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Fatigue-related Symptom Clusters and their Relationship with Depression, and Functional Status in Older Adults Hospice Patients with Cancer.

Suzan Fouad Abduljawad

University of South Florida, suzan.aj@hotmail.com

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Fatigue-related Symptom Clusters and their Relationship with Depression, and Functional Status
in Older Adults Hospice Patients with Cancer.

by

Suzan Fouad Abduljawad

A dissertation proposal submitted in partial fulfillment
of the requirements for the degree of
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College of Nursing
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Major Professor Hsiao-Lan Wang, Ph.D., RN, CMSRN, HFS
Jason W. Beckstead, Ph.D.
Debra Dobbs, Ph.D.
Carmen S. Rodriguez, Ph.D., ANP-BC, AOCN
Constance Visovsky, PhD

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Dedication

This dissertation is dedicated to my outstanding mother Khadija Elmoujarrad. Her devotion, hard work, and thirst for knowledge inspired my motivation to pursue my Doctor of Philosophy degree. Thank you is never enough, my mother, for your unconditional love, support, endless prayers and encouragement which put me on the road to success and completion of this dissertation. To my deceased father, Fouad Abduljawad, who had always encouraged me to pursue art and science and dream big. I wish you were here to witness the success of your daughter getting the honor of being the first female to attain the doctoral degree in our family.

I dedicate this to my beloved family, my friends, my educators, and mentors, I hope that you may find this dissertation a source of pride and inspiration. I am blessed to have each and every one of you in my life.

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Abstract

The hospice care population with cancer are often older adults who report many cancer-related symptoms experienced often in clusters. Most prevalent of these symptoms is fatigue and often it co-occurs with depressive symptoms and poor physical functioning. This dissertation examined fatigue, symptom clusters, depression, physical activity, and functional status in older adults with cancer. The aims of the literature review were to understand the relationship among physical functioning, cancer fatigue, fatigue-related symptom clusters, and their relationship with functional status in older adults. The literature related to these associations is insufficient and inconclusive. The methods section aimed to investigate the reliability and validity of the Center for Epidemiology Studies-Depression scale, Boston Short Form (CESD-10). Using Structural Equation Modeling (SEM) for confirmatory factor analysis, the factor structure of responses in a cross-sectional sample (N = 200) of adults with different types and stages of cancer was examined. Internal consistency reliability estimate Cronbach's alpha = 0.737. The CESD-10 four-factor model (positive affect, depressive affect, somatic complaints, and interpersonal challenges) fits the data well. The CESD-10 was a valid and reliable measure for assessing depressive symptoms in this study. The final section examined fatigue related symptom clusters and their relationships with functional status in older adult hospice patients with cancer (N=519). The fatigue-related symptom cluster (lack of energy, feeling drowsy and lack of appetite), significantly predicted poor functional status. Experiencing physical and psychological symptoms has a significant impact on functional dependence. Hospice healthcare professionals should be alert to older adults' symptom cluster experience during assessment and management.

Dissertation Overview

Introduction

In 2018, over a 1.7 million new cancer cases and more than 609,000 cancer deaths are estimated to occur in the United States (Siegel, Miller, & Jemal 2018). The anticipated demographic changes of the U.S. are derived from the rapidly aging population. By 2030, new cancer diagnoses are projected to reach 2.3 million a year, approximately (60%) of those patients, and up to 70% of all cancer mortality will be occurring in 65 years of age or older (Smith, D., Smith, L., Hurria, Hortobagyi, & Buchholz, 2009). This estimated dramatic spike in cancer incidence of older adults in future cancer population will shift the healthcare system and the direction of research, towards new cancer therapies and care pathways. Which in turn creates a need for further investigations of cancer symptom science, to solidify older people's health care approach toward optimum quality of life (QOL).

Fatigue in Older Adult Cancer Population

Fatigue is one of the most prevalent, persistent, and distressing symptoms experienced by older adult patients across the cancer trajectory (Beck, Towsley, Caserta, Lindau, & Dudley, 2009; Luctkar-Flude, Groll, Woodend, & Tranmer, 2009). A significant number of those older adults with cancer exhibit functional impairment (Jacobson, 2013; Garrison et al., 2011). When compared to their younger counterparts, older adults with cancer often present with other chronic illnesses, such as arthritis, myalgia, and insomnia. These co-morbidities dispose them with great risks of psychological distress, depression, limited functional status with manifestation of constrained overall performance status and inability of carrying out activities of daily living

(Barbera et al., 2010; Beck et al., 2009; Luctkar-Flude et al., 2009; Giacalone et al., 2013; Hellstadius et al., 2016; Palgi, Shrira, & Zaslavsky, 2015; Rha & Lee, 2017). Nevertheless, over 75% of the studies in recent systematic reviews failed to report co-morbidities and appeared to discount the importance of evaluating multimorbidities and fatigue-related symptoms relationship with functional status (Cramp & Byron-Daniel, 2012; Puetz & Herring, 2012; Mishra et al., 2012; Rha & Lee, 2017).

Researchers have repeatedly identified that fatigue is at the center of the cancer symptoms experience, especially in symptom cluster research (Van Lancker, Beeckman, Verhaeghe, Van Den Noortgate, & Van Hecke, 2016; Yeo et al., 2012). Older adult patients with cancer often present with an accentuated fatigue experience secondary to such experience that interferes with their physical/psychological well-being and QOL (Beck et al., 2009; Luctkar-Flude et al., 2009). Research findings show consistent symptom clusters that are most relevant to cancer fatigue including pain, sleep disturbance, anorexia, dyspnea, and gastrointestinal (constipation, nausea, and diarrhea) complications (Tsai, Wu, Chiu, Hu, & Chen, 2006; Van Lancker et al., 2016). However, in addition to the physical symptoms, psychological distress and/or depression are more often co-occurring in the fatigue symptom clusters and found to increase cancer fatigue experienced (Hwang, Cho, & Yoo, 2016; Nho, Kim, & Nam, 2017; Tsai, Wu, Chiu, & Chen, 2010)). A broad range of cancer studies, with different genders, ages, and various cancer stages, notably identified the correlation between psychological symptoms, fatigue, and functional status (Rha & Lee, 2017; Van Lancker et al., 2016). Recent and ongoing investigations consistently conclude that high psychological distress and lack of social support has a direct impact on physical deterioration of the patient, no matter what form of cancer, or which symptom cluster (Okuyama et al., 2008)). Understanding the importance of these fatigue-

related clusters in older adults with cancer is integral to future interventions, treatments, and care.

Symptom Clusters

Understanding symptoms is essential in palliative care. Much research in this area is still needed. Throughout the terminal cancer stages, specific symptom clusters and their proper identification are often overlooked. Recent research in the latter phases of advanced cancer and older adult patients indicates more attention is needed to the details of the symptoms within the clusters. Van Lancker et al., (2016) compared older adults in geriatric hospital units to those in non-geriatric units in a cross-sectional study. Four hundred palliative patients with cancer were evaluated using validated and agglomerated clustering studying the physical, psychological, functional, social and existential aspects of their experience. Results from this study indicated a need for more acute attention to the analyzing of symptoms within clusters that would better distinguish a patient symptom experience from the other in order to provide more personalized and accurate care. In this case, 3 patient groups were identified as 1) symptom-free 2) physical discomfort 3) physical and psychological discomfort. Group 3 had a significantly higher geriatric risk profile on their functional dependency in tandem with feeling less meaning in their lives, prone to or with depression and other psychological disorders. This reflects a stronger need to better assess the impact that the psychosocial dynamic has on both the physical symptoms which cluster with cancer fatigue and their predictability of functional status or lack thereof.

Further supporting the connection between the psychological and physical discomforts, a study conducted by Okuyama et al., (2008) stresses that fatigue, a primary symptom of the terminal cancer spectrum, was found to be much more severe when coupled with psychological distress. Greater fatigue was directly correlated with psychological distress indicating the

importance of psychological intervention in the inclusion of treatment and care for fatigue and its' associated symptoms. Conversely, Hui, dos Santos, Chisholm, and Bruera, (2015), found that depression dissipates while increasing discomfort and pain continue to persist. This study, assessing symptoms during the last seven days of the life, suggests that it is precisely the detachment from depression experience could serve as a predictor of pending death. Therefore, this study reinforces the priority and urgency to focus on the psychosocial and mental experience of the palliative care patients, in equal tandem with all of the psychological symptoms, throughout all crucial phases from their admission into hospice care.

Alternatively, Tsai et. al, (2006) assessed symptom clusters in cancer patients of the lung, liver, stomach, the most prevalent symptoms identified were fatigue, weakness, anorexia, abdominal/gastrointestinal pain, and depression. Following this, the authors undertook a deeper investigation into the change patterns of severity between one week after admission and two days before death. Six clusters were identified, and their severity was measured against the time frames from admission to their death. This study demonstrated that the most prevalent symptom clusters (gastrointestinal complications, insomnia, depression, and aggression) with an emphasis on both physical and psychological symptoms, were improved through palliative care. On the other hand, fatigue was in the group associated with anorexia and dyspnea and showed no improvement. The conclusion from this study once again emphasizes a stronger focus needed, not just on symptom management, but a holistic approach that will equally tend to the psychosocial and spiritual dynamic of the patients near the end of life experience.

Symptom Clusters, Functional Status, and Quality of Life

Identifying symptoms within symptom clusters supports the imperative to define QOL. This is the primary objective, and most rational solution, for palliative care and anyone in the late

stages of their lives. There is a lack of longitudinal studies to understand relationships between symptom clusters, functional status, and QOL. Prior research has focused on the cluster symptoms, rather than symptoms within the clusters; this leads to a tendency to over-generalize the concept of functional status impact on QOL. Ongoing investigations have supported this need to distinguish. Two earlier studies of ovarian cancer patients identified specific symptom clusters as a result of the cancer disease itself and the cancer therapy (Hwang et al., 2016; Nho et al., 2017). In the Hwang (2016) study, prevalent symptom clusters were found to include fatigue, depression, psychological distress, and abdominal discomfort; its effects were amplified by patients with high depression. These clusters influenced all aspects of their QOL. In the other study Nho et al. (2017) deciphered two clusters. The first cluster was anxiety, depression, fatigue, sleep disturbances. The second cluster was pain and chemotherapy-related symptoms. It was the combination of both that led to the poorer QOL. That said, both studies concluded that, while the symptom clusters varied depending on age, onset, disease duration, recurrence, the combination of physical with emotional symptoms did indeed affect the overall quality of the ovarian cancer patients' lives. While this may seem an obvious conclusion, palliative care research is now lending itself to more definitive observations on the impact of psychosocial well-being amidst the specific symptom clusters, leading to better ways to predict and manage functional status.

In a more recent study that determined differential contributions of symptom cluster to functional status and QOL, Rha & Lee (2017) assessed 300 patients undergoing palliative chemotherapy. Four symptom clusters were identified, while nausea/vomiting/appetite symptoms were categorized with a poor emotional experience to negatively affect the role and social functioning, fatigue and its' correlated cluster symptoms such as dyspnea, constipation, and sleep

disorders negatively affected physical functioning. Role functioning was found to have a direct impact on QOL. All of the other symptom, symptom clusters and/or subsets of symptoms indirectly impacted QOL, these symptoms included both physical and psychosocial symptoms. Once again, these findings support the urgency to understand the coupling of psychological distress, such as depression, with the recurring physical symptoms. The psychosocial dynamic seems to be a prevalent predictor to negatively affect both functional status and QOL. Similarly, another study concluded severity of psychological distress as having a direct and immediate impact on physical deterioration (Tsai et al., 2010).

Depression

Depression is one of the most important symptoms at the time of hospice admission (Garrison et al., 2011; McMillan, Small, & Haley, 2012). Progressively close to the end of life, greater losses may become at stake including relationship connections, personal privacy, dignity, freedom, liberty, and independence, as well as cognitive and physical capacity. In response to such suffering, many of cancer patients endure a significant emotional distress. (Choi, Ransom, & Wyllie, 2008). This normal response to tragic life events is a part of a spectrum of depressive symptoms which range from normal feelings of sadness to adjustment disorder with depressed moods or a full-blown major depression (Rhondali et al., 2012; Widera & Block, 2012). Living with chronic stress response had been linked to increased mortality in cancer patients. Such adversities include reduced body tumor surveillance, reduced tumor suppressor gene activity, and cellular apoptosis, and increased cancer invasiveness (Smith 2015). Neglecting depression assessment and management in hospice care settings can be equated with hastening death in this population.

Despite the highlighted demand for a change in detecting depression in the cancer population, recent studies showed that psychosocial assessments for depression were missing about 75% of the time from hospice patient's records (McMillan et. al, 2012). According to the National Comprehensive Cancer Network (2018), only about 5% of the patients with cancer obtain psychological care (Watson et al., 2016). Besides the stigma associated with mental illness, researchers report that a likely barrier to the adequate diagnosis and treatment of depression is a common belief that experiencing depression is universal at the end of life (Widera & Block, 2012). The underdiagnosis of depression was not attributed to the clinicians' lake of knowledge or care providers' neglect, Rhondali et al., (2012) suggested the lack of time as reported by oncology palliative care clinicians is an important factor. Perhaps the fast and busy clinical pace of the work environment urged the move towards electronic symptom screening both nationally and internationally (Burstin, Leatherman, & Goldmann, 2016). However, active management of depression and systematic assessments of depression in hospice remains inadequate and difficult to implement (McMillan et. al, 2012; Rhondali et al., 2012).

Depression can worsen the overall symptom burden, it affects the patient's ability to adhere to treatment recommendations, it affects how people cope with their cancer, and adversely affects not only the patient's but also the patient's family and caregivers' QOL (Lloyd-Williams, Dennis, & Taylor, 2004; Lloyd-Williams, Shiels, Taylor, & Dennis, 2009; Satin, Linden, & Phillips, 2009). The issues with depression in older adults with cancer are very unique compared to the general cancer population. Older adults experience depressive symptoms differently, unexplained physical complaints such as fatigue and headaches, or sleep disturbances are often a sign of depression in this age group, rather than feeling sad or depressed. Also, they may appear confused, have memory loss, or be agitated. Delirium is also common (90%) among

older adults with advanced disease in the final days of life, making it even more challenging for detecting depression in the hospice population with cancer (Nelson, et al., 2010). In addition, when it comes to assessing depression, there's the challenge of choosing the most appropriate instrument for this group. Many depression measures have been validated for use with the general population of older adults, and with patients with cancer, however, there are fewer reported data on the validity and reliability of these most commonly used instruments in older adult hospice patients with cancer (Marks & Heinrich, 2013).

Moreover, prior hospice research on depression and symptom assessments had focused on studying symptoms separately rather than exploring how different symptoms co-occur in certain patterns (i.e. symptom cluster) and how they interact and influence each other (Lloyd-Williams et al., 2017; Widera & Block, 2012). While hospice care is covered by Medicaid and most private insurance plans, approximately 85% of enrollees receive hospice coverage through the Medicare hospice benefit. Quality and effective utilization and management of government resources are warranted. All health organizations are called out for better and innovative measures to detect depression. Understanding symptom clusters, how they can influence each other, and how they predict certain health-related outcomes may contribute to improving symptoms assessment in hospice care settings.

This dissertation research seeks to discern the myriad symptoms experienced by older adult cancer patients in hospice care. There are three sections/manuscripts in this dissertation. Using this proposed model, this dissertation will examine the associations among fatigue-related symptom clusters (physical symptoms), functional status, and depression (psychological symptoms) in older adults with cancer in hospice. In the first section of the dissertation, an integrative review is presented that was to understand the effect of physical activity interventions

that improved fatigue and functional status in older adult cancer population (Title: Physical Activity, Cancer-related Fatigue, and Functional Status in Older Adults with Cancer: A Review of Literature). In the second section, a psychometric evaluation of a clinical relevant depression scale (CESD-10) is described while depression is considered as the psychological symptom in the conceptual model (Title: Validity and Reliability of the Center for Epidemiologic Studies Depression, Boston Short Form: A Clinically Relevant Scale for Depression Detection in Cancer Patients). In the third section, the fatigue-related cluster is identified. Its relationships with functional status and depression are examined and confirmed (Title: Fatigue-Related Symptom Clusters, Depression and Functional Status of Older Adults in Hospice).

Definitions of Relevant Terms

For the purpose of this study, the following terms and definitions were used.

1. **Fatigue in cancer:** A physical symptom; an unusual, sustained, subjective sense of tiredness, malaise or lack of energy, related to cancer or cancer treatment that interferes with usual functioning (The National Comprehensive Cancer Network [NCCN], 2018).
2. **Depression:** A psychological symptom; includes a series of depressive symptoms such as lack of energy, inability to concentrate, lack of interest and pleasure in daily activities, significant weight loss or gain, insomnia or excessive sleeping, feelings of worthlessness or excessive guilt and recurrent thoughts of death or suicide (American Psychological Association, 2018).
3. **Symptom cluster:** The presence of a group of related co-occurring symptoms which may not have a shared etiology but can have a combined effect on outcomes as patient's morbidity (Miaskowski, Aouizerat, Dodd & Cooper, 2007).

4. **Physical activity:** a bodily movement produced that requires energy expenditure as a part of a structured or prescribed exercise intervention (World Health Organization, 2018).
5. **Functional status:** A functional measure that attempts to estimate the patients' general well-being and ability to independently perform activities of daily living.
6. **Older adults:** The World Health Organization (2010) defines older age based on a range of characteristics including the change in social role and functional abilities. For the purpose of this research older adults are defined as: adults 65 of age and older.
7. **Hospice:** A facility which delivers hospice care programs and services designed to provide palliative care and emotional support to the terminally ill in a home or home-like setting where symptoms are controlled, and QOL is maintained. cite

Theoretical Background

Clinical experts and researchers alike have an agreement concerning the symptom cluster phenomenon in patients with cancer (Agasi-Idenburg, Thong, Punt, Stuijver, & Aaronson, 2017; Nieder & Kämpe, 2017; Nho et al. 2017; Reich et al., 2017; Van Lancker et al., 2016). The focus on symptom cluster research stems from the innovations and advances in science and cancer therapies (Aktas, Walsh, & Rybicki, 2010; Dong et al., 2016; Yeh, Chien, Lin, Bovbjerg, & Van Londen, 2016). A key principle of the Theory of Unpleasant Symptoms (Lenz, Suppe, Gift, Pugh, & Milligan, 1995), is that multiple disease-related symptoms often occur simultaneously and have interactive and adversative interaction. In cancer research, this premise is supported by findings indicating the worst fatigue and sleep quality were related to the most severe pain (Lenz, Pugh, Milligan, Gift, & Suppe, 1997). Patient factors influencing the symptom experience include age, living arrangement disease stage, and months from diagnosis.

The outcome of the symptom experience is conceptualized as functional status. In summary, the Theory of Unpleasant Symptoms helps guide the current study by providing a framework that postulates (1) cancer symptoms are interrelated; (2) patient contextual factors influence the experience of physical and psychological symptoms and fatigue-related symptom cluster; (3) Functional status is an outcome of the symptom experience.

Behavioral Logical Model:

To answer the research questions and test the proposed theoretical relationships a conceptual framework that integrates the selected constructs of fatigue-related symptom clusters (FSC) of participation, and functional status is presented (Figure 1). Using a logical model, the relationships among the factors of FSC (physical and psychological symptom) and predictors of functional status (outcome) are delineated.

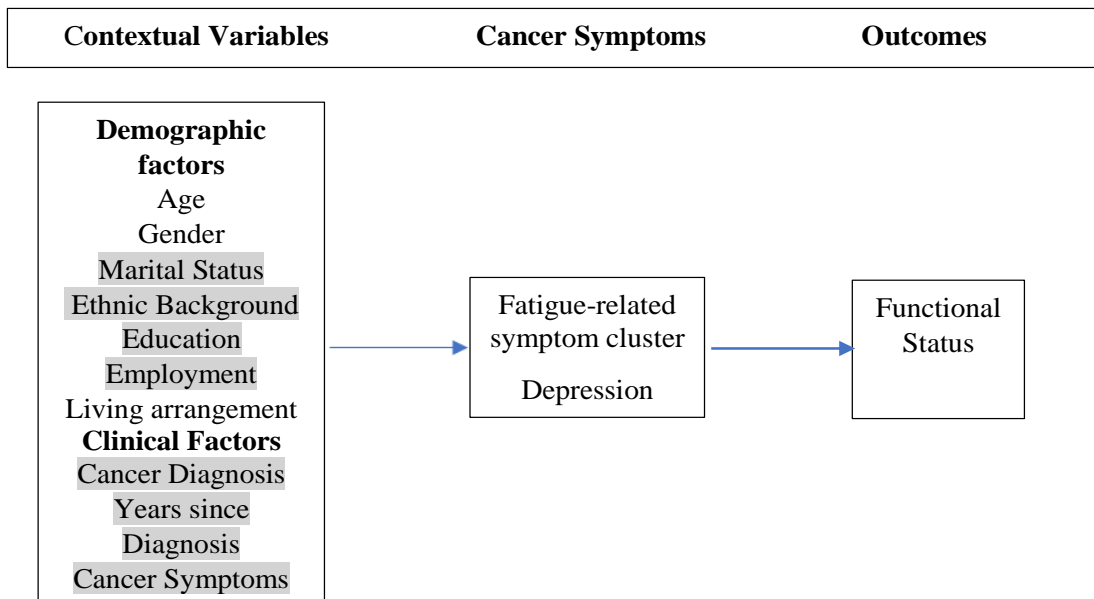


Figure 1. Directional pathways of fatigue-related symptoms and functional impairment with psychosocial, behavioral, and physiological variables.

Statement of the Problem

Patients in hospice care who were treated with surgery, radiation or chemotherapy and are in advanced or terminal stages of their cancer illness, often experience an array of distressing symptoms that occur simultaneously in clusters (Kirkova, Walsh, Aktas, & Davis, 2010). Over one-third of patients with cancer experience symptoms significantly. Among these symptoms, fatigue has been the most frequent, severe, and distressing symptom reported (Beck et.al, 2009; Luctkar-Flude et. al, 2009). More importantly, a mix of fatigue, depression, sleeplessness, and poor appetite renders them with a struggle to carry activities of daily living, a decline in functional status (Dodd, Cho, Cooper, & Miaskowski, 2010). Functional status operationally defined by performance was significantly influenced by fatigue and/or fatigue-related symptom cluster.

When the purpose of hospice care is to alleviate suffering and maximizing the QOL for the patients who are in the last phases of an incurable disease, focusing on detecting symptom cluster should be a priority. Many studies which addressed older adult functional status in patients with cancer included patients who are cancer survivors or have an early-stage disease (Beck et.al, 2009; Luctkar-Flude et. al, 2009; Sprod et al., 2012). There is limited research on predictors of functional status in hospice settings. Few nursing studies report the percentage of the population with advanced disease, and even fewer included patients near the end of life or those receiving hospice care services (Dy et al., 2012; Garrison et al., 2011). There is a need to explore whether the functional status is influenced by the experience of FSC in hospice patients with advanced cancer disease. Several studies concluded that more than half of all patients with advanced cancer disease who are receiving treatment experience co-occurring symptoms (Delgado-Guay, Yennurajalingam, Parsons, Palmer, & Bruera, 2011; Nho et al., 2017; Nieder &

Kämpe, 2017). The stability of symptom clusters remains unclear, whether patients with advanced cancer continue to experience similar fatigue-related symptom clusters after transitioning to hospice care is an area in need of further nursing research.

Significance to Nursing Research

Identifying the fatigue-related symptom cluster and understanding its relationship with functional status and depression, in older adult hospice patients, will inform fatigue symptom management interventions so that nursing researchers will be able to detect what other symptoms in the cluster are likely to change. The desired symptom cluster research outcome is similar to novel treatments, which aim to manage several symptoms by targeting their common pathway. Living in chronic stress response had been linked to reduced lifespan in patients with cancer (Smith, 2015; Denieffe, Cowman, & Gooney, 2014). Considering symptom clusters as a major source of chronic stress in the hospice patients, this study will inform the future symptom cluster researcher priorities and the clinical practice of every compassionate nurse who strives to make a difference in older adult lives.

Implications for Clinical Practice

While hospice care is covered by various public and private insurance plans, approximately 85% of enrollees receive hospice coverage through the Medicare hospice benefit (National Hospice and Palliative Care Organization: Facts and Figures Hospice Care in America, 2016). Quality and effective utilization and management of government resources are warranted. All health organizations are called out for better and innovative measures to detect health outcomes. Experiencing cancer symptoms in clusters can worsen the overall symptom burden as it extenuates symptom distress, it affects the patient's ability to adhere to treatment recommendations, how people cope with their cancer, and adversely affects not only the

patient's but also the patient's family and caregivers' QOL (Stapleton, Hplden, Epstein, & Wilkie, 2016; Lloyd-Williams et al., 2009; Satin et al., 2009). Understanding fatigue-related symptom clusters, how they relate to each other, and how they influence functional status may contribute to improving older adults' symptom assessment and management in hospice care settings.

The use of symptom cluster analysis to predict and detect functional status is a contemporary approach to utilizing health information, it will contribute to the enhancement of hospice and palliative care clinicians' sensitivity for identifying risk factors, and older adults at risk for impaired cognitive or physical capacity (Widera & Block 2012). Also, it will help promote and advance the statistical methods and assessment tools use for cancer-related symptom cluster research (Aktas, Walsh, & Hu, 2014; So et al., 2009). In addition, fatigue-related symptom cluster is considered as a physical symptom relating to functional status while depression is defined as a psychological symptom with confounding effects in this relationship. This study will shed light on symptom predictors of functional status, it will provide an understanding of the risk factors that warrant initiating referrals and appropriate interventions to optimize health outcomes and reduce the potential symptom distress among older adult hospice patients with cancer.

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Section One: Physical activity, fatigue, and functional status in older adults with cancer. A Review of Literature

Abstract

More than half of the older adults with cancer report fatigue as the most common symptom that is experienced with moderate to severe intensity most of the time, and often is complicated with concurrent symptoms and comorbidities. We undertook a systemic review of the current literature to summarize the evidence exploring fatigue-related symptom cluster, and what relationships, if any, exist between fatigue, physical activity, and functional status. To synthesize data about older adults' fatigue and functional status, systematic reviews are included in the narrative of the literature in this area from 2011 to 2018.

Empirical evidence supports the benefits of physical activity for the management of cancer fatigue and improving physical functioning in the older adult cancer population. Multimodal interventions including aerobic and resistance exercises showed significant improvements in cancer fatigue. Future research is warranted to determine the most effective physical activity parameters for fatigue in older adults with cancer including intensity level, duration, and frequency of sessions. Consensus on the most appropriate fatigue outcome measure also is needed as are studies that are sufficiently powered to detect changes in fatigue. Further work should include patients with advanced disease who are receiving palliative care. This review concluded a need for further research regarding comprehensive physical activity interventions for the management of cancer fatigue. in older adults with cancer in hospice care.

Keywords: palliative care, exercise, physical functioning, symptom cluster, frail.

Introduction

Clinically, fatigue in cancer is highly distressing, and prevalent, occurring in about 70% of older adults with cancer. If left unmanaged fatigue can compromise patients' functional status in a way that alters their health-related quality of life and changes their lives forever. Given that fatigue is almost never occurring in isolation, both physical and psychological factors associated with fatigue have been implicated in increased suffering, increased symptom intensity and burden reduced treatment adherence and ultimately reduced survival time. Increasing physical activity and committing to exercise is highly recommended as an effective non-pharmacological intervention for the management of fatigue during the cancer continuum (Agasi-Idenburg, Thong, Punt, Stuver, & Aaronson, 2017; Barbera et al., 2010; Deckx et al., 2011; Giacalone et al., 2013; Van Lancker, Beeckman, Verhaeghe, S., Van Den Noortgate, & Van Hecke, 2016; National Comprehensive Cancer Network, 2018; Palgi, Shrira, & Zaslavsky, 2015; Rock et al., 2012; Sprod et al., 2012; Yennurajalingam et al., 2016).

There are tangible benefits of physical activity when it comes to cancer symptom management. Physical activity is associated with significantly reduced fatigue during and after the course of cancer treatment and has beneficial effects on functional status and quality of life (QOL). Physical activity also is recommended for its' significant beneficial effect on depression and pain as well as the sleep disturbances and older adults' cognitive health integrity. However, such an effective intervention is yet to be explored when addressing fatigue as a symptom cluster with multiple co-existing symptoms. Aging is typically associated with a decline in functional, physical, and cognitive conditions, and when exposed to cancer treatments(Beck, Towsley, Caserta, Lindau, & Dudley 2009; Costarella, Monteleone, Steindler, & Zuccaro, 2010; Cramp & Byron-Daniel, 2012; Davis & Goforth, 2014; Fuller, Hartland, Maloney, & Davison, 2018; Northey, Cherbuin, Pampa, Smees, & Rattray, 2018; Payette et al., 2011; Puetz & Herring, 2012).

Older adults experience a rapidly progressive debility, which consequently has detrimental effects on their physical and psychological well-being,

In a Cochrane Collaboration Review, 56 randomized controlled trials (RCTs) of physical activity interventions for 4068 adults were included and investigated their effectiveness for fatigue (Cramp & Byron-Daniel, 2012). This meta-analysis published in 2012, included randomized controlled trials (RCT) published between 1861 and 2011. The authors found that aerobic exercise was effective and beneficial for the management of fatigue; however, only one reported RCT was conducted specifically for an older adult population (mean age 65) who were all diagnosed with breast cancer (Payne, Held, Thorpe, and Shaw, 2008). More recently, a group of 20 older women with cancer (mean age = 62) were examined during a cancer rehabilitation exercise program (Smith, Broomhall, and Crecelius, 2016). The study evaluated the impact of moderate levels of physical activity on functional status, cancer-related symptoms of fatigue and depression, and QOL. Participants attended 12-sessions of supervised aerobic and resistance training, for an hour, twice weekly during a 6- to 10-week period. The authors found that all functional status tests improved significantly, including aerobic endurance and muscle strength and endurance. Also, QOL was improved significantly, however, neither fatigue nor depression had a detectable change.

It is time to investigate whether there is an update of literature with regards to new evidence relevant to older adult people with cancer, or any missed trials that have been published since 2011. This integrative review aimed to understand, in the physical activity RCTs among older adults, (1) measurement of fatigue in older patients (2) physical activity interventions that mitigated fatigue symptom, and (3) physical activity interventions that improved functional status.

Method

A systematic computer-aided search using PubMed, Web of Science, and PsychINFO, was completed (05.01.2018). The search terms used for each database were cancer-related fatigue AND physical activity, OR physical exercise, AND functional status, OR performance status, AND older adults OR elders OR geriatrics. In total 1,647 articles were screened (Figure 2), title and abstract of the articles were examined to determine their relevance to this review; then the full-text articles were assessed for the adherence to the inclusion criteria Reference lists from the retrieved articles were also screened for relevant publications which may have been missed by the computer-aided search.

Inclusion and exclusion criteria.

To be included in this review studies had to be: (1) articles published in the English language; (2) primary research articles conducted in the United States; (3) RCTs with physical activity interventions; (4) articles published after 2011; (5) participants were older-adults (≥ 65 years of age), either women or men diagnosed with cancer; (6) articles examining fatigue and/or functional status as an outcome; and (7) articles published in peer-reviewed journals. Exclusion criteria included: (1) animal model trials; (2) non-adult human studies; (3) abstract-only articles; (4) case studies; and (5) unpublished studies. The study selection, data extraction, and screening were verified using the inclusion and exclusion criteria.

Results

Nine randomized controlled trials (RCTs) with physical activity interventions (Table 1) were included (Bourke et al., 2011a, 2011b; Culos-Reed et al., 2010; Edvardsen et al., 2015; Galvão, Taaffe, Spry, Joseph, and Newton 2010; Hawkes et al., 2013; Oldervoll et al., 2011; Wenzel et al., 2013; Yeo et al., 2012).

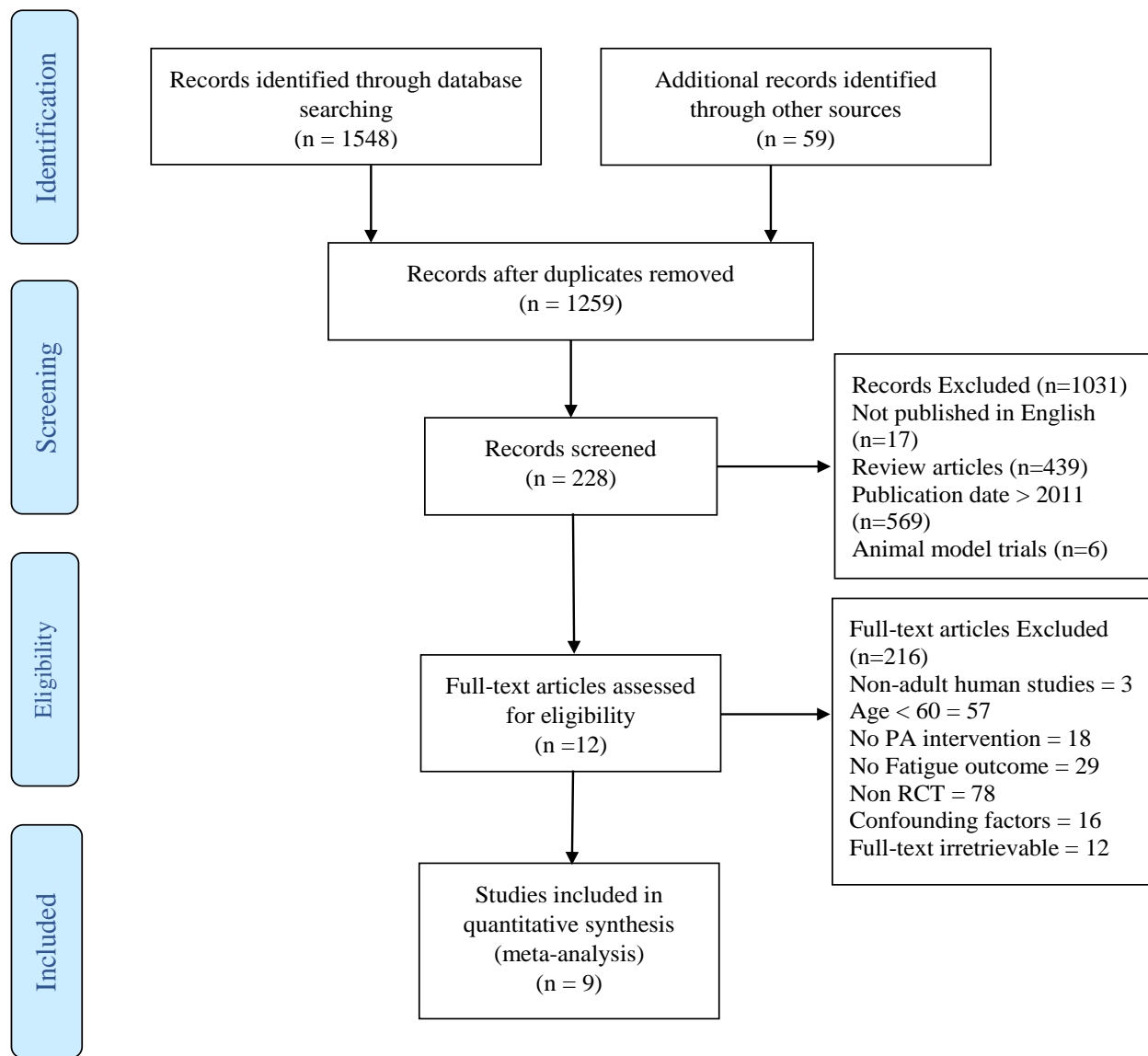


Figure 1.2. Flow diagram of study selection for integrative review (PRISMA).

The small number of RCTs that were eligible is owing to the challenge of segregating the effects on older adults in studies with mixed populations of patients. This review included those RCTs with older adult participants only. The intervention studies included patients who had

completed adjuvant treatment and were with or without hormone therapy. The physical activity interventions included aerobic exercise; resistance exercise; and impact training exercise under direct supervision and/or home-based. Sample sizes ranged from 57-192 participants. All studies were conducted in older adults with the average age of participants being 65 years old (SD= 8.1).

Review of Fatigue Measurements

All articles but one (Yeo et al., 2012) lacked theoretical definitions of fatigue, meaning there was no consensus on operational definitions. Eight different measures were used to assess the fatigue including the following:

The Functional Assessment of Cancer Therapy-Fatigue subscale (FACT-F).

The FACT-F was the fatigue measure used in Bourke et al., (2011a, 2011b) studies. It is a measure of QOL in cancer treatment, derived from the FACT general form (Cella et al., 1993), with more focus to the problems of fatigue. The fatigue subscale is a separate 13-item reliable measure of fatigue that has been used in a number of fatigue intervention studies (Dhillon et al., 2012; Giacalone et al., 2013; Pertl, Hevey, Collier, Lambe, & O'Dwyer, 2013; Si et al., 2012; Yennurajalingam et al., 2016). FACT-F has a strong reliability (coefficient alpha range = 0.93–0.95), and it showed a significant positive correlation with other measures of fatigue. Yellen, Cella, Webster, Blendowski, and Kaplan, (1997) have been able to derive a change in scale scores that correspond to minimum clinically significant differences which is especially useful for intervention studies. Scores on this measure range from 6 (high fatigue) to 52 (low fatigue), and it is considered a valid measure of the physical and functional effects of fatigue (Yellen et al., 1997).

The Fatigue Severity Scale (FSS).

The seven-point 9 item Fatigue Severity Scale utilized by Culos-Reed et al., (2010) was originally validated in a non-cancer population (namely multiple sclerosis and systemic lupus erythematosus patients). While it has been extensively used in chronic fatigue and neurological disease, it has had very limited use in cancer patients (Stone, & Richards, 2001). The total score for this measure is calculated by averaging the scores of each item resulting in scores that range from 0 To 10 (Minton & Stone, 2008). The greater the number, the worse the fatigue. Culos-Reed et al., (2010) defined severe fatigue as being a score of 4.5 or greater. However, this study failed to demonstrate a significant change in FSS scores among the cancer patients in comparison with two other fatigue measures that showed significant changes.

Fatigue subscale of the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire C30 (EORTCQLQ-C30).

The EORTC QLQ C30, used by Galvão et. al, (2010), is a 30-item quality-of-life measure which incorporates 9 multi-item scales: 5 functional scales (physical, emotional, social, role, and cognitive); 3 symptom scales (pain, fatigue, nausea and vomiting); a global health and quality-of-life scale. It also includes several single-item symptom measures. The fatigue subscale has three-items and has been independently validated as a separate fatigue measure. The items are rated on a Likert-type scale from 1 (not at all) to 4 (very much), with a higher score on the subscale indicating a greater fatigue severity. While this measure has weaker psychometric properties than more extensive fatigue scales (Cronbach's alpha = .80-.85, convergent validity with other scales $r = 0.49-75$), it is short and easy to administer which may compensate for this drawback. However, it has been reported to have a floor/ceiling effect in advanced cancer

patients and is not recommended as a single measure to measure fatigue (Paiva et al., 2014; Minton & Stone, 2008; Aaronson et. al, 1993).

Functional Assessment of Chronic Illness Therapy-Fatigue Scale (FACIT-F).

Hawkes et al. (2013) used the FACIT Fatigue scale, a self-report questionnaire that has been validated for use with older adults. It is a short 13-item, easy to administer tool that measures the level of fatigue on a four-point Likert-type scale (4 = not at all fatigued to 0 = very much fatigued) during one's usual daily activities over the past week. Scores may range from 0 to 52 with higher scores indicating less fatigue and better QOL (Cella et. al, 1993). The FACIT Fatigue Scale is written at the 4th-grade reading level and takes 5-10 minutes to complete. A score of < 30 indicates severe fatigue (Webster, Cella, & Yost, 2003). The FACIT-F scale has demonstrated high internal consistency reliability (Cronbach's alpha = 0.96, inter-item correlation = 0.95). High correlation with other measures of fatigue (r = .79 with FSS) and sensitivity to change in older adult patients with chronic health conditions support construct validity (Chandran, Bhella, Schentag, & Gladman, 2007).

Chalder Fatigue Scale/Fatigue Questionnaire (FQ).

Oldervell et al., (2011) assessed fatigue using the Chalder Fatigue Scale that is also known as the Fatigue Questionnaire (FQ) (Chalder et al., 1993). This is an 11-item multidimensional scale that measures physical fatigue (PF), mental fatigue (MF), and total fatigue (TF) on a 4-point Likert-type scale that was originally validated in the general population, and its main use has been in the assessment of chronic fatigue syndrome. The FQ is considered brief and easy to administer and score, with higher scores indicating more fatigue, with acceptable psychometric properties across different populations; it has been recommended for use in cancer patients (Minton & Stone, 2008).

Revised Piper Fatigue Scale (PFS).

In the study by Wenzel et al. (2013) fatigue was measured by the revised Piper Fatigue Scale (PFS) a 22-item 10-point Likert-type self-report scale. The PFS is a comprehensive instrument that measures total fatigue and four subjective dimensions of fatigue including sensory, cognitive/mood, affective meaning, and behavioral/severity. The entire scale (22 items) demonstrated high internal consistency reliability with Cronbach's alpha = 0.97 (Piper et al., 1998). While it has been validated in a group of breast cancer survivors, there are limited data on the psychometric properties of the PFS modified version for use in other cancer population (Minton & Stone, 2008).

Profile of Mood States (POMS) Fatigue Subscale.

The POMS scale was initially developed to evaluate changes in mental and psychological state. The shortened version used by Wenzel et al., (2013) is composed of six emotional distress subscales including fatigue, anxiety, depression, anger, vigor, and confusion. The POMS-F is a 7-item fatigue/inertia subscale (score range 0–28); higher scores indicate more fatigue experienced during the past seven days (Shacham, 1983). This measure has been reported to have adequate internal consistency reliability ($\alpha > .80$), and correlated with other fatigue measures, such as the revised Piper Fatigue Scale ($r = .75, P = .01$), and the Functional Assessment of Cancer Therapy fatigue subscale ($r = -.74, P < .05$) which supports its construct validity.

Schwartz Cancer Fatigue Scale.

Schwartz Cancer Fatigue Scale is a six-item scale used by Smith et al. (2016). This self-report tool allows individuals to rate their tiredness, difficulty thinking, and feelings of being overcome, worn out, and helpless. The highest score is 30 points, where a higher score indicates a greater fatigue. This test has been shown to be valid and reliable. Preliminary construct validity

was demonstrated by differences in fatigue between two groups of cancer therapy and by scores on a visual analog scale of fatigue. Cronbach's alpha for the total scale was 0.96 and estimated to be between 0.82 and 0.93 for the subscales for the population of patients with cancer (Schwartz, 1998).

Physical Activity Interventions

Of the eight studies that implemented an intervention for cancer fatigue, seven trials found positive results of physical activity interventions for the improvement of fatigue in older cancer patients. Intervention periods ranged from 8 weeks to 12 months and included: home-based aerobic exercise only program (Wenzel et al., 2013; Yeo et al., 2012), combination of supervised and home-based aerobic/resistance exercise program with dietary advice (Bourke et al., 2011a, 2011b), supervised and home-based aerobic and light resistance training (Culos-Reed et al., 2010), supervised only aerobic and resistance exercise program (Galvão et al., 2010), telephone-based multiple health behavior change education intervention (Hawkes et al., 2013), and a supervised aerobic exercise only program (Oldervoll et al., 2011).

Non-supervised interventions.

Home-based aerobic exercise.

Two RCTs applied a structured home-based aerobic exercise intervention without supervised sessions and were able to draw similar conclusions. Yeo et al., (2012) tested the effects of the walking program *Every Step Counts* in a sample (N=102) of adults with pancreas and periampullary cancer. *Every Step Counts* walking program intervention consisted of a walking prescription based on the American College of Sports Medicine (ACSM) guidelines. The exercise prescription for the intervention group included a brisk 20- to 30-minute walk, with a 5-minute warm-up period, and followed by a 5-minute cool-down period for 5 days per week.

Participants were randomized into intervention group (n =54, mean age= 66) or usual care control group (n=48, mean age 67). Cancer-related fatigue was measured by FSS and the Fatigue Visual Analog Scale at baseline, at 3 months (intervention completion), and at 6 months follow up. Comparing pre-test post-test scores between groups, only patients in the intervention group had significantly improved fatigue scores (p= 0.05) by both fatigue measures at the end of the study.

Similarly, Wenzel et al., (2013) evaluated the impact of *Every Step Counts* walking intervention during cancer treatment on fatigue, sleep quality, and emotional distress, in a sample of patients with mixed types of cancer (N=126; Age M= 60.2, SD=10.6) randomized to exercise (n=68) or usual care control (n=58) groups. Assessment of fatigue was made using the modified PFS at baseline and at the end of intervention (5 to 35 weeks) depending on the chemotherapy regimen. Participants who reported more aerobic exercise, regardless of group assignment, had significantly lower fatigue scores: PFS total fatigue (P=.035) and POMS fatigue subscale (P=.020). Greater participation in the aerobic exercise was associated with 11% less fatigue (P=.001).

Telephone-based behavior modification.

Hawkes and colleagues (2013) examined the effect of a 6-month telephone-based intervention focusing on health behavior change related to physical activity, weight management, dietary habits, alcohol, and smoking. A sample of 410 colorectal cancer survivors was randomized into two groups. The intervention group (n=205 Age M=65.9 years, SD= 10.8) received a total of 11 health change telephone sessions, 10 delivered as twice-monthly sessions for 5 months followed by a final telephone session 4 weeks later, to promote self- management techniques and maintenance of behavioral improvements promotion. The control group (n=205,

Age $M= 67.8$, $SD= 9.2$) received usual care. To promote physical activity in the intervention group, participants were given a pedometer and encouraged to achieve 10,000 steps per day as the recommended goal, no individualized exercise prescription was given; exercise intensity was not reported. There were no significant group differences found at 6 or 12 months for cancer-related fatigue.

Supervised interventions with the home-based component.

Aerobic and resistance exercise with behavior modification.

A combination of aerobic and resistance training programs under the supervision of an experienced exercise physiologist can produce parallel results even without a home-based component. Galvão et. al, (2010) compared the effect of a twice a week for 12 weeks exercise intervention to usual care. In a sample of 57 men who received androgen suppression therapy for treatment of prostate cancer, randomized into an exercise intervention group ($n=29$) with an average age of 69.5 years ($SD= 7.3$), and a usual care control group ($n=28$; Age $M= 70.1$, $SD= 7.3$). The aerobic component of the training program was moderate to high intensity and included 15 to 20 minutes of cardiovascular exercises (cycling and walking/jogging) at 65% to 80% maximum heart rate and perceived exertion at 11 to 13 (6 to 20-point, Borg scale). Significant differences were found between the groups favoring the exercise intervention group in the reduction of fatigue ($P=.021$), nausea, and dyspnea, as well as improvements in the role and cognitive functioning (Galvão et al., 2010).

Culos-Reed and colleagues (2010) tested a 16-week exercise program designed to promote physical activity in 100 prostate cancer survivors receiving androgen suppression therapy. Participants were randomized into either the physical activity intervention group ($n=53$; Age $M= 67.2$, $SD= 8.8$) or the one-year waitlist control group ($n=47$; Age $M= 68.0$, $SD= 8.4$).

This program consisted of home-based and supervised group individualized sessions tailored to participants' ability. Aerobic exercises consisted of walking, stretching, and light resistance exercises with the use of resistance bands and core strengthening work using training ball. The weekly group sessions lasted one and one-half hours and included physical activities and education followed by group discussions that focused on shared concerns such as exercise goals setting and overcoming barriers. The authors reported a non-significant trend toward improvement in average fatigue scores on the FSS measure, in favor of the intervention group which did drop from 4.49 at pre-test to 4.15, while the control group scores stayed virtually unchanged (4.50 at pre-test and 4.46 at post-test).

Bourke and colleagues (2011a) tested a lifestyle intervention in cancer-related fatigue for prostate and colorectal cancer patients. The intervention combined aerobic and resistance exercises, dietary advice, and a behavioral modification strategy to help improve compliance. Fifty sedentary men with advanced prostate cancer, average age= 72, range= 60 – 87 years, who had been receiving androgen suppression therapy (AST) for at least 6 months were randomized into 2 groups: a 12-week intense exercise program with dietary advice (n =25; Age $M= 72.2$, $SD= 7.7$) or standard care (n = 25; Age $M= 71.3$, $SD= 6.4$). During the intervention period, men attended supervised exercise sessions for 30 minutes aerobic and 2 to 4 sets of resistance training (body weight resistance and free weights) twice weekly for the initial 6 weeks and then once weekly for the following 6 weeks. Also, the participants were instructed to perform a home-based exercise such as brisk walking, cycling, or gym exercise for 30-minute at least one session per week during the first 6 weeks and a minimum of 2 sessions per week for the following 6 weeks, using an exercise diary to record activity. Intervention participants were encouraged to reach a total of 5 sessions per week of exercise. Results of this feasibility study indicated that a

pragmatic lifestyle intervention can produce significant improvement in fatigue ($P = 0.002$), exercise behavior ($P < 0.001$), aerobic exercise tolerance ($P < 0.001$), and muscle strength ($P = 0.033$) compared with standard care controls during AST treatment.

In another feasibility study of older colorectal cancer survivors cohort ($N=18$) with a mean age of 69 years (range= 52–80 years) Bourke et al.'s (2011b) physical activity program was able to evoke similar significant improvement in cancer related fatigue ($P=.005$), replicating the same lifestyle intervention in Bourke et al., 2011a' trial.

Finally, a two-arm randomized controlled trial by Oldervoll et al., (2011) aimed to determine the efficacy of an exercise intervention for reducing fatigue and improve physical performance. Two hundred and thirty-one palliative care patients were randomized to a physical exercise group ($n=121$; Age $M=62.6$, $SD= 11.3$) or a usual care group ($n=110$; Age $M= 62.2$, $SD= 10.7$). The exercise group attended supervised biweekly sessions for 8 weeks. Each session consisted of 10 to 15-minute aerobic warm up, 30 minutes of strengthening and resistance exercises, and 10-15 minutes stretching and relaxation. Fatigue Questionnaire scores at baseline and 8 weeks showed no significant difference between-groups effect in physical fatigue ($P= .20$), total fatigue ($P=.12$), or mental fatigue ($P=.13$).

Functional Status

To explore the relationship between physical activity, fatigue, and functional status, we must understand the effect of physical activity on functional status. A single-blinded RCT aimed to evaluate the effects of exercise on functional status, investigating the changes in pulmonary function, muscular strength, total muscle mass and peak oxygen uptake (Edvardsen et al., 2015). Shortly after lung cancer surgery, 61 older adults with lung cancer were randomized into high-intensity endurance and strength training ($n = 30$, Age $M= 64.4$, $SD= 9.3$), compared with

controls ($n = 31$; Age $M = 65.9$, $SD = 8.5$) who received standard postoperative care. The intervention group attended exercise sessions at fitness centers near the patients' homes. Each session was 60 minutes. Participant attended three times a week for 20 weeks. The session started 5–7 weeks after surgery. The session included 1 hour a week group exercise. The sessions were monitored by highly qualified personal trainers and under physiotherapists' supervision. The exercise was well tolerated. Test scores of the medical outcomes short form health survey (SF36), showed a clinically significant improvement in physical health, functional status and QOL in the intervention group compared with the controls.

Galvao et al. (2010) assessed functional performance as a primary outcome of their exercise intervention. The maximal weight lifted one time (1-RM) was a measure for the dynamic muscle strength (chest press, seated row, leg extension, and leg press). Using the maximal number of repetitions performed at 70% of 1-RM (for the chest press and leg press exercises) muscle endurance was measured. Several measures of functional performance were used. Using electronic timing gates, the 6-meter usual and fast walk and repeated chair rise to standing (5 times) were assessed, and the 400-meter walk assessed cardiovascular capacity. Dynamic balance was assessed by the 6-meter backward walk the sensory organization test and the Neurocom Smart Balance Master. Galvao and his colleagues (2010) reported significant improvements, in the exercise group compared with control group, of all functional performance, muscle strength, and balance measures. The resistance/aerobic exercise was also able to reverse total body and regional lean mass loss.

The study of Wenzel et al., (2013) also assessed physical functioning and fitness for secondary study outcomes, controlling for age, cancer treatments, and gender. Comparing patients with prostate cancer to non-prostate cancer groups, this study reported improvements of

peak maximal oxygen uptake (8%) in prostate cancer patients, compared to > 9% loss in the non-prostate cancer group. Findings for those participants who engaged in more aerobic exercise also included significant improvement in self-reported physical function, compared to other participants who were less physically active. Participants' mental and psychological status was also measured, the Profile of Mood States Scale (POMS) assessments revealed that participants who exercised more had significantly less emotional distress than their less active counterparts.

The study of Yeo et al., (2012) measured performance ability using the Eastern Cooperative Oncology Group (ECOG) performance status scale. Functional status was assessed using the Short Form-36v2 health survey which addressed 8 functional domains (cognitive functioning, family and marital functioning, sexual functioning, social support, sleep, health distress, physical symptoms and psychological symptoms). The findings of this study were consistent with previous reports, performance (ECOG) and functional status (Short Form-36v2) improvements were evident in the intervention group compared to the control (usual care) group. Improvements in functional status were distinct in the Physical Component Summary (PCS) and the Mental Component Summary (MCS) in both the intervention and the control group, however, those with higher baseline score of MCS, depression, and poor functional status reported less depression, higher physical functioning scores, and had lower cancer stage by the end of the study.

Comparably, Oldervoll et al., (2011) hypothesized that the exercise intervention would improve participants' physical performance. Physical functioning as an indicator of physical performance was a secondary outcome of the exercise intervention. This study included several measurements of performance, the Karnofsky performance status scale (KPS) was used as an indicator of survival. Measures of physical performance included sit to stand test, an indirect

measure of strength in the lower limbs, the grip strength test as a measure of general strength, and the maximal step length test as an assessment of balance. Functional capacity was measured using the Shuttle Walk Test (SWT).

These authors reported both clinically and statistically significant intervention effects, between exercise and control groups, in all measures of functional capacity and physical performance. In those who completed the exercise intervention, KPS was a significant indicator of survival after controlling for age and gender. Physical performance as well as general well-being improved after 6 weeks, and physical functioning parameters significantly improved 8 weeks post exercise intervention. Of note, those who dropped out of the intervention lost to follow up, and participants who were in the waitlist were the ones with significantly lower KPS scores, lower mean scores of all functional capacity and performance tests at baseline, compared to those who completed the exercise intervention. These findings further support the contribution of physical exercise in physical function maintenance, for older adult patients with advanced and progressive cancer disease (Oldervoll et al., 2011).

Finally, Culos-Reed et. al, (2010) also included assessments of physical functioning as a secondary study outcome. Measures of functional and aerobic capacity included the 6-min walk test, the handgrip strength test, and assessed flexibility using the modified sit and reach test. The European Organization for the Research and Treatment of Cancer, Quality of Life Study Group (EORTC QLQ C30) was included as a measure of physical function. While the study findings revealed significant improvements in physical fitness indicators for the intervention group, compared to the control group participants, the mean scores for the functional subscale decreased slightly for both groups from baseline to end of the study. However, those changes did not reach significance, the EORTC QLQ C30 physical function subscale was reported to have poor

reliability, therefore the authors did not include it in the final analyses. In this study, participants' mental and psychological status was also assessed as a secondary outcome. The Center for Epidemiological Studies Depression scale scores revealed that participants in the exercise group had a decrease in depression, compared to an increase in the control group depression from pre-intervention. Of note, the study had a high dropout rate (34%) before post-testing, of the 100 participants 66 did not complete assessments, in their discriminant function analysis dropout participants were revealed to be older and had higher depression scores.

Discussion

The current review of cancer-related fatigue emphasizes the management of fatigue among adult cancer patients age 65 and older during and after completing cancer treatment. For patients with prostate cancer who are undergoing androgen suppression therapy, research indicated that implementing moderate to high intensity aerobic and resistance exercise programs to promote physical activity may result in improved functional status and lower fatigue during treatment, in either combination of supervised and home-based sessions or supervised sessions alone without home-based component (Culos-Reed et al., 2010; Galvão et al., 2010; Bourke et al., 2011a, 2011b).

The quality of the studies included in the review was variable; only one of the reviewed studies included a theoretical definition of fatigue and presented a conceptual framework (Yeo et al., 2012). The period of physical activity intervention varied from study to study (8-weeks-6-months), there were also inconsistencies in the duration of activity and frequency, which may have affected fatigue outcomes differently. Few of the studies reviewed included information about the potential participant who declined participation in the trial; thus, the study participants

may have been motivated to receive treatment, and so they would be systematically different than those people who refused to participate, limiting the generalizability of the results.

Only one study adhered to the recommendations of the ACSM (Wenzel et al., 2013). According to ASCM adults should undertake a moderate-intensity physical activity for 30 minutes 5 times a week, or a minimum of 20 minutes vigorous-intensity aerobic physical activity 3 times a week (Garber et al., 2011). Much of physical activity interventions reviewed did not follow these recommendations.

Only four studies identified fatigue as a primary outcome (Hawkes et al., 2013; Oldervoll et al., 2011; Wenzel et al., 2013; Yeo et al., 2012). In the rest of the studies, fatigue was either one of two or more secondary outcomes (Bourke et al., 2011a, 2011b) or reported and measured as a QOL indicator or subscale (Culos-Reed et al., 2010; Galvão et al., 2010).

In comparison to supervised exercise sessions, structured home-based walking exercise programs that adhere to the recommendations of safety, intensity and guidelines of ACSM showed significant improvement of fatigue among older cancer patients with different types of cancer diagnoses. Patients who participate more in home-based aerobic exercises with moderate intensity such as brisk walking had significantly less fatigue (Yeo et al., 2012; Wenzel et al., 2013). On the contrary, other randomized controlled trials did not have significant fatigue reduction results, including one that did not incorporate an exercise prescription (Culos-Reed et al., 2010), another one depended on telephone counseling alone (Hawkes et al., 2013), and the last did not provide a structured physical activity intervention that adhered to the standards and guidelines (Yeo et al., 2012). Incorporating physical activity interventions in cancer fatigue symptom management can also be beneficial in improving functional status objectively (Bourke et al., 2011a, 2011b). The improved measures included aerobic exercise tolerance, functional

capacity and muscle strength for older adult cancer patients. Furthermore, the frailty associated with older age, besides cancer patients' disease and treatment, as well as the relative occasions of inactivity associated with the cancer symptom experience disposes this population to a major risk for falls and injury. Exercise-based interventions are able to modify this risk. Regular participation in moderate to high-intensity exercise programs mitigate falls risk through improvement of functional status: increasing muscle strength, muscle mass, improving gait patterns and balance control (Galvão et al., 2010). Older adults with cancer can benefit from different exercise modalities to target each of those areas of impairment selectively or in combination (Sherrington et al., 2016).

Contributing factors of successful physical activity interventions must be taken into consideration. The timing of physical activity interventions for patients during or after completion of cancer treatment may evoke significant improvement in fatigue compared to advanced stage or short life expectancy periods (Oldervoll et al., 2011). In 2017, a meta-analysis of systematic reviews supported the evidence found in this review. In agreement with our proposed research study, it acknowledged the significance of the challenge facing both cancer population and clinicians (Stout, Baima, Swisher, Winters-Stone, & Welsh, 2017). The challenge seems to be optimizing functional status and survival. Despite the growing and robust body of evidence identified which supports the need to include exercise in most of the care plans of patients with cancer, there is a lack of practice guidelines for older adult hospice patients.

In addition to the absence of practice guidelines for older adult hospice patients with cancer, the lack of structure or precise prescription of physical activity hinders its effect on fatigue (Hawkes et al., 2013). Equally important is adhering to ACSM guidelines when constructing physical activity programs and maintaining adequate exercise intensity levels

appropriate to the age and health status of the participants (Yeo et al., 2012; Wenzel et al., 2013). The randomized controlled trials in this review demonstrated effectiveness of structured physical activity interventions in reducing fatigue for older adult cancer patients with fatigue compared to controls (Bourke et al., 2011a, 2011b; Culos-Reed et al., 2010; Galvão et al., 2010; Oldervoll et al., 2011; Wenzel et al., 2013; Yeo et al., 2012).

There is also evidence that functional status and physical performance have a considerable response to earlier interventions (Edvardsen et al., 2015;), with improvements in physical health and QOL (Wenzel et al., 2013; Yeo et al., 2012; Oldervoll et al., 2011; Galvão et al., 2010). Perhaps fatigue and other fatigue-related symptom management interventions for older adults need further investigation to gauge timing, duration, and intensity to clarify dose response for future research (Minton, Jo, & Jane, 2015).

The management of clustered symptoms such as fatigue-related symptom cluster should aim at multimodal interventions, which are supported by evidence of improvements in self-reported physical and role functioning (Culos-Reed et al., 2010; Galvão et al., 2010). Yeo et al. (2012) examined the participants' symptoms profile for evidence of symptom clusters, the most predominant fatigue-related cluster (fatigue, bodily pain, depression, weakness, and anxiety) was identified, this was considered as a preliminary evidence of the existence of a fatigue-related symptom cluster. Also, several studies measured other symptoms including pain, emotional distress, and depression. Key findings of those studies correspond to a decrease in total depression scores (Culos-Reed et al., 2010; Yeo et al., 2012), significantly less emotional distress, less pain in addition to less fatigue, physical functioning, and more vigor in patients who exercised compared to those who were less active (Wenzel et al., 2013). Incorporating behavioral

modification strategies, to promote compliance with physical activity programs, can help improve fatigue and its clustered symptom outcomes in older adult cancer patients.

Future Implications for Research and Practice

This review offers evidence that physical activity is beneficial for fatigue management and maintenance of functional status. Further research is warranted to determine the most effective physical activity parameters for older adults with cancer including intensity level, duration, and frequency of sessions and safety for frail older patients. Also needed is consensus on the most appropriate fatigue outcome measure. Further work needs to include patients with advanced disease and hospice populations as the majority of the studies included in this review had participants undertaking cancer therapy during the study period. In addition, future research needs to sufficiently power trials to detect changes in depression, a psychological distress concurrent with fatigue. Future research should also consider strategies to promote self-efficacy to exercise and boost adherence rates. There is a great opportunity to benefit from the increased public use of smartphones and health-related apps, as well as the availability of global positioning systems and physical activity trackers. While tracking exercise and adherence can benefit from trend following and the social media wave of the public desire for approval, setting up effective regimens that conform to the recommended guidelines is essential. This makes it amenable for researchers to customize physical activities to evoke precise outcomes, such as monitoring exercise dose-response, self-efficacy, and adherence. Future physical activity applications should be tailored to older adult cancer populations. A significant improvement in cancer symptoms, functional status, and QOL becomes readily attainable as people with cancer become self-motivated to change.

Limitations

There are few limitations to this systematic review, one limitation is that it does not evaluate the methodological quality of the studies using a validated technique. Also, as this article is a part of a dissertation requiring independent student work, this constitutes a methodological limitation because two independent reviewers is the gold standard for validating the systematic review flowchart. Inclusion criteria limited the additional evidence available in the non-English literature, as well as excluding abstract-only articles when the full text was not available for review.

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Table 1. Summary of Characteristics of the RCT Studies Findings

Authors, Date of Publication	Research Design/ conceptual framework, model	Purpose	Sample Characteristics	Measures	Findings	Limitations
Bourke et al., 2011	RCT; 2 group conceptual framework not indicated.	To evaluate the feasibility of a lifestyle intervention designed to improve fatigue, physical/functional fitness, QoL.	N=50 prostate cancer (PCA) on ADT: age 60 or older 25 randomized to exercise/diet intervention + 25 usual care control group.	FACT-F at baseline, 12 weeks (end of lifestyle intervention) and 6 months in both groups.	Lifestyle group improvements in exercise behavior ($P < 0.001$), aerobic exercise tolerance ($P < 0.001$), and muscle strength ($P = 0.033$) compared with standard care. Significant fatigue differences at 12 weeks ($p=0.002$) in intervention group compared with control, at 6 months $P = 0.006$.	The high rate of attrition at 6 months (44%) increase the possibility of differential selection bias.
Bourke et al., 2011	RCT; 2 group parallel conceptual framework not indicated.	To evaluate the feasibility of a lifestyle intervention designed to improve fatigue, physical/functional fitness, QoL, aerobic exercise tolerance, functional capacity, muscle strength.	N=18 colorectal cancer survivors 6 to 24m post-surgery (mean age 69y) randomized to (n=9) lifestyle intervention or control standard care (n=9).	FACT-F at baseline, and at 12 weeks (end of intervention).	Lifestyle intervention had significant improvements in fatigue ($P=.005$, $d=.52$), exercise behavior ($P=.068$), aerobic exercise tolerance ($P=.010$), functional capacity ($P=.003$). No change in QOL.	Small sample size. Responses were subject to recall bias.
Culos-Reed et al., 2010	RCT; 2 groups, waitlist control conceptual framework not indicated.	To investigate the effects of physical activity (PA) intervention on PA behavior, QOL, and fitness measures. Theoretical framework not indicated.	N=100 PCA survivors receiving ADT Mean age 67.6y.	FSS at baseline and 16 weeks (end of intervention).	Non-significant change in scores ($P>.05$) However, average fatigue scores for the intervention group did drop from 4.49 to 4.15, the controls remained almost unchanged (4.50 at pre-test and 4.46 at post-test).	77.8% adherence, 34% drop out. Low statistical power. Blinding not done. Randomization method not described.

Table 1. (Continued)

Galvão et al., 2010	RCT 2 group parallel design conceptual framework not indicated.	To compare the effects of a 12-week combined resistance and low volume aerobic exercise compared to usual care on muscle mass, strength, physical function, enhanced health status.	N=57 PCA patients, randomized into exercise group n=29 and usual care control group n=28.	EORTC QLQ-C30	Significant differences between the groups favoring exercise intervention: reduction in fatigue (P=.021), nausea, and dyspnea, and improvements in role and cognitive functioning.	EORTC QLQ-C30 is not a valid measure of Fatigue as an endpoint.
Hawkes et al., 2013	RCT, 2 group design conceptual framework not indicated.	To determine effects of a 6 months telephone behavioral intervention on health outcomes including PA, HRQoL, fatigue, (BMI), diet, and smoking.	N= 410, CRC survivors randomized to health coaching intervention (n=205) or usual care (n=205)	FACIT-F at baseline, 6 months and 12 months	There were no significant intervention effects at 6 or 12 months for mental HRQoL or cancer-related fatigue	Participants were not blinded to study condition.
Oldervoll et al., 2011	RCT 2 group design conceptual framework not indicated.	Determine the efficacy of an exercise intervention for reducing fatigue and improve physical performance.	N=231 palliative care patients randomized to physical exercise group (n=121) or usual care group (n=110).	Fatigue Questionnaire (FQ).	There is no significant between-groups effect in physical fatigue (P= .20), total fatigue (P=.12), or mental fatigue (P=.13).	High drop-out rate (35 % intervention group, 22% usual care controls).
Wenzel et al., 2013	RCT 2 group design conceptual framework not indicated.	Evaluate the impact of a home-based walking intervention during cancer treatment on sleep quality, emotional distress, and fatigue.	N=138 patients with prostate (55.6%), breast (32.5%), other solid tumors (11.9%) randomized to a home-based walking exercise (n=68) or usual care control (n=58).	Profile of Mood States (POMS) Fatigue Subscale, Modified piper fatigue scale (PFS) at baseline and at end of intervention (5 to 35 weeks).	Participants who reported more aerobic exercise, regardless of group assignment, had significantly lower fatigue scores: PFS total fatigue (p=.035) and POMS fatigue subscale (p=.020) greater participation in the aerobic exercise was associated with 11% less fatigue (p=.001). Using intention to treat analysis the PFS showed no significant difference in fatigue between groups (p=.46).	Exercise cross-over effect in both groups, 32.4% of participants assigned to exercise “dropped out” and 12% of controls “dropped in” to exercise. Lack of racial/ ethnic diversity.

Table 1. (Continued)

Yeo et al., 2012	RCT 2 group design, conceptual framework: Levine Conservation of Energy Theory.	Examine the effects of a walking program on CRF, physical functioning, QOL, and to explore symptom burden and clustering.	N=100 pancreas/periampullary cancer patients n =50 intervention and n=50 usual care control groups.	Fatigue severity scale (FSS) and fatigue Visual Analog Scale at baseline and at 3 to 6 months.	Comparing pre-test post-test scores between groups, only patients in the intervention group had significantly improved fatigue scores by both fatigue measures at the end of the study, as compared with their own baseline (p= 0.05).	Lack of racial/ethnic diversity primarily white sample well educated The sample was motivated to receive treatment, limiting the generalizability of the results.
Edvardsen et al., 2015	RCT 2 group single blinded design, conceptual framework not indicated.	Evaluate the effects of high-intensity endurance and strength training on change in peak oxygen uptake from baseline to after intervention. Explore changes in pulmonary function, muscular strength, total muscle mass, daily physical functioning, and QOL.	N= 61 Lung cancer patients after lung cancer surgery, n= 30 intervention, n= 31 usual care control group.	SF-36, EORTC QOL-C30, and a battery of physical functioning tests before surgery, 4–6 weeks after surgery and immediately after the intervention.	High-intensity endurance and strength training is well tolerated and significantly improves cardiorespiratory fitness, muscular strength, daily physical functioning, total muscle mass and quality of life.	Low response rate to the QOL questionnaires. technicians were possibly not blinded during the last data collection.

*RCT-Randomized Controlled Trial, QOL-Quality of Life, ADT-Androgen Deprivation Therapy, FACT-F- Functional Assessment of Cancer Therapy-Fatigue, FSS- The Fatigue Severity Scale, EORTC QOL-C30- European Organization for Research and Treatment of Cancer Quality of Life Questionnaire C30, Fatigue subscale, HRCOL-Health-Related Quality of Life, BMI-Body Mass Index. POMS- Profile of Mood States Fatigue Subscale.

Section Two: Validity and Reliability of the Center for Epidemiologic Studies Depression, Boston Short Form: A Clinically Relevant Scale for Depression Detection in Cancer Patients

Abstract

The purpose of this study was to investigate the reliability and validity of the Center for Epidemiology Studies-Depression scale, Boston Short Form (CESD-10), as a clinically relevant depression measure used for cancer center outpatients. A secondary data analysis from a larger study was conducted. Using Structural Equation Modeling (SEM) for confirmatory factor analysis, the factor structure of responses in a cross-sectional sample ($n = 200$) was examined. Internal consistency of the instrument was estimated using Cronbach's alpha. The factor analysis demonstrated that the CESD-10 contains the same underlying factors of positive affect, depressive affect, somatic complaints, and interpersonal challenges found in the full CES-D; the four-factor depression model fits the data well. Internal consistency reliability coefficient was satisfactory (Cronbach's alpha=0.737). The CESD-10 is a valid and reliable measure for assessing depressive symptoms among patients with cancer who are participating in a research study. Using this simple and brief scale in clinical settings can help clinicians detect depression in older adults with cancer.

Keywords: cancer, depression, oncology, psychological assessment, psychometrics, structural modeling.

Note to Reader

Portions of this chapter have been submitted for publication and are currently under the review of *The Journal of Psycho Oncology*.

Introduction

Depressive symptoms are highly prevalent among cancer population (Massie, Lloyd-Williams, Irving, & Miller, 2011). A diagnosis of cancer can be mostly sad and traumatic, however, when it's said to be terminal it sets the person who receives it for a greater sense of loss and pervasive hopelessness. There are so many losses which people with cancer face; the loss of health, wealth, self-image, and the sense of control are initially experienced early on along the cancer continuum. These psychological symptoms always present in a physiological number of symptoms that interfere with the individual's quality of life and are associated with a significant decline in performance status and functional ability, as well as a reduction in the utilization of health care and treatment adherence. Depressive symptoms have been measured in research using a variety of scales. The Center for Epidemiologic Studies-Depression (CES-D) scale has been extensively used as a self-administered screening tool for identifying depressive symptoms, both in clinical and research settings (Comstock & Helsing, 1976; Radloff, 1977; Radloff & Lock, 1986; Nezu, A., Nezu, C., McClure, & Zwick, 2002; Murphy, 2002; Eaton, Muntaner, Smith, Tien, & Ybarra, 2004). Even though the full 20-item CES-D remains one of the most widely used instruments in the field of psychology, its length impedes its use in a variety of clinical settings, especially among vulnerable populations. This has led to the development of a shorter version, the Center for Epidemiologic Studies-Depression-Boston Short Form, also known as CESD-10 scale. This adapted scale balances respondent burden and psychometric

integrity. Radloff originally reported that the 20 items of the scales could be summarized into four factors: positive affect, depressed affect, interpersonal challenges, and somatic complaints. Mogos et al. (2015) have recently confirmed the longitudinal invariance of the four-factor structure. The factor structure of the CESD-10 has been debated in the literature (Amtmann et al., 2014; Carpenter et al., 1998; Kohout et al., 1993). Although the four-factor structure had been replicated in other studies (Irwin, Artin, & Oxman, 1999; Kohout et al., 1993), its structural validity has not been verified in the people with all types of cancer. The 10 items that were retained from the original CES-D scale for the CESD-10 are shown in Table 1.1.

It is generally acknowledged that symptoms of depression exist in patients with cancer. Understanding depression in cancer patients calls for understanding measurement of its symptoms. While self-report assessment measures can never adequately diagnose a psychiatric disorder without a complete clinical assessment, they can help identify depression symptoms provided that these measures demonstrate acceptable reliability and validity. It is important to examine the CESD-10 for evidence of reliability using Cronbach's alpha coefficient, and for evidence of construct validity. Using structural equation modeling (SEM) to conduct confirmatory factor analysis this study aimed to: examine the factor structure of CESD-10 for evidence of validity, and reliability. It was hypothesized that CESD-10 would be a reliable scale that exhibits the same symptom dimensions found in the original 20-item CES-D, supporting construct validity.

Method

Sample.

The initial sample consisted of 201 adults with cancer who were enrolled in a large Patient-Centered Outcomes Research Institute (PCORI) funded clinical trial (CE-12-11-4025). Participants were outpatients recruited at a large and comprehensive National Cancer Institute-

designated center in southwest Florida. They were included in the parent study if they had baseline scores of a cancer symptom intensity, distress, and/or interference ≥ 4 for at least 2 symptoms on the Cancer Symptoms Scale (McMillan, Tofthagen, Choe, & Rheingans, 2015). The participants had to be 18 years old or older, were fluent and literate in the English language, had passed mental and functional status screenings, and were near the beginning of their therapy for cancer (at least 3 chemotherapy cycles or three weeks of radiation therapy remaining for treatment). Only participants who consented to participate in the parent study and completed CESD-10 assessments were included in this secondary baseline data analysis. Individuals who were within six weeks following surgery, planned to leave Florida during the intervention, were in hospice care, confused, or were expected to die within 3 months were excluded from participation.

Measures.

Following approval by the university's Institutional Review Board, the CESD-10 was administered as part of a larger battery of instruments used in the clinical trial (CE-12-11-4025). The demographic data were collected from electronic health records.

Center for Epidemiology Studies-Depression, Boston Short Form (CESD-10). This 10-item depression screening tool has been widely used in research. However, it should be noted that it is not a diagnostic tool, but rather a symptom assessment scale with only 10 items and yes/no answers. It combines ease of administration and reduced questionnaire burden with only 2 minutes' administration time. It has been utilized in cancer research, in samples of patients with breast cancer (Carpenter et al., 1998; Hann, Winter, & Jacobsen, 1999; Stagl, et. al, 2015), and elderly hospice cancer patients (Garrison, Overcash, & McMillan, 2011), but this is the first validation study of CESD-10 in a sample of patients that included all types of cancers and both

sexes. This short version was developed in the multi-site research project led by Kohout et al. (1993). The 10 items that were selected for the short form were based on the original scale factor analysis; these items had high correlations with the 20 items of the widely validated full scale (Cronbach's alpha = .88) and had a similar pattern of loadings to the four dimensions reported by Radloff (1977) depressed affect, positive affect, somatic complaints, and interpersonal challenges.

Kohout et al. (1993) reported that shortening the scale did not compromise its reliability (Cronbach's alpha = 0.80 versus 0.86), and the total proportion of the variance in all 10 variables explained by the four factors was 66%. The value of variance explained along with the similar pattern of loadings indicates that the short form strikes the same symptom dimensions of depression found in the original CES-D.

In the shortened form, the items are coded dichotomously as present or absent, rather than the frequency rating in the full CES-D where scores ranged from 0 to 20. Total scores of the shortened scale range from 0 to 10. Simplifying the response options to "yes" or "no" had demonstrated convenience for use among patients who may find the questions of the scale emotionally distressing. This approach also reduced respondents' confusion associated with scoring responses on the Likert-type scales (Irwin et. al, 1999). Using a sample of clinically diagnosed middle-aged individuals with major depression as a criterion standard ($n = 40$) and healthy comparison controls ($n = 43$) who had no lifetime history of psychiatric diagnosis and were never mentally ill, Irwin and colleagues (1999) set the cutoff score to ≥ 4 to detect depression in those depressed patients, a low cutoff score that is consistent with the screening purpose of CESD-10. Of the 40 depressed patients, 39 were positively identified and one was a false negative, using this cutoff score yielded a high sensitivity of 97%, specificity of 93%, and a

predictive value of 85%. Both internal consistency (Cronbach's alpha = .92) and test-retest reliability with 3 to 4 weeks' delay ($r = .83$) were reported to be very strong (Irwin et. al, 1999).

Procedures.

The present study proposal was approved by the University of South Florida Institutional Review Board. For this secondary data analyses of the CESD-10, de-identified data were obtained from the principal investigator. Data were examined for outliers and missing data.

Data analysis.

SPSS software version 24.0 was used to describe sample characteristics, compute depression scores, and conduct reliability analyses. A minimum of 0.70 for Cronbach's alpha reliability coefficient was used to indicate the internal consistency of the scale. To assess the construct validity of CESD-10, the statistical software package LISREL 9.2 (Jöreskog & Sörbom, 2015) was used to conduct confirmatory factor analysis (CFA). To evaluate the CFA models, we relied on several measures of fit: Root Mean Square Error of Approximation (RMSEA), Standardized Root Mean Square Residual (SRMR), Adjusted Goodness of Fit Index (AGFI), Goodness of Fit Index (GFI), and Comparative Fit Index (CFI). Since 1999, Hu and Bentler conducted extensive simulation studies on covariance structure analysis (Hu & Bentler, 1999). These investigators reported that some of the conventional cutoff criteria for those fit indices tend to overly reject true-population models, especially for small size samples. It is suggested that a relatively good-fitting model will have RMSEA cutoff values close to .06, SRMR cutoff values close to .08, CFI cutoff value close to .95, GFI and AGFI cutoff values close to .90 (Bentler, 2007).

Results

Sample demographics and clinical characteristics.

One case was excluded due to a missing CESD-10 item response, leaving 200 cases for analysis. Demographic and clinical characteristics are summarized in Table 1.2. The sample accrued for this analysis included 200 patients with a wide variety of cancers including 25% diagnosed with breast cancer, 7% with colon cancer, 6.5% with ovarian cancer, and 6.5% lung cancer, as well as other types of cancer. The mean age of the participants in this sample was approximately 58 years old ($SD=12.2$); there were 76 males and 125 females. Of the total participants, 61.2% reported being married, 62% were females, and had an average education of 14.9 years. The sample was predominantly White/non-Hispanic (83.6%); the remainder of the sample self-identified as Black/non-Hispanic (9.5%), White/Hispanic (4%), and other/nondisclosed (2%). The mean CESD-10 score was 2.57, with a standard deviation of 2.2 (Table 1.2). Overall, 29.5% of the participants reported total scores on CESD-10 to be ≥ 4 , which is indicative of a certain degree of depression. More women (64.4%) than men (35.6%) in the sample reached the cutoff score for depression.

Reliability.

Reliability analysis was conducted using SPSS reliability procedure. The correlation matrix, presented in Table 1.3, shows that the average inter-item correlation was .233. Item-total correlations are shown in Table 1.4. The item-total correlations ranged between .205 and .570. Using Cronbach's coefficient of internal consistency, the overall reliability coefficient for the scale scores in this sample was .737.

Validity.

Prior to conducting the analysis, the data were examined for their suitability for analysis.

First, the average inter-item correlation within the scale was .233. Second, the determinant of the

correlation matrix approached zero (.060) and the Kaiser-Meyer-Olkin Index of Sampling Adequacy was .691, which is above the recommended value of .60. Finally, the Bartlett's Test of Sphericity was significant ($\chi^2 = 546.75$, $df = 45$, $p < .001$). Based on these criteria, the inter-item correlation matrix was deemed adequate for factor analysis.

Confirmatory factor analyses were conducted to compare two models, a simple one-factor model to evaluate unidimensionality of the CESD-10 scale, and a second model, a four-factor theory-driven model based on the work of Irwin et al. (1999), Kohout et al. (1993), and Radloff (1977). The models were specified to include Lambda-X, Phi, and Theta-Delta matrices, and both models were fit to the data. The goodness of fit indices of the single factor model ($\chi^2 = 265.057$, $df = 35$) were not within an acceptable range (RMSEA = 0.181, GFI = 0.791, CFI = 0.554, SRMR = 0.114, and AGFI = 0.672).

The theory-driven four-factor model, including depressed affect (DA), positive affect (PA), somatic complaints (SC), and interpersonal challenges (IP), was also fitted to the data ($\chi^2 = 37.012$, $df = 29$). A formal test comparing the two models was conducted by comparing this Chi-square with that of the one-factor model. The change in comparison was significant ($\chi^2 = 227.988$, $df = 6$, $p < .001$). The four-factor model fits the data significantly better than the single factor model. Improvements in the other indices of fit are shown in Table 1.5. The parameter estimates from the four-factor model are shown in Table 1.6. All of the factor loadings were statistically significant. Standardized factor loadings were ranging from .237 to .883. Item 3 ('restless sleep') had the lowest loading and item 7 (people unfriendly) had the highest loading. The pattern of each factor loadings was as follows: Depressed Affect (Items 5, 6, 8), Positive Affect (Items 1, 4), Somatic Complaints (Items 2, 3, 10), and Interpersonal Challenges (Items 7,

9). The highest factor correlation was between the interpersonal challenges and somatic complaints factors ($r = .634$), and all factor correlations were modest in size (Table 1.6).

Discussion

Reliability.

The present study examined the reliability and factorial structure of the CESD-10 scale in a mixed sample of patients with cancer. Reliability of the data was assessed by Cronbach's alpha coefficient prior to testing the measurement structure of the CESD-10 scale. The coefficient was satisfactory (Cronbach's alpha= 0.737) for the overall sample; while this is an acceptable value of reliability, it is considered relatively low compared to what was reported by earlier authors (Kohout et al., 1993).

To examine this relatively low-reliability coefficient, we considered various aspects, including scale attributes or items specific factors such as low inter-item correlations, a small number of items, or heterogeneous constructs (Cortina, 1993), and possible reliability measure limitations. Cutting the length of the CES-D from the original 20 items to the Boston Short form might be expected to decrease the value of Cronbach's alpha (Tavakol & Dennick, 2011). Particularly in the context of internal consistency, consideration must be given to the source of error related to the assumption of homogeneity of the scale items. A set of scale items is said to be homogeneous when they measure to some degree the same concept on a unidimensional scale. Both the magnitude of inter-item correlations as well as the number of items in the scale also have an influence on homogeneity and the value of Cronbach's alpha (Tavakol & Dennick, 2011).

In other words, symptom measurement scales usually involve multiple items, each item is an indicator of the same attribute or symptom of a construct (e.g., depression). When using the

CESD-10 with the intention to measure attributes of depression, clinicians and researchers are measuring co-occurring, unique, interrelated, and possibly exchangeable symptoms. Through calculating a total score from the unweighted sum of item scores, the attribute levels can be identified. Researchers suggest that computing a total or composite score from a set of scale items would only be meaningful if all the scale items were unidimensional (Widhiarso & Ravand, 2014). In our sample, an inspection of the scale dimensionality reveals that the items have low intercorrelations, despite the theoretical supposition that these 10 items assess the same construct. In this case, the assumption of multidimensionality holds, and the literature suggests that using a unidimensional reliability measure such as Cronbach's alpha coefficient would have limited application in such situations (Green & Yang, 2009; Widhiarso and Ravand, 2014).

However, the 10 items of the CESD-10 provide a measure of depression using different indicators, including depressed affect, the lack of positive mood, somatic complaints, and social or interpersonal challenges. The heterogeneity of the constructs in this scale can potentially contribute to underestimating its internal consistency using the Cronbach's alpha reliability coefficient. Retaining the somatic complaints and interpersonal challenges items in the shortened CESD-10 was done specifically by the scale developers to preserve the original scale factorial structure (Kohout et al., 1993) capturing the multidimensions of depression symptoms.

Construct validity.

Confirmatory factor analysis was used to assess the construct validity of the single factor and four-factor structures of the scale that are hypothesized in the literature. In general, the results indicate that the single-factor structure was far from fitting the data adequately. The four-factor model proposed by Kohout et al. (1993) was a better fit for the present study's data. In another study, Irwin et. al, (1999) demonstrated that a four-factor structure of CESD-10 was

valid for screening for major depression in older adults. Their results replicate the four-factor solution originally proposed by Radloff (1977) with only minor differences in factor loading patterns on the four CESD-10 subscales.

The four factors found in this sample of cancer patients are consistent with the components of depression built in the original CES-D scale. It is important to note that all 10 items of the scale are indicators of symptoms or moods of depression; although they are related to each other, their dimensions are unique. However, despite the focus of theory and empirical evidence on the orthogonal four factors, the literature does not imply an undue emphasis on separate factors or subscales. In presence of high internal consistency and Cronbach's alpha values, a simple total CESD-10 score should always be considered as an estimate of depression symptoms.

The present findings generated in a sample of both men and women with a variety of types of cancer show that the abbreviated version of the CES-D has a reliability and validity comparable to that reported for the original 20-item scale (Kohout et al., 1993). The mean scores on the CESD-10 were relatively low, but almost 30% of patients reported scores above 4 on the CESD-10 indicating that they had depression symptoms that needed to be reported. The sample's mean age was approximately 58 years old; collectively 38.8% of which reported being single, divorced or widowed, and the majority were females. All of these are factors that may be important to explore in future studies to evaluate independent contributions to these depression scores.

Implications for Practice

Cancer patients who are in treatment may experience distressing physical symptoms such as fatigue, nausea or pain that may render them unwilling to complete long questionnaires. The

CESD-10 is a brief and easy-to-use tool to assess depressive symptoms. If patients report symptoms of depression, oncology providers may need to refer them for further assessment by mental health providers. It is common practice to ask patients about symptoms when they are in the clinical setting. This secondary data analysis confirmed the importance of asking patients about depressive symptoms when assessing other symptoms in clinical settings. The CESD-10 represents a valid and reliable means of measuring depressive symptoms in a vulnerable population in which respondent burden to longer instruments is a key concern.

Implications for Research

If symptom assessment measures are found to be multidimensional, researchers should consider applying alternative reliability coefficients. The appropriate coefficient to choose depends on the study design, the construct being measured, and the data analysis method used in the study. For example, studies that use structural equation modeling methodology for data analysis should employ reliability coefficients based on the results of the confirmatory factor analysis. Nonetheless, findings of this secondary analysis were limited by applying a single measure for the assessment of reliability. Perhaps applying alternative methods of reliability assessment in concurrence with Cronbach' alpha should be explored in future research.

Summary

In conclusion, this study suggests that a four-factor CESD-10 depression model fits the data well. The factor analysis demonstrated that the CESD-10 contains the same underlying factors of positive and depressed affect, interpersonal challenges, and somatic complaints, all of which were reported by the developer of the original 20-item CES-D (Radloff, 1977). To our knowledge, this is the first report of construct validity using SEM factor analysis of the CESD-10 among cancer patients. Data collected using the CESD-10 appears both reliable and valid among

patients with cancer who were in active treatment for their cancers. Using the short form is warranted in situations where the desire to maintain psychometric properties is paired with a need to reduce the respondent burden for vulnerable populations.

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Table 1.1 Full CES-D Items vs Boston Short Form.

Standard CES-D twenty items	Boston Short Form 10 items	Intended factor
1. I was bothered by things that usually don't bother me.	—	
2. I did not feel like eating; my appetite was poor.	—	
3. I felt that I could not shake off the blues.	—	
4. I felt that I was just as good as other people.	—	
5. I had trouble keeping my mind on what I was doing.	—	
6. I felt depressed.	x	DA
7. I felt that everything I did was an effort.	x	SC
8. I felt hopeful about the future.	—	
9. I thought my life had been a failure.	—	
10. I felt fearful.	—	
11. My sleep was restless.	x	SC
12. I was happy.	x	PA
13. I talked less than usual.	—	
14. I felt lonely.	x	DA
15. People were unfriendly.	x	IP
16. I enjoyed life.	x	PA
17. I had crying spells.	—	
18. I felt sad.	x	DA
19. I felt that people disliked me.	x	IP
20. I could not "get going."	x	SC

**IP = Interpersonal Challenges, DA = Depressive Affect, PA = Positive Affect, SV = Somatic Complaints. Items included in the Boston Short Form indicated by x.*

Table 1.2 Sample Characteristics.

Characteristic	Over-all sample N=201
Age (years), mean (SD)	57.95 (12.2)
Gender n (%)	
Male	76 (38)
Female	125 (62)
Education (years), mean (SD)	14.9 (2.6)
Ethnicity n (%)	
White/non-Hispanic	168 (83.6)
White/Hispanic	8 (4)
Black/non-Hispanic	19 (9.5)
Other	4 (2)
Marital status n (%)	
Single	27 (13.4)
Married	123 (61.2)
Divorced	36 (17.9)
Widowed	15 (7.5)
CESD-10, mean (SD)	2.57 (2.2)
Total score \geq 4, n (%)	59 (29.5)
Male	21 (35.6)
Female	38 (64.4)

*SPMSQ = Short Portable Mental Status Questionnaire, CESD-10 = Center for Epidemiologic Studies-Depression (Boston Short form)

Table 1.3 Correlation Matrix, Means, and Standard Deviations of Item Scores.

Depressive Symptoms	CESD1	CESD2	CESD3	CESD4	CESD5	CESD6	CESD7	CESD8	CESD9	CESD10
Enjoyed life	1									
Everything was effort	.297	1								
Sleep was restless	.158	.125	1							
Happy	.659	.319	.194	1						
Lonely	.186	.141	.092	.277	1					
Depressed	.281	.234	.208	.263	.517	1				
People unfriendly	.206	.040	.061	.253	.196	.157	1			
Sad	.260	.232	.102	.324	.419	.661	.131	1		
People disliked me	.153	.120	.043	.209	.223	.124	.655	.042	1	
Couldn't get going	.274	.375	.062	.307	.169	.211	.177	.133	.208	1
Means	.145	.405	.605	.165	.225	.280	.040	.325	.035	.340
Standard deviations	.353	.492	.490	.372	.419	.450	.196	.470	.184	.475

* all correlations were significant at the 0.01-0.05 level (2-tailed)

Table 1.4 CESD-10 Reliability Analysis Statistics.

	Corrected Item-Total Correlation	Squared Multiple Correlation
Enjoyed life	.494	.459
Everything was effort	.389	.228
Sleep was restless	.204	.075
Happy	.559	.508
Lonely	.438	.321
Depressed	.570	.542
People unfriendly	.296	.460
Sad	.488	.484
People disliked me	.283	.461
Couldn't get going	.366	.213
Scale Mean		2.57
Scale Standard deviations		2.207

*CESD-10= *Center for Epidemiologic Studies-Depression (Boston Short form)*

Table 1.5 Summary of Competing Model Fit Statistics for the CESD-10.

Model	χ^2	<i>df</i>	RMSEA	SRMR	AGFI	GFI	CFI
1.1 One factor model	265.0	35	0.181	0.114	0.672	0.791	0.554
1.2 Four-factor model	37.012	29	0.0372	0.0422	0.934	0.965	0.984

* χ^2 = Chi-square, *df* = Degrees of Freedom, RMSEA = Root Mean Square Error of Approximation, SRMR = Standardized Root Mean Square Residual, AGFI = Adjusted Goodness of Fit Index, GFI = Goodness of Fit Index, CFI = Comparative Fit Index.

Table 1.6 Standardized Loadings and Factor Correlations for the CESD-10.

Indicator variable		Latent factor loading			
Item	Label	PA	DA	IP	SC
CESD1	Enjoyed life	.766	-	-	-
CESD4	Happy	.859	-	-	-
CESD6	Depressed	-	.873	-	-
CESD8	Sad	-	.753	-	-
CESD5	Lonely	-	.588	-	-
CESD7	People unfriendly	-	-	.883	-
CESD9	People disliked me	-	-	.742	-
CESD2	Everything was effort	-	-	-	.616
CESD3	Sleep was restless	-	-	-	.237
CESD10	Couldn't get going	-	-	-	.570
Factor Correlations					
	IP	DA	PA	SC	
IP	1.000				
DA	.416	1.000			
PA	.319	.213	1.000		
SC	.634	.450	.240	1.000	

* *IP = Interpersonal Challenges, DA = Depressive Affect, PA = Positive Affect, SV = Somatic Complaints.*

Section Three: Fatigue-Related Symptom Clusters and Functional Status of Older Adults in Hospice

Abstract

Symptom control and improving quality of life (QOL) are important components of comprehensive hospice care where palliation is the goal. Patients with advanced cancer experience frequently complex and distressing co-occurring symptoms which affects their functional ability and functional status. Fatigue in cancer remains one of the most prevalent, persistent, and distressing symptoms experienced by this population. Although highly prevalent, the relationship of fatigue symptom cluster on functional status remains inconclusive among hospice patients. Fatigue-related symptoms experienced by hospice patients were examined. Physical and psychological symptoms that co-occur together were explored, and the identified cluster was used to discover predictors of functional status. The current study was conducted as a secondary analysis of data from a hospice outcomes improvement initiative.

Findings will be discussed with respect to sample characteristics and results of cluster and regression analysis. These data may contribute to a better understanding of fatigue symptom cluster as predictors of functional status, also it could identify benefits of symptom cluster assessment in patients with advanced cancer in hospice. This study will inform clinical practice of innovative ways of utilizing systematic assessment for detection of functional outcomes which can ultimately improve the QOL of patients who receive hospice services.

Keywords lack energy, physical activity, functionality, symptom co-occurrence, elders.

Introduction

Symptom cluster refers to the presence of a group of related co-occurring symptoms which can have an adverse effect on patient' outcomes and may also have a combined effect as a predictor of patient's morbidity (Miaskowski, Aouizerat, Dodd, & Cooper, 2007; Nugent, 2013). Patients in hospice care who were treated with surgery, radiation or chemotherapy, often experience multiple symptoms that occur simultaneously (Kirkova et. al, 2010). Depression, sleep disturbances, pain, poor appetite and difficulty of concentration are all symptoms that often occur cluster with fatigue (Tsai, Wu, Chiu, & Chen, 2010; Dong, Butow, Costa, Lovell, & Agar, 2014; Nieder & Kämpe, 2017). Current interventions that manage fatigue symptom in cancer patients only focus on fatigue as the single symptom outcome. Therefore, there is a need to understand fatigue-related symptom cluster in order to improve future designs of fatigue intervention research.

More than 1.7 million of the cancer population receive hospice services each year. It is estimated that 83.3% of Medicare hospice patients are 65 years of age or older. Even with new advancements in the treatment of cancer, it continues to be the number 1 diagnosis in hospice admissions, accounting for 27.2%. The vast majority (97%) of hospice care is received as a routine home care (National Hospice and Palliative Care Organization (2017). On average, patients with a primary diagnosis of cancer receives 47 days (median 19) of health care under hospices services, and close to 85% of the discharges are reported "deceased". From these estimates, it is understandable that older adults in hospice services with cancer are admitted near the end of life, perhaps in late stages of their illness.

They frequently experience a complex of distressing and co-occurring symptoms, as well as higher levels of fatigue than their younger counterparts (Butt et al., 2010). Symptom management is one of the most crucial components in their comprehensive hospice care.

The fatigue research in the cancer symptoms science has not been a focus in the older adult' population. There is a pressing need to investigate fatigue-related symptom cluster, as it may be associated with a decline in functional status among older adult hospice patients (Esper, 2010; Cheng & Lee, 2011; Lengacher et al., 2012; Thomas et al., 2013; Dong et. al. 2014; Reich et al., 2017). The treatment-limiting frailty and other age-related concerns such as slowed metabolism, and multi-morbidities keep these patients from participating in research studies and subject them to experience a rapidly progressive course of illness and increased disability (Butt et al., 2010). Hence, there are detrimental effects on their well-being, mortality, and survival (Beck, Towsley, Caserta, Lindau, & Dudley 2009; Costarella, Monteleone, Steindler, & Zuccaro, 2010; Payette et al., 2011). Additional studies are needed to delineate the fatigue-related symptom cluster and its relationship with functional status among older adult hospice patients with cancer. Fatigue has been considered a physical symptom due to complaints of physical lack of energy (Kim, Puymon, Qin, Guru, & Mohler, 2014). Its relationship with psychological distress, such as depression, is supported in the previous literature (Francoeur, 2014). There is a necessity to control for depression when one investigates the relationship of fatigue-related symptom clusters with functional status.

Research Aims and Hypotheses

This was a secondary data analysis study from a randomized clinical trial (RCT) Symptom Assessment to Improve Hospice Outcomes funded by the National Institute of Health

(McMillan, R01/5R01NR008252) of a sample of adult hospice patients (N=709). The following aims and hypotheses were tested:

Aim 1. To explore the relationships between symptoms and identify fatigue-related symptom clusters in older adult hospice patients.

Hypothesis 1. Older adult patients in hospice care experience multiple correlated symptoms that cluster with fatigue.

Aim 2. To which extent fatigue-related symptom clusters predict functional status while controlling for depression.

Hypothesis 2. Fatigue-related symptom clusters significantly predict functional status while controlling for depression.

Method

The parent study description.

The parent study used a multisite, randomized controlled trial design, where interested patient and caregiver dyads who were receiving hospice home care received standardized symptom assessment. Two equivalent research teams were identified in each hospice service involved in the study, and patients were recruited by these teams. The sample population was patients and their caregivers in two hospices in Southwest Florida. The hospices provided services to an average of 475 patients per day, who resided in a predominantly white with urban, suburban, and rural areas. Approximately 25% of the deaths in these counties are due to cancer. The largest proportion of the hospice patients have a cancer diagnosis (50%). Interdisciplinary teams provide care to approximately 65% patients each. The average length of stay was 39 days.

The study sample consisted of patients who were receiving hospice home care. The inclusion criteria for participation were: Patients were identified by admission face sheets as those who had a cancer diagnosis, had an identified family caregiver, were adults (18+ years

old), either male or female, able to read and understand English, and able to pass screening with the Short Portable Mental Status Questionnaire for cognitive competency (score > 8). Exclusion criteria were confused, excessively debilitated, comatose or actively dying patients. The original sample included 709 participants. 533 of them were 65 years or older and were included in this secondary analysis.

The parent study was approved by the administrators of the involved hospice service and the University of South Florida (USF) Institutional Review Board for the Protection of Human Subjects (IRB). The data collectors for patient data were experienced hospice nurses. Baseline data collection took place after admission to hospice. Patients who met the admission criteria were asked to fill out their questionnaires during a home visit. Those patients who met sample selection criteria and signed the informed consent were asked to answer the following questionnaire: Palliative Performance Scale (PPS), Center for Epidemiological Studies Depression, Boston Short Form (CESD-10), and the Memorial Symptom Assessment Scale MSAS. A demographic and clinical survey was completed as well.

Research design.

This study conducted a cross-sectional correlational study using baseline dataset from a large multicenter parent study (R01/5R01NR008252), of hospice patients with cancer. The purpose of choosing this design was to examine relationships among variables, so that inference about symptom cluster relationship with functional status could be made. In addition, as it is the intent of this study to evaluate the association between multiple fatigue-related symptoms, this design allows the investigator to compare multiple variables at the same time at no additional cost.

Sample.

To be included in this secondary data analysis, the participants' data had to have met the inclusion criteria: older adults (65+ years old), males and females, and had completed the MSAS, CESD-10, and the PPS scales, as well as demographic and clinical survey. The exclusion criteria were the same as the parent study.

Measures.

Patient demographic/clinical survey. Variables included age, gender, ethnic background, education level, marital status, living arrangement, cancer type, and length of time since diagnosis in years. Age was a continuous variable, gender and living arrangement were categorical variables. Living arrangement had 7 items: "Living alone, living with a spouse, living with spouse and child, living with the child, living with a parent, living with a roommate, and living with other".

Functional status. *Palliative Performance Scale (PPS)* assessed the functional status of persons receiving palliative care (Anderson, Downing, Hill, Casorso & Lerch, 1996). It was a validated measure of performance status, was based on the Karnofsky Performance Scale (KPS) and was proposed to provide a framework for measuring the progressive decline in palliative care patients. The PPS measures three broad areas: mobility, intake, and level of consciousness in five categories (degree of ambulation; ability to do activities and extent of disease; ability to do self-care; food/fluid intake; and state of consciousness). The PPS was scored from 0-100% at 10% increments (0% = "worse performance vs. 100% = "best performance"). The validity of this instrument was assessed by comparing the PPS score with the length of survival (McMillan et al, 2012). The strong positive correlations between PPS and KFS ($r=.88-.97$, $n=23$) support

construct validity. Inter-rater reliability between two raters was strong ($r=.95$) (McMillan et. al, 2012).

Symptoms. The *Memorial Symptom Assessment Scale (MSAS)* was designed to differentiate among frequency, intensity, and distress from symptoms that are commonly associated with cancer. MSAS demonstrated reliability, validity, and ease of use (Portney, et al, 1994). The original MSAS has 33 items assessing cancer symptoms. The items are scored by summing the items in each subscale (i.e., physical, psychological). The higher the score, the more severe, frequent, or distressing the symptoms are. (Portney, et al, 1994). A revised MSAS was used for this study that was developed for use with hospice patients with cancer, retaining items from the original MSAS that were most relevant to hospice patients' symptom experience (McMillan et. al, 2012). A total of 25 items were included in the revised version of the MSAS. Participants were asked whether they had a symptom or not (symptom occurrence). If their answer was positive. They were further asked about the symptom severity and distress. Symptom occurrence was a perception of the symptom frequency in the past 7 days in the MSAS, so this variable was treated as a continuous variable from 0 ("No") to 1 ("Yes"). Symptom severity and distress items were rated from 0-4 for severity and from 0-4 for distress. The scores were transformed into a 0-100 score respectively. For this secondary data analysis fatigue was operationally defined as lack of energy in this scale. Assessment of the validity of the MSAS for use with cancer patients receiving hospice home care was conducted and included correlation Hospice Quality of Life Index-14 (HQLI-14) scores. The correlation between MSAS distress scores and HQLI-14 scores were moderately strong and negative ($r= -.72$; $p<.001$). This provided further support for construct validity of the MSAS for use with cancer patients near the end of

life. In addition, the reliability of the intensity and distress scores were acceptably high ($r=.73-.74$) using coefficient alpha.

Depression. Depressive symptoms were assessed using the *Center for Epidemiologic Studies Depression-Boston Short Form (CESD-10) Scale*. The CESD-10 is a 10-item, self-report questionnaire that was developed to measure symptoms of depression in community populations. It is rated on a dichotomous Yes/No scale (Kohout et al., 1993). CESD-10 scores range from 0 to 30; higher scores indicate higher depressive symptoms. It combines ease of administration and reduced questionnaire burden with only 2-minutes of administration time. It had a very good reliability and validity and had been utilized successfully in the assessment of depressive symptoms in cancer research (Carpenter et al., 1998; Hann, Winter, & Jacobsen, 1999; Stagl, et al., 2015; Garrison, Overcash, & McMillan, 2011). The Cronbach's alpha for this study was .703. It is expected that shorter scales with fewer items like CESD-10 have lower alpha coefficients, thus, this result is acceptable.

Procedures.

The study protocol was approved by the University of South Florida IRB. Only baseline dataset was analyzed in this dissertation study. The recruitment process, study findings, and limitations of the parent study were discussed with the research team. The data were examined for completeness.

Data cleaning. To improve the quality of data for advanced analyses, data cleaning was performed. A common limitation of secondary data analysis is the single data source. Data quality problems of single data collection include misspellings of variables during data entry, invalid data, and missing information (Rahm, & Do, 2000). Statistical Package for Social Sciences SPSS version 25.0 (SPSS, Chicago, IL, USA) was used to detect and remove errors and

discrepancies. The parent study sample included patients who were 18 years and older, the parent study data file was split into $64 \leq$ and $65 \geq$ years. The current data analyses included only participants that were 65 years and older. The new data file (N= 533) had a substantial amount of missing data on MSAS severity and distress scale. A major problem with using the MSAS was that the symptom severity or distress items were dependent on the occurrence items. This meant that if there was no symptom occurrence, both symptom severity or distress would not be answered which led to a large amount of missing data. For that reason, we limited the analyses to include MSAS symptom occurrence. Furthermore, the dummy coding method was used to transform categorical variables. Variables with “0” entry were excluded from the analysis because they were missing data. One item of living arrangement, “live with a parent,” was considered to not appropriate for the target population, because very few older adults still live with parents. This item was removed from analyses. For the remaining variables, missing data were managed with pairwise deletion techniques assuming that data were missing completely at random. After data cleaning, 519 cases were available for data analyses.

Data analyses.

Descriptive statistics were used to analyze the demographic and clinical variables. For the first research question, bivariate Pearson correlations were used to explore the relationships among study variables and identified the symptoms which correlations reached statistical significance with fatigue. MSAS occurrence symptoms were clustered by exploratory factor analysis (EFA) extraction method used was principal component analysis (PCA) of the Statistical Package for the Social Sciences (SPSS) version 25 (SPSS Chicago, IL, USA). We used oblique rotation methods, (direct Oblimin and Promax), as we hypothesized to have nonzero correlations among the factors and aim to make inferences about physical and psychological symptoms

relationships, orthogonal rotations may be inappropriate. The number of factors extracted was determined using the eigenvalue 1.0, a scree plot, and parallel analysis with the Monte Carlo data simulation technique.

For the second research question, first, bivariate correlations were conducted among fatigue-related symptoms clusters (mean of clustered symptoms cooccurrence), depression (CESD_10), and functional status (PPS). Second, hierarchical multiple regressions with a functional status variable as the outcome variable were applied. In the first step, the predictor variable was fatigue related symptom cluster. In the second step, the predictor variable was fatigue related symptom cluster controlling for age, gender, and living arrangement. In the third step, the predictor variable was fatigue related symptom cluster controlling for age, gender, living arrangement, and depression.

Results

Sample characteristics.

The sample included 519 hospice patients. The mean age of the sample was 78.13 years, (SD= 7.4), with a mean of 12.6 years of education (SD= 3.1 years). Fifty-seven percent of the participants were males. Ninety-seven percent were Caucasian. The majority of the patients were partnered (64%) and living with spouse/partner. Cancer diagnoses included lung (n=193, 36%), pancreas (n=50, 9.4%) colon (n=39,7.3%), prostate (n=36, 6.8%), and breast (n=25, 4.7%) among others (n=147, 27.5%), with a mean of 2.25 years from diagnosis (SD= 4.1). The average CESD-10 score was 2.89 (SD= 2.2). In the MSAS, the total number of symptoms had a mean of 9.63 (SD= 4.19). The average of total PPS scores was 56.83 (SD= 10.72). Sample characteristics are presented in Table 3.1.

Research Question 1: which symptom relationships identify fatigue-related symptom cluster?

Relationships among symptoms.

Fatigue (lack of energy) had a significant positive correlations with the following items in relationship strength order: lack of appetite ($r=.267, p<.05$), feeling drowsy ($r=.220, p<.05$) lack of concentration ($r=.164, p<.05$), shortness of breath ($r=.132, p<.05$), dizziness ($r=.128, p<.05$), feeling sad ($r=.127, p<.05$), feeling irritable ($r=.126, p<.05$), nausea ($r=.122, p<.05$), dry mouth ($r=.117, p<.05$), feeling nervous ($r=.115, p<.05$) problems with sex ($r=.101, p<.05$), problems with urination ($r=.097, p<.05$), and sweats ($r=.091, p<.05$). Lack of energy had apposite correlation with CESD-10 ($r=.217, p<.01$). (Table 3.2).

Currently, in symptom cluster research, there are no standard or cutoff points for a symptom to be included in a cluster (Dong et. al. 2014). However, it is generally agreed that symptoms should moderately correlate with each other ($r=.30-.70$) (Chan, Richardson, A., & Richardson, J., 2005). However, all the Pearson correlations were less than 0.3 in the results. Therefore, 0.2 of Pearson r was set for clustered symptom selection. As a result, fatigue-related symptoms cluster identified in this analysis included lack of energy, feeling drowsy, and lack of appetite. In the total of 519 participants, there were 201 (39%) who reported lack of energy, feeling drowsy, and lack of appetite simultaneously.

Symptom Clusters.

Due to the low Pearson correlations for the three clustered symptoms. This cluster was further examined by conducting EFA to check if these three symptoms clustered in one factor. Initially, the data suitability for the cluster analysis was examined. MSAS symptom occurrence for this sample ($N=519$) was reliable. The average inter-item Cronbach's alpha coefficient of reliability was .735. The determinant of the correlation matrix approached zero (.076). The

Kaiser-Meyer-Olkin Index of Sampling Adequacy was .761. Finally, the Bartlett's Test of Sphericity was significant ($\chi^2 = 1318.530$, $df = 231$, $p < .001$). Based on these criteria, the inter-item correlation matrix was deemed adequate for factor analysis. Four symptom clusters were identified, with 40.837% of the variance explained, the symptom cluster PCA factor structure with the solution is presented in Table 3.3.

On Factor 1, seven symptoms (worrying, feeling sad, feeling irritable, feeling nervous, difficulty concentrating, problem with sex, and feeling drowsy) loaded together, which explained 15.470% of the factor's variance. Cronbach's alpha coefficient, for this cluster, was 0.63 which indicated the symptoms within cluster occurred in a homogeneous pattern. This factor was labeled "psychological." However, one symptom (feeling drowsy) loaded on both Factor 1 and Factor 3. The loading score for feeling drowsy was higher for Factor 3 than Factor 1, suggesting it was a stronger symptom indicator for Factor 3 and it was excluded from Factor 1 accordingly. Thus, only six of the seven symptoms (worrying, feeling sad, feeling irritable, feeling nervous, difficulty concentrating, problem with sex) were considered as indicators of Factor 1.

On Factor 2, four symptoms loaded together (nausea, vomiting, pain, sweats, and lack of appetite) which explained 7.058% of the factor's variance. Cronbach's alpha coefficient for this cluster was 0.607 which indicated the symptoms within the cluster occurred in a homogeneous pattern. Factor 2 was labeled "pain, gastrointestinal".

On Factor 3, nine symptoms (constipation, lack of appetite, feeling bloated, difficulty sleeping, dry mouth, lack of energy, feeling drowsy, problems with urination, dizziness) loaded simultaneously, which explained 6.007% of the factor's variance. Cronbach's alpha coefficient for this cluster was 0.472 which suggested the symptoms within cluster occurred in a homogeneous pattern. However, as previously mentioned the symptom (feeling drowsy) loaded

on both Factor 1 and Factor 3. The loading score for feeling drowsy was higher on Factor 3 than Factor 1 and was retained as an indicator of the symptom cluster for Factor 3. Factor 3 was labeled “somatic vegetative”. At the same time, Factor 3 supported that fatigue-related cluster contained the three symptoms (lack of energy, feeling drowsy, and lack of appetite) found in the Pearson correlations.

On Factor 4, four symptoms (dizziness, shortness of breath, cough, difficulty swallowing) loaded together, which explained 5.451% of the factor’s variance. Cronbach’s alpha coefficient for this cluster was 0.444 which suggested the symptoms within cluster occurred in a homogeneous pattern. However, the symptom (dizziness) loaded on both Factor 3 and Factor 4. The loading score for dizziness was higher for Factor 3 than Factor 4, suggesting it was a stronger indicator for Factor 3 than Factor 4 and so it was eliminated from Factor 4 and retained as an indicator of the symptom cluster for Factor 3. This resulted in three symptoms being considered as indicators of Factor 4. Factor 4 was labeled “dyspnea, throat”. Symptom clusters factor correlation matrix is presented in Table 3.4.

Research Question 2: To which extent fatigue-related symptom clusters predict functional status while controlling for depression?

Fatigue, depressive symptoms, and functional characteristics.

On average, older adult hospice patients experienced 9 concurrent symptoms (SD= 4.2), and the prevalence of fatigue (lack of energy) was 86.9%. Approximately 34% of the patients reported feeling depressed, and 37.6% felt sad. FSC reached a negative low but highly significant correlation ($r = -.117$ $p=.008$) with the functional status measure PPS, and positive significant correlation with CESD-10 ($r=.253$, $P<.000$). Also, depressive symptoms CESD-10 had a negative low and significant correlation with PPS ($r= -.096$, $p=.027$).

Predictors of functional status.

Hierarchical multiple regression was performed to investigate the ability of fatigue-related symptom cluster (lack of energy, feeling drowsy, and lack of appetite) to predict functional status, after controlling for depressive symptoms. The first step of the hierarchical regression conducted with the independent variable fatigue related symptom cluster regressed onto functional status explained 1.2 % of the total variance of the PPS scores ($R^2=.012$, $F(1,515) = 7.113$, $p = .008$). To control for confounding variables that correlate with functional status, a second step of the hierarchical regression was conducted controlling for age, gender and living arrangement. The second model of the hierarchical regression, $F(8,508) = .176$, $p = .000$, FSC significantly predicted PPS accounting for 4.5% of the variance controlling for age, gender, and living arrangement.

In an attempt to further the investigation of functional status predictors, as the fatigue-related symptom has a significant positive correlation with CESD-10. The third step, depressive symptoms CESD-10 total scores were entered as a covariate variable, in addition to FSC, age, gender, living arrangement variables. The third model increased the functional status predictability of fatigue-related symptom cluster by 3.5 points, ($R^2 \Delta = .047 - .012 = .035$), which was a small but a significant change ($F\Delta = 4.983$, $df(1,507)$, $P < .05$).

Discussion

This study aimed to identify fatigue-related symptom cluster in older adult hospice patients with cancer and to evaluate the extent to which the identified cluster and depression can predict functional status. The correlation analysis revealed three clinically relevant symptoms of fatigue: lack of energy, feeling drowsy, and lack of appetite. Atkas, Walsh, and Hu (2014), as well as Van Lancker et al., (2016), had recently reported similar clustering with fatigue. The

relationship between fatigue and feeling drowsy is suggested to be indicative of a parasympathetic nervous system dysfunction (Van Lancker et al., 2016). On the other hand, the lack of appetite can result in loss of energy and feeling of weakness that can be linked to functional status decline. A clinically and statically significant predictive relationship that was confirmed in our regression analysis. This close direct linkage of fatigue symptom cluster and functional status, however, only accounted for a small (1.2%) portion of the total variance in PPS scores. The increase in total variance explained by fatigue-related cluster (4.7%), which further supports the independent negative relationship of fatigue-related symptom cluster with functional status. Also, a trend was observed in the patients' age and living arrangement differences, suggesting that younger patients who lived with children may report more fatigue-related symptoms, higher depression and lower functional status. An explanation of such a trend is possibly related to older adults' fewer reports of symptoms severity and distress. It could also be inferred that living with adult children comes with many stresses and it may involve living with grandchildren and married children. Although living alone presents its own set of challenges, such as needing a caregiver. Perhaps old age among many virtues come with better and more effective coping skills. Finally, even though we used Pearson correlation coefficients to identify the symptom cluster, our study was able to confirm the finding with further factor analysis, and replicate findings of the literature specific to fatigue-related symptom clusters (Aktas, Walsh, & Hu, 2014; Van Lancker et al., 2016).

There have been some pilots and studies on more effective symptom management for a single symptom, such as physical activity interventions. However, we are still in a rudimentary phase researching the more precise ways to identify symptom clusters and their predictive tendencies on the various cancer patients' functional status. Therefore, research remains limited

and requires continuous longitudinal and empirical case evaluations. However, as it stands, research beckons a need for a shift in paradigm, in the overall palliative care management, to refocus its lens on the more psychological aspects of the patients' difficult experience. Education on physical symptom attributes, no matter what the recurring clusters, are only a primary catalyst of an overarching theme; that is, the effect of psychological distress on worsening or even expediting the inevitable physical symptoms. A similar linkage of physical and psychological symptoms is evident in symptom science literature, Kwekkeboom (2016) found that fatigue, pain, and anxiety were tremendously increased in those participants undergoing chemotherapy with little to no social support. Symptom experience begins with the occurrence, first, the perception of a change is noted. However, the actual experience lies in the process of evaluation and response. The judgment of the physical symptom severity, frequency and location is what evokes the subjective psychological, physiological or behavioral response. The symptom assessment scale must capture the full experience feelings, thoughts, and behaviors related to the symptom experience. The reason fatigue was not clustered with pain, depression, or sleep disturbance is perhaps a limitation of the way fatigue was defined, relying on lack of energy symptom occurrence only.

Recent studies in cancer patients of urban settings attempted to distinguish symptoms between minorities and Caucasians and while concluded there was currently none but not enough long-term research to validate this definitively adds another layer of research needed. Furthermore, the findings emphasize the necessity of educating patients as well, involving them in their own ability to identify the concurrent symptoms and potential extraneous catalysts that may exacerbate or conversely ameliorate these symptoms. Implications for nurses is to be as informed as possible of potential high-risk predictors directly related to the psychosocial aspect

of the patient. Therefore, increased proper tracking of physical symptoms in tandem with psychological impacts on the symptoms themselves.

Conclusions

Current research is indicating three important gaps that may be considered for further investigations in future research:

1. More statistical and scientific derivations for assessing symptom clusters and their predictive impacts on functional status, in the progressive stages of the hospice patients, would better assist methodical guidance in symptom management.
2. Emphasis on the psychosocial impacts needs to be better addressed and reviewed, as well as new interventions to facilitate and ameliorate symptom cluster management.
3. While not discussed much in this review, biological underpinnings need to be further investigated both on how it impacts predictive symptom clusters as well as more ethnic and cultural implications of psychosocial symptoms experienced.

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Table 3.1 Demographics and Clinical Characteristics of Patients

	Frequency	Percent	Mean	Std. Deviation
Age			78.18	7.351
Gender				
Male	300	57.8		
Female	219	42.2		
Marital status				
Never married	18	3.5		
Currently married	332	64.0		
Separated	4	.8		
Divorced	42	8.1		
Widowed	122	23.5		
Ethnicity				
Caucasian	503	96.9		
African American	8	1.5		
Hispanic	5	1.0		
Asian/pacific islander	1	.2		
other	2	.4		
Years of formal education			12.61	3.121
Cancer diagnosis	8.65	8.719		
Lung	188	36.2		
Pancreas	49	9.4		
Colon	39	7.5		
Prostate	32	6.2		
Breast	23	4.4		
other	329	63.8		
Years since diagnosis			2.27	4.16
Living arrangement				
Alone	39	7.5		
Spouse/partner	342	65.9		
Spouse/partner and children	19	3.7		
Children (no spouse/ partner)	46	8.9		
Roommate (no spouse/ partner)	5	1.0		
other	68	13.1		
Cancer symptoms				
Lack of energy (yes)	451	86.9		
Pain at all (yes)	363	69.9		
Difficulty sleeping (yes)	202	38.9		
Depression (CESD-10)			2.89	2.2
Functional status (PPS)			56.83	10.72

Table 3.2 Bivariate Correlations Matrix of Study Variables with Fatigue Symptom Cluster.

	Age	Gender	PPS	CESD -10	FSC	MSAS severity	MSAS distress	MSAS occurrence	living arrangement	Mean	SD
age	1									78.18	7.34
gender	-.063	1								.43	.49
PPS	-.036	-.066	1							57.05	10.72
CESD-10	-.045	.021	-.096*	1						2.84	2.15
FSC	-.171**	-.005	-.117**	.253**	1					2.07	.90
MSAS severity	-.181**	.017	-.114**	.443**	.548**	1				20.49	11.14
MSAS distress	-.179**	.025	-.103*	.451**	.479**	.887**	1			19.72	13.43
MSAS occurrence	-.206**	-.007	-.046	.421**	.617**	.882**	.820**	1		9.65	4.10
Living arrangement	-.002	.251**	.153**	-.045	-.103*	-.026	-.052	-.028	1		

*N=533; *Correlation is significant at the 0.01 level (2-tailed). **Correlation is significant at the 0.05 level (2-tailed). PPS=palliative performance scale; functional status measure, CESD-10=Center for Epidemiological Studies Depression, Boston Short Form, FSC= fatigue-related symptom cluster. MSAS=Memorial Symptom Assessment Scale.

Table 3.3 Symptom Clusters Structure Matrix

Symptom experiences	Factors			
	Factor 1	Factor 2	Factor 3	Factor 4
worrying	.688			
feeling sad	.684			
feeling irritable	.612			
feeling nervous	.580			
difficulty concentrating	.532			
prob with sex	.337			
nausea		.817		
vomiting		.785		
pain		.542		
sweats		.412		
constipation			.500	
lack of appetite			.489	
feeling bloated			.483	
difficulty sleeping			.476	
dry mouth			.460	
fatigue; lack of energy			.455	
feeling drowsy			.417	
problems with urination			.370	
dizziness			.341	
shortness of breath				.726
cough				.703
difficulty swallowing				.459
Variance explained	15.470%	7.058%	6.007%	5.451%
Total Variance explained	33.987%			

Table 3.4 Symptom Clusters Factor Correlation Matrix

	Factor 1	Factor 2	Factor 3	Factor 4
Factor 1	1.000			
Factor 2	.278	1.000		
Factor 3	.324	.270	1.000	
Factor 4	.235	.168	.229	1.000

*Factor 1 = "psychological". Factor 2 = "pain, gastro-intestinal". Factor 3 = "somatic, vegetative, physical". Factor 4 = "dyspnea, throat). Extraction Method: Principal Component Analysis. Rotation Method: Promax with Kaiser Normalization.

Table 3.5 Hierarchical Multiple Regression Predicting Functional Status

Model		B	Std. Error	β	t	Sig.	Adjusted R Square	Std. Error of the Estimate	R Square Change
Step 1	(Constant)	59.50	1.169		50.877	.000			
	FSC	-1.38	.520	-.117	-2.667	.008	.012	10.755	.014
Step 2	(Constant)	67.39	5.482		12.294	.000			
	FSC	-1.406	.527	-.118	-2.668	.008			
	Living other	6.188	1.464	.193	4.227	.000			
	age	-.098	.066	-.067	-1.479	.140			
	gender	-2.489	1.034	-.114	-2.407	.016	.045	10.575	.046
Step 3	(Constant)	67.844	5.483		12.374	.000			
	FSC	-1.209	.542	-.102	-2.232	.026			
	Living other	6.164	1.462	.193	4.216	.000			
	age	-.097	.066	-.066	-1.460	.145			
	gender	-2.425	1.033	-.111	-2.347	.019			
	CESD-10 Total	-.336	.220	-.068	-1.524	.128	.047	10.561	.004

*PPS=palliative performance scale, CESD-10=Center for Epidemiological Studies Depression, Boston Short Form, FSC= fatigue-related symptom cluster.
Dependent Variable: PPS Total

Summary of Dissertation

Discussion

This dissertation study explored the relationships between fatigue, depressive symptoms and functional status in older adults with cancer. Guided by the Theory of Unpleasant Symptoms, our framework postulated that fatigue in cancer is a physical symptom and has interrelations with other cancer symptoms; fatigue related symptom clusters. Depression is considered a psychological symptom in the conceptual framework. Patient contextual factors influence the experience of fatigue-related symptom cluster and depression. Functional status is an outcome of the symptom experience.

In the first section of the dissertation, we summarized the current science stands on fatigue in the older adult cancer population, in relation to physical activity interventions, and explored functional status outcomes. There is evidence that moderate to intensive physical activity interventions are well tolerated by older adults. Motivation and adherence were also similar to their younger counterparts. The interventions showed significant improvements in fatigue cancer symptom. Objective improvements were also evident in measures of functional status, including muscle strength, mass, and endurance, balance, peak oxygen uptake reflecting increases in physical and functional capacity.

There is yet a lack of consonance on the measures of fatigue, and specifics of exercise modalities, and duration. An important aspect of the Theory of Unpleasant Symptoms is symptom defined in multidimensional measures, including intensity, distress, frequency, and interference. Therefore, a multidimensional symptom as fatigue should be captured with a scale

that considers fatigue-related symptom cluster. Interventions that included behavioral aspects and counseling could benefit patients with depression. Also, future physical activity interventions should adhere to the American College of Sports Medicine guidelines when prescribing physical activity programs to maintain adequate levels of intensity, duration, and frequency that are appropriate for the older adult cancer patients for the purpose of producing the desirable positive and significant health improvements.

Because depression, as a psychological symptom, was detected by many previous cancer studies as a core component of symptom clusters, in the second dissertation section we examined the Center for Epidemiological Studies Depression, Boston Short Form (CESD-10). We confirmed CESD-10 has appropriate structural validity. The reliability for use to assess depression in patients with cancer was also satisfactory. Physical symptoms, such as fatigue, are linked to emotional distress which negatively affects functional status. Both physical and psychosocial symptoms and symptom clusters have a direct and indirect impact on quality of life, supporting the urgency to understand the relationship between depression, fatigue, and functional status.

In the third dissertation section, we examined the relationship of fatigue to cancer-related symptoms and identified a fatigue-related cluster of symptoms (feeling drowsy, lack of energy, and lack of appetite) that was evident in prior research as well. Depression was positively associated with fatigue-related symptom cluster, and negatively with functional status. While functional status was operationalized as scores of PPS. Both fatigue related symptom cluster and depression were significantly associated with PPS. Experiencing fatigue-related symptom cluster was a predictor of participants' low functional status, and depression had a significant contribution to this predictive relationship. Although one can argue the effect of sample size in

producing inflated results, this relationship is evident in clinical context and prior research.

A common limitation of secondary data analysis studies is the constrain researchers to have towards the choice of instruments. Probably conceptualizing fatigue as lack of energy does not capture the full dimensions of fatigue symptom, which may explain the weak but significant results of this dissertation. In future studies, researchers should consider using a valid and reliable fatigue measurement scale. A multi-symptom measure that lacks a specific fatigue subscale may contribute to the weak correlations with the functional status outcome we found.

This study is informative of the potential significant predictors of functional status directly related to the physical and psychological aspects of the patient. Therefore, clinicians and researchers alike should gain increased sensitivity and proper detection of cancer symptoms in tandem with their psychological impacts.

Appendix A: Institutional Review Board Approval for Section Two



RESEARCH INTEGRITY AND COMPLIANCE
Institutional Review Boards, FWA No. 00001669
12901 Bruce B. Downs Blvd., MDC035 • Tampa, FL 33612-4799
(813) 974-5638 • FAX (813) 974-7091

May 17, 2018

Suzan Abduljawad
College of Nursing Tampa,
FL 33612

RE: **Expedited Approval for Initial Review**

IRB#: Pro00035101

Title: Validity and reliability of the Center for Epidemiologic Studies Depression, Boston Short Form for Use with Cancer Patients.

Study Approval Period: 5/16/2018 to 5/16/2019

Dear Ms. Abduljawad:

On 5/16/2018, the Institutional Review Board (IRB) reviewed and **APPROVED** the above application and all documents contained within, including those outlined below.

Approved Item(s):

Protocol Document(s): [Cesd-10 protocol](#)

Consent/Assent Document(s)*: Waiver of Process granted.

Appendix B: Institutional Review Board Approval for Section Three



RESEARCH INTEGRITY AND COMPLIANCE
Institutional Review Boards, FWA No. 00001669
12901 Bruce B. Downs Blvd., MDC035 • Tampa, FL 33612-4799
(813) 974-5638 • FAX(813)974-7091

6/5/2018

Suzan Abduljawad
College of Nursing
5201 Cypress Palms Ln

Tampa, FL 33647

RE: **Not Human Subjects Research Determination**

IRB#: Pro00035809

Title: Fatigue-Related Symptom Clusters and Functional Status of Older Adults in Hospice

Dear Mrs. Abduljawad:

The Institutional Review Board (IRB) has reviewed your application. The activities presented in the application involve methods of program evaluation, quality improvement, and/or needs analysis. While potentially informative to others outside of the university community, study results would not appear to contribute to generalizable knowledge. As such, the activities do not meet the definition of human subject research under USF IRB policy, and USF IRB approval and oversight are therefore not required.

While not requiring USF IRB approval and oversight, your study activities should be conducted in a manner that is consistent with the ethical principles of your profession. If the scope of your project changes in the future, please contact the IRB for further guidance.

If you will be obtaining consent to conduct your study activities, please remove any references to "research" and do not include the assigned Protocol Number or USF IRB contact information.

If your study activities involve collection or use of health information, please note that there may be requirements under the HIPAA Privacy Rule that apply. For further information, please contact a HIPAA Program administrator at (813) 974-5638.

Sincerely,

About the Author

Suzan Abduljawad grew up in Saudi Arabia and Morocco and moved to Florida in 2007. She earned a M.S. in Nursing, with a concentration in oncology from the University of South Florida (USF) College of Nursing. She actively participates in educational and research activities; she has served as a Teaching Assistant and a Graduate Research Assistant at USF and volunteered as a substitute teacher in Hillsborough County and Pasco county schools. She is currently a reviewer and a facilitator for the Annual Research Conferences at USF, and a reviewer for the Journal of Nursing Measurement. Suzan has worked as a Registered Nurse, and an Advanced Oncology Nurse Practitioner in the adult oncology unit and the ambulatory care clinics at the Saudi Arabian National Guard Hospital. She has nursing students mentoring, and nursing leadership experiences while caring for young and older adults with cancer. She developed an interest in cancer symptom research while taking care of her patients. Her research interests are fatigue, depressive symptoms, physical activity, functional status, and quality of life of adults with cancer. During her doctoral studies, Suzan co-authored four peer-reviewed publications. She has collaborated on many posters and oral presentations. She received the Advanced Nursing Practice Clinical Excellence Award from USF and was awarded a King Abdelaziz Medical City, and a Saudi Arabian Cultural Mission full scholarship for her graduate studies. She was inducted into the Sigma Theta Tau International Honor Society of Nursing and is a member of the Oncology Nursing Society and the Southern Nursing Research Society. Suzan is a Yogi, and a Tae Kwon Do practitioner. She enjoys traveling and has plans for international and global collaborations.