, 1489-1494. Retrieved from doi:10.2147/CIA.S113530

Nicklas, B. J., Beavers, D. P., Mihalko, S. L., Miller, G. D., Loeser, R. F., & Messier, S. P. (2016). Relationship of objectively-measured habitual physical activity to chronic inflammation and fatigue in middle-aged and older adults. *The Journals of Gerontology, Series A, 71*(11), 1437-1443. doi:10.1093/gerona/glw131

Nolte, S., Coon, C., Hudgens, S., & Verdam, M. G. E. (2019). Psychometric evaluation of the PROMIS® depression item bank: An illustration of classical test theory methods. *Journal of Patient-Reported Outcomes, 3*(1), 1-10. https://10.1186/s41687-019-0127-0

Norberg, E., Boman, K., & Löfgren, B. (2010). Impact of fatigue on everyday life among older people with chronic heart failure. *Australian Occupational Therapy Journal, 57*(1), 34-41. https://10.1111/j.1440-1630.2009.00847.x

O'Connor, S. (2020). Secondary data analysis in nursing research: A contemporary discussion. *Clinical Nursing Research, 29*(5), 279-284. https://10.1177/1054773820927144

Oh, E., Kim, C., Lee, W., & Kim, S. (2004). Correlates of fatigue in Koreans with chronic lung disease. *Heart & Lung, 33*(1), 13-20. https://10.1016/j.hrtlng.2003.09.001

Oh, H., Park, J., & Seo, W. (2018). Identification of symptom clusters and their synergistic effects on quality of life in rheumatoid arthritis patients. *International Journal of Nursing Practice, 25*(2), e12713-n/a. https://10.1111/ijn.12713

Opinions 4 Good (2020). *Health care panel. Op4G.* https://op4g.com/our-panel/health-care-panel

Osborne, J., & Waters, E. (2002). Four assumptions of multiple regression that researchers should always test. *Practical Assessment, Research, and Evaluation, 8*(2). https://doi.org/10.7275/r222-hv23

Oude Voshaar, M. A., Ten Klooster, P. M., Glas, C. A., Vonkeman, H. E., Taal, E., Krishnan, E., Bernelot Moens, H. J., Boers, M., Terwee, C. B., van Riel, P. L., &

van de Laar, M. A. (2015). Validity and measurement precision of the PROMIS physical function item bank and a content validity-driven 20-item short form in rheumatoid arthritis compared with traditional measures. *Rheumatology (Oxford, England)*, *54*(12), 2221–2229. https://doi.org/10.1093/rheumatology/kev265

Overcash, J., Tan, A., Patel, K., & Noonan, A. M. (2018). Factors associated with poor sleep in older women diagnosed with breast cancer. *Oncology Nursing Forum*, *45*(3), 359-371. https://10.1188/18.ONF.359-371

Paddison, J. S., Effing, T. W., Quinn, S., & Frith Peter, A. (2013). Fatigue in COPD: Association with functional status and hospitalisations. *The European Respiratory Journal*, *41*(3), 565-570. https://10.1183/09031936.00021412

Painter, P., Stewart, A. L., & Carey, S. (1999). Physical functioning: Definitions, measurement, and expectations. *Advances in Renal Replacement Therapy*, *6*(2), 110-123. https://10.1016/s1073-4449(99)70028-2

Paraschakis, A., Douzenis, A., Michopoulos, I., Christodoulou, C., Vassilopoulou, K., Koutsaftis, F., & Lykouras, L. (2012). Late onset suicide: Distinction between “young-old” vs. “old-old” suicide victims. how different populations are they? *Archives of Gerontology and Geriatrics*, *54*(1), 136-139. https://10.1016/j.archger.2011.02.011

Park, J., Oh, H., Park, W., Kwon, S., Ham, O., Suh, Y., & Jeong, H. (2018). Causal relationships between modifiable risk factors of cognitive impairment, cognitive function, self-management, and quality of life in patients with rheumatic diseases. *Orthopaedic Nursing*, *37*(5), 305-315. doi: 10.1097/NOR.0000000000000481

Pascal de Raykeer, R., Hoertel, N., Blanco, C., Lavaud, P., Kaladjian, A., Blumenstock, Y., Cuervo-Lombard, C., Peyre, H., Lemogne, C., Limosin, F., Adès, J., Alezrah, C., Amado, I., Amar, G., Andréi, O., Arbault, D., Archambault, G., Aurifeuille, G., Barrière, S., . . . Zendjidjian, X. (2019). Effects of depression and cognitive impairment on quality of life in older adults with schizophrenia spectrum disorder: Results from a multicenter study. *Journal of Affective Disorders, 256*, 164-175. https://10.1016/j.jad.2019.05.063

Pereira, T., Cipriano, I., Costa, T., Saraiva, M., & Martins, A. (2019). Exercise, ageing and cognitive function - effects of a personalized physical exercise program in the cognitive function of older adults. *Physiology & Behavior, 202*, 8-13. https://10.1016/j.physbeh.2019.01.018

Plach, S. K., Heidrich, S. M., & Jeske, L. (2006). Fatigue representations in women with heart failure. *Research in Nursing & Health*, *29*(5), 452-464. Retrieved from doi:10.1002/nur.20156

Polikandrioti, M., Tzirogiannis, K., Zyga, S., Koutelekos, I., Vasilopoulos, G., Theofilou, P., & Panoutsopoulos, G. (2018). Effect of anxiety and depression on the fatigue of patients with a permanent pacemaker. *Archives of medical sciences. Atherosclerotic diseases*, *3*, e8–e17. https://doi.org/10.5114/amsad.2018.73231

Pope, J. E. (2020). Management of fatigue in rheumatoid arthritis. *RMD Open*, *6*(1), 1-9. https://10.1136/rmdopen-2019-001084

Pouraboli, B., Poodineh, Z., & Jahani, Z. (2019). The effect of relaxation techniques on anxiety, fatigue and sleep quality of parents of children with leukemia under chemotherapy in south east iran. *Asian Pacific Journal of Cancer Prevention: APJCP*, *20*(10), 2903-2908. https://10.31557/APJCP.2019.20.10.2903

Ream, E., & Richardson, A. (1996). Fatigue: A concept analysis. *International Journal of Nursing Studies, 33*(5), 519-529. Retrieved from doi:10.1016/0020-7489(96)00004-1

Redeker, N. S., Lev, E. L., & Ruggiero, J. (2000). Insomnia, fatigue, anxiety, depression, and quality of life of cancer patients undergoing chemotherapy. *Scholarly Inquiry for Nursing Practice*, *14*(4), 275–298

Reishtein, J. L. (2005). Relationship between symptoms and functional performance in COPD. *Research in Nursing & Health, 28*(1), 39-47. https://10.1002/nur.20054

Richards, A., Kanady, J. C., & Neylan, T. C. (2019). Sleep disturbance in PTSD and other anxiety-related disorders: An updated review of clinical features, physiological characteristics, and psychological and neurobiological mechanisms. *Neuropsychopharmacology (New York, N.Y.), 45*(1), 240-241. https://10.1038/s41386-019-0529-y

Roets-Merken, L. M., Zuidema, S. U., Vernooij-Dassen, Myrra J. F. J., & Kempen, Gertrudis I. J. M. (2014). Screening for hearing, visual and dual sensory impairment in older adults using behavioural cues: A validation study. *International Journal of Nursing Studies, 51*(11), 1434-1440. https://10.1016/j.ijnurstu.2014.02.006

Saffer, B. Y., Lanting, S. C., Koehle, M. S., Klonsky, E. D., & Iverson, G. L. (2014). Assessing cognitive impairment using PROMIS® applied cognition-abilities scales in a medical outpatient sample. *Psychiatry Research, 226*(1), 169-172. https://10.1016/j.psychres.2014.12.043

Salter, A., Fox, R. J., Tyry, T., Cutter, G., & Marrie, R. A. (2019). The association of fatigue and social participation in multiple sclerosis as assessed using two different instruments. *Multiple Sclerosis and Related Disorders, 31*, 165-172. https://10.1016/j.msard.2019.04.014

Sanborn, V. E., Spitznagel, M., Crosby, R., Steffen, K., Mitchell, J., & Gunstad, J. (2018). Cognitive function and quality of life in bariatric surgery candidates. *Surgery for Obesity and Related Diseases, 14*(9), 1396-1401. https://10.1016/j.soard.2018.06.010

Schakel, W., Bode, C., Elsman, E. B. M., van der Aa, H.P.A, de Vries, R., van Rens, G.H.M.B, & van Nispen, R.M.A. (2019). The association between visual impairment and fatigue: A systematic review and meta-analysis of observational studies. *Ophthalmic & Physiological Optics, 39*(6), 399-413. https://10.1111/opo.12647

Schmidt, H., Nordhausen, T., Boese, S., Vordermark, D., Wheelwright, S., Wienke, A., & Johnson, C. D. (2018). Factors influencing global health related quality of life in elderly cancer patients: Results of a secondary data analysis. *Geriatrics (Basel, Switzerland), 3*(1), 5. https://doi.org/10.3390/geriatrics3010005

Schreier, A. M., Johnson, L. A., Vohra, N. A., Muzaffar, M., & Kyle, B. (2019). Post-treatment symptoms of pain, anxiety, sleep disturbance, and fatigue in breast cancer survivors. *Pain Management Nursing, 20*(2), 146-151. https://10.1016/j.pmn.2018.09.005

Shakoor, N., Block, J. A., Chua, J., Bradley, L. A., & Catsrejon, I. (2017). Ethnic group differences in pain and physical function in patients with osteoarthritis and rheumatoid arthritis. *Osteoarthritis and Cartilage, 25*(Supplement 1), S373-S374. https://https://doi.org/10.1016/j.joca.2017.02.641

Silva, J. P., Pereira, D. S., Coelho, F. M., Lustosa, L. P., Dias, J. M. D., & Pereira, L. S. M. (2011). Clinical, functional and inflammatory factors associated with muscle fatigue and self-perceived fatigue in elderly community-dwelling women. *Brazilian Journal of Physical Therapy, 15*(3), 241-248. doi:10.1590/S1413-35552011000300011

Silva, J., Truzzi, A., Schaustz, F., Barros, R., Santos, M., Laks, J., Silva, J., Truzzi, A., Schaustz, F., Barros, R., Santos, M., & Laks, J. (2017). Impact of insomnia on self-perceived health in the elderly. *Arquivos De Neuro-Psiquiatria, 75*(5), 277-281. https://10.1590/0004-282x20170031

Smith, E. M., Imam, B., Miller, W. C., Silverberg, N. D., Anton, H. A., Forwell, S. J., & Townson, A. F. (2016). The relationship between fatigue and participation in spinal cord injury. *Spinal Cord, 54*(6), 457-462. https://10.1038/sc.2015.149

So, W. K. W., Leung, D. Y. P., Ho, S. S. M., Lai, E. T. L., Sit, J. W. H., & Chan, C. W. H. (2013). Associations between social support, prevalent symptoms and health-related quality of life in Chinese women undergoing treatment for breast cancer: A cross-sectional study using structural equation modelling. *European Journal of Oncology Nursing, 17*(4), 442-448. https://10.1016/j.ejon.2012.11.001

Soares, W. J. S., Lima, C. A., Bilton, T. L., Ferrioli, E., Dias, R. C., & Perracini, M. R. (2015). Association among measures of mobility-related disability and self-perceived fatigue among older people: A population-based study. *Brazilian Journal of Physical Therapy, 19*(3), 194-200. https://10.1590/bjpt-rbf.2014.0091

Soyuer, F., & Şenol, V. (2011). Functional outcome and depression in the elderly with or without fatigue. *Archives of Gerontology and Geriatrics, 53*(2), e164–e167. https://doi.org/10.1016/j.archger.2010.08.006

StataCorp. (2019). Stata Statistical Software (Version 16). StataCorp LLC. https://www.stata.com

Stephen, S. A. (2008). Fatigue in older adults with stable heart failure. *Heart & Lung: The Journal of Critical Care, 37*(2) doi:10.1016/j.hrtlng.2007.03.006

Stites, S. D., Karlawish, J., Harkins, K., Rubright, J. D., & Wolk, D. (2017). Awareness of mild cognitive impairment and mild alzheimer's disease dementia diagnoses associated with lower self-ratings of quality of life in older adults. *The Journals of Gerontology: Series B, 72*(6), 974-985. https://10.1093/geronb/gbx100

Teresi, J. A., Ocepek-Welikson, K., Kleinman, M., Ramirez, M., & Kim, G. (2016). Measurement equivalence of the patient reported outcomes measurement information system ® (PROMIS ®) anxiety short forms in ethnically diverse groups. *Psychological Test and Assessment Modeling, 58*(1), 183-219. https://www.ncbi.nlm.nih.gov/pubmed/28649483

Teshale, S. M., Molton, I. R., & Jensen, M. P. (2019). Associations among decisional autonomy, fatigue, pain, and well-being in long-term physical disability. *Rehabilitation Psychology, 64*(3), 288–297. https://doi.org/10.1037/rep0000279

Tolstrup Larsen, R., Tang, L. H., Brochmann, N., Meulengracht Flachs, E., Illemann Christensen, A., Hasselbalch, H. C., & Zwisler, A. D. (2018). Associations between fatigue, physical activity, and QoL in patients with myeloproliferative neoplasms. *European Journal of Haematology, 100*(6), 550–559. https://doi.org/10.1111/ejh.13048

Torossian, M., & Jacelon, C. S. (2021). Chronic Illness and Fatigue in Older Individuals: A Systematic Review. *Rehabilitation Nursing: the official journal of the Association of Rehabilitation Nurses*, *46*(3), 125–136. https://doi.org/10.1097/RNJ.0000000000000278

van de Mortel, T.F. (2008). Faking it: Social desirability response bias in self-report research. *Australian Journal of Advanced Nursing, 25*(4), 40-48

van Hees, S. G. M., van den Borne, B.H.P., Menting, J., & Sattoe, J.N.T. (2020). Patterns of social participation among older adults with disabilities and the relationship with well-being: A latent class analysis. *Archives of Gerontology and Geriatrics, 86,* 1-12. https://10.1016/j.archger.2019.103933

van Lummel, R. C., Walgaard, S., Pijnappels, M., Elders, P. J. M., Garcia-Aymerich, J., van Dieën, J. H., & Beek, P. J. (2015). Physical performance and physical activity in older adults: Associated but separate domains of physical function in old age. *PLoS ONE, 10*(12), 1–16. doi:10.1371/journal.pone.0144048

van Seben, R., Reichardt, L. A., Aarden, J. J., van der Schaaf, M., van der Esch, M., Engelbert, R. H. H., Twisk, J. W. R., Bosch, J. A., & Buurman, B. M. (2019). The course of geriatric syndromes in acutely hospitalized older adults: The hospital-

ADL study. *Journal of the American Medical Directors Association, 20*(2), 152-158. https://10.1016/j.jamda.2018.08.003

Vassend, O., Røysamb, E., Nielsen, C. S., & Czajkowski, N. O. (2018). Fatigue symptoms in relation to neuroticism, anxiety-depression, and musculoskeletal pain. A longitudinal twin study. *PLoS ONE, 13*(6), 1-21. https://10.1371/journal.pone.0198594

Veldhuijzen van Zanten, J., Douglas, M. R., & Ntoumanis, N. (2021). Fatigue and fluctuations in physical and psychological wellbeing in people with multiple sclerosis: A longitudinal study. *Multiple Sclerosis and Related Disorders, 47*, 1-7. https://10.1016/j.msard.2020.102602

Verma, J. P., & Abdel-Salam, A. G. (2019). *Testing statistical assumptions in research*. Wiley.

Vitiello, M. V., McCurry, S. M., Shortreed, S. M., Baker, L. D., Rybarczyk, B. D., Keefe, F. J., & Von Korff, M. (2014). Short-term improvement in insomnia symptoms predicts long-term improvements in sleep, pain, and fatigue in older adults with comorbid osteoarthritis and insomnia. *Pain*, *155*(8), 1547–1554. https://doi.org/10.1016/j.pain.*2014*.04.032

Wennberg, A. M., Canham, S. L., Smith, M. T., & Spira, A. P. (2013). Optimizing sleep in older adults: Treating insomnia. *Maturitas*, *76*(3), 247-252. https://10.1016/j.maturitas.2013.05.007

Yamada, Y., Vlachova, M., Richter, T., Finne-Soveri, H., Gindin, J., van der Roest, H., Denkinger, M. D., Bernabei, R., Onder, G., & Topinkova, E. (2014). Prevalence and correlates of hearing and visual impairments in european nursing homes:

Results from the SHELTER study. *Journal of the American Medical Directors Association, 15*(10), 738-743. https://10.1016/j.jamda.2014.05.012

Yazici, Y., Kautianen, H., & Sokka, T. (2007). Differences in clinical status measures in different ethnic/racial groups with early rheumatoid arthritis: Implications for interpretation of clinical trial data. *Journal of Rheumatology, 34*(2), 311-315

Yoo, J. S., Yang, H. C., Lee, J. M., Kim, M. S., Park, E., & Chung, S. H. (2020). The association of physical function and quality of life on physical activity for non-small cell lung cancer survivors. *Supportive Care in Cancer, 28*(10), 4847-4856. https://10.1007/s00520-020-05302-6

Yu, L., Buysse, D. J., Germain, A., Moul, D. E., Stover, A., Dodds, N. E., Johnston, K. L., & Pilkonis, P. A. (2011). Development of short forms from the PROMIS™ sleep disturbance and sleep-related impairment item banks. *Behavioral Sleep Medicine, 10*(1), 6-24. https://10.1080/15402002.2012.636266

Zizza, C. A., Ellison, K. J., & Wernette, C. M. (2009). Total water intakes of community-living middle-old and oldest-old adults. *The Journals of Gerontology: Series A, 64A*(4), 481-486. https://10.1093/gerona/gln045