CHANGES IN PHYSICAL ACTIVITY AND QUALITY OF LIFE OF CANCER SURVIVORS

PARTICIPATING IN A GROUP EXERCISE PROGRAM

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Sarah Jane Greterman

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The Supervisory Committee certifies that this ***disquisition*** complies with North Dakota

State University's regulations and meets the accepted standards for the degree of

DOCTOR OF PHILOSOPHY

SUPERVISORY COMMITTEE:

Bryan Christensen
Chair

Brad Strand

Won Byun

Mark Strand

Approved:

4/28/2017	Yeong Rhee
Date	Department Chair

ABSTRACT

Although cancer survival rates are improving, cancer treatment is often associated with adverse biopsychosocial symptoms, including increased risk of anxiety, depression, and social isolation, and reduced physical fitness and quality of life (QOL) (Courneya, 2003; Howlader, et al., 2012; Rajotte, et al., 2012). Since the early 1990's, interest in the potential benefits of participation in exercise on the well-being of cancer survivors has been growing (Pinto & Floyd, 2007). Although physical activity (PA) has shown to improve physical functioning and QOL many adverse biopsychosocial effects often impact one's ability to engage in regular PA, and challenges overall well-being. (Knobf, Musanti, & Dorward, 2007). To overcome some of these barriers, the LIVESTRONG® Foundation partnered with numerous YMCA's establishing a structured 12-week post-treatment group exercise program for cancer survivors. The purpose of this study was to evaluate changes in PA and QOL among cancer survivors participating in a LIVESTRONG® at the YMCA group-exercise program. Subjects (N=47) participating in a program in Fargo, North Dakota, between July 2011 and August 2014, were grouped into cohorts based on their monthly start date. PA was monitored using the SenseWear armband activity monitor and QOL was assessed using the FACT-G. Both PA and QOL were evaluated at three different time points: end of week 1, week 6, and week 12. Overall, results indicated participants engaged in more than 4 hours of PA each day, with more than 40 minutes of moderate-vigorous PA per day. Furthermore, significant declines in sedentary activity were observed from week 1 to week 6 and week 6 to week 12, based on wear time. In addition, participants started the program with relatively high QOL. All areas of QOL improved, with the most significant improvements correlated with physical well-being. Although it was difficult to determine exact cause and effect relationships relative to participation in the LIVESTRONG® at

the YMCA group exercise program, the fact that participants met the minimum ACSM PA

recommendations at each time point, expressed a significant decline in sedentary activity, and

displayed improvements in QOL is promising.

Keywords: cancer, physical activity, group exercise program, quality of life, FACT-G,

biopsychosocial

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LIST OF ABBREVIATIONS

ACSM……………………….American College of Sports Medicine

ATP……………………….Adenosine Triphosphate

BMI……………………….Body Mass Index

BRFSS……………………….Behavior Risk Factor Surveillance System

CDC……………………….Centers for Disease Control and Prevention

CRP……………………….C-Reactive Protein

CVD……………………….Cardiovascular Disease

DLW……………………...Doubly Labelled Water

DNA……………………....Deoxyribnucleic Acid

EORTC QLQ…………….…...European Organization for Research and Treatment of Cancer
                                      Quality of life Questionnaire

EXMOS……………………...Exercise-Mediated Oxidative Stress

FACT-G……………………...Functional Assessment Cancer Therapy-General

IDEEA……………………….Intelligent Device for Energy Expenditure and Physical Activity

IPAQ……………………......International Physical Activity Recall Questionnaire

LIT……………………….....Light Physical Activity

METs……………………….Metabolic Equivalents

MOD……………………….Moderate Physical Activity

MVPA……………………….Moderate-Vigorous Physical Activity

NHANES……………………….National Health and Nutrition Examination Survey

PA………………………..….Physical Activity

PACT……………………...Physical Activity after Cancer Treatment

PAEE…………………….……Physical Activity Energy Expenditure

QOL………………………...….Quality of Life

ROS……………………………Reactive Oxygen Species

RNS…………………………….Reactive Nitrogen Species

SED……………………………Sedentary

SOFIT……………………..……System for Observing Fitness Instruction Time

TAM…………………………....Tumor-Associated Macrophages

TEE……………………………Total Energy Expenditure

VIG…………………………..Vigorous

CHAPTER 1. INTRODUCTION

According to the Centers for Disease Control and Prevention (CDC) (2013), about one in every seven adults will develop cancer at some point in their life with approximately 1.7 million new cancer cases diagnosed annually. Furthermore, this estimate does not include carcinoma in situ (non-invasive cancer) of any site except urinary bladder, and does not include basal cell and squamous cell skin cancers, which are not required to be reported to cancer registries (American Cancer Society, 2013). In 2013 alone, more than 575,000 Americans are expected to die of cancer, equating to almost 1,600 people per day (American Cancer Society, 2013; CDC, 2013). In fact, cancer is the second most common cause of death, accounting for nearly one of every four deaths in the United States (American Cancer Society, 2013).

Without a doubt, the number of cancer cases is substantial; however, only about 5% of all diagnosed cancers are cancers that originate from inherited genetic alterations (American Cancer Society, 2013). Most cancers are caused by non-inherited genetic damage due to internal or external factors either acting together, or in sequence, to initiate or promote the development of cancer (American Cancer Society, 2013). Indeed, the World Cancer Research Fund estimates that about one-quarter to one-third of new cancer cases could be related, specifically, to obesity, physical inactivity, and poor nutrition, all of which are controllable factors (American Cancer Society, 2013). These causal factors may inhibit or delay cancer detection, treatment, survival rate, and quality of life.

Advancements in early detection and treatment have improved the overall cancer survival rate, with a 66% all-site five-year survival rate following diagnosis for adults (Howlader, et al., 2012) (see Table 1). Such advancements project the number of cancer survivors in the U.S. to increase from 13.7 million to 20 million by 2020 (American Cancer Society, 2013; Howlader, et

al., 2012). This five-year survival rate is useful for monitoring progress in early detection and treatment of cancer; however, it doesn't distinguish between those patients who are still in treatment, have relapsed, or have been cured permanently, since cancer deaths can occur beyond five years after diagnosis (American Cancer Society, 2013). Although relative survival rates provide an indication of the average survival experience of cancer patients, such rates may or may not predict long-term prognosis. Therefore, early diagnosis and post-cancer treatments may play an integral role in the cancer patients' long-term survival and overall well-being.

Despite these survival rate estimates, "cancer survivors are at an increased risk for recurrence, secondary cancers, late effects of treatment, and a variety of symptoms that can adversely affect quality of life" (Bellizzi, Rowland, Jeffery & McNeel, 2005, p. 8884). In addition, cancer treatment is often associated with adverse psychosocial and physical symptoms, including increased risk of anxiety, stress, depression and social isolation, as well as reduced physical fitness and quality of life (QOL) (Courneya, 2003; Howlader, et al., 2012; Rajotte, et al., 2012). Furthermore, the responses to these stressors are often dependent on a variety of components, including the stage of disease, the intensity of treatment, patient's coping style, support network, and adaptation skills (Knobf, Musanti, & Dorward, 2007). Therefore, how cancer patients respond to these stressors can play an integral role in their overall outcome and, ultimately, survival.

The biopsychosocial responses cancer patients and survivors related to the multifaceted aspects that come with the diagnosis, treatment, and follow-up of cancer can have a big impact on physical activity levels and overall QOL. Physical exercise has been shown to improve physical functioning, cardiovascular fitness, sleep, QOL, and a variety of other psychological and social factors in cancer patients (Knobf, et al., 2007).

Table 1

5-year survival rates for the top 10 cancer sites in the United States, 2005-2011.

Cancer type	Survival rate
All-sites	66.5%
Prostate cancer	98.9%
Thyroid Cancer	97.9%
Melanoma of the Skin	91.5%
Breast Cancer (female)	89.4%
Endometrial Cancer	81.7%
Kidney and Renal Pelvis	73.2%
Non-Hodgkin Lymphoma	70%
Colon and Rectum cancer	64.9%
Leukemia	58.5%
Lung and bronchus cancer	17.4%
Pancreatic Cancer	7.2%

Note: Howlader, et al., 2012

Purpose

Research examining changes in physical activity and its impact on QOL is still in its infancy. Physical activity and QOL interventions vary from individual to group-based programs and encompass a variety of training modalities. The LIVESTRONG® organization has collaborated with numerous YMCAs nationwide as a means to assist participants in recovery by developing their own physical fitness program, reduce therapy side effects, prevent unwanted weight changes, and improve self-esteem (LIVESTRONG Foundation, 2015; YMCA of Cass

Clay, 2016). In addition, their goal is to promote a healthy lifestyle in a supportive environment and a feeling of community with fellow survivors, YMCA staff, and members (LIVESTRONG Foundation, 2015; YMCA of Cass Clay, 2016).

The problem is there is limited research evaluating changes in physical activity and its impact on QOL both during and after participation in the LIVESTRONG® at the YMCA program. Furthermore, there are no evidence-based exercise programs for cancer survivors. Therefore, the purpose of this study is threefold. First, the information presented will identify the biopsychosocial impact of cancer on both cancer patients and cancer survivors. Secondly, this paper will discuss research examining physical activity as a treatment modality for cancer patients and cancer survivors and its impact on quality of life, survival rate, and related biopsychosocial factors. Third, methodologies will aim to examine changes in physical activity (PA), sedentary time (SED), and QOL, and determine the impact of physical activity on quality of life measures during participation in a post-treatment, 12-week, LIVESTRONG® at the YMCA group exercise program in Fargo, North Dakota.

Hypothesis

While it is logical to think that greater PA leads to higher levels of QOL, it could be deemed that those with a higher QOL had more energy to engage in greater levels of PA. This research study will examine quantitative changes in PA and SED time, will qualitatively assess changes in QOL using the FACT-G, and will determine the relationship between PA, SED time, and QOL measures among 30 cancer survivors participating in the 12-week, LIVESTRONG® at the YMCA exercise program in Fargo, North Dakota. Therefore, the hypotheses are two-fold. First, it is hypothesized that PA will increase and SED activity will decrease from baseline to week 12 of the LIVESTRONG® at the YMCA exercise program. Secondly, it is hypothesized

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that QOL will increase from baseline to week 12 of the LIVESTRONG® at the YMCA exercise program.

Limitations

Because the study is limited to the YMCA in Fargo, North Dakota, the ability to generalize the findings may be limited. In addition, the population itself is extremely unstable, which could result in drop-outs due to the strenuousness of the program, cancer recurrence, or other individual limitations. Furthermore, those enrolled in the program have various backgrounds, such as type of cancer and timeframe of diagnosis and treatment, which could also impact their PA levels and QOL during the study.

Conclusion

This research will strive for specific and fundamental changes in physical activity levels and QOL measures among cancer survivors enrolled in a structured and planned group exercise program. In the short term, the goal of participation in the LIVESTRONG® at the YMCA program is to establish an increase in physical activity levels and improved overall quality of life among cancer survivors during and following participation in a 12-week LIVESTRONG® at the YMCA wellness program. In the medium term, researchers and the health professionals administering the program aim to identify maintenance of these physical activity improvements and enhanced quality of life among the cancer survivor participants enrolled in the LIVESTRONG® at the YMCA program. Finally, in the long term, continued research aims to validate the LIVESTRONG® at the YMCA program as an evidence-based program to improve physical activity and quality of life among cancer survivors in order to provide oncologists and health professionals with an evidence-based wellness program to improve physical activity and quality of life among cancer survivors.

CHAPTER 2. LITERATURE REVIEW

Since the early 1990's, there has been considerable growing interest in the potential benefit, both physically and psychologically, that participation in exercise can have on cancer patients (Pinto & Floyd, 2007). Declining physical, psychological, and social functioning observed in cancer patients and survivors illustrate the need for post-treatment interventions for improving overall well-being. Anticipated benefits include cardiovascular fitness, muscular fitness, less fatigue and pain, and a general improvement in patient-rated physical functioning and improved overall quality of life (Courneya, Mackey, et al., 2003). Therefore, tertiary prevention, such as increasing levels of physical activity, may play a key role in controlling the adverse effects of cancer and treatment (Bellizzi, et al., 2005).

Etiology of Cancer

Cancer is a complex disease that can originate almost anywhere in the human body. The human body is made up of trillions of cells, all with specific, specialized functions. Normal human cells follow an orderly process of growth, division, and death, or apoptosis. This orderly process allows our bodies to form new cells as the body needs them by replacing old or damaged cells. When cancer develops, this orderly process is broken down. Cancer cells are abnormal cells that lack the specific functionalities of normal cells. Because of this, the abnormal cancerous cells grow out of control in that they continue to divide without stopping, thereby allowing old or damaged cells to survive and forming new cells where they are not needed. This out-of-control growth of abnormal cells often forms malignant cancerous tumors, which means they have the ability to spread or invade nearby tissues. Furthermore, as they grow, they have the ability to break off and travel to other parts of the body and form new tumors (National Cancer Institute, 2015).

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Although many cancer diagnoses are due to the formation of tumors, not all cancers form tumors. Some cancers arise in the blood, bone marrow, or other cells, such as lymph cells. However, there are similarities to tumors in that there is an abnormal out of control growth of the production of specific blood cells or immune cells that lead to cancer (National Cancer Institute, 2015). Just as with tumors, these cancerous cells have the ability to metastasize to other parts of the body.

Regardless of where the cancer originates, cancer is viewed as a genetic disease because carcinogenesis causes changes to genes that control how cells function at the cellular, molecular, and morphological levels (Demarzo & Garcia, 2004). The three main types of genes affected by cancer are proto-oncogenes, tumor suppressor genes, and deoxyribonucleic acid (DNA) repair genes. Proto-oncogenes are primarily responsible for cell growth and division, but alterations in these genes may cause them to become oncogenes (cancer-causing genes) by allowing cells to grow and survive when they shouldn't (National Cancer Institute, 2015). Tumor suppressor genes also control cell growth and division, but alterations in these genes may cause division in an uncontrolled manner (National Cancer Institute, 2015). Activation of oncogenes or suppression of the tumor suppressor genes can then lead to cancer progression (Jones and Thompson, 2009). The third genes leading to cancerous cells are DNA repair genes. DNA repair genes are involved in fixing damaged DNA; however, cells with mutated DNA repair genes may encourage mutations in other genes causing them to become cancerous (National Cancer Institute, 2015). Research suggests that certain mutations are common among specific types of cancer. Therefore, cancers are sometimes characterized by the types of genetic alterations that are driving them, as well as where they develop (National Cancer Institute, 2015).

As a genetic disease, the basic understanding behind carcinogenesis follows the processes of tumor initiation, tumor promotion, and tumor progression (Yuspa and Poirier, 1988). Tumor initiation develops due to genetic changes (primarily in the genes discussed above) caused by inherited genes, or more commonly, by environmental exposures, such as tobacco smoke or ultraviolet rays, or lifestyle behaviors, such as poor diet or lack of physical activity (Kavazis and Powers, 2013; National Cancer Institute, 2015). These genetic changes magnify the replication rate of cancerous cells compared to normal cells (Kavazis and Powers, 2013). During the tumor promotion stage, the initiated cells are quickly cloned leading to hyper proliferation, tissue remodeling, and inflammation, which can bring about additional alterations in gene expression and DNA damage in tumor cells (Kavazis and Powers, 2013; Rogers, Colbert, Greiner, Perkins, and Hursting, 2008). The last step in the process is tumor progression, which is characterized by enhanced clonal expansion and invasive or metastatic tumors (Pitot, 1989). Although this is deemed the terminal stage of carcinogenesis, the multi-step process of carcinogenesis may be disrupted at any point.

Before tumor initiation takes root, normal cells progress through a cyclical course of growth, division, and apoptosis, which is fueled by specific metabolic pathways imperative to the normal cell lifecycle. Normal cells rely on two metabolic pathways for energy production, oxidative phosphorylation and anaerobic glycolysis. Oxidative phosphorylation accounts for 70-88% of the energy needs and glycolysis accounts for the remaining energy needs (Seyfried and Shelton, 2010; Zheng, 2012). When oxygen is sufficient, the metabolic energy pathways are regulated using oxidative phosphorylation as the primary means for energy balance, and thereby inhibiting glycolysis. This reduction in glucose flux in the presence of oxygen is known as the "Pasteur Effect" (Gatenby & Gillies, 2004). Mitochondrial oxidative phosphorylation is highly

efficient, thereby generating more adenosine triphosphate (ATP) than glycolysis (38 ATP vs 2 ATP, respectively) (Gatenby & Gillies, 2004; Zheng, 2012). However, when oxygen levels are low, glycolysis takes over to compensate for the weakened function of oxidative phosphorylation in order to maintain sufficient cellular energy. Glycolysis requires the conversion of glucose to pyruvate and then to the waste product lactic acid. This metabolic versatility of normal cells is critical for maintaining energy production during changes in oxygen concentrations (Gatenby & Gillies, 2004). As genes mutate into cancerous cells, the fundamental metabolism of these normal cells pose specific challenges in order for the cancerous cell to resist apoptosis, a key biochemical aspect of the normal cell lifecycle.

Although this ebb and flow of metabolic changes is normal in healthy cells, carcinogenesis presents common phenotypic traits. That is, cellular metabolism and nutrient uptake in cancerous cells and tissues must be modified to support growth and proliferation, survive metabolic stress, and maintain viability as the cells accumulate (Jones and Thompson, 2009). One foundational phenotypic trait is that of altered glucose metabolism. The metabolic change from oxidative phosphorylation to aerobic glycolysis involves converting glucose to lactic acid in the presence of oxygen (Gatenby & Gillies, 2004, Seyfried & Shelton, 2010). Aerobic glycolysis as the primary means for cellular energy in cancerous cells was first proposed by Otto Warburg in the 1920's. Since then, research has revealed the "Warburg effect" (Warburg, 1956) to be a metabolic trademark of most cancerous cells, regardless of tissue or cellular origin. Therefore, the fundamental underlying problem in cancer cell physiology is primarily due to impaired or damaged respiration (Warburg, 1956). The continued production of lactic acid in the presence of oxygen presents an abnormal Pasteur Effect, which is the situation in most cancerous cells (Seyfried and Shelton, 2010). Therefore, Warburg's (1956) observations

suggest that cells with the ability to increase glycolysis during intermittent respiratory damage have the ability to form cancers. Such respiratory damage develops in the presence of hypoxic environments.

In addition to changes in metabolism, other biological changes occur in the presence of exogenous and/or endogenous carcinogens. Although the exact biological changes aren't fully understood, it is well understood that physiological mechanisms may become altered at any point. The three key physiological mechanisms associated with cancer initiation, promotion, and progression are oxidative stress, inflammation, and suppressed immune system (Ulrick, Steindorf, & Berger, 2013).

Oxidative stress is a condition that occurs when the balance between free radicals and their enrichment via the antioxidant defense system becomes disrupted (Halliwell and Cross, 1994). Many different free radicals exist; however, those derived from oxygen and/or nitrogen, known as reactive oxygen species (ROS) or reactive nitrogen species (RNS), appear to be the most important class of free radicals produced in living systems (Bogdan, Rollinghoff, & Diefenbach, 2000; Valko, Leibfritz, Moncol, Cronin, Mazur, & Telser, 2007). ROS and RNS are well recognized as having both harmful and beneficial effects on living systems (Fisher-Wellman and Bloomer, 2009; Valko, et al., 2007). Under normal physiological conditions, low-to-moderate concentrations of ROS and RNS play important roles in gene expression, regulation of cell-signaling pathways, and in defending against infections agents (Kavazis and Powers, 2013; Valko, et al., 2007). Harmful effects, known as oxidative stress or nitrosative stress, occur when there is an overproduction of ROS/RNS and insufficient production of enzymatic and non-enzymatic antioxidants (Valko, et al., 2007). Elevated levels of ROS and RNS can directly cause DNA base modifications and gene instability, thereby altering gene expression, a key aspect in

the development of cancer (Kavazis & Powers, 2013). Furthermore, high levels of ROS and RNS can act as signaling molecules in cell pathway systems, which can potentially cause metastasis of tumor cells (Kavazis & Powers, 2013). The precise balance between the beneficial and potential harmful effects of ROS and RNS is critical to living organisms, and imbalances may lead to a disruption of homeostatic functioning, which could increase the likelihood of the development and/or progression of cancerous cells (Kavazis & Powers, 2013; Valko, et al., 2007).

In addition to oxidative stress, inflammation appears to be a key contributing factor to the development of cancer. In fact, oxidative stress and inflammation share similar, corresponding signaling pathways (Sallam & Lahar, 2015). More specifically, key transcription factors are considered to be major regulators of gene expression and metabolism in response to cellular oxidative or inflammatory stress (Kim, et al., 2009). These transcription factors promote the expression of specific rate-limiting enzymes, which assist in mediating inflammatory processes (Kim, et al., 2009). For instance, inflammation is an important physiological response when tissues, such as the skin, are damaged or injured, and work to protect the host and engage the immune system as a means to promote repair and protect against invading pathogens (Rogers, et al., 2008). In contrast, chronic, low-grade, systemic inflammation has been associated with certain chronic diseases, such as obesity and cancer. Chronic, low-grade systemic inflammation, has been identified as a condition where there is a 2- to 3-fold increase in the circulating levels of key cytokines, without the presence of a foreign pathogen (Rogers, Colbert, Greiner, Perkins & Hursting, 2008). It is speculated that adipose tissue increases the expression of inflammatory-specific genes and inappropriate overexpression of such enzymes have been observed in numerous premalignant and malignant tissues (Coppack, 2001; Mohan & Epstein, 2003; Rogers, et al., 2008; Williams, Mann, & DuBois, 1999). Therefore, the type and amount of specific

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transcription factors and cytokines may have the ability to encode proteins involved in inflammation, immune responses, and cancer (Kim, et al., 2009).

A key relationship between inflammation and the development of cancer is activation of the immune system. The immune system is essential for protecting the human body from the invasion of foreign pathogens, resolving inflammation, and controlling and eliminating pathogens and tumor cells (Swann & Smyth, 2007). When normal tissues are disrupted by the presence of a pathogen or tumor cell, the immune system is put into action. Current research suggests that the control of cancer tumor growth is dependent on three phases of the immune system: tumor elimination, tumor immune cell equilibrium, and tumor escape (Meng & Rogers, 2013; Swann & Smyth, 2007). During tumor elimination, the immune system is able to recognize tumor antigens on cells and eliminate them either completely or partially (Swann & Smyth, 2007). Partial tumor elimination leads to a temporary state of equilibrium, which either inactivates the tumor cell or continues the evolutionary changes in gene expression initiated by the tumor cells (Swann & Smyth, 2007). Tumor cells that continue to evolve follow the process as indicated above, in which copies are made. The immune system works to eliminate as many clones of the tumor cells as it can in order to control tumor progression (Swann & Smyth, 2007). However, if the immune system fails to completely eliminate the tumor, the tumor cells are able to resist apoptosis, thereby leading to the escape phase (Swann & Smyth, 2007). During the escape phase, the immune system can no longer contain tumor growth, and tumor progression continues (Swann & Smyth, 2007). When the immune system is functioning optimally, it can provide significant protection to the human body in decreasing disease risk. However, a suppressed or unhealthy immune system, whether innate or acquired, may pose challenges when fighting, or trying to eliminate or prevent, pathogenic invasion or tumorigenesis.

Although the immune system serves a remarkable protective role in preventing and fighting tumor growth, a suppressed immune system, whether it be innate or adapted, may pose significant risks for the development of disease, such as cancer. When the immune system is functioning optimally and there's a greater number of prominent adaptive and innate immune cells, research has shown improved prognosis and better survival rates in patients with ovarian, colorectal, and gastric cancer (Ishigami, et al., 2000; Kondo, Shen, & Issa, 2003; Sato, et al, 2005). On the contrary, some studies have shown an increased risk for cancer formation in immunosuppressed patients, whether the immunosuppression was inherent or due to the use of immunosuppressive medications (Buell, Gross, & Woodle, 2005; Penn, 1988). In addition, a suppressed immune system resulting from other factors, such as advanced disease, obesity, or stress, may stimulate tumor progression by inducing tumor cell proliferation, angiogenesis, or altering the metastatic potential of tumor cells (Ostrand-Rosenberg, 2008). Furthermore, immunosuppression may alternatively activate specific immune cells, such as tumor-associated macrophages (TAMs), which appear to regulate the development of tumors (Meng and Rogers, 2013). For example, the presence of TAMs was associated with poor prognosis in numerous human malignancies, such as breast, prostate, cervical, lung, and bladder cancer (Lewis & Pollard, 2006). Largely, the immune system plays a critical role in the potential development and progression of cancer; however, chronic inflammation and unresolved immune responses may pose challenges to this generally protective system. Since the exact mechanisms relating immunosuppression to increased cancer risk isn't fully understood, more research is needed to better understand host immunity, better understand how to enhance the immune response to better control tumor development, and better understand what may be needed for effective cancer prevention and therapies.

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Physical Activity

Overview

Physical *fitness*, as opposed to physical *activity*, is a set of attributes related to the "ability to respond to routine physical demands, with enough reserve energy to cope with a sudden challenge" and encompasses the following five health-related components of fitness: body composition, cardiorespiratory endurance, muscle strength, muscle endurance and flexibility (Hales, 2015, p. 220). Although fitness is an important component of both health and athletic performance, one doesn't have to be athletic in order to have good physical fitness and overall health. One of the concerns in the literature is that these terms are often used interchangeably, despite their differences. Physical *activity*, then, "refers to any movement produced by the muscles that results in expenditure of energy" and includes any movements at home, work, school or performed in leisure-time physical activity (Hales, 2015, p. 223). The American College of Sports Medicine recommends 150 minutes per week of moderate physical activity or 75 minutes of vigorous physical activity for general health (Garber, et al., 2011). However, more than 60% of adults in the United States do not meet these recommendations and at least 25% don't engage in any leisure time physical activity (CDC, 2013).

Although many individuals may associate physical activity with exercising at a gym, exercise is considered a subset of physical activity, requiring "planned, structured and repetitive bodily movement with the intent of improving one or more components of physical fitness" (Hales, 2015, p. 223)**.** Current research suggests individuals can be physically active without engaging in routine exercise (Loprinzi & Cardinal, 2013). In a landmark study of more than 6,000 American adults (age 18-85), Loprinzi and Cardinal (2013) evaluated the accelerometry data from the NHANES 2003-2004 and 2005-2006 cycles and compare that data to the following

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biologically related variables: blood pressure, cholesterol, triglyceride levels, glucose levels, waist circumference, triceps skinfold, subscapularis skinfold, and body mass index (BMI). An unadjusted and multivariate regression analysis was used to examine the association between each physical activity intensity and each biologic health outcome for (model 1) <10 minute durations of PA (nonbout), (model 2) >10 minute durations of PA (bout), (model 3) PA in nonbouts while controlling for >10 minute bouts of PA (unadjusted results). The fourth model used an adjusted Wald test to investigate differences in each biologic variable for those who met the PA guidelines (as mentioned above) for both bout and nonbout PA. Results showed that less than 10% of the participants who reported longer structured exercise sessions (bout) met the ACSM guidelines for physical activity, compared to almost 43% of those who did short bouts of exercise (nonbout) (Loprinzi & Cardinal, 2013). In addition, after controlling for potential confounding variables, physical activity intensity for both bouts and nonbouts had similar strengths of association with all biologic variables, except BMI (R^2_{adj} = -.0007 to -.09; $p<.0001$). Furthermore, with respect to the adjusted coefficient, none of the biologic variables were statistically significant among those meeting the PA guidelines for both bout and nonbouts, except for BMI (bouts R^2 = .24 and $p <.0001$ vs. nonbouts R^2 = .18) (Loprinzi & Cardinal, 2013). Overall, short stretches of physical activity, such as taking the stairs or walking several blocks, during the day may be as beneficial as a trip to the gym. Therefore, an active lifestyle approach with more frequent stretches of physical activity may be as effective in providing overall health benefits.

Physiological impact of PA on cancer development

Numerous studies have shown that appropriate levels of physical activity are associated with a reduced risk of many cancers, such as breast and colon cancer, and improved health

benefits (Courneya, 2003; Courneya, Mackey, et al. 2003; Demarzo & Garcia, 2004; Rajotte, et

al., 2012). Overall, physical activity can have various effects on carcinogenesis based on energy

supply, intensity, and frequency of exercise. When evaluating responses to specific types of

exercise, exercise is classified as acute exercise when it lasts less than two hours on one day or

chronic exercise when it lasts longer than two hours and over many days or months (as indicated

in Shephard & Shek, 1999). Intensity is generally classified as moderate when it is between 50

and 65 percent of one's maximal oxygen uptake, and high intensity or vigorous when the

exercise is between 75 and 100 percent of one's maximal oxygen uptake or supramaximal

anaerobic exercise ranging from 30 seconds to 20 minutes (as indicated in Shephard & Shek,

1999). As previously discussed, it is well known that moderate intensity and rates of exercise

appear to have the greatest impact on reducing cancer risk and recurrence, and has been

associated with significant health benefits. However, single exhaustive exercise or unaccustomed

high intensity training actually may increase the risk of some carcinogenesis. Some studies

suggest exhaustive exercise actually increases free radical DNA oxidative damage and

suppresses immune function, both which have been related to an increase in cancer development

(Banerjee, Mandal, Chanda, & Chakraborti, 2003; Poulsen, Loft, & Vistisen, 1996). For

example, Demarzo and Garcia (2004) examined 16 male Wistar rats injected with the chemical

carcinogen 1,2-dimenthylhydrazine (DMH), a colorectal carcinogen often detected by the assay

of precursor legions known as abberant crypt foci. A group of eight rats were given one

exhaustive swimming endurance test, which consisted of each rat swimming to exhaustion with a

weight equivalent to 2% of body weight tied to the tail (Demarzo & Garcia, 2004). The control

group (the other eight rats) were contained in a small chamber with a small amount of water

(Demarzo & Garcia, 2004). Following the conclusion of the exhaustive swimming bout, each rat

was injected with DMH. The number of abberant crypt foci in the exercise group was statistically significantly higher (p<0.01) than the control group after 15 days post neoplasic induction (10.85 $\pm$ 3.20 vs. 3.72 $\pm$ 0.70, respectively). Another study found an increase in pancreatic carcinogenesis when high intensity treadmill exercise began at the 13th week of age in rats compared to high intensity treadmill exercise introduced at the 6th week of age (Roebuck, McCaffrey, & Baumgartner (1990). Therefore, the precise dose (frequency, intensity, and duration) and mode of exercise needed to elicit key changes to improve cancer survival isn't clear. Although the molecular mechanisms underlying these differences aren't fully understood, the degree of exercise-mediated oxidative stress, degree of inflammatory response, and degree of immunosuppression seem to be key contributing factors in phenotypic carcinogenesis (Kavazis & Powers, 2013; Na & Oliynyk, 2011).

One of the potential correlating factors between physical activity and level of carcinogenesis has to do with exercise-mediated oxidative stress. Although the body works hard to regulate this balance between ROS and RNS, certain elements, such as exercise, can disrupt this preferred redox homeostatic state (Vollaard, Shearman, & Cooper, 2005). Exercise, particularly whole-body exercise, is associated with an increase in oxygen uptake, which increases the production of ROS and RNS, thereby inducing oxidative and nitrosative stress (Kavazis & Powers, 2013; Na & Oliynyk, 2011). For the purpose of this paper, this will be collectively known as exercise-mediated oxidative stress (EMOS). In a study conducted by Goto, et al. (2007), the researchers evaluated oxidative stress in eight healthy, inactive men following 30 minutes of exercise at mild-intensity (25% VO_{2max}), moderate-intensity (50% VO_{2max}), and high-intensity exercise (75% VO_{2max}). Results indicated a significant increase in oxidative stress both during the 30 minutes of high-intensity exercise and following the 10-minute recovery

period, but not with either the mild-intensity or moderate intensity exercise and recovery period (p<0.05) (Goto, et al., 2007). These results are similar to other studies that found high intensity exercise related to an increase in oxygen consumption, and increase in nitric oxide production, and an overall increase in oxidative stress (Davies, Quintanilha, Brooks, & Packer, 1982; Lovlin, Cottle, Pyke, Kavanagh, & Belcastro, 1987; Matsumoto, Hirata, Momomura, Fujita, Yao, Sata, et al., 1994). This increase in formation of ROS and RNS has shown to cause lipid, DNA, and protein oxidation in the blood and other cells (Kavazis & Powers, 2013). Oxidation of these key biological molecules, as a result of increased production of ROS and RNS, "can severely compromise cell health and viability or induce a variety of cellular responses through generation of secondary reactive species" (Dalle-Donne, Rossi, Colombo, Giustarini, & Milzani, p. 601, 2006). Such oxidative damage may impair exercise performance, alter contractile function, accelerate muscle damage or fatigue, and may promote various human disease states, such as cancer (Dalle-Donne, et al., 2006; Reid, 2001; Watson, Callister, Taylor, Sibbritt, Macdonald-Wicks, & Garg, 2004).

Cellular damage and oxidative stress may have significant consequences on exercise performance and pathophysiological conditions, such as atherosclerosis and cancer, with some epidemiological studies suggesting an increased risk of disease in those who regularly engage in large volumes of exercise (Knez, Coombes, & Jenkins, 2006; Lee, Hsieh, & Paffenbarger, 1995; Quinn, Sprague, Van Huss, & Olson, 1990). For example, Quinn, et al., (1990) reported that the most active adults had the same risk for CVD as those that were the least active. This is similar to other studies that found that those who engaged in a cumulative energy expenditure greater than 14,700 kJ/week, particularly if the activity exceeded 12,600 kJ/week of vigorous-intensity activity, had higher rates of heart attacks and an increase in mortality (Lee, et al., 1995; Shaper,

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Wannamethee, & Weatherall, 1991). It is understood that higher levels of ROS and RNS can directly damage DNA, which can lead to carcinogenesis. In addition, exercise-induced increases in ROS and RNS production may contribute to the cell's mutation rate, thereby altering DNA base modifications by serving as a secondary messenger in intracellular signaling pathways (Kavazis & Powers, 2013; Valko, et al., 2006). Furthermore, high levels of ROS and RNS may not only contribute to tumor initiation, but they may also play a role in the metastasis of tumor cells. For example, as ROS increases in the mitochondria of the cells, the oxidation targets key molecules which can alter the major signaling pathways, thereby driving cancer cell invasion and metastasis (Kavazis & Powers, 2013; Li, Yan, Ming, & Liu, 2011). However, the exact production of ROS and RNS appears to be highly dependent on the mode (aerobic or anaerobic), intensity, and duration of exercise, all which vary in energy requirements, oxygen consumption, and mechanical stresses on the tissues (Jackson, 2000).

Excessive exercise not only causes free radical generation and oxidative stress, but exercise intensity that causes significant muscle damage also increases the inflammatory response, which may further the free radical production as well (Kavazis & Powers, 2013; Kim et al., 2009). Exercise-induced oxidative stress can stimulate several inflammation signal transduction pathways by activating redox-sensitive transcription factors (Kavazis & Powers, 2013). Activation of these key transcription factors serve as tumor promoters, which can increase the production of specific protein factors involved in such processes as inflammation and immune response, thereby triggering inflammation-associated carcinogenesis (Kavazis & Powers, 2013; Rogers, et al., 2008). It is suggested that a single bout of maximal exercise can accelerate activation of the redox-sensitive transcription factors, thereby, stimulating cancer development (Kavazis & Powers, 2013; Kim, et al., 2009; Na & Oliynyk, 2011). For example,

Kim, et al. (2009) found a dose-response relationship between single bouts of varying exercise intensity and expression and binding of key transcription factors related to a pro-inflammatory response in the human blood cells of 13 healthy male subjects. As exercise intensity increased, expression and DNA binding of specific transcription factors were significantly elevated in human peripheral blood cells ($p<0.05$ at 80% HRR and $p<0.01$ at 100% HRR) (Kim, et al., 2009). This activation suggests a pro-inflammatory response, which has been implicated in a number of inflammation-associated chronic disorders, such as cancer (Kim, et al., 2009; Mohan & Epstein, 2003).

Exercise not only increases inflammation within the body, but it has also been shown to suppress the immune system. As indicated above, immunosuppression may activate or enhance the risk of tumor growth and/or metastasis. Therefore, engaging in specific types of exercise, such as longer duration or higher intensity, may pose challenges to this normally protective system by negatively influencing immune cell functions. For example, acute fatiguing exercise in mice showed an increase in infection risk when exposed to a virus 20 minutes after completing the exercise (Kahut, Boehm, & Moynihan, 2001). In addition, various studies conducted by Nieman (1997) have shown increased illness, white blood cell counts, and suppression of both critical immune cells following high intensity, acute exercise. Lastly, Campbell, et al., (2008) found no statistically significant changes in any immune cell markers following a 12-month exercise program involving overweight and obese postmenopausal women. In conclusion, changes to the immune system either during or post exercise may induce alterations at any point of the carcinogenesis process.

Exercise appears to cause considerable damage to the molecular functioning of bodily cells; however, there exists unique defense mechanisms, which may offer significant advantages

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to the potential harmful results of physical activity. To prevent oxidative damage, a well-organized defense system of antioxidants work together to regulate ROS and RNS (Fisher-Wellman & Bloomer, 2009; Kavazis & Powers, 2013). Regular and consistent exercise has shown to be a significant factor in the upregulation of antioxidant enzymes, as well as non-enzymatic repair systems, which assist in the prevention and/or repairing of damage caused by ROS and RNS (Ji, 1999; McArdle & Jackson, 2000; Wittwer, et al., 2004). Numerous studies have shown increases in gene expression and/or protein levels of antioxidant enzymes in skeletal muscle (Ennezat, et al., 2001; Nakatani, et al., 2005). For example, following treatment of a renal carcinogen in rats, 10 weeks of swimming increased key antioxidant enzymes in both the diaphragm and kidney (Nakatani, et al., 2005). In addition to antioxidant enzymes, DNA repair enzymes are also upregulated (Wittwer, et al., 2004). As previously discussed, cancer is a genetic disease in that it results from damaged or mutated DNA; therefore, upregulation of such key enzymes as the result of regular physical activity may pose preventative factors in the initiation or recurrence of cancer, as well as disrupt the promotion and/or progression of tumor cells. Lastly, physical activity and exercise increases mitochondrial and oxidative capacity, which provides energy for synthesizing new proteins in the antioxidant defense system (Sallam & Lahar, 2016). In addition, low-to moderate intensity has shown to decrease tumor hypoxia by up to 50%, with long-term exercise displaying upwards of 90% reduction in tumor hypoxia in rats (McCullough, Stabley, Siemann, & Behnke, 2014). Overall, exercise activates enzymatic and non-enzymatic antioxidant and repair systems, which triggers the release of specific enzymes that work to combat harmful radicals.

Although some types of physical activity appear to increase tissue inflammation, previously established as a contributing factor to the development of cancer, the pro-

inflammatory response is acute. When evaluating the relationship between inflammation and carcinogenesis, research suggests a correlation between primarily chronic, low-grade, systemic inflammation and cancer (Erlinger, Platz, Rifai, & Helzlsouer, 2004; Lehrer, et al., 2005). Various epidemiological studies display an association between systemic inflammation and physical inactivity (Abramson & Vaccarino, 2002; Geffken, et al., 2001). However, different types of physical activity may have different effects on specific inflammatory markers (King, Carek, Mainous, & Pearson, 2003). For example, King, et al., (2003) assessed over 4000 individuals in the NHANES III study and found significantly lower levels of three inflammatory markers measured in participants who engaged in 12 or more times per month of either jogging ($p < 0.01$) or aerobic dance ($p < 0.01$) activities compared to other types of exercise, such as cycling and swimming. In another study, researchers evaluated key inflammatory biomarkers in 320 postmenopausal women (Friedenreich, et al., 2012). The women ($n = 154$) in the exercise group participated in a yearlong progressive exercise program at 70-80% heart rate reserve, with the remainder participants classified into the control group (Friedenreich, et al, 2012). Results indicated a significant difference in one inflammatory biomarker particularly, c-reactive protein (CRP), in the exercise intervention group compared to the control group (TER = 0.87; 95% CI = 0.79-0.96) (Friedenreich, et al., 2012). Further evaluation of CRP shows a statistically significant trend ($p = 0.021$) with increasing exercise adherence during the program, thereby, suggesting higher doses of exercise may contribute to greater reductions in this key inflammatory marker (Friedenreich, et al., 2012). Lastly, although vigorous intensity exercise may increase the inflammatory response, it is speculated that this is an acute pro-inflammatory response, and may have more beneficial effects long term (King, et al., 2003). Overall, the training effect associated

with regular participation in different types of physical activity may be the key factor in lowering inflammatory biomarkers, and, thereby, reducing overall cancer risk.

As indicated above, the immune system plays an important role in reducing inflammation and controlling carcinogenesis. Although longer duration or higher intensity individual bouts of exercise may have a negative impact on the immune system, other types of exercise, particularly moderate-intensity aerobic exercise, have shown the opposite. Sustained aerobic exercise at 50-65% maximum oxygen uptake have shown statistically significant increases in a number of immune cells, with cumulative repetitive moderate training posing even greater enhancements in these vital immune cells (Shephard & Shek, 1999). Circulating immune cells, such as the natural killer cells, appear to rise throughout a workout, and the magnitude of this increase is significantly correlated with the duration of moderate intensity exercise ($r^2 = 0.791$; $p < 0.0001$) (Shephard & Shek, 1999). Light intensity exercise below 50% maximal oxygen uptake showed increasing levels of immune cells, but at lower levels overall compared to moderate-intensity exercise (Shephard & Shek, 1999). Vigorous-intensity exercise displays a greater impact on the initial peak of immune cells at the beginning of a workout; however, the magnitude of this increase appears to be indirectly correlated with duration of higher intensity physical activity (Shephard & Shek, 1999). However, research shows that the immune cells return to baseline generally within 2-24 hours post-exercise (Shephard & Shek, 1999). Although there appears to be conflicting evidence regarding the impact of certain types of exercise and the potential disease risk, sedentary lifestyles have also been associated with a decrease in immune function (Shephard & Shek, 1999). However, the phenotypic cancers associated with an impaired immune system appear to be different from those associated with lack of physical activity (Pan & Morrison, 2011). Therefore, engaging in regular physical activity may have a greater impact on

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reducing a wide array of cancer risk and recurrence in both immunosuppressed and healthy individuals.

As stated earlier, intensity-specific exercise causes fluctuations in oxidative stress, inflammation, and immune response, which can affect the innate antioxidant defense system, thereby increasing potential disease risk in certain individuals. However, in order to surpass the present antioxidant defense system, the physiological stimulus, for example the amount of ROS and RNS produced to induce exercise-mediated oxidative stress, must reach a minimum threshold to effectively overload the system (Dalle-Donne, et al., 2006; Fisher-Wellman & Bloomer, 2009). This process is similar to other exercise science principles, suggesting that once this overload is achieved, the physiological capacity of the human body will be able to adapt, thereby leading to improved health and/or human performance (Fisher-Wellman & Bloomer, 2009). However, physical activity over and above this threshold may pose significant increased risk in disease and negatively influence performance. Therefore, although there is a vast amount of literature on the effects of exercise on the antioxidant system, no clear consensus has been established (Kavazis & Powers, 2013). This may be due to the ambiguity and variation in intensity and duration exercise protocols, particularly for cancer patients and survivors (Kavazis & Powers, 2013). Overall, further research is needed to determine exercise protocols necessary to optimize health benefits and reduce disease risk.

Sedentary behaviors and health risks

Physical activity, whether in one long bout or short frequent bouts, is arguably one of the most important components of overall health and quality of life. Health benefits associated with regular PA encompass improvement in multiple factors, including enhanced physical fitness, self-esteem, stress response, and social functioning; a decreased risk of heart disease and cancer;

and lower levels of psychological distress (Bellizzi, et al., 2005; Knobf, et al., 2007). Physical activity recommendations for special populations, such as those with cancer, for achieving such benefits are similar to the general health recommendations of 150 minutes of moderate physical activity or 75 minutes of vigorous physical activity per week (Garber, et al., 2011). However, significant declines in physical activity have been shown among cancer survivors both during and post-treatment. For example, the CDC (2012) evaluated more than 45,000 respondents in the 2009 Behavior Risk Factor Surveillance System (BRFSS) and found that during the past 30 days, almost 31.5% of cancer survivors had not participated in any leisure-time physical activity compared to 24.2% of the general population in this report (CDC, 2012). In another study, Kim, et al. (2013) evaluated 11,000 individuals who participated in the questionnaire-based interview related to PA and SED behavior from the 2007-2010 National Health and Nutrition Examination Survey (NHANES). Questions in the interview relating to physical activity assessed frequency and duration of PA in a typical week. Questions in the interview relating to SED behavior included average time per day, over the last 30 days, spent sitting or lying, aside from sleeping. Results indicated that cancer survivors are more likely to report engaging in regular PA compared to the non-cancer participants (multivariable adjusted OR = 1.17, 95% CI (0.94,1.46)) (Kim, et al., 2013). However, cancer survivors are also more likely to report spending more than eight hours per day engaged in SED behavior (OR = 1.42, 95% CI (0.98, 1.53)) (Kim, et al., 2013). Although these studies show conflicting results for physical activity between cancer survivors and the general population, both reports are based on self-report analysis. Furthermore, Kim et al. (2013) indicated that the cancer survivors are more likely to engage in more than eight hours of SED behavior, which could pose additional health concerns.

Sedentary behaviors are often identified in the contexts of TV viewing, computer or game-console use, sitting in automobiles, and workplace sitting (Owen, Healy, Matthews, & Dunstan, 2010). Owen, et al. (2010) proposed that too much sitting is distinct from too little exercise with observable physiological variances between these two measures. Healy, Dunstan, Salmon, Cerin, et al. (2008) examined the dose-response associations of television-viewing time with continuous metabolic risk variables among 4064 physically active Australian adults aged $\geq$ 25 years. Information was gathered from the national, cross-sectional Australian Diabetes, Obesity and Lifestyle study from 1999-2000. Results indicated that among those participants who met the recommended guidelines of 150 minutes of moderate-vigorous physical activity each week, increased television-viewing time was positively associated with waist circumference, systolic blood pressure and 2-h plasma glucose in men ($p < 0.001$; $p < 0.023$; $p < 0.001$, respectively) and women ($p < 0.001$; $p < 0.039$; $p < 0.001$, respectively) and for fasting plasma glucose ($p < 0.011$), triglycerides ($p < 0.001$) and HDL-cholesterol ($p < 0.001$) in women (Healy, Dunstan, Salmon, Cerin, et al., 2008). Therefore, large doses of sedentary behaviors may have significant impacts on various health factors.

Although the above-mentioned studies are based off self-report, objectively assessed studies on sedentary time have shown consistent results compared to the self-report studies. In a study of 178 adults, Healy, et al. (2007) tracked physical activity over the course of seven days using uniaxial Actigraph accelerometers. Results indicated that higher sedentary time is associated with significantly higher 2-h plasma glucose ($p = 0.042$) and both light intensity activity and moderate-to-vigorous intensity activity are associated with significantly lower 2-h plasma glucose ($p = 0.006$ and 0.005, respectively) (Healy, et al, 2007). In a continuation study, Healy, Dunstan, Salmon, Shaw, et al. (2008) further discovered that the total number of breaks in

sedentary time is associated with significantly lower waist circumference ($p = 0.027$), BMI ($p = 0.026$), triglycerides ($p = 0.029$), and 2-h plasma glucose ($p = 0.025$). Therefore, prolonged SED time may be the key factor to chronic disease risks, such as cancer.

The development of chronic diseases tends to coincide with declines in physical activity and/or increases in sedentary behaviors. When it comes to cancer, such declines may be associated with the considerable toll cancer has on an individual's body, whether it's due to the pathology of the disease, treatment regimens, or inactivity. Such physiological repercussions may include an increase in fatigue and pain, a decrease in physical functioning (i.e., strength, muscle stiffness, joint pain, etc.) and cardiovascular fitness, increased depression and anxiety, social implications, and lower quality of life (Tompkins-Stricker, Drake, Hoyer, & Mock, 2004; Courneya, 2003). On the contrary, various studies have shown physical exercise improves physical functioning, cardiovascular fitness, sleep, QOL, and a variety of other psychological and social factors in cancer patients (Courneya, 2003; Courneya, Mackey, et al., 2003, Forsythe, et al., 2013; Haas, 2011; Knobf, et al., 2014; Rajotte, et al., 2012). Therefore, as previously discussed, physical activity may be a valuable intervention tool for overcoming the many obstacles related to physical, psychological, and social functioning, as well as overall quality of life among cancer patients and survivors.

Physical activity associated with fatigue and pain

Fatigue is one of the most common and distressing symptoms associated with cancer treatments and interventions and occurs in almost all of persons with cancer (Curt, et al., 2000; Tompkins-Stricker, et al., 2004). Haas (2011) examined fatigue among 73 breast cancer patients using the 22-item Piper Fatigue Scale. Scores suggested that fatigue interferes with mood and concentration, as well as the cancer patients' ability to socialize, work, enjoy activities, and

engage in sexual activity. Furthermore, fatigue perceived as unpleasant, destructive, and negative enhances feelings of listlessness and weakness (Haas, 2011). However, there is strong evidence indicating exercise can have a positive impact, or even reverse, the feelings and experiences associated with fatigue. In a study of over 220 cancer survivors, Rajotte, et al. (2012) measured fatigue ratings using the 13-item Fatigue Symptom Inventory, which is a scale designed to assess the duration, intensity, and disruptiveness of fatigue on the cancer population. After completion of a 12-week program, consisting of 90 minute sessions two days/week, participants displayed a significant decrease in overall fatigue (Rajotte, et al., 2012). Furthermore, a systematic review of over 20 research studies indicated that fatigue significantly declined and energy improved following exercise treatments in at least 17 of those evaluated (Tompkins-Stricker, et al., 2004). The other three studies did show decreases in fatigue, but results were not significant (Tompkins-Stricker, et al., 2004). Although several forms of exercise were tested in the studies evaluated, the majority were considered aerobic and all activities were performed at effective intensities similar to other chronic disease populations. Overall, engaging in regular physical activity may help cancer patients and survivors to either stabilize or reduce fatigue levels during and post-treatment (Tompkins-Stricker, et al., 2004).

Although fatigue appears quite prevalent among cancer patients and survivors, pain is another common ailment often experienced during, immediately post-treatment and even many years post-treatment. The exact cause and course of pain associated with cancer survivors isn't fully understood, but prevalence estimates suggest 12-29% of cancer survivors more than five years post-treatment continue to report pain attributed to cancer (Deimling, Sterns, Bowman, & Kahana, 2005). Furthermore, pain associated with cancer is associated with various negative sequelae in cancer survivors, such as depression, changes in mood, poorer general health and

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physical and social functioning (Greene, Hart-Johnson, & Loeffler, 2011). In many cases, pain is a coinciding factor with cancer treatment and survivorship. However, there is limited research on the relationship between physical activity and its impact on chronic pain and pain management.

With the high prevalence of pain associated with cancer treatment and post-treatment, finding ways to manage or reduce pain becomes a key aspect associated with long-term survival. A handful of research studies have looked at the impact of physical activity and its relationship to pain management and have shown a significant improvement in body pain, as well as pain that interferes with mood, normal work situations, and relationships, following participation in physical activity (Durak, Harris, & Ceriale, 2001; Rajotte, et al., 2012). In a more specific study examining pain in long-term breast cancer survivors (10 years post-treatment), high television time was associated with more pain ($p < 0.05$) and survivors meeting the physical activity guidelines as indicated above were half as likely to report above-average pain as inactive survivors (p , 0.01) (Forsythe, et al., 2013). In addition, those survivors who decreased BMI were less likely than those who increased BMI to be in the pain worsened group ($p = 0.02$) (Forsythe, et al., 2013). Therefore, engaging in, or increasing, regular physical activity may be a beneficial addition to decreasing or minimizing pain often associated with cancer treatments and survivorship.

Physical activity and physical functioning

As a chronic disease, cancer patients and survivors often suffer from not only fatigue and pain, but overall physical functioning can be highly impacted. In fact, cancer survivors have a projected 2-fold increased risk for functional limitations compared to age-matched peers (Hewitt, Rowland, & Yancik, 2003). Physical functioning relates to cardiovascular and pulmonary issues, muscle aches and joint pain, and a decrease in strength and flexibility (Rajotte, et al., 2012).

However, exercise may serve as a protective factor against the loss of physical functions. For example, following a 12-week exercise intervention study with 221 cancer survivors from different cancer diagnoses, results displayed significant improvement in systolic ($p < 0.001$) and diastolic ($p = 0.035$) blood pressure, walking endurance as measured by the 6-min walk test ($p = 0.004$), upper and lower body strength as measured by one repetition maximums ($p < 0.001$), and flexibility ($p < 0.001$) (Rajotte, et al., 2012). Improvements in resting heart rate, weight, and waist circumference were also noted; however, these values were not significant (Rajotte, et al., 2012). Another study examining 26 breast cancer participants participating in a 4-6 month community-based exercise program showed improvements in musculoskeletal symptoms, such as aches, joint pain, and muscle stiffness; however, muscle stiffness was the only symptom to significantly decrease over time ($p = 0.04$) (Knobf, et al., 2014). These results are consistent with other exercise interventions that have shown additional physiologic improvements, including immune function, systolic and diastolic blood pressure, peak oxygen consumption, upper and lower body strength, walking endurance and flexibility (Courneya, 2003; Courneya, Mackey, et al. 2003; Rajotte, et al., 2012). Overall, physiological improvements appear substantial for cancer survivors engaged in routine physical activity.

As indicated above, regular physical activity has shown beneficial to various physiological facets. Not only can patients improve biologically in such areas, but outlook and perception of the engaged activity may also enhance these outcomes. Durak, et al. (2001) attempted to relate perception of physical functioning to endurance and strength outcomes in 50 cancer patients engaged in an exercise treatment program. Results displayed a significant improvement in overall perception of their individual endurance and strength (Durak, et al., 2001). Therefore, such physiologic improvements appear enhanced by the individual's

perception of the exercise intervention, which could play a role in other dynamics, such as quality of life.

Psychosocial responses to physical activity

Cancer treatments are often prolonged and rigorous, causing not only physical distress (as mentioned above), but also psychological distress. This psychological stress is often characterized by uncertainty, vulnerability, loss of control, and existential concerns, which may lead to some type of psychological disorder, whether it be depression, anxiety, or some other adjustment disorder (Knobf, et al., 2007; Trask, 2004). Largely, the two most common psychological responses to cancer are depression and anxiety. The prevalence of depression among cancer patients and survivors ranges dramatically, anywhere from 1.5-57% (Massie, 2004). In addition, Stark, et al. (2002) estimates the number of cancer patients and survivors experiencing anxiety to range from 20% to 50%. Nonetheless, such variations in the prevalence of any type of psychological disorder may relate to varying conceptualizations of the disorder, differing criteria for assessment, different populations studied, and type of cancer diagnosis (Massie, 2004).

Although these statistics appear rather high, there is growing evidence suggesting exercise interventions may decrease anxiety and lower levels of depressive symptoms and/or depression. In a study of 91 cancer patients engaged in a six-week, multidimensional exercise program, both anxiety (-1.14 ±2.91, P < 0.001) and depression (-0.44 ±2.77, P = 0.042) were significantly reduced (Midtgaard, et al., 2005). Similar findings were found in a study conducted by Badger, Segrin, Dorros, Meek and Lopez (2007) following a six-week self-managed exercise program. Moreover, research suggests exercise interventions may have a positive impact on the psychological distress many cancer patients often experience.

Cancer survivors are at a heightened health risk and studies show that cancer survivors engage in unhealthy behaviors on the same level as the general population (Bellizzi, et al, 2005). Therefore, a key psychosocial factor associated with making healthy behavior changes in both the general population and cancer survivors is social support (Park, Edmondson, Fenster, & Blank, 2008). In a study examining social support and its impact on exercise participation among women treated for early-stage breast cancer, Pinto, Trunzo, Reis, and Shiu (2002) evaluated changes in exercise participation over 12 months. Results indicated a non-significant increase in participation of vigorous (VIG) and moderate-vigorous PA (MVPA); however, greater confident social support ($z = 2.61$, $p < 0.01$, 95% CI = 0.03, 0.20) and living with a partner or spouse ($z = 2.5$, $P < 0.01$, 95% CI = 0.18, 1.40) were positively associated with vigorous intensity activity (Pinto, et al., 2002). In addition, affective social support positively predicted physical role functioning ($z = 2.56$, $p = 0.01$, 95% CI = 0.04, 0.29) (Pinto, et al., 2002). These results are similar to other studies, which demonstrated perceived social support and its association with healthy behaviors in cancer survivors (Park, et al., 2008).

As indicated above, several studies have examined the relationship between healthy behaviors, particularly exercise, and perceived social support, but little research has addressed the impact of social support on exercise intervention as a means for cancer treatment (Park, et al., 2008; Pinto, et al., 2002). However, social support may play a critical role in exercise adherence, feelings of confidence to participate in exercise, and general psychosocial well-being (Knobf, et al., 2007; Rajotte, et al., 2012). For example, a longitudinal cohort of 658 participants enrolled in a 12-week rehabilitation group program for cancer patients showed improved social functioning following the completion of the 30-item, EORTC QLQ-C30 self-report questionnaire for cancer patients (Korstjens, Mesters, van der Peet, Gijsen, & van den Borne, 2006). Furthermore, an

increase in social support predicted exercise participation in a 12-month prospective longitudinal study of 69 breast cancer survivors (Pinto, et al., 2002). Although research in this area appears limited, the majority of studies incorporated the social impact of exercise treatments on cancer patients by evaluating quality of life, which will be addressed later on.

Physical activity training modalities

Although PA participation may have benefits, cancer diagnosis is often followed by a decrease in physical activity. In a study conducted of 978 breast and prostate cancer survivors, only 58% admitted to engaging in regular PA; however, 80% indicated an interest in the need for health promotion programs during and post treatment (Demark-Wahnefried, Peterson, McBride, Lipkus, & Clipp, 2000). Research indicates that many of the exercise programs geared towards cancer patients vary in overall modalities. Training programs may be supervised or home-based, or may incorporate either aerobic exercise or resistance training, with only a few investigations involving cancer patients receiving both aerobic and resistance training (Pinto & Floyd, 2007). In addition, overall intensity has shown considerable variability across all aspects.

Little attention has been given to examining exercise interventions and long-term follow-ups, leaving little explanation regarding maintenance of exercise and its associated benefits (Pinto & Floyd, 2007). One study found benefits in physical training, physical strength and fighting spirit were maintained following a one-year follow-up after intervention (Berglund, Bolund, Gustafsson, & Sjoden, 1994). In contrast, Pinto, et al. (2002) conducted a longitudinal observation study examining the course of exercise participation in breast cancer survivors following therapy. Results indicated that 35% of the sample did not meet guidelines for PA over the 12-month study. Pinto, et al. (2002), determined predictors of exercise participation to be associated with age, level of social support, having a partner or not, and length of diagnosis.

Although many variables exist among treatment modalities and outcomes, current research demonstrates significant, post-treatment benefits of exercise indicating that physical activity may be a suitable intervention for cancer survivors. Various studies have shown physical exercise improves biopsychosocial factors, as well as overall QOL (Courneya, Mackey, et al., 2003; Durak, et al., 2001; Knobf, et al., 2007; Rajotte, et al., 2012). Therefore, future research is needed to examine the long-term effects of exercise participation, both during and following intervention.

Instrumentation for Measuring Physical Activity

Active lifestyles are a key component of both preventing and controlling chronic diseases, such as cancer. Therefore, finding valid methodologies for evaluating physical activity behaviors under daily life conditions is imperative. Currently, both subjective and objective approaches are used to estimate and/or measure daily physical activity, which may include self-report measures, such as questionnaires, activity logs or diaries and proxy reports, direct observation, indirect calorimetry techniques, heart rate monitors, and activity monitors, such as pedometers and accelerometers. Evaluating these measures is critical for determining the best approach for monitoring physical activity behaviors among cancer patients and cancer survivors.

Subjective measures

Subjectively evaluating physical activity among a variety of populations includes an assortment of self-report measures, such as self-administered or interviewer-administered recall questionaires, activity logs or diaries, and proxy reports (Sallis & Saelens, 2000). Fundamentally, subjective measures, whether qualitative or quantitative in nature, enhance the researchers' ability to collect data from a large number of people at relatively low costs. Such measures primarily focus on the intensity, duration, frequency, and total amount of PA performed, with

less attention given to the type of activity (aerobic or resistance) and environmental context (Shephard, 2003). However, the flexibility of subjective evaluation allows for the assessment over age ranges, for the adaptation to fit the needs of a particular population or research question, and for the inclusion of domain or activity-specific questions (Chastin, Culhane, & Dall, 2014; Sallis & Saelens, 2000). Overall, subjective evaluations provide large scale evaluation of PA for both epidemiological studies and general PA prescription.

Recall questionnaires. One of the most commonly used subjective means for evaluating PA behaviors are self-report recall questionnaires. Physical activity recall questionnaires, both self-administered and interviewer-administered, rely on subjective recall of physical activity over a period of days or months, and allow activities to be categorized into varied intensities, such as very active, active, or SED (Van Remoortel, et al., 2012). In addition, administration of such questionnaires can be done either quantitatively or qualitatively depending on the type of instrument used and the goals of the researchers. Of the many published questionnaires, the International Physical Activity Questionnaire (IPAQ) is one of the most widely used recall questionnaires in several populations and can be administered either by telephone interview or self-administered (Craig, et al., 2003). The IPAQ was developed by the World Health Organization in 1998 with the purpose of quantitatively estimating and comparing PA on large populations of individuals ages 15-69 (Craig, et al., 2003; Lee, et al., 2011; International Physical Activity Recall Questionnaire (IPAQ), 2015). There are two versions of the questionnaire, with the short version suitable for national and regional surveillance systems and the long version suitable for research or evaluation purposes (IPAQ, 2015). Questions in the IPAQ pertain to PA over the last seven days and include activities related to the following five domains: at work; during transportation; housework, house maintenance, and caring for family;

recreation, sport, and leisure-time; and time spent sitting. In addition, the activities listed further reference time (hours and/or minutes) spent engaged in each activity, as well as intensity. Therefore, the IPAQ provides broad capabilities for evaluating free-living, daily PA levels of large populations.

With physical inactivity becoming a growing health concern throughout the world, identifying reliable and valid means for assessing physical activity at population levels and across countries has become increasingly noteworthy. Since the IPAQ can be administered either in person or over the telephone, it has undergone extensive reliability and validity testing across many different domains. For example, Craig, et al. (2003) examined the reliability and validity porperties of both the short and long versions of the IPAQ in 14 centers in 12 different countries. Reliability measures were evaluated at one week intervals and validation measures were tested against objective data collected on the Computer Science and Application's Inc. (currently known as the ActiGraph) accelerometer. Results of the test-retest reliability data for the long version indicated a pooled repeatability coefficient of $p = 0.81$ (95% CI 0.79-0.82), and for the short version a pooled repeatability coefficient of $p = 0.76$ (95% CI 0.73-0.77) (Craig, et al., 2003). The criterion validity between the IPAQ and Computer Science and Application's Inc accelerometers showed fair to moderate agreement between the two measures for both the long version (pooled $p = 0.33$, 95% CI 0.26-0.39) and the short version (pooled $p = 0.30$, 95% CI 0.23-0.36) (Craig, et al., 2003). Overall, the IPAQ is a valuable means for evaluating activities, for guiding policy development to increase physical activity, and for providing comparable and valid measures of physical activity within and between countries (IPAQ, 2015).

Although the IPAQ appears to be a reliable tool for estimating physical activity levels of large populations to enhance epidemiological and public health research, there are limitations.

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For example, in a study of 69 adults, Chastin, et al. (2014) compared SED time between the self-reported measure of the IPAQ and the activPal. Results indicated a negative correlation of the IPAQ sitting items and the activPal, thereby underestimating sitting time in a range of 2.2 h*d^{-1} on the weekdays (r = -0.250, p = 0.002 Kendall Tau correlation) and 4.6 h*d^{-1} on the weekends (r = -0.156, p = 0.057 Kendall Tau correlation). Furthermore, the IPAQ has been shown to consistently overestimate walking frequency and duration (Lee, Macfarlane, Lam, & Stewart, 2011; Rzewnicki, Auweele, & De Bourdeaudhuij, 2003). Overall, therefore, when compared to objectively measured physical activity, self-report measures, such as the IPAQ, have been shown to have low correlations in the range of 0.14-0.53 (Sallis & Saelens, 2000).

Activity logs or diaries. Another popular tool for subjectively calculating daily PA behaviors are activity logs or diaries. Activity logs or diaries allow individual documentation of daily activities, which may include frequency, duration, and intensity. Diaries can be used to document hour-by-hour or activity-by-activity record of one's physical activity and sedentary behaviors (Strath, et al., 2013). Information recorded can vary, but generally includes start and stop time of activity, type of activity, and intensity of activity (Strath, et al., 2013). Diaries are primarily used to measure psychometric properties of PA questionnaires, as an adjunct to objective monitoring, or as part of an ecological momentary assessment to evaluate social and physical contextual information (Strath, et al., 2013). To document the activity, individuals may use a standard paper and pencil booklet method or a form of technology, such as a cell phone. A more standardized means for logging activity would be the Bouchard Physical Activity Record or the log developed by Ainsworth and colleagues. Such logs assist the individual in identifying specific activity movements or behaviors and categorizes them into ratings based on intensity

(low, moderate, vigorous) (Strath, et al., 2013). Regardless of the method used to document the activity, it is imperative the researchers remain consistent in the evaluation between participants.

Although diaries are an effective means for documenting activities as they are occurring or immediately after, these means pose a fairly high burden on the subjects. In addition, they have been criticized for self-report bias and missing activities, especially for short and/or incidental activities (Stopher & Greaves, 2007; Tudor-Locke, Bittman, Merom, & Bauman, 2006). In a study developing and testing an automated algorithm to determine walking and nonwalking activities from accelerometer data, 750 participants were instructed to wear a hip-mounted accelerometer, carry a GPS unit, and record their activity in a diary for seven days (Kang, Moudon, Hurvitz, Reichley, & Saelens, 2013). Results indicated that 43% of 40 walking bouts documented by the GPS were not reported in the travel diary. In addition, travel frequency was 0.5 less walking bouts and 3.8 fewer total minutes of walking time compared to the GPS data, thereby, suggesting that travel diaries underestimated walking behavior (Kang, et al., 2013). Therefore, although travel diaries allow for hour-by-hour subjective documentation of various activities and can be beneficial in supplementing additional qualitative and quantitative means for evaluating physical activity, caution should be used when using travel diaries as the sole research protocol.

Proxy reports. Epidemiological studies often rely on subjective reporting of PA because information can be obtained from a large number of individuals in a rather short amount of time and inexpensively. However, the accuracy of self-reported PA in cognitively impaired individuals, very young children (<10 years), ill-striken individuals, or individuals who are too fatigued to complete such reports is unpredictable (Middleton, Kirkland, Mitnitski, &

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Rockwood, 2010; Sallis, 1991; Varni, Limbers, & Burwinkle, 2007). Therefore, an alternative to the self-report measures, as mentioned above, are proxy reports.

Proxy reports rely on proxy-respondents to classify and categorize PA for individuals who are unable to self-report their own PA. The proxy-responder is generally a person who is close to the individual of study, such as a parent, spouse, or other close family member. Even when children or individuals are able to self-report, proxy-responders may be considered as a secondary outcome measure depending on the proxy's role in clinical decision-making and/or home treatment regimens (Varni, et al., 2007). Depending on the research protocol, proxy responders may complete either daily diaries or recall questionnaires for the subjects at large. Therefore, using valid and reliable proxy-respondent instruments are critical to the primary outcome measures of PA for the specific individuals under study. In a secondary analysis of the Canadian Study of Health and Aging, a prospective cohort study of dimentia in people aged 65 or older, Middleton, et al. (2010) evaluated two questions on a risk-factor questionnaire addressing frequency and intensity of exercise. The risk-factor questionnaire was completed by both cognitively impaired and non-cognitively impaired individuals aged 65 and older. The same questionnaire was also administered to a proxy-responder for both groups, thereby, comparing both self- and proxy-reports using an intraclass correlation coefficient. Results indicated a moderate reliability between self- and proxy-reports for frequency (ICC = 0.49; 95% CI: 0.38-0.58, $p < 0.001$) and intensity (ICC = 0.48; 95% CI: 0.37-0.57, p , 0.001) of PA. Similar results were also noted when comparing proxy-reports against accelerometers in children. Tulve, et al. (2007) found a moderate association ($r = 0.42$) and low to moderate concordance (57-78%) when comparing proxy-report PA diaries against accelerometers in nine children aged 4-17 months over the course of 4 days. In addition, Burdetter, Whitaker, and Daniels (2004) found similar

moderate association (r = 0.33) for total activity when comparing a proxy-reported recall questionnaire against both a three day activity checklist and three days of accelerometer monitoring. Such positive, moderate relationships between proxy-reports and PA measures indicate proxy reports may provide a useful tool for evaluating PA levels in special populations.

Proxy reports are a cost-effective, time-efficient, and valid means to measure PA and establish epidemiological relationships among special populations (as mentioned above) (Middleton, et al., 2010). However, there are limitations. First of all, proxy reports are only recommended for specific populations, which may limit their usability on a grander scale. Secondly, results rely on the proxy's subjective responses to questionnaires and/or interpretation of PA, which increases the risk for bias. Thirdly, proxy reports, as indicated above, provide only a moderate association at best between the subjective responses and PA levels; therefore, using alternative objective measures, in addition to proxy reports, may provide stronger correlations and enhance the statistical significance of PA measures in said populations.

Overall, subjective measures are valid, reliable, easy to administer, and frequently cited in literature; however, they do present limitations. For example, self-reported descriptions of physical activity often fail to classify the possible differences in patterns of accrued physical activity and may lack the precision to detect changes on a regular, day-to-day basis (Metzger, et al., 2007; Van Remoortel, et al., 2012). Furthermore, self-report of physical activity often suffers from significant reporting bias, potentially due to challenges associated with estimating frequency, intensity, and duration (Metzger, et al., 2007; Sallis & Saelens, 2000). Lastly, subjective measures vary greatly in their detail, the period surveyed, the extent of supervision of respondents, time to complete, and assistance needed to complete the forms and/or requirements.

Therefore, consideration must be taken when interpreting ordinal scales, because intercategory increments of energy expenditure or total activity may not be uniform (Shephard, 2003).

Objective measures

In contrast to subjective measures, objective methods eliminate subjective reporting bias by empirically measuring PA and other daily activities through discrete units of measurement. As mentioned previously, the PA guidelines for Americans include the following recommendations: avoid inactivity; accumulate a minimum of 150 minutes of moderate-intensity or 75 minutes of vigorous intensity physical activity each week in at least 10 minute bouts; for additional health benefits, upwards of 300 minutes of moderate intensity or 150 minutes of vigorous physical activity per week or an equivalent combination of both; and include muscle-strengthening activities at least two days per week (Garber, et al., 2011; Strath, et al., 2013). Accurately measuring frequency, duration, intensity, and mode, or type, of activity becomes critical in identifying if, how, and when, individuals are meeting these recommended guidelines. Assessing such components of PA, therefore, can be quantified by determining energy expenditure, using metabolic equivalents (METs) of the activity, computing how much time is spent in different physical activity intensity categories on a given day or over a given week, or a combination of these (Strath, et al., 2013). Objective methodologies typically include methods that directly measure one or more biosignals, such as acceleration, heart rate, energy expenditure, or some other indicator of physical activity, as they occur (Strath, et al., 2013). Common objective methods for assessing PA include direct observation, doubly labeled water, indirect calorimetry, heart rate monitoring, and activity monitors.

Direct observation. Observational studies involve trained observers watching or a video recording an individual who is partaking in PA by monitoring and recording movement intensity,

activity type or domain, duration, and location in which the activity ocurred (Strath, et al., 2013). The purpose of this particular assessment is to generate key contextual information, as well as objectively measure the mode/type of PA, along with the when, where, and with whom it occurs (Strath, et al., 2013). Data is collected using a momentary time sampling observation technique in which the various aspects of individuals' physical activity (as indicated above) are monitored, documented, and coded every five to upwards of 60 seconds, depending on the instrument in use (Brown, et al., 2006). In addition, direct observation tools tend to be inexpensive and can be used in a wide range of settings and age groups.

Although direct observation can be used for any age group, it is primarily used to assess PA among children either at school, home and/or neighborhoods/communities, or during sporting events. In fact, direct observation is often considered the gold standard means for assessing PA and sedentary behaviors in children (Loprinzi & Cardinal, 2011; Oliver, Schofield, & Kolt, 2007). A widely used observational tool is the System for Observing Fitness Instruction Time (SOFIT), which was designed to assess PA levels during physical education classes (Honas, Washburn, Smith, Greene, Cook-Weins, & Connelly, 2008). The SOFIT has been validated using heart rate monitors and accelerometers and has been used in a variety of studies, including the Sports, Play, and Active Recreation for Kids (McKenzie, Sallis, & Armstrong, 1994; Row, Schuldheisz, & VanDer Mars, 1997; Sallis, et al., 1997). Therefore, direct observation provides an inexpensive, reliable, and valid means for assessing physical activity in a variety of settings.

Observational studies have many positive uses; however, there are limitations to such instruments. For example, there is considerable education and training of potential researchers on proper recording and coding of physical activity domains dependent on the specific instrument

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used. In addition, observations generally need to be conducted at specific locations, which makes documenting PA over different days, different locations, or during free-living conditions difficult (Loprinzi & Cardinal, 2011). Finally, although these types of studies are inexpensive, they can be highly time consuming, particularly of the coding process, which poses additional limitations (Oliver, et al., 2007).

Indirect calorimetry. One objective method for measuring PA is with indirect calorimetry, which quantitatively measures total energy production by the body. Total energy production is composed of three main factors: basal, or resting, energy expenditure, thermic effect of food or diet induced thermogenesis, and physical activity (Volp, deOliveira, Alves, Esteves, & Bressan, 2011). Indirect calorimetry measures carbon dioxide production and oxygen degradation to estimate the total amount of energy expenditure of the body, and is considered the reference, or criterion, under controlled conditions (eg., laboratory) (Ainslie, Reilly, & Westerterp, 2003; Strath, et al., 2013; Volp, et al., 2011). Two methods of indirect calorimetry are doubly labelled water (DLW) and open-circuit methods, such as computerized metabolic cart systems, which are used to express PA as a measure of total energy expenditure (Ainslie, et al., 2003; Van Remoortel, et al., 2012).

Doubly labelled water. The doubly labelled water method assesses total energy expenditure of free-living humans for a period of 4-20 days. The individual consumes an "oral dose of water containing a known amount of stable (nonradioactive) isotopes of both hydrogen and oxygen" (Ainslie, et al., 2003, p. 684). These two isotopes mix with the normal levels of hydrogen and oxygen in the body within a few hours. As energy is expended, carbon dioxide and water are produced. Carbon dioxide is breathed out, while the water is lost in breath, urine, sweat, and other evaporations (Ainslie, et al., 2003). Since oxygen is found in both water and

carbon dioxide, it is lost more readily than hydrogen, which is only found in water. The difference between the rate of loss of oxygen and hydrogen reflects the rate at which carbon dioxide is produced, which, in turn, can be used to estimate energy expenditure (Ainslie, et al., 2003).

The isotopes used in DLW were first discovered in the late 1920's and 1930's, and by 1949, several studies had been conducted on the energy expenditure in mice (Speakman, 1998). This method was first used to measure energy expenditure on small animals, and it wasn't until 1980 when it was used to evaluate the energy expenditure of a human. The DLW method's initial validation study on humans was published in 1982 (Schoeller & van Santen, 1982) and by the mid-1990's, about 70-90 studies were published each year including the following research topics: clinical conditions; routine activities of a range of human subjects of varying body masses, age, and activities; extreme activities, such as mountain climbing and competitive bicycle racing; and free-living conditions (Speakman, 1998). Doubly Labelled Water is now considered a gold standard for measuring total energy expenditure (TEE) under free-living conditions, with a 97-99% accuracy rate, and is the only method available to accurately measure TEE during daily life (Plasqui & Westerterp, 2007).

The purpose of this method is to determine the average daily metabolic rate, and, combined with an estimate of resting metabolic rate, provides reliable means for measuring energy expenditure associated with physical activity over the course of 1-3 weeks and can be used for a wide range of age groups (Bouten, Verboeket-Van De Venne, Westerterp, Verduin, & Janssen, 1996; Plasqui & Westerterp, 2007). However, there are limitations to using DLW. For example, although this technique provides accurate depictions of TEE and average level of daily physical activity, it provides no information on PA patterns in terms of frequency, duration, or

intensity (Plasqui, et al., 2007). In addition, administering the technique is expensive, thereby restricting its use to small study populations (Johannsen, et al., 2010; Plasqui, et al., 2007). Therefore, the DLW technique is generally used as a criterion measure for validating other instruments.

Computerized metabolic cart systems. Computerized metabolic cart systems are ventilated open-circuit indirect calorimetry techniques in which a person breathes either room air or a mixture of gases of known concentration, thereby, analyzing the expired amounts of oxygen and carbon dioxide (Strath, et al., 2013). Indirect calorimetry is a noninvasive, highly reproducible and accurate method, has an error lower than 1%, and is considered a gold standard method (Volp, et al., 2011). The ventilated open-circuit technique requires the participant to breath through either a mouthpiece or a facemask, which is connected to a metabolic cart. The metabolic cart contains a unidirectional valve, which collects and mixes expired air, measures flow rate, analyzes gas concentrations, and pumps air through the system (Haugen, Chan, & Li, 2007; Levine, 2005; Volp, et al., 2011). This method of indirect calorimetry, therefore, assesses the amount of heat generated indirectly according to the amount and pattern of oxygen used and carbon dioxide produced (Haugen, et al., 2007). Energy expenditure is then calculated by measuring the amount of oxygen used (oxygen consumption or VO_2) and amount of carbon dioxide gas produced by the cells (carbon dioxide production or VCO_2) (Haugen, et al., 2007).

Although indirect calorimetry via metabolic carts are extremely reliable and accurate, and are considered a gold standard, they do pose limitations. First of all, machines used to measure indirect calorimetry are fairly expensive and relatively complex, thereby, requiring trained personnel to correctly use the machines and analyze the data (Haugen, et al., 2007; Volp, et al., 2011). Additional technical considerations that may pose limitations include lack of appropriate

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calibration and validation of the machine or potential system leaks (either with the mouthpiece, facemask, or system itself), which may prevent the correct measurement of amount of gases (Haugen, et al., 2007). Lastly, the metabolic cart method is generally a one-time test and isn't used over extended periods of time to evaluate mode, intensity, duration, or frequency of physical activity, whether it be minute-by-minute or over days or weeks (Van Remoortel, et al., 2012). Therefore, although metabolic cart systems are great at evaluating energy expenditure, they aren't effective at evaluating PA levels during free-living conditions.

Heart rate monitors. Another objective means for measuring PA and energy expenditure is through the use of heart rate monitors. Heart rate monitoring has become a practical and feasible means for objectively assessing daily physical activity, as it has shown a strong positive association with energy expenditure during large muscle, dynamic movments (Strath, et al., 2000). The basic physiological principle behind heart rate monitor assessment of physical activity lies with the understanding that changes in heart rate are indicative of cardiorespiratory stress during any and all movement, including physical activity and exercise (Strath, et al., 2013). Heart rate monitors are portable, non-restraining, unobtrusive, and relatively inexpensive devices allowing measurement of physical activity to be carried out and stored at high resolution over several days (Strath, et al., 2013; Volp, et al., 2011). In addition, heart rate monitors are able to provide quantitative data on frequency, intensity, and duration of PA with high reproducibility rates (Strath, et al., 2000). According to Volp, et al., (2011), the mean error for estimating energy expenditure using heart rate monitors is $3\pm20\%$ during light activity. In addition, heart rate monitoring has been validated against indirect calorimetry, doubly labelled water, and whole-room respirometry with reported measures differing from -20% to +25% (Luke, Maki, Barkey, Cooper, & McGee, 1997).

However, heart rate and energy expenditure are not always linearly related, in that heart rate changes with many variables, including caffeine consumption, hydration status, intensity of physical activity, emotional state, ambient temperature, type of contraction, and even posture (Strath, Kaminsky, et al., 2013; Strath, et al., 2000; Volp, et al., 2011). Heart rate appears to increase linearly and proportionately during moderate to vigorous PA, which relates to an approximate heart rate range of 90-150 beats per minutes (Ceesay, et al., 1989; Keytel, et al., 2005; Rennie, Hennings, Mitchell, & Wareham, 2001). However, this linear relationship is disrupted with activities involving strictly upper-body movement resulting in a higher heart response per given rate of total energy expenditure as compared to activities involving primarily lower body movements, or using just the legs (Strath, et al., 2013). In addition, a non-linear and discontinuous relationship appears evident during inactivity and light activity (Rennie, et al., 2001; Strath, et al., 2013). Since cancer patients and survivors may be limited in the intensity and duration of PA engagement, heart rate monitors may not be suitable for such populations. Furthermore, heart rate monitors may not be effective in evaluating sedentary lifestyles, which has previously been established as a key contributor to the development of many chronic diseases.

Activity monitors. Significant advances have been made in the assessment of physical activity patterns in free-living conditions. Physical activity monitoring devices, such as pedometers and accelerometers, can monitor multiple days with relatively low subject burden, have the ability to capture "real time" intensity, duration, and frequency of activity, and provide discrete units for objective data collection (Chen & Bassett, 2005; Westerterp, 2009). Furthermore, these devices are increasingly affordable and reliable (Strath, et al., 2013; Troiano, et al., 2007). Therefore, pedometers and accelerometers may provide potential solutions to the

problems associated with various subjective data, as well as the high cost and burden of other objective measures as previously indicated.

Pedometers. Pedometers are simple body-worn sensors used primarily to estimate step counts through mechanical or digital measurements in the vertical plane (Van Remoortel, et al., 2012). In addition to monitoring step accumulation, pedometers may also be able to determine walking distance and total walking or running activity when stride length is known, and, if body weight is provided, possibly the total number of calories expended (Freedson & Miller, 2000; Plasqui & Westerterp, 2013). Pedometers are often used in research as a means to track overall steps over days or weeks, are fairly inexpensive, and allow insights into general physical activity among large samples. Furthermore, pedometers are commonly used as motivational tools to increase daily levels of ambulatory physical activity.

Although pedometers offer some insight into one's PA and are widely available, they have limited capabilities for measuring habitual activity. For example, pedometers only calculate step counts over the course of the day and are unable to provide any temporal information regarding PA. In addition, pedometers are limited in their capabilities to determine frequency, duration, or intenstiy of PA, nor are they able to differentiate between walking, running, upper body activities, or isometric exercises (Bassett, 2000; Freedson & Miller, 2000; Plasqui & Westerterp, 2013). Therefore, pedometers tend to assume a person expends a constant amount of energy per step, despite many of these factors (Bassett, 2000). Lastly, step counts may be misrepresented when an individual's gait is unstable or slower than average, such as within chronic disease or special populations (Van Remoortel, et al. 2012). A study examining slow, normal, and fast self-paced walking speeds and gait using the Performance-Oriented Mobility Assessment of 26 nursing home residents and 28 community-dwelling older adults found that

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slower walking speeds and unstable gait impacted step counts when using the Yamax Digiwalker pedometer. At normal pace, gait scores were significantly correlated with pedometer error (r_s =0.46, p<0.0001) for both nursing home residents and community-dwelling older adults. In addition, pedometer accuracy improved as walking speed increased ($F(1,84) = 34.9$, p<0.0001) (Cyarto, Myers, & Tudor-Locke, 2004). These results are similar to Bassett, et al. (1996), whom indicated a 25% reduction in pedometer accuracy when walking speeds are less than 54 m*min^{-1} (equivalent to 2.0 mph). Overall, the applicability of pedometers to accurately assess PA measures among free-living conditions is limited, particularly among special populations.

    Accelerometers. Although pedometers are a useful tool for measuring PA, accelerometers offer significantly more insight into overall PA. Accelerometers measure PA in one, two, or three directions (uni-, bi-, or tri-axial accelerometers), determine quantity, frequency and intensity of movements, and store minute-by-minute data over days or weeks (Plasqui & Westerterp, 2007; Van Remoortel, et al, 2012). In addition, accelerometers can identify accelerations during SED or low-intensity activities, such as sitting or walking, as well as high-intensities activities, such as running or jumping. Furthermore, accelerometers are relatively inexpensive and well tolerated by participants. Because of these many factors, accelerometers have been the primary means for evaluating physical activity in a variety of research studies, such as the NHANES (Troiano, et al., 2007). Overall, being able to distinguish between type, frequency, duration, and intensity of PA is imperative for evaluating changes in physical activity, particularly in chronic disease populations, in order to establish reliable and effective interventions.

    ActivPal. Increased use of objective monitoring, particularly with accelerometers, has significantly advanced the understanding of PA and SED behaviors of both healthy and disease

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populations within the literature. The ActivPal accelerometer is a commonly used device for measuring PA levels primarily in cross-sectional and intervention research studies (Stanton, Guertler, Duncan, & Vandelanotte, 2014). The device is a lightweight, uniaxial accelerometer that analyzes time spent in different postures, postural transitions, step count and cadence, and energy expenditure (PALtechnologies Limited, 2010; Stanton, et al., 2014). The ActivPal attaches to the upper thigh using a dual layer hydrogel and can be waterproofed by wrapping a medical grade adhesive covering along with another sheet of dressing, which can provide 3-7 days of continual wear (PALtechnologies Limited, 2010). Overall, the ActivPal may be an effective means for evaluating PA and SED behaviors in both laboratory and free-living conditions, as well as a wide range of ages.

While there are a number of devices available for assessing PA and SED behaviors, the ActivPal is a significant contender with its ability to measure step counts, differentiate between postural transitions, and assess sedentary behavior. In a study to examine the validity and reliability of the ActivPal in measuring step number and cadence, inter device reliability was excellent for both step number and cadence (ICC(2,1)$\geq$ 0.99) at five different speeds, 0.90, 1.12, 1.33, 1.56, and 1.78 m/s (Ryan, Grant, Tigbe, & Granat, 2006). Assessing postural transitions has also been validated with the ActivPal. For example, Grant, Ryan, Tigbe, and Granat (2006) assessed the accuracy of the ActivPal to differentiate between sitting, standing, and walking postures while comparing against direct observation. Results indicated intraclass correlation coefficients for interdevice reliability ranging from 0.79 to 0.99 (Grant, et al., 2006). Overall agreement between the ActivPal and observer was 95.9%, with the following mean percentage differences for specific postures: total time spent sitting, 0.19%; total time spent upright, -0.27%, total time spent standing, 1.4%; and total time spent walking, -2.0% (Ryan, et al., 2006). Further

evaluation of SED behaviors with the ActivPal compared to direct observation showed an underestimation of SED behaviors by 7.7 minutes, with a standard error of 2.5 min (95% CI = -12.5, -2.9 min) (Kozey-Keadle, Libertine, Lyden, Staudenmayer, & Freedson, 2010). Overall underestimated percent bias was 2.8% (SE = 1.0%; 95% CI = -4.7% to 0.9%), which was not statistically different (Kozey-Keadle, et al., 2010). Lastly, the ActivPal was able to detect changes between SED and active conditions (p < 0.05) (Kozey-Keadle, et al., 2010). In general, the ActivPal appears to be a valuable tool for assessing key aspects of PA behaviors, particularly for SED and light activities.

Although the ActivPal has been widely used in the literature, it may not be suitable for evaluating a range of activities and intensities. For example, during nonsedentary time, the ActivPal "only provides an ouput of stepping time and cadence of the steps," which limits the ability to estimate activity intensity and/or the type of activity being performed (Kozey-Keadle, et al., 2010, p. 1566). Moreover, the device is only capable of measuring sitting, lying, walking, and standing postures, thereby, the device is unable to detect movements of the upper body, which can and do attribute to estimated total energy expenditure (Kozey-Keadle, et al., 2010). Lastly, from a design perspective, the device is attached by adhesive tape directly to the skin, and several studies have indicated skin irritations, with some studies resulting in participant withdrawal (Clark, et al., 2013; De Decker, et al., 2013). In the end, the ActivPal may be beneficial in assessing SED behaviors, but is limited in measuring other key aspects of PA, such as total energy expenditure, intensity, and type.

Actigraph. Considering the purpose of the study and type of activity being investigated is critical when selecting a monitor for objective assessment of PA behaviors. The ActiGraph monitor is one of the most widely used and accepted accelerometers for measuring PA and SED

behaviors among all ages (Trost, Loprinzi, Moore, & Pfeiffer, 2011; Welk, McClain, Eisenmann, & Wickel, 2007). ActiGraph accelerometers are available as uni-, bi- or tri-axial models, are worn at the hip, waist, or ankle, and measure energy expenditure, step counts, PA intensity, and body position (ActiGraph, 2015; Strath, et al., 2013). Overall, the versatility of these monitors allow for investigations of PA in both laboratory and field-based studies, assessment of free-living PA in larger populations, and usability in a variety of age groups (Herman-Hanson, et al., 2014).

The flexibility of the ActiGraph makes it a highly used device in the literature, including numerous validation studies. For example, in a study examining the convergent and concurrent validity of the ActiGraph (formerly known as the Computer Science and Application activity monitor) during a bout of rehabilitative exercises among older adults with chronic disease, results were two-fold (Focht, et al, 2003). First, the study evaluating convergent validity resulted in significant ($p < 0.01$) positive, moderate relationships between average activity counts and estimated METs ($r = 0.60$), pedometer readings ($r = .47$), and a six minute walk test ($r = 0.62$) (Focht, et al., 2003). The second study evaluating concurrent validity revealed a significant ($p < 0.01$) positive correlation between activity counts and oxygen uptake ($r = 0.72$) (Focht, et al., 2003). These results are comparable to other studies, which found the ActiGraph to be fairly accurate when estimating energy expenditure and PA duration under free-living conditions as compared to the Intelligent Device for Energy Expenditure and Physical Activity (IDEEA) (Welk, et al., 2006). The IDEEA is a portable system that uses a series of electrodes and a complex neural network to detect type, onset, duration, and intensity of PA with 98% accuracy (Zhang, Werner, Sun, Pi-Sunyer, & Boozer, 2003). Mean correlations between the ActiGraph and IDEEA were consistently high ($r = 0.62-0.88$) for type of PA behavior, with multiple

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variations between lying and walking (Welk, et al., 2006). Differences in energy expenditure ranged from -1.10 METs to 0.46 METs with the wide range resulting from the use of different algorithms (Welk, et al., 2006). Therefore, although the ActiGraph appears to be a valid and reliable tool for PA assessment in a variety of populations, cut-off points and calibration equations may provide challenges.

Another crucial limitation of the ActiGraph is its ability to accurately measure SED behaviors. For example, in a study examining the ability of the ActiGraph to assess SED behaviors when compared to direct observation, results indicated the ActiGraph underestimated SED behaviors by 16.9 min (SE = 8.5 min; 95% CI = -33.6 to -0.3 min) (Kozey-Keadle, et al., 2011). In addition, Bland-Altman plots indicated a poor to moderate relationship between direct observation and the ActiGraph ($R^2 = 0.39$) with regards to percent SED time (Kozey-Keadle, et al., 2011). Lastly, the ActiGraph monitor was not sensitive to reductions in sitting time between SED and active conditions (p = 0.3) (Kozey-Keadle, et al., 2011). Since increased SED behaviors have been shown to be associated with increased health risks, the ActiGraph may not be a suitable device for measuring all aspects of activity behaviors.

SenseWear. Although the traditional accelerometers offer technical and practical implications for objectively measuring PA, two key limitations are suggested: (a) they selectively record movement based on the location of the devices attachment on the body, making certain types of PA indistinguishable or unmeasurable; and (b) PA is established over a predetermined time epoch, which may limit the predictability of energy expenditure over a wide range of types and intensities (Chen & Bassett, 2005). Strategies for overcoming such limitations include the use of a multi-sensor device, which combines the capabilities of an accelerometer with additional physiological sensors in a single-site device (Chen & Bassett, 2005). One of the

more popular multisensor accelerometers used in the literature is the BodyMedia® SenseWear armband monitoring devices. The SenseWear armbands are unobtrusive external monitors worn on the upper-arm (situated on the triceps) via an elastic band, are light weight, and comfortable to wear (Johannsen, et al., 2010). These multi-sensor devices combine all the capabilities of a bi- (SenseWear Pro_2 and Pro_3 Armband) or tri- axial (SenseWear Mini Armband) device, along with several other physiological sensors, such as heat flux, skin temperature, and galvanic skin response (Johannsen, et al., 2010; BodyMedia, Inc., 2015**;** Welk, et al., 2007). In addition, the devices can be used to quantify daily durations spent in various intensities of physical activity (e.g., sedentary, light PA, moderate PA, vigorous PA, and very vigorous PA) (BodyMedia, Inc., 2015). Overall, the additional sensors of the SenseWear armbands may provide increased sensitivity for detecting subtle changes in energy expenditure, as well as more accurate depictions of varying intensities when engaged in a wide range of activities.

The added physiological sensors included in the SenseWear armbands allow for improvements in estimating free-living energy expenditure, and have been validated against DLW and indirect calorimetry (e.g., two criterion standards for quantifying energy expenditure) to estimate energy expenditure (Johannsen, et al., 2010; Welk, et al., 2007). In a validation study of the SenseWear Pro_3 Armband and the SenseWear Mini Armband, Johannsen, et al. (2010) compared total energy expenditure and physical activity energy expenditure (PAEE) under free-living conditions in healthy adults by direct comparison to DLW. Results indicated both the SenseWear Pro_3 (4%) and SenseWear Mini (<0.1%) underestimate total energy expenditure compared to DLW, but results are non-significant (p = 0.07 and p = 0.69, respectively) (Johannsen, et al., 2010). Regression analysis showed significant agreements between the SenseWear Pro_3 Armband and DLW measurements of total energy expenditure ($R^2 = 0.68$, p <

0.001), as well as between the SenseWear Mini and DLW measurements of total energy expenditure ($R^2 = 0.71$, $p < 0.001$) (Johannsen, et al., 2010). Examination of the agreement in total energy expenditure between the two armband monitors and DLW shows an ICC of 0.80 (95% CI = 0.89-0.70) for the SenseWear Pro$_3$ Armband and DLW and an ICC of 0.85 (95% CI = 0.92-0.76) for the SenseWear Mini and DLW (Johannsen, et al., 2010). Overall, SenseWear Armbands appear to be valid monitors for measuring energy expenditure in free-living conditions, with the SenseWear Mini showing slightly better performance, which may be due to the inclusion of the tri-axial accelerometer.

Although the SenseWear Armbands have been validated in the literature as valuable tools for assessing PA (as indicated above), limitations have been suggested when engaged in very high intensities. In a recent validation study of two SenseWear Armband devices, breakdown of PAEE between the SenseWear Pro$_3$ Armband and DLW and the SenseWear Mini and DLW suggested significant underestimation of both devices when compared to DLW (SenseWear Pro$_3$ Armband, $p < 0.02$ and SenseWear Min, $p < 0.03$), ICC for PAEE for both devices with DLW was 0.63 (95% CI = 0.77-0.47), and regression analysis indicated moderate agreement between SenseWear Pro$_3$ Armband and DLW ($R^2 = 0.51$, $p < 0.001$) and SenseWear Mini and DLW ($R^2 = 0.48$, $p < 0.001$) (Johannsen, et al., 2010). In addition, both monitors significantly underestimated energy expenditure at higher activity levels (SenseWear Pro$_3$ Armband: $R^2 = 0.56$, $p < 0.001$; SenseWear Mini: $R^2 = 0.49$, p , 0.001) (Johannsen, et al., 2010). This is consistent with other studies, which reported inaccuracies in the SenseWear armbands at running speeds greater than 6.0 mph and activities greater than 10 METs (Drenowatz & Eisenmann, 2011; Koehler, et al., 2010). However, such discrepancies could be due to the device's algorithms and its reliablitiy on the measurement of body acceleration; therefore, it doesn't take into account the load being

moved during resistance training (Benito, et al., 2012). In addition, cancer survivors may have physical limitations, which would inhibit running activities at higher speeds, as well as engaging in vigorous or high intensity activities greater than 10 METs.

Overview of accelerometers. As mentioned previously, properly evaluating PA is critical to examining epidemiological changes in PA, as well as intervention strategies. Therefore, understanding which method is best for different populations and research is imperative. Most accelerometer devices are worn on either the hip, wrist, ankle or thigh, are, as mentioned previously, available as uni-, bi-, or tri-axial instruments, as well as multi-sensor devices, and perform many basic functions. Furthermore, many accelerometers have the capabilities to record and store high resolution data for several days and/or weeks. This becomes critical when assessing PA levels during free-living activities, as it is recommended at least seven days are monitored in order to get an accurate depiction of average PA levels over time (Matthews, Ainsworth, Thompson & Bassett, Jr., 2002). Therefore, determining which accelerometer will work for each specific study and population is imperative for proper appraisal of PA and SED behaviors.

As indicated previously, accelerometers provide an effective means for measuring PA behaviors in both healthy and chronic disease populations. Selecting the appropriate type of activity monitor is critical, particularly in regards to specific functions and their relation to specific research questions and populations. However, determining which activity monitor is best for specific studies and populations can be daunting. In a systematic review, Van Remoortel, et al. (2012) evaluated 40 activity monitors tested in validation studies using both healthy individuals and those with chronic diseases. Activity monitors included uniaxial, triaxial and multi-sensor devices, all of which included validation studies against DLW. Results indicated

that uniaxial devices (4 = 0.52; 95% CI = 0.29, 0.70) had significantly lower pooled r compared

to multisensor devices (r = 0.84; 95% CI = 0.78, 0.88; p < 0.001), but there were no significant

differences compared to the triaxial devices (r = 0.61; 95% CI = 0.45, 0.73; p = 0.37). Meta-

regression analysis showed that 53% of the between-study heterogeneity was accounted for by

type of device (Van Remoortel, et al., 2012). Furthermore, change in total energy expenditure

was less accurate in uniaxial accelerometers (-12.07%) compared to triaxial accelerometers (-

6.85%; p = 0.39) and multisensor devices (-3.64%; p = 0.03). In addition, a change in total

energy expenditure was smaller, though not statistically significant, in studies with chronic

disease populations than in studies with healthy populations (-9%; p = 0.09). In regards to active

energy expenditure, correlations for active energy expenditure were higher in triaxial

accelerometers (0.59; 95% CI = 0.45, 0.70) and multisensor devices (0.54; 95% CI = 0.39, 0.65)

compared to uniaxial accelerometers (0.39; 95% CI = 0.16, 0.58; p = 0.12 for triaxial and p =

0.32 for multisensor devices against uniaxial accelerometers) (Van Remoortel, et al., 2012).

Moreover, all monitors underestimated active energy expenditure (-24.22% in uniaxial, -21.01%

in triaxial, and -24.35% in multisensor devices), but no significant differences were found

between the devices. However, changes in active energy expenditure were statistically

significantly smaller in studies with chronic disease populations compared to studies with

healthy populations (-44%; 95% CI = -73, -13; p = 0.006) (Van Remoortel, et al., 2012). Overall,

using a triaxial or multisensor activity monitor appears to provide the most accurate outcomes,

particularly when measuring total and active energy expenditure.

  Although there are outcome differences between the different types of activity monitors,

most accelerometer devices perform similar basic functions, such as steps, PA level/intensity,

and energy expenditure, but vary in additional measures, such as body position/posture, METs,

and/or activity type/counts (Strath, et al., 2013). Furthermore, accelerometer devices can vary in accuracy of the calculations, even among the most basic functions. For example, Berntsen, et al., (2010) assessed the ability of four activity monitors (SenseWear Pro$_2$ Armband, Actigraph, ikcal, and ActiReg) to determine the time spent in moderate-to-vigorous physical activity (MVPA) and total energy expenditure compared to indirect calorimetry in 120 minutes of daily free living activity. Results indicated an overestimation of average MVPA minutes in both the Actigraph (2.5% overestimation) and the SenseWear Pro$_2$ Armband (2.9% overestimation) and an underestimation of average MVPA minutes by the ikcal and ActiReg by 11.6% and 98.7%, respectively (Berntsen, et al., 2010). When evaluating total energy expenditure, the ikcal and SenseWear Pro$_2$ Armband showed lower estimation error of total energy expenditure (5% and 9% estimation errors, respectively) compared to the Actigraph (15% estimation error) and ActiReg (21% estimation error) (Berntsen, et al., 2010). Understanding whether devices are more prone to overestimating or underestimating physical activity is critical for improving research strategies.

Although accelerometers have been shown to be highly effective in evaluating locomotor activities, limitations have been noted when assessing the energy cost of low intensity activities during daily living. Light activity makes up the majority of daily PA under free-living conditions, particularly within special populations, such as cancer patients and survivors. However, low intensity activities are often difficult to measure because of its intermittent and arrhythmic nature (Chen & Bassett, Jr., 2005). Therefore, finding the most precise means for assessing light intensity activity becomes critical for public health research, accurate assessment of total energy expenditure, and successful intervention strategies (Calabro, Lee, Saint-Maurice, Yoo, & Welk, 2014).

It has been suggested that multi-sensor activity monitors that incorporate physiological paramaters (heart rate, body temperature, etc.) within the accelerometers to evaluate energy expenditure offer improved estimates at lower intensity activities (Calabro, et al., 2014). A recent study evaluated the validity of five commercially available accelerometers (ActivPal, SenseWear Pro$_3$ Armband, SenseWear Mini Armband, ActiHeart monitor, and ActiGraph GT3X) and their ability to estimate energy expenditure at lower intensities (1.5-2.9 METs) (Calabro, et al., 2014). All five devices were evaluated against a portable indirect calorimetry device (Oxycon Mobile 5.0), which served as the criterion measure for this study. Participants wore all six devices while participating in 60 minutes of structured activities and 60 minutes of unstructured free-living activities at low intensity (total duration 120 minutes). Results indicated the SenseWear Mini and SenseWear Pro$_3$ Armband overestimated energy expenditure by 0.9% and 3.9%, respectively, but were the most accurate for estimates of total energy expenditure compared to the ActiGraph, ActiHeart, and ActivPal, which all underestimated total energy expenditure by 25.5%, 7.8%, and 22.2%, respectively (Calabro, et al., 2014). Sensitivity and specificity values were assessed for all five devices based on three intensities: SED (1.0-1.4 METs), light intensity (1.5-2.9 METs), and moderate intensity (3.0-5.9 METs) (Calabro, et al, 2014). All five devices produced high sensitivity to SED activities; however, the ActiGraph had the lowest specificity for SED activities (Sp = 0.64, 95% CI: 0.52, 0.77), which may indicate this device overestimates the amount of time spent in SED activities by counting light intensity as SED (Calabro, et al., 2014). The sensitivity rating for light activities was significantly lower for the ActiGraph (Se = 0.14, 95% CI: 0.01, 0.27) (Calabro, et al., 2014). In addition, the ActiGraph (Sp = 0.38, 95% CI: 0.21, 0.54) and the ActivPal (Sp = 0.19, 95% CI: 0.05, 0.32) had the lowest specificity rating for light activities, suggesting that moderate intensities are classified as light (Calabro, et al., 2014).

Similar inconsistencies for sensitivity of these two devices were seen in the moderate intensity activities as well (ActiGraph: Se = 0.29, 95% CI: 0.12, 0.45; ActivPal: Se = 0.07, 95% CI: 0.00, 0.17) (Calabro, et al, 2014). Overall, the misclassifications of intensities enhance the understanding of errors in estimation and the impacts it may have on total energy expenditure differences. Therefore, multi-sensor monitors (SenseWare Mini, SenseWear Pro Armband, and ActiHeart) appear to have advantages over the standard accelerometry-based monitors (Actigraph and ActivPal).

Overall, since accelerometers can vary in the many different functions and outcomes, knowing how studies were conducted and which monitor was used in the literature becomes critical. In addition to the limitations related to intensity measures, monitoring compliance (non-wear time) and inactivity are of concern when using traditional uni-, bi-, or tri-axial accelerometers alone. Therefore, using a multisensor accelerometer that combines all aspects of the tri-axial accelerometer with other sensors that capture physiological responses to activity, such as heart rate or skin temperature, to optimize assessment of body posture and PA may provide added benefits to research (Van Remoortel, et al., 2012). Furthermore, the additional physiological responses of the multisensor accelerometers aim to increase the sensitivity of such devices for improving pattern recognition and detecting subtle changes in energy expenditure associated with various lifestyle tasks. These additional components of the multi-sensor accelerometers, such as the SenseWear Pro Armband, may be optimal when measuring PA levels of special populations, particularly cancer patients and survivors. In conclusion, selecting the appropriate assessment tool is imperative and should be dependent on the PA component of interest, overall objectives of the study, target population characteristics, and feasibility relative to cost and logistics (Butte, Ekelund, & Westerterp, 2012).

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Quality of Life

It is well known that during the course of cancer diagnosis, treatment, and follow-up, cancer patients and survivors are likely to experience a variety of physical, psychological, and social difficulties. Physical activity has been shown to have significant health benefits, as indicated above; however, the fatigue, pain, and loss of function may have a greater impact on cancer survivors' ability to engage in regular and routine PA. Therefore, these culminating side effects may present significant challenges in a cancer survivor's overall well-being.

Well-being refers to one's physical, psychological, and social satisfaction, complete life satisfaction, and the emotional responses therein (Diener, Suh, Lucas & Smith, 1999). Evaluating an individual's judgment of their global well-being is often reflected in the term quality of life (QOL). Quality of life is defined as a multidimensional concept including physical, psychological, and social well-being (Knobf, et al., 2007; Rummans, Bostwick, & Clark, 2000). In addition, QOL represents an individual's subjective perspective, and when it comes to participation in PA and disease-free, overall survival, QOL is a significant outcome (Knobf, et al., 2007).

Numerous studies suggest that exercise interventions in cancer survivors are generally associated with a positive increase in overall QOL (Courneya, Mackey, et al., 2003; Hayes, et al., 2011; Knobf, et al., 2007; Korstjens, et al., 2006; Mendelbatt, et al., 2011; Schwartz, 2004). As indicated by Knobf, et al. (2007) cross-sectional retrospective studies involving men and women from a variety of cancer backgrounds, those who exercised reported better QOL than those who did not engage in routine exercise. Furthermore, in a study conducted by Mandelbatt, at al. (2011), researchers found that individuals with breast cancer who reported the highest levels of moderate and vigorous PA also had the highest QOL. Although most studies have shown a direct

correlation between PA and QOL, some studies have not reported improved QOL associated with exercise. Pinto, et al. (2002) found no improvement in overall mood or cancer-related symptoms over the course of a 12-month, longitudinal observational study. Although the literature relating PA behaviors to QOL is inconclusive, evaluating the association between PA behaviors and the multidimensional concept of QOL commonly involves three core domains: psychological, physical, and social (Knobf, et al., 2007).

Psychological domains

Psychological distress is one of the most common results of the diagnosis and treatment of cancer, and is often characterized by uncertainty, vulnerability, loss of control, and existential concerns (Knobf, et al., 2007). Psychological responses associated with these factors include depression, anxiety, death anxiety, worry about health problems, perceived risk of recurrence, or decision regrets (Simard, et al., 2013). The varying aspects of these cancer-related psychological stressors are often dependent on the stage of diagnosis. Immediately post-diagnosis, most of the cancer patients' concerns focus on treatment and survival prognosis. Once treatment begins, concerns shift to the potential risks of invasive procedures or noxious effects of treatment. After treatment, fear or concerns of cancer recurrence tend to be most prominent. Although worries of recurrence may decline over time, additional worries arise, such as concerns about another cancer resulting from treatment, distress with continued testing and monitoring, additional health concerns associated with aging, functional difficulties, and depression and anxiety (Deimling, Bowman, Sterns, Wagner & Kahana, 2006).

Depression and anxiety, as indicated above, are highly prevalent in cancer patients and survivors, and are the two more commonly assessed psychological factors in PA-related studies and cancer patients and survivors (Knobf, et al., 2007). In addition to these more common

associations of psychological distress, self-esteem is viewed as a key component of the psychological domain of QOL. Self-esteem is defined as a multifaceted structure relating to overall feelings of self-worth; however, its description and conceptualization are limited within cancer-related QOL models (Knobf, et al., 2007). Therefore, many QOL frameworks include self-esteem within the general outline of the psychological domain rather than as a separate entity (Knobf, et al., 2007). Regardless, self-esteem plays a significant role in QOL and the impact of PA on QOL in cancer patients and survivors.

Although self-esteem is identified as part of the psychological domain of QOL, there appears to be a reciprocal relationship between self-esteem and PA behaviors as measured by QOL. The Exercise and Self-Esteem Model (EXSEM) is a long-standing hierarchical theory of self-esteem, which confirms this relationship between physical activity, physical self-worth, and global self-esteem (Sonstroem & Morgan, 1989). Therefore, the basis of this theory suggests engaging in routine PA may influence the self-perceptions of physical functioning.

Physical functioning has been shown to improve with PA, but specific changes within the physical domain, such as physical conditioning, self-efficacy, attractive body, and strength, are theorized to be associated with physical self-worth, a precursor to overall self-esteem (Baldwin & Courneya, 1997; McAuley, et al., 2005). For example, in a study of over 170 sedentary older adults (mean age = 66.7 years) involved in a 6-month exercise program, McAuley, et al. (2005) examined self-efficacy and exercise-related self-esteem changes at one and five year follow-ups. At the one-year follow-up, bivariate correlations indicated a statistically significant association between PA and physical self-worth ($r = 0.35$, $p < 0.05$), exercise self-efficacy and physical self-worth ($r = 0.37$, $p < 0.05$), and exercise self-efficacy and global self-esteem ($r = 0.29$, $p < 0.05$) (McAuley, et al., 2005). The five-year follow-up showed similar results with statistically

significant associations between PA and physical self-worth ($r = 0.31$, $p < 0.05$), exercise self-efficacy and physical self-worth ($r = 0.34$, $p < 0.05$), and exercise self-efficacy and global self-esteem ($r = 0.19$, $p < 0.05$), along with the addition of PA and global self-esteem ($r = 0.68$, $p < 0.05$) (McAuley, et al., 2005). These results are similar to other studies that found statistically significant associations between global self-esteem with physical competence ($r = 0.70$, $p < 0.001$), perceived physical ability ($r = 0.53$, $p < 0.001$), and strenuous activity ($r = 0.21$, $p < 0.05$) in 64 breast cancer survivors (Baldwin & Courneya, 1997). Therefore, engaging in routine physical activity may be influenced by one's own perception of self-esteem, but self-esteem and physical self-worth can also be enhanced by participating in exercise programs, thereby coinciding with the proposed EXSEM theory.

Physical domains

The physical aspect of PA and its relationship to QOL is highly impacted by the level of fatigue, pain, cardiovascular fitness, strength, and subjective physical well-being. It is suggested that physical activity may have a positive impact on survival rates of cancer patients with sustained adherence a dependent factor for this potential impact of PA on disease outcomes (Courneya, 2009; Holmes, Chen, Feskanich, Kroenke, & Colditz, 2005; Meyerhardt, et al., 2006; Midtgaard, et al., 2012; Kenfield, Stampfer, Giovannucci, & Chan, 2011). Therefore, understanding the key aspects attributing to adherence and maintenance of PA becomes a primary goal for research and subsequent interventions. Overall, QOL has been shown to have a direct impact on one's ability to engage in PA, as well as the motivation to stay physically active (Midtgaard, et al., 2012).

Although quantitative methods provide standardized and measurable concepts related to physical activity outcomes, qualitative methods can contribute, through observational insights

and theoretical perspectives, to the understanding of the relationship between physical activity and QOL. Two key aspects associated with the physical domain related to QOL are self-efficacy and adherence. As a social cognitive variable, self-efficacy is defined as the "belief in one's ability to accomplish a goal or change a behavior" (Hales, 2015, p. 20). Self-efficacy has repeatedly shown to be a strong contributor to physical activity behavior and adherence (Coups, et al., 2009; Pinto, Rabin, & Dunsiger, 2009). Understanding the basis of self-efficacy and its impact on motivation, adherence, and QOL can assist researchers and medical professionals in developing intervention strategies and resources for increasing physical activity, improving physical activity maintenance and adherence, and enhancing QOL, both during and after cancer treatment.

The second key aspect of the physical domain associated with QOL refers to the ability to identify not just quantified adherence rates, but, more so, the underlying reasoning and motivation to adhering to PA programs and maintaining active lifestyles long term. For example, in an exploratory study evaluating the Copenhagen PACT (Physical Activity after Cancer Treatment) Study, Midtgaard, et al. (2012) attemptted to identify post intervention experiences and their associations with physical activity maintenance through semi-structured focus group interviews. The Copenhagen PACT Study was a 12-month rehabilitation program promoting sustained regular PA in cancer survivors who had completed chemotherapy less than six months prior to the start of the program. The rehabilitation program consisted of weekly, high intensity supervised physical exercise training coupled with tri-monthly presentations from invited experts, bimonthly in-group coaching, and 3 x 1 hour individual coaching sessions (Midtgaard, et al., 2012). Following the completion of this program, Midtgaard, et al. (2012) recruited 23 individuals from the Copenhagen PACT Study to participate in four semi structured focus group

interviews a minimum of six months post intervention. Results indicated five overriding categories related to physical activity maintenance post-treatment and post-intervention: 1) a new agenda; 2) an act of autonomy; 3) goal setting; 4) prioritizing; and 5) tamed fear. These five categories provide an insightful look into the basis of the cancer survivors' post-intervention PA maintenance and furthers the understanding of adherence-enhancing PA programs and resources.

The "new agenda" that the PACT study articulated is achieved because all participants were able to increase their physical activity levels during the treatment leading them to "confront old habits" and "decide on a new agenda in life" (Midtgaard, et al., 2012, p.2002). Furthermore, the intervention gave them enough personal experience to prefer regular exercise to sedentary behavior, felt a reduction in fatigue, and viewed breaks in PA as temporary interruptions, rather than threats to their maintenance. In addition, the program demonstrated "an act of autonomy" for the cancer patients to follow upon completion of the program (Midtgaard, et al., 2012, p. 2002). Following the intervention, the participants felt confident, optimistic, and enthusiastic about maintaining their PA program. They further described their maintenance as "a conscious act of will," "a personal choice," and "a decisional power" (Midtgaard, et al., 2012, p. 2003). The third category, goal setting, is described as a key strategy behind adherence and maintenance of PA because it allows cancer patients and survivors to look to the future, focus on hopes and dreams, and a challenge for maintaining PA. Participants who viewed PA as having value and importance in comparison to other obligations were more likely to prioritize and plan PA into their daily routines. Therefore, giving priority to exercise increased feelings of self-satisfaction and rewards because the participants were investing in a healthy lifestyle. Finally, an increase in fearful outlooks often coincided with the diagnosis of cancer, whether it is related to fear of the diagnosis, fear of the treatment, fear of reoccurrence, or fear of death. Participants described PA

as inseparable from the cancer, with fear lying only in what would happen if the participants quit their exercise routines. Furthermore, fear of disease recurrence appeared to be controlled or minimized by PA maintenance. Overall, the researchers in this study described physical activity maintenance as a "psychological act of balance" by helping the participants take control of an otherwise uncontrollable disease, enhance self-awareness, and restore power and order in one's life (Midtgaard, et al., 2012, p. 2005).

Social domains

Not only can cancer have an impact on an individual physically and psychologically, but their overall social functioning can be greatly affected as well. The social domain of overall QOL is often related to social support, social well-being, and/or role performance. Social support, specifically, reflects one's perceived comfort, care, assistance, and esteem one receives from others (Wallston, et al., 1983). In regards to cancer survivorship, Hodges and Winstanley (2012) suggested that optimism and social support may directly or indirectly contribute to levels of positive affect. In a study of over 100 cancer survivors, positive affect was positively correlated with both optimism ($r = 0.63$, $p < 0.001$) and social support ($r = 0.45$, $p < 0.001$), with optimism also displaying a positive correlation with social support ($r = 0.38$, $p < 0.001$) (Hodges & Winstanley, 2012). This is consistent with other studies that suggested perceptions of social support during and immediately post cancer treatment showed a positive association with well-being and expectations of future social support to predict overall levels of well-being (Sarason, Pierce, & Sarason, 1990; Shelby, et al., 2008). Hence, optimism at the start, during, and post cancer treatment, may have a significant impact on perceived and actual social support, both of which contribute to overall well-being and QOL.

Although social support appears to play a key role in QOL and well-being, added physical and psychological stresses may have a negative impact on social support throughout diagnosis, treatment, and post-treatment of cancer patients and survivors. Mayfield (1999) qualitatively evaluated this idea in a sample of seven female cancer patients selected from a community-based support group and suggested that social support may actually decrease for cancer survivors, particularly when it comes to support from physicians and health care staff. In fact, one subject stated, "Once treatment is over, you have no one to talk to" (Mayfield, 1999, p. 30). In addition, Polinsky (1994) examined the role of social support in a study of 223 breast cancer survivors and, although fewer than 5% of the respondents reported changes in their social activities, 64% of the respondents indicated the need to discuss concerns about breast cancer, with 8% reporting they had no one to talk to. While 8% seems low in reporting such concerns, 73% of the cancer survivors thought their spouse or significant other understood what they were going through well or very well, 57% thought their family members understood well or very well, and only 45% thought their friends understood well or very well (Polinsky, 1994). Therefore, the level of understanding could impact the cancer patients' and survivors' ability to communicate and express all of their psychosocial symptoms, which could further impact overall social support and social functioning.

Even though the role of social support and social well-being has not been clearly addressed in the cancer literature, it is proposed that physical activity may have a positive impact on social functioning as a component of QOL. Such improvements may include social well-being and functional ability in work and family roles, and enhanced feelings of life satisfaction and overall happiness (Knobf, et al., 2007). Korstjens, Mesters, van der Peet, Gijssen, & van den Borne (2006) examined this theory following the completion of a 12-week physical and psycho-

education rehabilitation program among almost 600 cancer survivors. The EORTC QLQ-C30 (Appendix B) was used to evaluate social functioning. Results indicated EORTC QLQ-C30 reference values for social functioning significantly increased from 77.3 at the midpoint for all cancer survivors (W = -6.785, p < 0.001) to 86.4 for breast cancer survivors (W = -5.03, p < 0.001) and 85.8 for all other cancer survivors (W = -6.429, p < 0.001) at the end of the rehabilitation program (Korstjens, et al., 2005). This is similar to other studies, which found significant improvements in social functioning (p = 0.009) following a 4-6 month community based exercise intervention program with 26 breast cancer survivors (Knobf, et al., 2014). Overall, social support appears to be a key aspect of both QOL measures and PA participation and adherence, and warrants more explicit research.

Instrumentation for Quality of Life Measures

Relatively little research has given attention to the chronic stressors and long-term implications of QOL on cancer survivors. In a study of 335 young adult cancer survivors, Yanez, Garcia, Victorson and Salsman (2013) found that the most physical, psychological, social and functional distress occurred 13-24 months post-treatment. Furthermore, psychosocial well-being and physical functioning ability have added to the overall indication of QOL (Knobf, et al., 2007). Therefore, it has become increasingly common for QOL to be used when evaluating all aspects of treatment (before, during, and after) for cancer patients.

Multiple instruments are available for measuring an individual's QOL; however, understanding what the instruments measure is critical to interpreting the overall findings. Instruments vary in conceptualization and key domains (physical, psychological or social) are either left out or combined as subscales, thereby, limiting the constructs of well-being and/or function (Knobf, et al., 2007). The two most commonly used instruments measuring QOL among

cancer patients and cancer survivors are: 1) the European Organization for Research and

Treatment of Cancer Core Quality of Life Questionnaire (EORTC-QLQ-C30); and 2) the

Functional Assessment of Cancer Therapy – General (FACT-G), all of which provide a total

summated score describing either global QOL, general well-being, or overall QOL (Knobf, et al.,

2007; Pearce, Sanson-Fisher, & Campbell, 2008; Tamburini, 2001). Since these instruments have

reporting inconsistencies, understanding the key similarities, differences, and reported outcomes

are imperative for identifying the overall impact of QOL on cancer survivors. Furthermore,

measuring QOL during and after treatment can help the clinician and other medical personnel

with weighing the benefits of treatment and interventions compared to any side effects, whether

they be physical, emotional, or psychosocial.

FACT-G

A frequently used measure for QOL is the FACT-G. The FACT-G is a 27-item

instrument divided into four well-being subscales: physical, social/family, emotional, and

functional (Tamburini, 2001; Victorson, et al., 2008). It was first developed in 1987 for adult

cancer patients and has since undergone four revisions, with its most recent revision in 1997

(Victorson, et al., 2008). Currently, the FACT-G uses a 5-point Likert-type scale (0-4) with a

seven-day recall period (Victorson, et al., 2008). Following the completion of the FACT-G, all

subscales are summed together, with a higher score indicating better quality of life (Victorson, et

al., 2008). Several (about 20) subscales of the FACT-G have been constructed to address

relevant disease-, treatment-, or condition-related issues (Tamburini, 2001). Each subscale

consists of the core FACT-G items with a specific scale relating to a particular type of cancer

(e.g., breast, prostate, etc.), treatment (e.g., chemotherapy, radiation, etc.), and/or other QOL

domains (e.g., fatigue, spirituality, etc.) (Victorson, et al., 2008). Overall, the FACT-G can be used with patients and survivors with any form of cancer.

Since its development, the FACT-G has been translated into 30 different languages, and has become one of the most widely used QOL measures in both clinical and medical treatment evaluation trials (Tamburini, 2001; Victorson, et al., 2008). One of the key components to using this measure is that the FACT scale is highly sensitive to classifying patients on the basis of performance status rating, stage of disease, and hospitalization status (Cella, et al., 1993). In accordance with its high sensitivity, the FACT-G has been validated in several thousand patients of different cancer types and across various cultures (Cella, Yost, Lai, & Zagari, 2003; Conroy, et al., 2004; Costet, Lapierre, Benhamou, & Le Gales, 2005; Fumimoto, et al., 2001; Victorson, et al., 2008). For example, the original validation study displayed a high correlation among test-retest reliability for the physical subscale ($r = 0.88$), functional subscale ($r = 0.84$), social subscale ($r = 0.82$), emotional subscale ($r = 0.82$), and overall total ($r = 0.92$) (Cella et al., 1993). In addition, internal consistency was also highly correlated with all domains: physical (0.82), functional (0.80), social (0.69), emotional (0.74), and total (0.89) (Cella, et al., 1993). These findings are in conjunction with a more recent meta-analytic reliability generalization study, which examined possible influences on the FACT-G and its subscale score variability across studies (Victorson, et al., 2008). The mean FACT-G alpha coefficient was .88 (range: .80-.96), with an average standard error of measurement of 5.32 (range: 1.9-8.6) (Victorson, et al., 2008). Furthermore, from an international standpoint, in a study examining the reliability and validity of the FACT-G in French cancer patients, the French version of the FACT-G showed moderate discrimination between patients of varied disease stage (metastatic, localized, or remission) and treatment status (chemotherapy on, chemotherapy off, or no chemotherapy), had significantly

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high test-retest correlation coefficients (r = 0.74-0.90; p < 0.001), had good internal consistency (all alphas ≥0.77), and was overall, highly acceptable (Costet, et al., 2005). All-in-all, the FACT-G appears to be a reliable and valid tool for assessing QOL in cancer patients and cancer survivors from a variety of cancer diagnoses.

EORTC-QL-30

In addition to the FACT-G, the EORTC-QLQ-C30 scale is one of the most widely used measures for evaluating QOL in cancer patients and has been primarily used in clinical trials, research, and practice assessing both functional and physical symptoms in patients and survivors from a variety of cancer diagnoses. The questionnaire has undergone considerable evaluation, with the current version consisting of 30 items summed and transformed into the following subscales: five functioning subscales (physical, role, social, emotional, and cognitive); a global quality of life subscale; three symptom subscales (fatigue, nausea and vomiting, and pain); and six individual items (Smith, Cocks, Parry, & Taylor, 2014). While there are other cancer specific questionnaires for each of these measures, the general qualitative measure is appropriate for populations involving more than one type of cancer.

The EORTC-QLQ-C30 is a validated questionnaire designed to assess the QOL of cancer patients and survivors, has been translated in 38 languages, and used in over 1500 studies worldwide (Tamburini, 2001). In a large study involving Brazilian cancer patients, reliability of the EORTC-QLQ-C30 was assessed using Cronbach's alpha coefficient (Paiva, et al., 2014). All domains of the questionnaire were greater than 0.70, with the exception of cognitive functioning (α= 0.57), social functioning (α= 0.69), and nausea and vomiting (α= 0.68). In addition, multi-trait scaling analysis resulted in adequate convergent validity (91.6%) and divergent validity (97.4%), with moderate to strong correlations compared to respected dimensions from the

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WHOQOL-bref, the Hospital Anxiety and Depression Scale, and the Edmonton Symptom Assessment System instruments (Paiva, et al., 2014). Furthermore, the EORTC-QLQ-C30 was able to distinguish between performance statuses and types of treatment within different groups of patients (Paiva, et al., 2014). These results are comparable to other studies demonstrating good reliability among all domains, except for cognitive functioning (Smith, et al., 2014). In general, the EORTC-QLQ-C30 is a reliable and valid tool for assessing QOL in cancer patients; however, care should be taken when evaluating specific domains more directly.

Some studies have questioned the internal reliability of the psychometric properties of the EORTC-QL-30 to be modest at best (Luckett, et al., 2011). Internal reliability is a key aspect to identifying the psychometric properties of patient-reported outcome measures and may vary across patient samples, administration method, and different languages. In a review of 30 studies related to the reliability of the EORTC-QL-30, internal reliability was strongly supported (Cronbach α >0.7 on all subscales) in only a single study (Luckett, et al., 2011). Furthermore, in 27 of the 30 studies reviewed, internal reliability was limited or showed mixed evidence, which was based on a criterion of at least 50% of subscales having a Cronbach α between 0.7 and 0.9 (Luckett, et al., 2011). In addition, research suggested that the QOL measures of the EORTC-QL-30 may not be as effective among cancer survivors and patients over the age of 70 (Fitzsimmons, et al., 2009). Furthermore, healthy individuals have reported age-related factors associated with QOL and overall well-being (Bowling, 2011). Since the majority of cancer diagnoses occur in adults over the age of 65, this could pose a limitation to the use of this qualitative measure for research purposes.

Conclusion

Various studies, as mentioned above, indicated physical activity is an important component in everyone's health, including cancer patients. Exercise interventions are emerging as a positive means for coping with a variety of biopsychosocial factors associated with the pathology and treatment of cancer. Biologically, physical activity has been shown to improve overall physical functioning, including fatigue, pain, strength, flexibility and cardiorespiratory fitness. Psychologically, engaging in regular physical activity may have a large impact on depression and anxiety, as well as their associated symptoms. Finally, although research is limited (as indicated above), social support and one's involvement in an exercise regimen may play an important role in the overall quality of life of cancer patients and their continued survival.

Although this is an exciting area of research, there are many limitations when studying cancer patients and cancer survivors directly. For example, there is a level of instability with an increase in potential drop-outs due to strenuous of the engaged program, remission, or poor self-esteem. In addition, most research is only examining a short period of their life, which makes it difficult to determine their PA and QOL prior to cancer, during treatment, and years following. For instance, depending on their activity levels prior to getting cancer, their overall view on the importance of PA could play a role in their PA levels following treatment. Therefore, ongoing research plays a key role in the development and integration of exercise programs as means of treatment for cancer patients, intervention strategies for cancer survivors, and the impact it may have on overall QOL.

CHAPTER 3. MATERIALS AND METHODS

Participants

Approximately 86 individuals enrolled in 12 different cohorts of the LIVESTRONG® at the YMCA cancer survivor program from July 2011 until August 2014 were recruited for this study. The LIVESTRONG® at the YMCA program is an elective 12 week exercise and education program for cancer survivors. In order to participate in the program, participants had to be over the age of 18 and needed clearance from their physician to participate in the program; therefore, this study followed the same guidelines. Anyone outside of these criteria were not eligible for participation. Participants were asked to join this study once they had signed-up for the LIVESTRONG® at the YMCA program and were in attendance on the first day of the 12-week program. Only those actively participating in the program were recruited for this study and all information was provided both verbally and in the Informed Consent (see Appendix A). Their choice to participate or not in the research had no bearing on their participation in the LIVESTRONG® at the YMCA program. Approval from the Internal Review Board at North Dakota State University (see Appendix B) was obtained and data was only collected from those who chose to participate and signed the Informed Consent.

Materials and Methods

Device: SenseWear® armband monitoring device

The SenseWear® armband monitoring device is an unobtrusive external monitor that allows for valid and accurate estimation of free-living energy expenditure (see Appendix C). In addition, the device can be used to quantify daily durations spent in various intensities of physical activity (e.g., moderate physical activity, vigorous physical activity). The SenseWear® armband monitor is worn on the upper-arm (situated on the triceps) and attached via an elastic

band (see Appendix C). The monitoring device collects data via multiple sensors (e.g., triaxial accelerometer, skin thermometer, step counter, and body position sensor) and has been validated against DLW and indirect calorimetry (e.g., two criterion standards for quantifying energy expenditure) to estimate energy expenditure.

Procedure: Physical activity

Cohorts were divided based on the monthly start date, and individuals enrolled in the LIVESTRONG® at the YMCA program were approached, as a group, on the first day of each respective cohort. Participants were given an introduction to the study and the SenseWear® armband monitoring device, including education of use and wear, which was conducted for all participants at the beginning of the study to ensure proper knowledge, understanding, and wear. The introduction was conducted in person by the researchers at the YMCA in Fargo, North Dakota.

Interested participants within each cohort were asked to complete a demographics form provided by the researchers (see Appendix D). In addition, these participants were advised to wear the SenseWear® armband monitoring device for seven consecutive days during the first week of their respective cohort. Participants were instructed to wear the armband monitoring device during all activities, including work, exercise, SED activities, chores, sleeping, etc. The only time the participants were advised not to wear the armband was when showering or engaging in other water activities, such as swimming. Following the seven days of the first week of each cohort, the monitoring devices were collected by the researcher(s) in person at the YMCA in Fargo, North Dakota. Participants in each cohort were again asked to wear the armband monitoring device for one week (seven days) at the midpoint (week six) and endpoint (week 12) of the LIVESTRONG® at the YMCA program.

An introduction to the armband monitoring devices, including education of use and wear, was conducted for all participants at the beginning of the study to ensure proper knowledge and wear. The introduction was conducted in person on the first day of the LIVESTRONG® at the YMCA program in Fargo, ND. The armband monitoring device was administered by the researchers at the start and end of each data collection time point at the YMCA, Fargo, North Dakota.

Procedure: QOL measure

At the end of each data collection time point (week one, week six, and week 12 of the LIVESTRONG® at the YMCA program), participants were asked to complete a FACT-G questionnaire (see Appendix E) as a means to assess QOL. The FACT-G is a validated quality of life instrument intended for use with a general cancer population. It is a self-administered questionnaire that takes about five minutes to complete. An introduction to the questionnaire was conducted by the researcher(s) for all participants at the beginning of the study to ensure proper knowledge. The questionnaire was administered by the researchers at the the end of each data collection time point (as indicated above) by one of the researchers.

<center>**Statistical Analysis**</center>

PA statistical analysis

Data from the SenseWear® armband activity monitors were downloaded to the SenseWear® BodyMedia, Inc. licensed software program. Each minute of activity monitor wear time during each time point (as indicated above) was classified as sedentary (SED), light (LIT), moderate (MOD), or vigorous (VIG). As indicated in the hypothesis, we predicted PA would increase and SED activity would decrease over the course of the 12 week, LIVESTRONG® at the YMCA cancer survivor group exercise program. In order to evaluate our hypothesis, a

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repeated measures ANOVA with mixed model framework was used to compare weekly time spent in SED, LIT, MOD, and VIG between weeks 1, 6, and 12 of the LIVESTRONG® at the YMCA program. A time-varying covariate was used to adjust for activity monitor wear time during each time point. If a significant difference was determined, a post-hoc paired t-test was conducted to determine the significance, and a Tukey-Kramer correction, based on the number of t-tests performed, was administered to hold the alpha level at $p<0.05$.

SAS version 9.4 was used to conduct all analyses with an alpha level set at $p<0.05$.

QOL statistical analysis

The FACT-G is a 27-item questionnaire composed of four components, including physical, social/family, emotional, and functional well-being. The total overall score is 0-108, with a higher score indicating better overall QOL. Three subscales, PWB, EWB, and FWB, have an individual score range of 0-28, with a higher value indicating better QOL within each specific area. The score range for EWB is 0-24, again, with a higher score equating to better emotional QOL. A total FACT-G score is calculated by adding all four subscales together for an overall QOL score. In addition, each subscale was individually assessed based on the individual score ranges.

Quality of life measures were hypothesized to improve over the course of the 12 week, LIVESTRONG® at the YMCA cancer survivor group exercise program. A repeated measures ANOVA with mixed model framework was used to determine significance across the three time points. If a significant difference was identified, a post-hoc paired t-test was conducted to determine the significance. A Tukey-Kramer correction, based on the number of t-tests performed, was administered to hold the alpha level at $p<.05$.

SAS version 9.4 was used to conduct all analyses with an alpha level set at $p<.05$.

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CHAPTER 4. CHANGES IN PHYSICAL ACTIVITY OF CANCER SURVIVORS PARTICIPATING IN A GROUP EXERCISE PROGRAM

Introduction

According to the Centers for Disease Control and Prevention (CDC) (2013), approximately one in every seven adults develop cancer at some point in their life with nearly 1.7 million new cancer cases diagnosed annually. In 2013 alone, more than 575,000 Americans died of cancer, equating to almost 1,600 people per day (American Cancer Society, 2013; CDC, 2013). In fact, as the second most common cause of death, cancer accounts for roughly one of every four deaths in the United States (American Cancer Society, 2013).

Without a doubt, the number of cancer cases is substantial; however, only about 5% of all diagnosed cancers originate from inherited genetic mutations (American Cancer Society, 2013). Therefore, the majority of cancers stem primarily from uncontrollable factors, such as age, biological sex, and ethnicity/race, and controllable factors, such as physical activity, tobacco use, and diet. In fact, the World Cancer Research Fund estimated that about one-quarter to one-third of new cancer cases are related to preventable factors, specifically including obesity, physical inactivity, and poor nutrition (American Cancer Society, 2013).

Advancements in early detection and treatment have improved the cancer survival rate to a 66% all-site five-year survival rate following diagnosis for adults (Howlader, et al., 2012). Such advancements estimate the number of cancer survivors in the U.S. to increase from 13.7 million to 20 million by 2020 (American Cancer Society, 2013; Howlader, et al., 2012). Despite these survival rate estimates, cancer survivors have an increased risk for recurrence, secondary cancers, late effects of treatment, and a variety of other symptoms and responses that may impact

physical activity (PA) levels, cardiovascular fitness, and overall physical fitness (Bellizzi, et al., 2005; Knobf, et al., 2007).

The multifaceted responses coinciding with the diagnosis, treatment, and follow-up cancer patients and survivors experience can dramatically affect PA levels and overall physical functioning. Physical activity recommendations for special populations, such as those with cancer, are similar to the general health recommendations of 150 minutes of moderate physical activity or 75 minutes of vigorous physical activity per week (Garber, et al., 2011). However, PA declines, both during and post-treatment, have been observed among cancer survivors. For example, the Centers for Disease Control and Prevention (CDC) (2012) evaluated more than 45,000 respondents in the 2009 Behavior Risk Factor Surveillance System (BRFSS), discovered that almost 31.5% of cancer survivors had not participated in any leisure-time PA in the past 30 days, compared to 24.2% of the general population in this report (CDC, 2012). In another study, Blanchard, Courneya, and Stein (2008) conducted a national cross sectional survey reviewing PA levels in over 9000 participants across six major cancer survivor groups and discovered only 30-47% of cancer survivors were meeting the ACSM PA. On the contrary, Kim, et al. (2013) evaluated 11,000 individuals who participated in a PA and sedentary (SED) interview-based questionnaire from the 2007-2010 National Health and Nutrition Examination Survey (NHANES). Results indicated that cancer survivors were more likely to report engaging in regular PA compared to the non-cancer participants (multivariable adjusted OR = 1.17, 95% CI (0.94,1.46)); however, cancer survivors were also more likely to report spending more than eight hours per day engaged in SED behavior (OR = 1.42, 95% CI (0.98, 1.53)) (Kim, et al., 2013). Although these studies show contradictory results in PA between cancer survivors and the general population, and PA and SED time, all reports were self-reported. Furthermore, as

indicated in Kim et al. (2013), the cancer survivors reported more than eight hours of SED behavior, which could pose additional health concerns.

In order to take a closer look at these specific health concerns, particularly for chronic disease risk, objectively assessed studies on SED time have shown consistent results compared to these self-report studies. For example, a study of 145 post-treatment colorectal cancer survivors using a tri-axial MOX activity monitor identified the average SED time to be 10.2 hr/day (van Roekel, et al., 2016). In addition, Healy, et al. (2007) used uniaxial Actigraph accelerometers to track the PA of 178 adults over the course of seven days. Results indicated that higher SED time was associated with significantly higher 2-h plasma glucose, whereas both light intensity PA and moderate-to-vigorous intensity PA were associated with significantly lower 2-h plasma glucose ($p = 0.006$ and 0.005, respectively) (Healy, et al, 2007). In a continuation study, Healy, Dunstan, Salmon, Shaw, et al. (2008) further revealed that more breaks in SED time was associated with significantly lower waist circumference ($p = 0.027$), BMI ($p = 0.026$), triglycerides ($p = 0.029$), and 2-h plasma glucose ($p = 0.025$). Therefore, prolonged SED time may be the key factor to chronic disease risks, such as cancer.

Not only does PA and SED time affect various biomarkers, but the length and intensity of PA may also influence whether or not individuals meet the recommended PA guidelines. For example, Loprinzi and Cardinal (2013) found that of the more than 6000 American adults participating in the NHANES 2003-2004 and 2005-2006 studies, less than 10% of the participants who reported longer structured exercise sessions (>10 minute bouts) met the ACSM guidelines for physical activity, compared to almost 43% of those who did regular, short bouts of exercise (<10 minute bouts). In regards to intensity, numerous studies have shown that appropriate levels of physical activity are associated with a reduced risk of many cancers, such as

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breast and colon cancer, and improved health benefits (Courneya, 2003; Courneya, Mackey, et al. 2003; Demarzo & Garcia, 2004; Rajotte, et al., 2012). Overall, physical activity can have various effects on carcinogenesis based on energy supply, intensity, and frequency of exercise. As previously discussed, it is well known that moderate intensity and rates of exercise appear to have the greatest impact on reducing cancer risk and recurrence, and has been associated with significant health benefits. However, single exhaustive exercise or unaccustomed high intensity training may actually increase the risk of some carcinogenesis. Some studies even suggest exhaustive exercise actually increases free radical DNA oxidative damage and suppresses immune function, both which have been related to an increase in cancer development (Banerjee, Mandal, Chanda, & Chakraborti, 2003; Poulsen, Loft, & Vistisen, 1996). Overall, short stretches of moderate intensity PA, such as taking the stairs or walking several blocks, during the day, appear to have a greater impact on reducing cancer risk and recurrence, improving health, and aid in meeting the ACSM guidelines. Therefore, an active lifestyle approach with more frequent stretches of PA may be as effective in providing overall health benefits.

Although regular PA is beneficial, chronic disease development, such as the diagnosis of cancer, appears to coincide with declines in PA and/or increases in SED behaviors. Following cancer diagnosis, such declines may be associated with the considerable toll cancer has on an individual's body, whether it is from the pathology of the disease, treatment regimens, or inactivity. Changes in PA may have further physiological repercussions, such as an increase in fatigue and pain, and a decrease in physical functioning (i.e., strength, muscle stiffness, joint pain, etc.) and cardiovascular fitness (Tompkins-Stricker, Drake, Hoyer, & Mock, 2004; Courneya, 2003). In fact, cancer survivors have a projected 2-fold increased risk for functional limitations compared to age-matched peers (Hewitt, Rowland, & Yancik, 2003). Coincidently, a

decline in physical functioning has been shown to instill cardiovascular and pulmonary issues, exacerbate muscle aches and joint pain, and decrease strength and flexibility (Rajotte, et al., 2012). However, regular exercise and PA may serve as a protective factor against the loss of physical functions, and various studies have exemplified improvements in physical functioning and cardiovascular fitness in cancer patients who engage in regular physical exercise (Courneya, 2003; Courneya, Mackey, et al., 2003, Forsythe, et al., 2013; Haas, 2011; Knobf, et al., 2014; Rajotte, et al., 2012). For example, following a 12-week exercise intervention study with 221 cancer survivors from different cancer diagnoses, results displayed significant improvements in systolic ($p < 0.001$) and diastolic ($p = 0.035$) blood pressure, walking endurance as measured by the 6-min walk test ($p = 0.004$), upper and lower body strength as measured by one repetition maximums ($p < 0.001$), and flexibility ($p < 0.001$) (Rajotte, et al., 2012). Improvements in resting heart rate, weight, and waist circumference were also noted; however, these values were not significant (Rajotte, et al., 2012). Therefore, PA may be a valuable intervention tool for overcoming the many obstacles related to physical functioning in both cancer patients and survivors.

Numerous individual and group-based programs are widely available to support cancer patients and survivors in curtailing the loss of physical functioning and maintaining or improving PA levels throughout the process. However, there lacks evidence-based exercise programs for cancer survivors, and the wide variation in training and program modalities often provides barriers to the validation of programs within the research.

As a means to overcome these obstacles, the LIVESTRONG® organization collaborated with numerous YMCAs nationwide to assist cancer survivors in recovery by developing their own physical fitness program. This program offers specific education and structured group

training to help reduce therapy side effects, prevent unwanted weight changes, engage in regular PA, and improve self-esteem (LIVESTRONG Foundation, n.d.). In addition, their goal is to promote a healthy lifestyle in a supportive environment and a feeling of community with fellow survivors, YMCA staff, and members (LIVESTRONG Foundation). However, there is limited research evaluating changes in physical activity during participation in the LIVESTRONG® at the YMCA program. Therefore, the purpose of this study is to examine changes in PA and SED time during participation in a post-treatment, 12-week, LIVESTRONG® at the YMCA group exercise program in Fargo, North Dakota.

While it is logical to think that PA levels will increase, higher intensity exercise has been shown to increase inflammation, oxidative stress, and free radical damage, which could increase the likelihood of the development or recurrence of cancer. However, regular moderate intensity exercise has displayed considerable benefits on disease reduction and moderating these effects. Although participants are able to be active at their own pace, because of the structure, types of training, involvement of a group trainer, and educational components of the LIVESTRONG® at the YMCA group exercise program, we hypothesized that PA would increase and SED would decrease from baseline to week 12 of the LIVESTRONG® at the YMCA group exercise program.

Materials and Methods

Participants

Approximately 86 individuals enrolled in 12 different cohorts of the LIVESTRONG® at the YMCA cancer survivor program from July 2011 until August 2014 were asked to participate in this study. The LIVESTRONG® at the YMCA program is an elective 12-week exercise and education program for cancer survivors. In order to participate in this study, participants had to

be over the age of 18, needed clearance from their physician, and were elligble for participation in the program based on the LIVESTRONG® at the YMCA criteria. Anyone outside of these standards were not eligible for participation. Participants were asked to join this study once they had signed-up for the LIVESTRONG® at the YMCA program and were in attendance on the first day of the 12-week program in each respective cohort. Only those actively participating in the program were recruited for this study and all information was provided both verbally and in the Informed Consent (see Appendix A). Their choice to participate or not in the research had no bearing on their participation in the LIVESTRONG® at the YMCA program. Approval from the Internal Review Board at North Dakota State University (see Appendix B) was obtained and data was only collected from those who chose to participate and signed the Informed Consent (see Appendix A).

Device: SenseWear® armband monitoring device

The SenseWear® armband monitoring device is an unobtrusive external monitor that allows for valid and accurate estimation of free-living energy expenditure (see Appendix C). In addition, the device can be used to quantify daily durations spent in various intensities of PA (e.g., moderate PA, vigorous PA). The SenseWear® armband monitor is worn on the upper-arm (situated on the triceps) and attached via an elastic band (see Appendix C). The monitoring device collects data via multiple sensors (e.g., triaxial accelerometer, skin thermometer, step counter, and body position sensor) and has been validated against doubly-labeled water and indirect calorimetry (e.g., two criterion standards for quantifying energy expenditure) to estimate energy expenditure (Johannsen, et al., 2010; Welk, et al., 2007).

Procedure: Physical activity

   Cohorts were divided based on the monthly start date, and individuals enrolled in each cohort were approached on the first day of the LIVESTRONG® at the YMCA program, as a group. Participants were given an introduction to the study and the SenseWear® armband monitoring device, including education of use and wear, which was conducted for all participants at the beginning of the study to ensure proper knowledge, understanding, and wear. The introduction was conducted in person by the researchers at the YMCA in Fargo, ND.

   Interested participants were asked to complete a demographics form provided by the researchers (see Appendix D). In addition, participants were advised to wear the SenseWear® armband monitoring device for seven consecutive days during week 1 of the LIVESTRONG® at the YMCA program. The device was to be worn during all activities, including work, exercise, SED activities, chores, sleeping, etc. The only time the participants were advised not to wear the armband was when showering or engaging in other water activities, such as swimming. Following the seven days (end of week 1), the monitoring devices were collected by the researcher(s) in person at the YMCA in Fargo, ND. Participants were again asked to wear the armband monitoring device for one week (seven days) at the midpoint (week 6) and endpoint (week 12) of the LIVESTRONG® at the YMCA program.

   An introduction to the armband monitoring devices, including education of use and wear, was conducted for all participants at the beginning of the study to ensure proper knowledge and wear. The introduction was conducted in person on the first day of the LIVESTRONG® at the YMCA program in Fargo, ND. The armband monitoring device was administered by the researchers at the start and end of each data collection time point at the YMCA, Fargo, ND.

<center>**Stastical Analysis**</center>

Data from the SenseWear® armband activity monitors were downloaded using the SenseWear® BodyMedia, Inc. licensed software program. Each minute of activity monitor wear time during each time point (as indicated above) was classified as sedentary (SED), light (LIT), moderate (MOD), or vigorous (VIG). Each activity level was determined based on the correlating metabolic equivalents (MET): SED activity is equivalent to a MET<1.5, LIT activity is equivalent to a MET of 1.5-2.9, MOD activity is equivalent to a MET of 3-6, and VIG is equivalent to a MET>6. SAS 9.4 was used to conduct all analyses with an alpha level set at $p<0.05$.

As indicated in the hypothesis, we predicted PA would increase and SED activity would decrease over the course of the 12 week, LIVESTRONG® at the YMCA cancer survivor, group exercise program. In order to evaluate our hypothesis, a repeated measures ANOVA using a mixed model framework was used to compare weekly time spent in SED, LIT, MOD, and VIG between weeks 1, 6, and 12 of the LIVESTRONG® at the YMCA program. A time-varying covariate was used to adjust for activity monitor wear time, thereby, adjusting for the amount of time each participant physically wore the device during each time point. A linear mixed model analysis allows the researchers to measure PA at each time point rather than assuming equal variances as in repeated measures ANOVA.

<center>**Results**</center>

Primary analysis

Forty-seven male and female cancer survivors enrolled in the LIVESTRONG® at the YMCA program volunteered to participate in this study. Only 12 completed all three time points, all of which were female, middle-aged (M = 53.08, SD = 11.01), and non-smokers. The mean

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BMI at week 1 was 29.55 (SD = 4.99), week 6 was 29.52 (SD = 4.94), and week 12 was 30.29 (SD = 5.41). Average wear time of the SenseWear® armband activity monitor was 18:16 hr:min (SD = 4:49) per day during week 1, 17:39 hr:min (SD = 4:43) per day during week 6, and 17:48 hr:min (SD = 4:37) during week 12. There were no statistically significant differences in number of days worn at each time point (p = 0.05, F = 4.48).

A repeated measures ANOVA using a mixed model framework, based on wear time (as described above), was conducted to evaluate total time engaged in PA, time engaged in each PA intensity, and total time spent SED (no sleep) at weeks 1, 6, and 12 of the LIVESTRONG® at the YMCA program. Average amount of total physical activity increased slightly from week 1 to week 6, but decreased, again, from week 6 to week 12 (see Table 2). The proportion of total wear time spent in PA at week 1 was 22 % (SD = 5), week 6 was 26% (SD = 6), and week 12 was 23% (SD = 4). There were no statistically significant changes in proportion of total PA based on wear time, over all three time points (p = 0.119, F = 1.83). Time spent in LIT, MOD, and VIG are listed in Table 2. Light activity, which accounted for 82% (SD = 6) of the PA during week 1, declined from week 1 to week 6 (78% (SD = 7) of PA), but remained fairly constant from week 6 to week 12 (79% (SD = 8) of PA). However, there were no statistically significant differences in the changes observed in the proportion of LIT PA, based on wear time, over the three time points (p = 0.152, F = 2.07).

Vigorous intensity PA individually ranged from zero to 38 minutes per week, but when averaged out to min/day per participant, the average min/day spent in VIG activity was less than or equal to one minute per day (see Table 2). Because of the minimal engagement in VIG activity at all three time points, moderate and vigorous PA were combined into one group, moderate-vigorous PA (MVPA). Moderate-vigorous PA, which accounted for 18% (SD = 6) of

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the total PA time at week 1, increased from week 1 to week 6 (22% (SD = 7) of PA), but declined slightly from week 6 to week 12 (21% (SD = 8) of PA) (see Table 2). Again, when based on wear time, there was insufficient evidence to suggest any statistically significant differences in proportion of MVPA over all three time points (p = 0.170, F = 1.94).

Total average SED time, not including sleep time (no sleep), was greatest during week 1, declined during week 6, and increased again slightly during week 12 (see Table 2). However, average SED time (no sleep) (min/day) during week 12 was still lower than average time spent SED (no sleep) (min/day) during week 1. Total average SED time (no sleep) accounted for 53% (SD = 10) of the total wear time during week 1, 52% (SD = 9) of the time during week 6, and 54% (SD = 12) of the time during week 12. Changes in proportion of time spent in SED (no sleep), based on wear time, showed statistically significant differences over all three time points (p = 0.015, F = 5.18). Following Tukey-Kramer correction, t-tests were performed to identify where these differences occurred. There was a statistically significant difference in the change in proportion of wear time engaged in SED (no sleep) activities from week 1 to week 6 (p = 0.029, t = 2.79) and from week 6 to 12 (p = 0.026, t = -2.85), but no statistically significant difference was observed from week 1 to week 12 (p = 0.999, t = 0.03).

Table 2

Summary of mean sedentary activity (no sleep), total physical activity, and each physical activity intensity per day during weeks 1, 6, and 12 for the full study participants (n=12)

	Week		
Type of Activity	1	6	12
SED activity (min/day)	557 (±127)	532 (±120)*	537 (±113)**
Total PA (min/day)	242 (±96)	255 (±94)	234 (±90)
LIT PA (min/day)	201 (±81)	197 (±69)	188 (±75)
MOD PA (min/day)	41 (±23)	56 (±30)	44 (±24)
VIG PA (min/day)	0 (±0)$^{\perp}$	1 (±2)	0 (±1)$^{\perp}$
MV PA (min/day)	41 (±0:23)	57 (±32)	45 (±24)

Note: *$p<.05$ between weeks 1 and 6 based on proportion of wear time
**$p<.05$ between weeks 6 and 12 based on proportion of wear time
$^{\perp}< 1$ minute of VIG activity per day per week

Secondary analysis

As indicated above, of the 47 cancer survivors enrolled in the 12 week, LIVESTRONG® at the YMCA group exercise program, only 12 completed all three time points. Therefore, due to the high drop out rate, the researchers further evaluated PA and SED (no sleep) levels of those who completed only week 1 of the study (group A) and of those who completed both weeks 1 and 6 (group B), and compared PA and SED (no sleep) levels of both groups at each time point to those 12 participants who completed the full study (group C). Group A (n = 15) consisted of 13 females, one smoker, and had a mean age of 55.20 years (SD = 13.85). Group B (n = 19) consisted of 15 females, one smoker, and had a mean age of 52.17 years (SD = 11.71). The average BMI for all three groups, and at all time points, was in the range of overweight (BMI range 27.83-29.55).

Group A vs. Group C. During week 1 of the study, mean wear time for group A was 19:19 hr:min (SD = 3:56) and average wear time for group C was 18:16 hr:min (SD = 4:49). The proportion of wear time spent engaged in SED (no sleep) activities was comparable between groups A and C (52-53%). Overall, group C spent the least amount of time SED (no sleep) (see Table 3), but there were no statistically significant differences in proportion of wear time spent SED (not including sleep) between groups A and C (p = 0.645, F = 0.22) during week 1.

In regards to PA, the proportion of wear time spent engaged in PA was slightly lower for group A (19% (SD = 6)) compared to group C (22% (SD = 5)). In addition, overall PA for group A was slightly lower than group C during week 1 of the study (see Table 3). However, there were no statistically significant differences in the proporiton of total PA (based on wear time) between group A and group C (p = 0.237, F = 1.47) during week 1. The majority of PA for groups A and C during week 1 was LIT PA (75% (SD = 17) and 82% (SD = 6) of PA, respectively), with group C accumulating the most LIT PA (see Table 3). However, there were no statistically significant differences in the proportion of LIT PA (based on wear time) between groups A and C (p = 0.155, F = 2.17) during week 1. Due to the minimal VIG PA for the two groups, MOD and VIG were again combined into one MVPA category. During week 1, group C had the least amount of time spent engaged in MVPA (see Table 3), but there were no statistically significant differences between groups A and C (p = 0.155, F = 2.17) for the proportion of wear time spent engaged in MVPA.

Table 3

Summary of mean sedentary activity (no sleep), total physical activity, and each physical activity intensity per day for group A (participants completing week 1 only; n = 15) and group C (full study participants; n = 12) during week 1

	Group	
Activity type	A	C
SED activity (min/day)	597 (±153)	557 (±127)
Total PA (min/day)	230 (±86)	242 (±96)
LIT PA (min/day)	176 (±73)	201 (±81)
MOD PA (min/day)	53 (±46)	41 (±23)
VIG PA (min/day)	01 (±01)	00 (±00) [⊥]
MV PA (min/day)	54 (±48)	41 (±23)

Note: [⊥] < 1 minute of VIG activity per day per week

Group B vs. Group C. The average amount of total wear time for group B was 18:52 hr:min (SD = 2:44) compared to 18:16 hr:min (SD = 4:49) for group C during week 1, and 18:35 hr:min (SD = 3:46) for Group B and 17:39 hr:min (SD = 4:43) for Group C during week 6. Most of the wear time for both groups and at each time point (week 1 and week 6) was spent engaged in SED activities (52-53%), not including sleep time. Group C noted a greater drop in total average SED time (no sleep) from week 1 to week 6 compare to Group B (see Table 4); however, there were no statistically significant differences in proportion of SED time (no sleep), based on wear time, between the two groups (p = 0.42, F = 0.67) or between weeks (p = 0.247, F = 1.40). Nor was there enough evidence suggesting a statistically significant interaction effect (group x week) (p = 0.228, F = 1.53).

Total PA during week 1 was comparable between the two groups (see Table 4), accounting for 22% of the total wear time in both groups B and C (SD = 0.10 and SD = 0.05, respectively). During week 6, the proportion of wear time engaged in PA increased slightly for Group C (26% (SD = 6)), but remained relatively consistent for Group B (22% (SD = 8)). In addition, group C spent more total time engaged in PA during week 6 compared to group B (see Table 4), but there were no statistically significant differences in the proportion of total PA, based on wear time, between the two groups (p = 0.54, F = 0.39) or between weeks (p = 0.3861, F = 0.78). In addition, there was no statisticaly significant difference in the interaction effect (group x week) (p = 0.33, F = 0.98). Both groups spent the majority of their PA time engaged in LIT activities during weeks 1 and 6 (see Table 4), but there were no statistically significant differences in the proportion of LIT PA (based on wear time) between the two groups (p = 0.731, F = 0.12), between weeks 1 and 6 (p = 0.164, F = 2.05), or with the interaction effect (p = 0.552, F = 0.36). Similar to above, MOD and VIG activity were combined into one MVPA group. Total MVPA for Group C was lower than Group B during week 1, but total MVPA was comparable between the two groups during week 6 (see Table 4). Nonetheless, there is insufficient evidence to suggest any statistically significant differences in the proportion of wear time spent engaged in MVPA between groups B and C (p = 0.730, F = 0.12), between weeks 1 and 6 (p = 0.164, F = 2.05), or with the interaction effect (group x week) (p = 0.552, F = 0.36).

Table 4

Summary of mean sedentary activity (no sleep), total physical activity, and each physical activity intensity per day for group B (participants completing weeks 1 and 6 only; n = 19) and group C (full study participants; n = 12) during weeks 1 and 6

	Group			
	B		C	
Activity type	Week 1	Week 6	Week 1	Week 6
SED activity (min/day)	578 (±149)	575 (±128)	557 (±127)	532 (±120)
Total PA (min/day)	241 (±86)	239 (±95)	242 (±96)	255 (±94)
LIT PA (min/day)	184 (±51)	183 (±63)	201 (±81)	197 (±69)
MOD PA (min/day)	56 (±43)	55 (±40)	41 (±23)	56 (±30)
VIG PA (min/day)	00 (±01)[⊥]	01 (±01)	00 (±00)[⊥]	01 (±02)
MV PA (min/day)	56 (±44)	56 (±42)	41 (±23)	57 (±32)

Note: [⊥]< 1 minute of VIG activity per day per week

Discussion

Cancer is a debilitating disease associated with an increase in physical and functional limitations, often related to a decrease in PA. In fact, a national cross sectional survey appraising PA levels in over 9000 participants across six major cancer survivor groups revealed that only 30-47% of cancer survivors were meeting the ACSM PA recommendations (Blanchard, et al., 2008). Nonetheless, regular PA has shown improvement in multiple factors, including enhanced physical fitness, self-esteem, stress response, and social functioning, as well as a decreased risk of heart disease and cancer (Knobf, et al., 2007). Although many variables exist among treatment modalities and outcomes, current research demonstrates significant, post-treatment benefits of exercise indicating that physical activity may be a suitable intervention for cancer survivors. The

purpose of this study was to examine changes in overall PA and SED time during participation in a post-treatment, 12-week, LIVESTRONG® at the YMCA group exercise program. Researchers hypothesized that total PA would increase, and SED activity would decrease over the 12-week program.

The majority of wear time was spent engaged in SED activities, not including sleep time, (52-54% per day) each week, and accounted for more than eight hr/day of SED activity (not including sleep) each week. These results are comparable to data reported in the 2007-2010 NHANES study, which indicated cancer survivors were more likely to spend more than eight hours a day engaged in SED activities, even if they met the recommended guidelines for PA (Kim, et al., 2013). These results pose concern considering the well-documented impact sedentary lifestyles can have on health and disease risk, particularly among cancer patients and survivors. Cancer diagnosis, pathology, treatment, and post-treatment often have a major influence on ability and willingness to participate in regular PA. Declines in PA, offset by increases in SED activity, may have further physiological repurcussions by not only increasing physical and functional limitations, but also increasing the risk for cancer recurrence and/or development of other chronic diseases (Hewitt, et al., 2003; Tompkins-Stricker, et al., 2004; Courneya, 2003).

Although the average SED time (no sleep) in this study was more than eight hr/day on each time point, these results were lower than the average SED time per day in a study of 145 post-treatment colorectal cancer survivors who averaged 10.2 hr/day of SED activity (van Roekel, et al., 2016). Furthermore, the fact that the proportion of wear time spent in SED activities (no sleep) significantly declined from weeks 1 to 6, and, although it increased significantly from week 6 to week 12, average SED time was lower at week 12 compared to

week 1, is promising. In addition, participants averaged almost four hours of total PA each day, with most of the time spent doing light activity. Exhaustive exercise or unaccustomed high intensity training has been shown to negatively affect immune function and cancer development, therefore, the fact that participants engaged in minimal VIG PA may be beneficial (Banerjee, et al., 2003; Poulsen, et al., 1996; Shephard & Shek, 1999). Furthermore, length of PA at one time, regardless of intensity, varied from short to long bouts throughout the day, which suggests regular breaks in SED time (no sleep). This is encouraging as intermittent PA spread throughout the day has shown to improve metabolic risk factors, decrease chronic disease risk, increase the likelihood of meeting the ACSM guidelines, and improve health (Healy, Dunstan, Salmon, Shaw, et al., 2008; Loprinzi & Cardinal, 2013).

Although there were no statistically significant changes in proportion of wear time spent engaged in PA over the three time points, overall PA levels of the participants was relatively high. Generally, participants averaged almost four hours of PA each day. Even though most of the time spent engaged in PA was light intensity, the average amount of MOD activity each day was over 40 minutes a day. Therefore, participants well exceeded the ACSM minimum recommendation of 150 minutes per week of moderate intensity activity (Garber, et al., 2011). Overall, 8-9 participants in this study met the minimum weekly PA guidelines, which coincides with the 71% of participants in the LIVESTRONG at the YMCA program in Connecticut and Massachusetts who reported at least 150 minutes of exercise per week (Irwin, et al., 2016). However, two of the participants who averaged over four hours of MVPA during weeks 1 and 12 only had 2 days of data for week 6, which could have affected the results of this study. Regardless, these results are similar to a 12-month study that examined exercise participation in breast cancer survivors following treatment, which identified 35% of the participants not meeting

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the recommended PA guidelines (Pinto, et al., 2002). In contrast, another study indicated only 58% of breast and prostate cancer survivors regularly engaged in routine PA (Demark-Wahnefried, et al., 2000). However, 80% of these participants indicated a need for health promotion programs, such as exercise, during and post treatment (Demark-Wahnefried, et al., 2000). Therefore, more research is needed to validate individual and group exercise programs to further meet the needs, wants, and goals of cancer patients and survivors.

Limitations

Although there was minimal evidence to suggest statistically significant differences in changes in PA and SED activity (not including sleep) over all three time points, there were some limitations that may have contributed to these results. For example, the drop-out rate was considerably high among the 12 cohorts of the LIVESTRONG® at the YMCA program studied between July 2011 and August 2014. Although this was not assessed directly, the researchers conducted some further analysis between Groups A, B, and C to try and draw some conclusions. Overall, there was insufficient evidence to suggest statistically significant differences between SED time (no sleep), total PA, LIT PA, or MVPA across all three groups. However, group C did have less SED time (no sleep) compared to both group A and group B at each time point assessed, and total SED time (no sleep) for group C dropped by an average of 25 minutes per day. Furthermore, SED time (no sleep) for group B remained relatively consistent from week 1 to week 6. However, In addition, group C had considerably less MVPA (although insignificant) than both groups A and B during week 1, which may indicate overexertion and increased the burnout of the participants in Groups A and B following the first week. Although there is no clear indication for the high drop-out rate, additional contributing factors, such as an unstable population, strenuousness of the program, cancer recurrence, type of cancer, lack of social

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support, poor self esteem, time frame of diagnosis and treatment, or other personal reasons, should be considered.

In addition to the high drop-out rate, two additional limitations reside. First, this study lacked a control group. Secondly, aside from using the first week of the LIVESTRONG® at the YMCA program, there lacked a true baseline comparison. Since participants of the program were not required to pre-register (although it was recommended), obtaining a true baseline assessment of PA was difficult to acquire. This draws concern for a number of reasons. One, without knowing the PA levels prior to enrolling in the LIVESTRONG® at the YMCA program it is difficult to identify the true impact the program may have had on the participants' PA levels. Secondly, depending on their activity levels prior to diagnosis, during treatment, and varying time frame for enrolling in the LIVESTRONG® at the YMCA program, their overall view on the importance or intensity of PA could play a role in their PA levels during participation in the program.

Conclusion

Various studies, as mentioned above, indicate physical activity is an important component in everyone's health, including cancer patients and survivors. It aids in overall physical functioning, responses to stress, adaptation strategies, and improved health and overall quality of life. In addition, prolonged SED time has also been associated with an increased risk of disease, including heart disease and cancer. The fact that the participants in this study met the minimum recommendations set forth by the ACSM at each time point is promising. In addition, although a little more than 50% of the total wear time was spent sedentary (not including sleep), researchers noted a slight decrease in SED time (no sleep) from week 1 to week 12, with statistically significant changes from week 1 to week 6, and week 6 to week 12. Furthermore, PA

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varied between short and long bouts, which suggests regular breaks in SED time throughout the day. Although there is no clear understanding explaining the high drop-out rate, current results leave many questions relative to the true impact participation in the LIVESTRONG® at the YMCA group exercise program may have. Therefore, additional research is needed to 1) better understand the relationship between cancer survivors and their perception of PA; 2) identify the relationship between cancer survivors and their PA capabilities; and 3) further validate the structure and education of the LIVESTRONG® at the YMCA group exercise program.

CHAPTER 5. CHANGES IN QUALITY OF LIFE OF CANCER SURVIVORS PARTICIPATING IN A GROUP EXERCISE PROGRAM

Introduction

Well-being refers to one's physical, psychological, and social satisfaction, associated with complete life satisfaction and the emotional responses therein (Diener, Suh, Lucas & Smith, 1999). Evaluating an individual's judgment of their global well-being is often reflected in the term quality of life (QOL). Quality of life is defined as a multidimensional concept including physical, psychological, social, and spiritual well-being (Knobf, et al., 2007; Rummans, et al., 2000). In addition, QOL represents an individual's subjective perspective, and when it comes to participation in physical activity (PA) and disease-free, overall survival, QOL is a significant outcome (Knobf, et al., 2007).

It is well known that during the course of cancer diagnosis, treatment, and follow-up, cancer patients and survivors are likely to experience a variety of physical, psychological/emotional, and social difficulties. Numerous studies suggest that exercise interventions in cancer survivors are generally associated with a positive increase in overall QOL (Courneya, Mackey, et al., 2003; Hayes, et al., 2011; Knobf, et al., 2007; Korstjens, et al., 2006; Mendelbatt, et al., 2011; Schwartz, 2004). As indicated by Knobf, et al. (2007) cross-sectional retrospective studies involving men and women from a variety of cancer backgrounds, those who exercised reported better QOL than those who did not engage in routine exercise. Furthermore, in a study conducted by Mandelbatt, at al. (2011), researchers found that individuals with breast cancer who reported the highest levels of moderate and vigorous PA also had the highest QOL. Although most studies have shown a direct correlation between PA and QOL, some studies have not reported improved QOL associated with exercise. Pinto, et al. (2002) found no improvement

in overall mood or cancer-related symptoms over the course of a 12-month, longitudinal observational study. Although the literature relating PA behaviors to QOL is inconclusive, evaluating the association between PA engagement and the multidimensional concept of QOL is key (Knobf, et al., 2007).

Physical QOL

Assessing the multidimensional components of QOL generally involves three core domains: physical/functional, psychological, and social. The physical aspect of PA and its relationship to QOL is highly impacted by the level of fatigue, pain, side effects of treatment, fulfilling duties, and subjective physical conditioning. As a chronic disease, cancer patients and survivors often suffer not only from fatigue and pain, but overall physical functioning can be highly impacted. In fact, cancer survivors have a projected 2-fold increased risk for functional limitations compared to age-matched peers (Hewitt, Rowland, & Yancik, 2003). When evaluating physical functioning in the realm of QOL, it is often related to muscle aches and joint pain, physical limitations when engaging in daily activities, and lack of energy (FACT-G, Rajotte, et al., 2012). In a study examining 26 breast cancer participants participating in a 4-6 month community-based exercise program showed improvements in musculoskeletal symptoms, such as aches, joint pain, and muscle stiffness; however, muscle stiffness was the only symptom to significantly decrease over time ($p = 0.04$) (Knobf, et al., 2014). These results are consistent with other exercise interventions that have shown additional physiologic improvements, including immune function, systolic and diastolic blood pressure, peak oxygen consumption, upper and lower body strength, walking endurance and flexibility (Courneya, 2003; Courneya, Mackey, et al. 2003; Rajotte, et al., 2012). Overall, improvements in physiological well-being appear substantial for cancer survivors engaged in routine physical activity.

Psychological QOL

Psychological, or emotional, distress is one of the most common results of the diagnosis and treatment of cancer and is often characterized by uncertainty, vulnerability, loss of control and existential concerns (Knobf, et al., 2007). Psychological responses associated with these factors include depression, anxiety, death anxiety, worry about health problems, perceived risk of recurrence, or decision regrets (Simard, et al., 2013). Depression and anxiety are highly prevalent in cancer patients and survivors, and are the two more commonly assessed psychological factors in PA-related studies and cancer patients and survivors (Knobf, et al., 2007). The prevalence of depression among cancer patients and survivors ranges dramatically, anywhere from 1.5-57% (Massie, 2004). In addition, Stark, et al. (2002) estimates the number of cancer patients and survivors experiencing anxiety to range from 20% to 50%. Nonetheless, such variations in the prevalence of any type of psychological disorder may relate to varying conceptualizations of the disorder, differing criteria for assessment, different populations studied, and type of cancer diagnosis (Massie, 2004).

Although these statistics may appear rather high, there is growing evidence suggesting exercise interventions may decrease anxiety and lower levels of depressive symptoms and/or depression. In a study of 91 cancer patients engaged in a six-week, multidimensional exercise program, both anxiety (-1.14 ±2.91, P < 0.001) and depression (-0.44 ±2.77, P = 0.042) were significantly reduced (Midtgaard, et al., 2005). Similar findings were found in a study conducted by Badger, et al. (2007) following a six-week self-managed exercise program. Moreover, research suggests exercise interventions may have a positive impact on the psychological distress many cancer patients often experience.

Social QOL

Not only can cancer have an impact on an individual physically and psychologically, but their overall social functioning can be greatly affected. The social domain of overall QOL is often related to social support, social well-being and/or role performance. Social support, specifically, reflects one's perceived comfort, care, assistance and esteem one receives from others (Wallston, 1983). In regards to cancer survivorship, Hodges and Winstanley (2012) suggested that optimism and social support may directly or indirectly contribute to levels of positive affect. In a study of over 100 cancer survivors, positive affect was positively correlated with both optimism ($r = 0.63$, $p < 0.001$) and social support ($r = 0.45$, $p < 0.001$), with optimism also displaying a positive correlation with social support ($r = 0.38$, $p < 0.001$) (Hodges & Winstanley, 2012). This is consistent with other studies that suggest perceptions of social support during and immediately post cancer treatment show a positive association with well-being and expectations of future social support to predict overall levels of well-being (Sarason, Pierce, & Sarason, 1990; Shelby, et al., 2008). Hence, optimism at the start, during, and post cancer treatment, may have a significant impact on perceived and actual social support, both of which contribute to overall well-being and QOL.

Although social support appears to play a key role in QOL and well-being, added physical and psychological stresses may have a negative impact on social support throughout diagnosis, treatment, and post-treatment of cancer patients and survivors. Mayfield (1999) qualitatively evaluated this idea in a sample of seven female cancer patients selected from a community-based support group and suggested that social support may actually decrease for cancer survivors, particularly when it comes to support from physicians and health care staff. In fact, one subject stated, "Once treatment is over, you have no one to talk to" (Mayfield, 1999, p.

30). In addition, Polinsky (1994) examined the role of social support in a study of 223 breast cancer survivors and, although fewer than 5% of the respondents reported changes in their social activities, 64% of the respondents indicated the need to discuss concerns about breast cancer, with 8% reporting they had no one to talk to. While 8% seems low in reporting such concerns, 73% of the cancer survivors thought their spouse or significant other understood what they were going through well or very well, 57% thought their family members understood well or very well, and only 45% thought their friends understood well or very well (Polinsky, 1994). However, group exercise programs may offer a positive alternative to enhancing social well-being. For example, Knobf, et al. (2014) found significant improvements in social functioning (p = 0.009) following a 4-6 month community based exercise intervention program with 26 breast cancer survivors. Therefore, social support, communication, and level of understanding among cancer survivors and those involved could be enhanced by participation in cancer support groups like group exercise programs.

Assessing QOL

Relatively little research has given attention to the chronic stressors and long-term implications of QOL on cancer survivors. In a study of 335 young adult cancer survivors, Yanez, Garcia, Victorson and Salsman (2013) found that the most physical, psychological, social and functional distress occurred 13-24 months post-treatment. Furthermore, psychosocial well-being and physical functioning ability have added to the overall indication of QOL (Knobf, et al., 2007). Therefore, it has become increasingly common for QOL to be used when evaluating all aspects of treatment (before, during, and after) for cancer patients, particularly with participation in group exercise programs. Furthermore, measuring QOL during and after treatment can help

the clinician and other medical personnel with weighing the benefits of treatment and interventions compared to any side effects, whether they be physical, emotional, or psychosocial.

Multiple instruments are available for measuring an individual's QOL; however, understanding what the instruments measure is critical to interpreting the overall findings. Instruments vary in conceptualization and key domains (physical, psychological or social) are either left out or combined as subscales, thereby, limiting the constructs of well-being and/or function (Knobf, et al., 2007). One of the most common instruments for measuring QOL among cancer patients and survivors is the Functional Assessment for Cancer Therapy – General (FACT-G). The FACT-G is a 27-item instrument generalized for all forms of cancers and is divided into four well-being subscales: physical, social/family, emotional, and functional (Tamburini, 2001; Victorson, et al., 2008). Currently, the FACT-G uses a 5-point Likert-type scale (0-4) with a seven-day recall period (Victorson, et al., 2008). Following the completion of the FACT-G, all subscales are summed together, with a higher score indicating better quality of life (Victorson, et al., 2008). Several (about 20) subscales of the FACT-G have been constructed to address relevant disease-, treatment-, or condition-related issues (Tamburini, 2001). Each subscale consists of the core FACT-G items with a specific scale relating to a particular type of cancer (e.g., breast, prostate, etc.), treatment (e.g., chemotherapy, radiation, etc.), and/or other QOL domains (e.g., fatigue, spirituality, etc.) (Victorson, et al., 2008). Overall, the FACT-G can be used with patients and survivors with any form of cancer.

Research investigating changes in QOL is still limited. While it is logical to think participation in an exercise program would lead to improvement in QOL, various factors, such as self-esteem, energy level, PA rigor, the type of program, whether individual or group-based, and training modalities can all play a role. To try and regulate some of these factors, the

LIVESTRONG® organization has partnered with numerous YMCAs nationwide as a means to assist cancer survivors in recovery by developing their own physical fitness program to reduce therapy side effects, prevent unwanted weight changes, and improve self-esteem (LIVESTRONG Foundation, 2015). In addition, their goal is to promote a healthy lifestyle in a supportive environment and a feeling of community with fellow survivors, YMCA staff, and members (LIVESTRONG Foundation, 2015). The problem resides in limited research evaluating changes in QOL while participating in the 12-week program and little to no access to evidence-based exercise programs and their impact on QOL among cancer survivors. Therefore, the purpose of this study was to evaluate changes in QOL at the end of week 1, week 6, and week 12 of those cancer survivors enrolled in the 12-week LIVESTRONG® at the YMCA group-exercise program. In addition, we hypothesized that the QOL of cancer survivors participating in the 12-week in the LIVESTRONG® at the YMCA exercise program would increase from baseline (week 1) to week 6, and again improve from week 6 to week 12.

Materials and Methods

Participants

Approximately 86 individuals registered between 12 different cohorts of the LIVESTRONG® at the YMCA cancer survivor program in Fargo, North Dakota from July 2011 until August 2014 were recruited to participate in this study. The LIVESTRONG® at the YMCA program is an elective 12-week exercise and education program for cancer survivors. Eligible participants had to be over the age of 18 and needed clearance from their physician, which was obtained by those leading the LIVESTRONG® at the YMCA cancer survivor program. Anyone outside of these criteria were not qualified for participation in this study. Only those in attendance on the first day of each 12-week LIVESTRONG® at the YMCA cohort were

asked to join this study. Only those actively participating in the program were recruited for this study and all information was provided both verbally and in the Informed Consent (see Appendix A). Participation in this study had no impact on their involvement in the LIVESTRONG® at the YMCA program. Approval from the Internal Review Board at North Dakota State University (see Appendix B) was attained and data was only collected from those who signed the Informed Consent.

Procedure

Participants were grouped into cohorts based on their monthly start date. On the first day of each LIVESTRONG® at the YMCA cohort, all individuals were approached as a group and asked to participate in this study. All participants were given an introduction to the study, asked to complete a demographics form (see Appendix D) provided by the researchers, and verbally given an explanation of the FACT-G (see Appendix E) as a means to assess their QOL. The FACT-G is a validated quality of life instrument intended for use with a general cancer population, and is composed of four components: physical well-being (PWB; 7 items, score range 0-28), social/family well-being (SWB; 7 items, score range 0-28), emotional well-being (EWB; 6 items, score range 0-24), and functional well-being (FWB; 7 items, score range 0-28). It is a self-administered questionnaire, and all 27 questions in the FACT-G are answered based on a 5-point likert scale (0 = Not at all; 1 = A little bit; 2 = Somewhat; 3 = Quite a bit; 4 = Very Much). Items that are negatively worded are reversed scored to ensure a higher score is equivalent to higher overall QOL. Each subscale is totalled individually, and the total FACT-G score (27 items, score range 0-108) is the sum total of all four subscales. The initial introduction to the study was conducted in person by the researchers at the YMCA in Fargo, North Dakota.

The QOL of participants in each cohort was assessed, using the FACT-G, at three

different time points: week 1, week 6, and week 12. On the last day of week 1 of participation in

the LIVESTRONG® at the YMCA, the FACT-G was administered to, and completed by, all

active participants. The FACT-G was again administered at the end of week 6 and the end of

week 12. This same protocol was followed for each cohort of the LIVESTRONG® at the YMCA

group exercise program.

An introduction to the FACT-G questionnaire was conducted by the researcher(s) for all

participants at the beginning of the study to ensure proper knowledge and understanding of the

questionnaire. The FACT-G questionnaire was administered by the researchers at the end of each

data collection time point (as indicated above).

Stastical Analysis

Quality of life measures were hypothesized to improve over the course of the 12 week,

LIVESTRONG® at the YMCA cancer survivor group exercise program. Scoring the FACT-G

followed all guidelines provided by the Functional Assessment of Chronic Illness Therapy

(FACIT) Measurement System and FACIT.org, which manages the distribution, administering,

scoring, and interpretation of the FACT-G (facit.org). Only the FACT-G questionnaires with an

overall item response rate of greater than 80% were considered for analysis. A repeated measures

ANOVA using a mixed model framework was used to determine significance across the three

time points for total FACT-G, and for each subscale. If a significant difference was determined, a

post-hoc paired t-test was conducted to examine significant differences between weeks 1, 6, and

12. A Tukey-Kramer correction, based on the number of t-tests performed, was administered to

hold the alpha level at $p < .05$. SAS version 9.4 was used for conducting all analyses.

Results

Primary analysis

Overall, 37 male and female cancer survivors enrolled in 12 different cohorts of the

LIVESTRONG® at the YMCA program between June 2011 and August 2014 participated in

this study. However, only 11 participants completed the FACT-G QOL questionnaire on all three

time points, all of which were female, middle-aged (M = 53.08 (SD = 11.01)), and non-smokers.

As indicated above, the FACT-G is composed of four components, including physical,

social/family, emotional, and functional well-being. The total overall score is 0-108, with a

higher score indicating better overall QOL. Three subscales, PWB, SWB, and FWB, have an

individual score range of 0-28, with a higher value indicating better QOL within each specific

area. The score range for EWB is 0-24, again, with a higher score equating to better emotional

QOL.

A repeated measures ANOVA using a mixed model framework was used to evaluate

changes in overall QOL (total FACT-G score) and QOL for each subscale. Results indicated a

slight improvement in total FACT-G score from week 1 to week 6, but a slight decrease from

week 6 to week 12 (see Table 5); however these changes were not statistically significant (p =

0.389, F = 1.00). Distribution of the total FACT-G scores are displayed in Figure 1. Similar

results were observed in PWB, SWB, EWB, and FWB subscales, which displayed a slight

improvement in QOL scores from week 1 to week 6, and a slight decrease in QOL within each

subscale from week 6 to week 12 (see Table 5). Although QOL scores for PWB, SWB, and

EWB decreased slightly from week 6 to week 12, the scores at the end of week 12 were still

somewhat higher than at the end of week 1. FWB was the only subscale to have a lower score at

week 12 compared to week 1 (see Table 5). There were no statistically significant changes in

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three of the four subscales: SWB (p = 0.916, F = 0.09), EWB (p = 0.345, F = 1.14), or FWB (p = 0.679, F = 0.40) at all three time points. PWB was the only subscale to show statistically significant changes over the three time points (p = 0.02, F = 5.09). Using Tukey-Kramer correction, t-tests were performed to identify significant differences between each time point. Changes in PWB between weeks 1 and 6 were statistically significant (p = 0.017, t = -3.14), but there was insufficient evidence to suggest any statistically significant differences between weeks 1 and 12 (p = 0.131, t = -2.05) or weeks 6 and 12 (p = 0.514, t = 0.28). Distributions for all four subscales are displayed in Figures 2 through 5.

Table 5

Mean Quality of Life (QOL) scores for total FACT-G and for all four subscales (physical well-being (PWB), social well-being (SWB), emotional well-being (EWB), and functional well-being (FWB) during weeks 1, 6, and 12 for the full study participants (n = 11)

	QOL scores				
Week	Fact-G	PWB	SWB	EWB	FWB
1	82.65 (±8.84)	20.64 (±2.80)	23.02 (±5.80)	19.45 (±3.24)	19.55 (±2.46)
6	88.73 (±10.74)	23.60 (±2.46)*	24.00 (±4.67)	20.46 (±3.70)	20.67 (±3.39)
12	85.38 (±14.09)	22.82 (±4.94)	23.66 (±3.50)	19.64 (±4.15)	19.27 (±3.61)

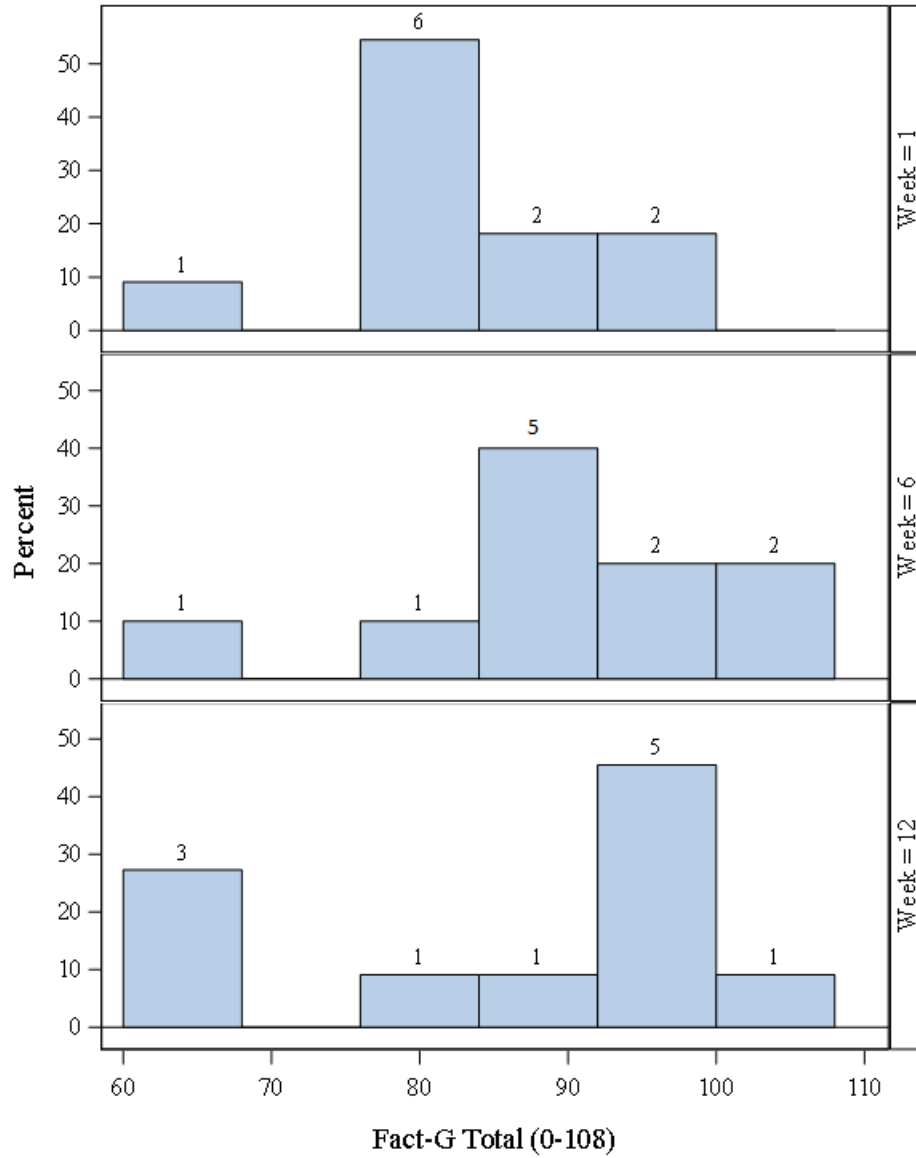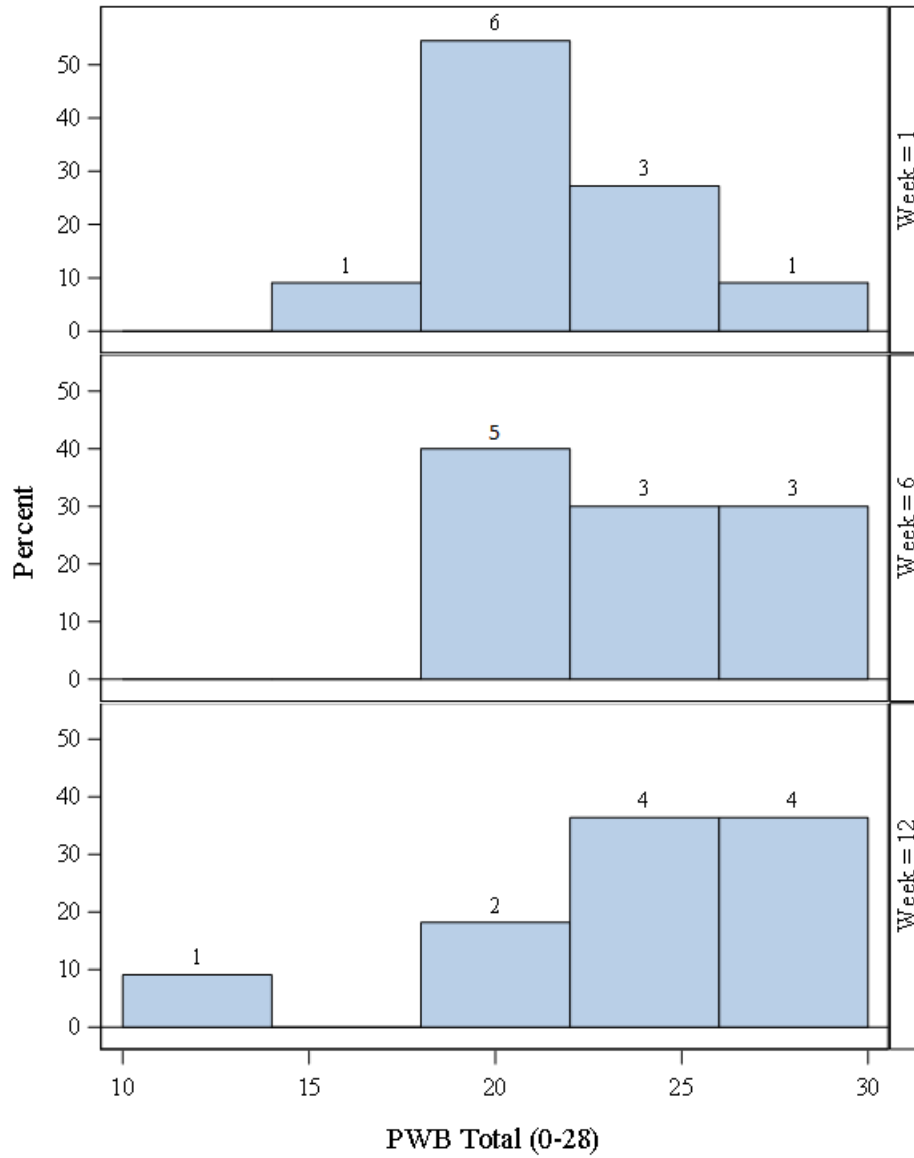Note: *p < .05 between week 1 and week 6

Figure 1. Distribution of FACT-G total scores for weeks 1, 6, and 12 for the full study participants (n = 11)

Figure 2. Distribution of physical well-being (PWB) scores for weeks 1, 6, and 12 for the full study participants (n = 11)
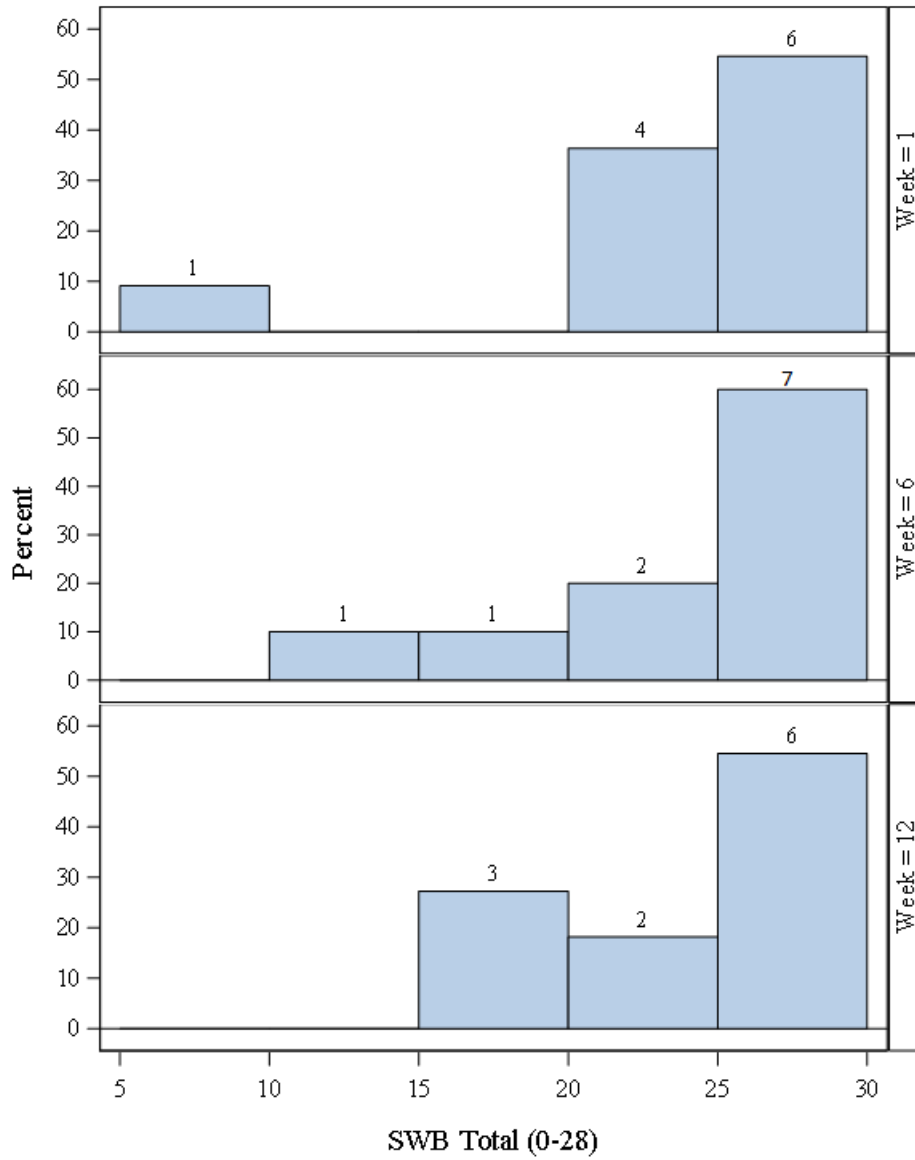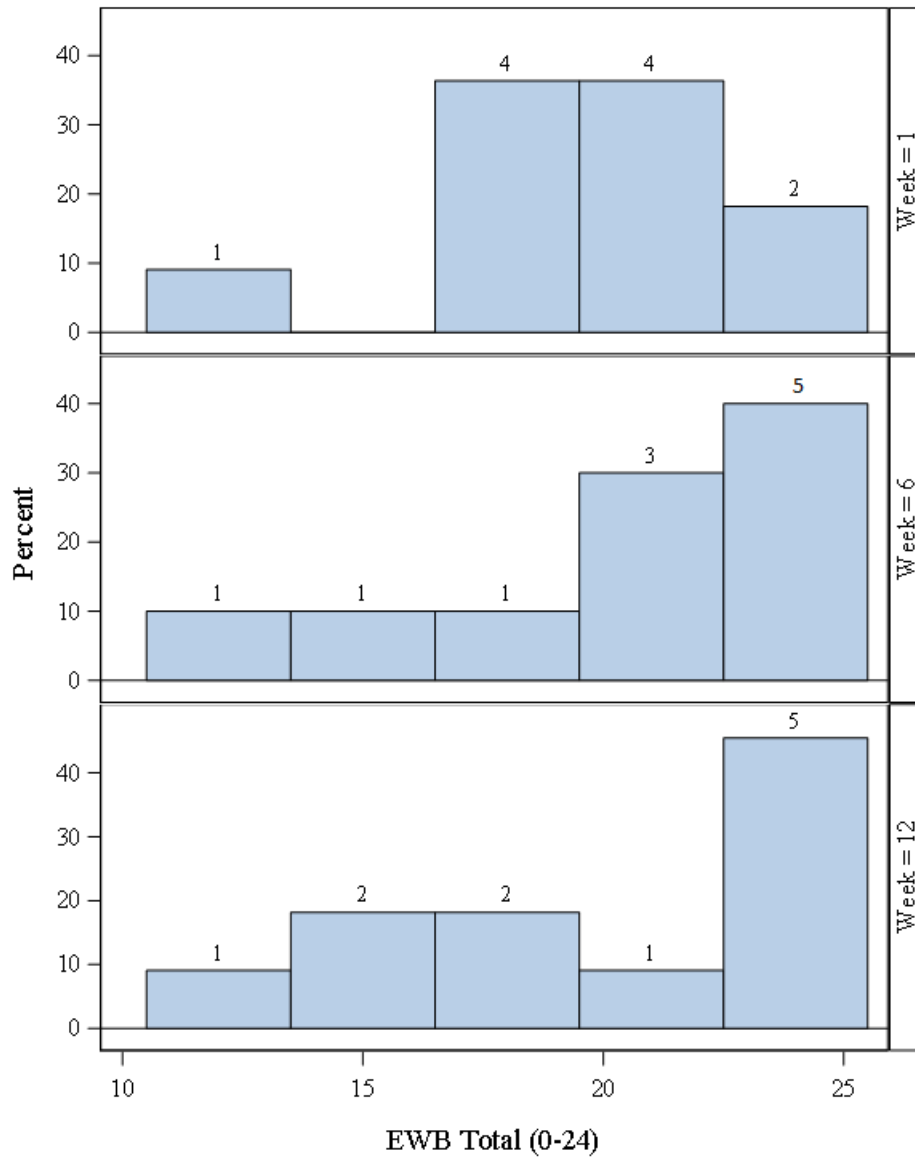
Figure 3. Distribution of social well-being (SWB) scores for weeks 1, 6, and 12 for the full study participants (n =11)

Figure 4. Distribution of emotional well-being (EWB) scores for weeks 1, 6, and 12 for the full study participants (n = 11)
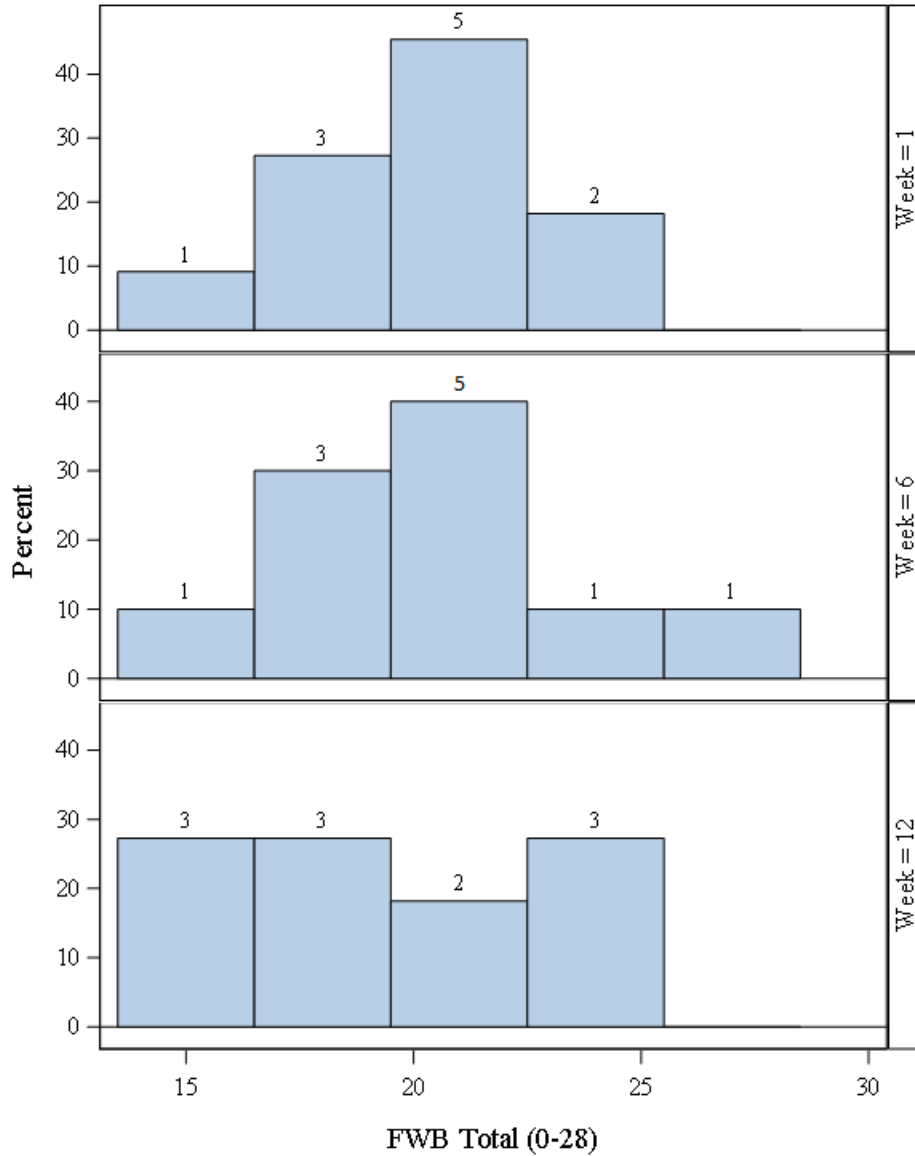
Figure 5. Distribution of functional well-being (FWB) scores for weeks 1, 6, and 12 for the full study participants (n = 11)

Secondary analysis

As indicated above, of the 37 cancer survivors enrolled in 12 different cohorts of the 12 week, LIVESTRONG® at the YMCA group exercise program, only 11 completed all three time points. Because of the high drop out rate, the researchers further evaluated QOL (total FACT-G score and scores of each subscale) of those completing only week 1 of the study (Group A) and

of those who completed both weeks 1 and 6 (Group B) of the study. The QOL results (total FACT-G score and each subscale score) from both Group A and Group B were each compared to the QOL scores of the 11 participants who completed the full study (Group C). A repeated measures ANOVA using a mixed model framework was used to evaluate changes in overall QOL (total FACT-G score) and QOL for each subscale between Groups A and C, and between Groups B and C. Group A (n = 7) consisted of 13 females, one smoker, and had a mean age of 55.20 years (SD = 13.85). Group B (n = 12) consisted of 15 females, one smoker, and had a mean age of 52.17 years (SD = 11.71). The average BMI for all three groups, and at all three time points, was in the range of overweight (BMI range 27.83-29.55).

Group A vs. Group C. The total FACT-G score for Group A was a little lower than Group C at the end of week 1 (see Table 6), but there was no statistically significant difference between the two groups (p = 0.53, F = 0.41). Physical well-being and FWB were both higher in Group A compared to Group C at the end of week 1 (see Table 6), but again, there were no statistically significant differences between the two groups (p = 0.592, F = 0.30 and p = 0.75, F = 0.11, respectively). Emotional well-being was comparable between the two groups at the end of week 1, with no statistical difference (p = 0.873, F = 0.03). Social well-being was quite a bit lower at the end of week 1 for Group A compared to Group C; however, there was not enough evidence to suggest a statistically significant difference between the two groups (0.236, F = 1.53).

Table 6

Summary of mean Quality of Life (QOL) scores for total FACT-G and each of the subscales for well-being (physical, social, emotional, and functional) for group A (participants completing week 1 only; n = 7) and group C (full study participants; n = 11) following week 1

	Group	
QOL score	A	C
Total FACT-G	79.95 ($\pm$14.64)	82.65 ($\pm$8.84)
Physical well-being	21.88 ($\pm$3.77)	20.64 ($\pm$2.80)
Social well-being	18.36 ($\pm$9.12)	23.02 ($\pm$5.80)
Emotional well-being	19.43 ($\pm$2.76)	19.45 ($\pm$3.24)
Functional well-being	20.29 ($\pm$4.07)	19.55 ($\pm$2.46)

Group B vs. Group C. Total mean FACT-G score for Group B was higher than Group C at the end of week 1, and although mean scores for both groups increased from week 1 to week 6, the mean FACT-G score for Group B was slightly lower than Group C at the end of week 6 (see Table 7). However, there were no statistically significant differences between groups ($p = 0.573$, $F = 0.33$), between weeks ($p = 0.146$, $F = 2.32$), or with the interaction effect (group x week) ($p = 0.57$, $F = 0.34$). Physical well-being increased for both Group B and Group C from week 1 to week 6, but PWB was higher for Group B compared to Group C at the end of both week 1 and week 6. When holding all other variables constant, results showed a statistically significant difference in weeks ($p = 0.002$, $F = 14.07$), but there were no statistically significant difference between groups ($p = 0.111$, $F = 2.76$) or in the interaction effect (group x week) ($p = 0.493$, $F = 0.49$). The mean score for SWB was a little higher for Group B compared to Group C at the end of week 1, but was comparable between the two groups at the end of week 6 (see

Table 7). However, the mean score for SWB decreased slightly from week 1 to week 6 for Group B, but increased slightly from week 1 to week 6 for Group C (see Table 7). Nonetheless, there were no statistically significant differences between groups ($p = 0.622$, $F = 0.25$), between weeks ($p = 0.964$, $F = 0.00$), or in the interaction effect (group x week) ($p = 0.895$, $F = 0.02$). The mean scores for EWB were comparable between Groups B and C at the end of week 1 (see Table 7). From week 1 to week 6, EWB for Group B decreased slightly, whereas EWB scores for Group C increased slightly (see Table 7). Although changes were observed in opposing directions, there was insufficient evidence to suggest any statistical significance between groups ($p = 0.467$, $F = 0.55$), between weeks (0.517, $F = 0.44$), or in the interaction effect (group x week) ($p = 0.11$, $F = 2.84$). The mean scores for FWB for Group B was slightly lower at the end of week 1 compared to Group C, and although scores for both groups increased from week 1 to week 6, the mean score for FWB was higher at the end of week 6 for Group B compared to Group C. Nevertheless, there were no statistically significant differences between groups (0.828, $F = 0.05$), between weeks (0.088, $F = 3.27$), or in the interaction effect (group x week) ($p = 0.71$, $F = 0.14$).

Table 7

Summary of mean Quality of Life (QOL) scores for total FACT-G and each of the subscales for well-being (physical, social, emotional, and functional) for group B (participants completing week 1 and week 6 only; n = 12) and group C (full study participants; n = 11) following weeks 1 and 6

	Week			
	1		6*	
QOL score	Group B	Group C	Group B	Group C
Total FACT-G	86.08 (±11.88)	82.65 (±8.84)	88.24 (±8.10)	88.73 (±10.74)
Physical well-being	23.08 (±4.03)	20.64 (±2.80)	25.00 (±1.60)	23.60 (±2.46)
Social well-being	24.03 (±4.87)	23.02 (±5.80)	23.99 (±3.15)	24.00 (±4.67)
Emotional well-being	19.47 (±3.32)	19.45 (±3.24)	18.00 (±3.98)	20.46 (±3.70)
Functional well-being	19.50 (±5.18)	19.55 (±2.46)	21.25 (±03.72)	20.67 (±3.39)

Note: *p<.05 between week 1 and week 6 only

Discussion

Perceived QOL plays a significant role in life satisfaction, engagement in physical activity, and physical, psychological, emotional, and social well-being. Although it may be logical to think that participation in physical activity would enhance life satisfaction and overall QOL, research is inconclusive. Therefore, the purpose of this study was to evaluate the overall QOL of participants enrolled in the LIVESTRONG® at the YMCA 12 week group exercise program using the FACT-G.

Initial results indicated no statistically significant difference in the change in overall QOL (FACT-G total) from week 1 of the program to week 12 for the full study participants. However, the average overall FACT-G score for the participants in this study were higher at all three time points (see Table 5) compared to FACT-G QOL normative data of 2236 cancer patients in the

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United States (FACT-G total = 80.9) (Brucker, Yost, Cashy, Webster, & Cella, 2005). Furthermore, Brucker, et al. (2005) evaluated the FACT-G total scores of more than 1075 U.S. healthy adults, who averaged an overall QOL score of 80.1. On the contrary, the total FACT-G score for participants in this study were lower at baseline compared to the average FACT-G score of participants enrolled in the LIVESTRONG® at the YMCA program in Connecticut and Massachusetts, who averaged a total QOL score of 90.4 (Irwin, et al., 2016). However, over the course of the 12 week program in each respective study, participants in this study displayed greater improvements in overall QOL compared to the improvements conveyed by the participants in Irwin, et al. (2016) (2.73 vs. 1.6, respectively). Overall, the participants in the LIVESTRONG® at the YMCA 12 week group exercise program both in this study and in Irwin, et al. (2016) began each respective study with relatively high overall QOL compared to both cancer patients and healthy U.S. adults. Therefore, further research is needed to identify specific physical, psychological, and/or social factors that may play a role in the aspirations to participate and finish the LIVESTRONG® at the YMCA 12 week group exercise program.

To further appraise specific aspects of QOL, evaluating the four subscales provides a clearer view of the relationship between participation in the group exercise program and individual components that affect life satisfaction. For cancer survivors, the physical domain of QOL, as mentioned previously, is often swayed by the amount of fatigue, pain, side effects of treatment, ability to fulfill duties, and increase in functional limitations (Hewitt, et al., 2003). When evaluating the different subscales of the FACT-G, the physical and functional domains are separated into individual subscales. The FWB component of the FACT-G includes the ability to work, fulfillment and enjoyment of life, work, and extracurricular activities, acceptance of illness, ability to sleep well, and contentment with current state of QOL. Participants in the

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LIVESTRONG® at the YMCA group exercise program displayed a slight, but statistically

insignificant, increase in FWB scores from weeks 1 to 6. However, the FWB scores at week 12

were somewhat lower than the original scores following week 1. Although this drop may suggest

concern, FWB scores at all three time points were still higher than normative data presented in

two other studies. Brucker, et al. (2005) determined a FWB score of 18.9 in a study of over 2000

cancer patients, which was comparable to the FWB score (18.8) in another study of over 300

patients with mixed cancer diagnoses (Cella, Hahn, et al., 2002). Therefore, higher levels of

FWB at the start of the study may offset limitations experienced later in the program.

The only subscale to show any statistical significance in this study was the PWB.

Questions evaluating PWB in the FACT-G relate to energy level, pain, nausea, inability to meet

physical needs, time spent in bed, side effects of treatment, and illness. The PWB score at week

1 (PWB = 20.64 (SD = 2.80)) of this study was lower than the average scores of cancer patients

with mixed cancers in two separate studies. In a study of 2236 cancer patients, the average score

for PWB was 21.3, which was comparable to the average PWB in another study consisting of

308 mixed cancer patients (PWB = 21.2) (Brucker, et al., 2005; Cella, Hahn, et al., 2002).

However, results indicated a significant increase in PWB from week 1 to week 6 (PWB = 23.6

(SD = 2.46)), which is higher than the normative data in both previously mentioned studies

(Brucker, et al., 2005; Cella, Hahn, et al., 2002). Although a slight, insignificant drop in PWB

was observed from week 6 to week 12 (see Table 5), the PWB score for week 12 was still higher

than the normative PWB scores indicated in Brucker, et al. (2005) and Cella, Hahn, et al. (2002).

The fact that the PWB scores were higher than the normative data at weeks 6 and 12 suggest

participating in the 12 week LIVESTRONG® at the YMCA group exercise program has a

positive influence on physical well-being, including improvements in pain, nausea, energy level,

ability to meet family needs, and side effects of treatment, as well as spending less time in bed and feeling ill less often.

Just as PA can influence physical and functional well-being, it can also greatly influence emotional well-being and QOL. Emotional, or psychological, distress is a common concern at the diagnosis of cancer, but also during and post-cancer treatment. Various responses to the disease may include depression, anxiety, worry, fear, or decisional regrets (Simard, et al., 2013). The EWB component of the FACT-G aims to target these concerns by evaluating feelings of sadness and nervousness, worry of dying and severity of condition, ability to cope, and hope to continue fighting the illness. Although there were no statistically significant differences in EWB scores, scores at all three time points (see Table 5) were higher than the average score in a study of more than 2000 cancer patients (EWB = 18.7) (Brucker, et al., 2005). In addition, the average EWB score from this study were higher than the average EWB score (18.1) of 308 patients with mixed cancers (Cella, Hahn, et al., 2002). Although the average EWB score was higher than participants from two different studies at week 1 of participation in the LIVESTRONG® at the YMCA group exercise program, the fact that the EWB scores were even higher at both weeks 6 and 12 suggests a positive relationship between participation in a group exercise program and overall EWB.

Another key component of overall QOL is social well-being. Numerous studies indicate social support, communication, and understanding have a significant impact on social well-being and QOL (Hodges & Winstanley, 2012; Sarason, Pierce, & Sarason, 1990; Shelby, et al., 2008). As current and expected social support increases, so does positive affect and QOL (Hodges & Winstanley, 2012). However, lack of communication has been shown to negatively impact perception of social support and overall QOL (Polinsky, 1994). Questions listed under the SWB

subscale related to support from, and closeness to, family, friends, and partner, as well as communication and acceptance of the cancer. Results from this study displayed relatively high SWB at all three time points, suggesting good overall SWB (see Table 5). In fact, the average SWB scores exhibited by participants in this study were higher than those expressed in a separate study of over 2000 cancer patients (SWB = 22.1) (Brucker et al., 2005). Furthermore, Cella, Hahn, et al. (2002) examined EWB in 308 patients with mixed cancers and found an average SWB score of 22.3, which was also lower than the average SWB of participants in this study. The fact that participants in the LIVESTRONG® at the YMCA group exercise program started the program with relatively high SWB suggests two things: 1) they may have good social support to begin with and/or 2) the expectations of participating in a group exercise program positively influence social well-being. In addition, the LIVESTRONG® at the YMCA group exercise program is also meant to be educational, which could enhance the communication efforts both during the exercise participation and outside. Therefore, participation in the 12-week LIVESTRONG® at the YMCA group exercise program may provide the necessary support, encouragement, and communication to enhance overall social well-being.

Although there were few statistically significant changes in total and subscale FACT-G scores, cancer patients and clinicians view QOL information and relevant outcome data important in assisting with treatment decisions (Cella, Hahn, et al., 2002). When it comes to oncology treatment specifically, small improvements or declines, even if statistically insignificant, may be very meaningful to patients and survivors. Therefore, assessing not only change, but meaningful change can provide additional information regarding clinical importance related to perceived benefits and overall management of the treatment and/or post-treatment activities (Cella, Hahn, et al., 2002).

When assessing clinical meaningful changes in total FACT-G scores and each subscale score, Cella, Hahn, et al. (2002) suggest a 5-7 point change in the raw total FACT-G score and a 2-3 point change in the raw score of each subscale to be of minimal clinically important difference. Applying this concept to the results of this study, a raw score increase of the total FACT-G score from week 1 to week 6 suggested meaningful clinical improvements in overall QOL within the first six weeks of participation in the LIVESTRONG® at the YMCA group exercise program. In addition, PWB displayed a score increase of almost 3 raw points from week 1 to week 6, which adds clinical meaning to the statistically significant improvement of this subscale. Overall, it appears that participationg in the 12-week LIVESTRONG® at the YMCA group exercise program may benefit overall QOL, but specifically, the greatest benefits may reside in the physical domain of well-being. Therefore, when seeking post-treatment programs, clinicians and cancer survivors may consider participation in such program as a means to combat fatigue, pain, side effects of treatment, nausea, and decreases in physical functioning.

Although the majority of the results of this study were insignficant, the drop-out rate was relatively high. Therefore, researchers further evaluated mean QOL scores for total FACT-G and each subscale for those who completed week 1 only (Group A) and those who completed weeks 1 and 6 only (Group B), and compared each score to that of those in Group C (full study participants). When first evaluating Group A with Group C, mean QOL scores for total FACT-G, and subscales EWB and SWB were all lower for Group A compared to Group C at the end of week 1. Furthermore, the mean total FACT-G score and mean SWB for Group A was lower than the mean FACT-G and SWB scores in two separate studies examining QOL in cancer patients (see values indicted above) (Brucker, et al., 2005; Cella, et al., 2002). On the contrary, mean scores for FWB and PWB, the two subscales relating most to physical capacity, were both lower

for Group C compared to Group A at the end of week 1, and the mean score for PWB in Group C was lower than the normative data previously mentioned (Brucker, et al., 2005; Cella, Hahn, et al., 2002). Therefore, participants in Group C may have felt a greater need to improve these areas, which may have provided the motivation necessary to continue with the program. In addition, although there were no statistically significant differences between the two groups, the SWB score for Group A was almost five points lower than those same scores in Group C following the first week, which suggests a clinical meaningful difference (as indicated above) (Cella, Hahn, et al., 2002). The large difference in SWB scores at the end of week 1 possibly sugggests that participants in Group A lacked the necessary social and family support to continue with the program, which may be something to evaluate prior to starting a group exercise program.

The second assessment examining participation drop-out evaluated differences in QOL, reflected in total FACT-G score and each subscale, between Group B and Group C. While holding all other variables constant, the only significant change was observed between week 1 and week 6. However, raw score data for total FACT-G score and each subscale displayed some discrepancies. Group B scores for total FACT-G, PWB, and SWB were all higher at the end of week 1 compared to Group C, but EWB and FWB scores were comparable between Group B and Group C at the end of week 1. When comparing each QOL score to normative data, scores for total FACT-G and all subscales, except PWB for Group C, were higher than each QOL assessment in Brucker, et al. (2005) and Cella, Hahn, et al., (2002). From week 1 to week 6, total FACT-G, PWB, and FWB scores all improved in both groups, with Group C surpassing Group B in overall QOL at the end of week 6. Scores in all three categories in both groups were higher than normative data indicated in two separate studies (Brucker, et al., 2005; Cella, Hahn, et al.,

2002). However, SWB and EWB scores both declined from week 1 to week 6 for Group B, but increased for Group C. The EWB score at the end of week 6 for Group B was below the national standards identified by both Brucker, et al., (2005) and Cella, Hahn, et al., (2002) of 18.7 and 18.1, respectively.

Overall, comparisons between Group B and Group C provide a vague illustration for identifying explanations for stopping the program. However, differences in total FACT-G score and PWB between the two groups do indicate clinical meaningful differences. Group B scores for total FACT-G and PWB were each 3-4 points higher than Group C at the end of week 1. And although scores for both groups in these two categories increased from week 1 to week 6, only the scores for total FACT-G (+6 points) and PWB (+3 points) in Group C showed any clinical meaningful change from week 1 to week 6. Although it's difficult to determine exact cause and effect, the fact that Group C experienced more improvements in overall QOL and PWB may have been enough of a change to encourage them to continue with the study. Therefore, examining the clinical meaningful differences between the two groups may provide a clearer understanding of participation, motivation, and follow-through with the LIVESTRONG® at the YMCA group exercise program.

Limitations

Despite the relatively consistent, but mostly statistically insignificant, findings of the present study, there are several limitations to consider. First, there was a fairly high drop out rate. The fact that only 11 of the 37 participants completed all three time points suggests volatility in the population studied. No significant differences were observed in the secondary analysis between those who dropped out at week 1 or week 6 compared to those who completed the full study. Therefore, speculations for the drop out, although not documented, may be attributed to

lack of readiness, rigorousness of the program, complications with disease or treatment, comfortability with questions on the questionnaire, scheduling conflicts, social or travel obligations, cancer recurrence, or even death. Second, there was no control group. The lack of control group may pose concern since time of year (season) and geographic location may impact QOL compared to normative data collected elsewhere. Third, there was no true baseline assessment of QOL. The data collection coincided directly with the 12 weeks of the program, and no baseline QOL data was collected on the very first day of the LIVESTRONG® at the YMCA group exercise program, which would've reflected the QOL prior to the start of the program rather than after the first week. Finally, there is no post-evaluation of QOL following completion of the 12 week LIVESTRONG® at the YMCA group exercise program, which would determine long-term effects following participation.

Conclusion

Health-related QOL measures are an integral component when evaluating treatments for cancer patients, and one of the most effect tools for evaluating QOL is the FACT-G. Although research examining the relationship between participation in a structured, group exercise program and impact on QOL is difficult to clearly identify, this study suggests greatest improvements in QOL occurred after 6 weeks, with a slight, but insignificant decline in all scores at week 12. In addition, the greatest improvements in QOL may fall in line with the physical domain compared to all other subscales. Pain, nausea, fatigue, inability to meet physical needs, and side effects of treatment, including illness, are often barriers to participating in regular PA. However, the results of this study suggest that engaging in a 12-week group exercise program can actually improve these limitations. Therefore, these results are encouraging for

cancer survivors and patients currently suffering from these ailments, and may enhance their willingness to participate in regular PA.

Looking to apply meaning to the scores in the form of low, average, or good is difficult considering the interpretation of the questions and overall scores are highly subjective. However, participants, on average, began the study with relatively high QOL compared to normative data, which may limit the value of participating in the LIVESTRONG® at the YMCA group exercise program and its impact on overall QOL. Because of this, further research is needed to assess the relationship between motivation and QOL considering only 11 of those recruited completed all 12 weeks of the study. Lastly, these results suggest a six week program may be long enough to provide the necessary means for enhancing QOL, but how QOL is affected long-term is inconclusive. Overall, there lacks a clear understanding of the connection between the duration, intensity, and type of PA used in the 12 week LIVESTRONG® at the YMCA group exercise program and its impact on QOL. Therefore, future research is needed to truly understand the relationship between participation in this group exercise program, length and intensity of the program, and overall QOL.

CHAPTER 6. DISCUSSION AND CONCLUSION

Discussion

Cancer is a highly prevalent and often debilitating disease. In fact, more than 1.7 million individuals are newly diagnosed with some form of cancer each year, and the number of individuals dying from cancer each year continues to increase (American Cancer Society, 2013; CDC, 2013). Although the all-site five-year survival rate following diagnosis for adults is approximately 66%, cancer is still the second leading cause of death in the U.S. (American Cancer Society, 2013; Howlader, et al., 2012). In addition, cancer patients and survivors are an unstable population, with an increased risk for late effects of treatment, secondary cancers, recurrence, immunosuppression, inflammation, other chronic diseases, poor quality of life, and adverse psychosocial and physical symptoms (Bellizzi, et al., 2005; Courneya, 2003; Howlader, et al., 2012; Rajotte, et al., 2012). Therefore, how cancer patients respond to these stressors can play an integral role in their overall outcome and, ultimately, survival.

While the development and repercussions of cancer are multifaceted, the World Cancer Research Fund estimates that about one-quarter to one-third of new cancer cases could be related to controllable factors, including obesity, physical inactivity, and poor nutrition (American Cancer Society, 2013). Although individuals cannot alter behaviors prior to the diagnosis of cancer, various biopsychosocial responses following the diagnosis, treatment, and follow-up can have dramatic impacts on the outcome and survival. For example, physical activity has been shown to improve overall physical functioning, cardiovascular fitness, QOL, and several other psychological and social factors in cancer survivors (Knobf, et al., 2007). Numerous programs, varying in training modalities, have been established to try and increase the level of PA among cancer survivors post treatment. However, it is estimated that less than 35% of cancer survivors

meet the ACSM guidelines for PA (Pinto, et al., 2002). With research examining changes in PA and QOL during participation in a structured exercise program still in its infancy, there continues to be a deficiency in evidence-based exercise programs for cancer survivors.

In order to combat the paucity of evidence-based exercise programs, the LIVESTRONG® organization collaborated with numerous YMCAs nationwide as a means to assist cancer survivors in recovery by developing their own physical fitness program to reduce therapy side effects, prevent unwanted weight changes, improve self-esteem, and promote a healthy lifestyle (LIVESTRONG Foundation, n.d.). The problem is there is limited research evaluating changes in physical activity and its impact on QOL both during and after participation in the LIVESTRONG® at the YMCA program. Therefore, the purpose of this study was to examine changes in PA and QOL of participants enrolled in the 12-week LIVESTRONG® at the YMCA group exercise program, and researchers hypothesized that PA would increase, SED activity would decrease, and QOL would increase from week 1 to week 12 of participation in the program.

Final results of this study question whether or not participation in the 12-week LIVESTRONG® at the YMCA group exercise program is effective. Although slight improvements in PA were observed at all three time points (week 1, 6, and 12), these changes were not statistically significant. Most of the PA at all three time points consisted of light intensity; however, the average amount of MVPA at weeks 1, 6, and 12 well exceeded the ACSM guidelines for PA. Although the changes in PA intensity were not statistically significant, these results are promising in the fact that MVPA increased from week 1 to 6, and remained fairly steady from week 6 to week 12. Furthermore, SED time significantly decreased from week 1 to week 6, and although SED time significantly increased from week 6 to week 12, total SED

time at week 12 was still lower than the total SED time at week 1. Therefore, such improvements, although slight, are encouraging, considering breaks in SED time and regular PA have been shown to enhance the biopsychosocial aspects of health, lessen the side effects of treatment, and reduce chronic disease risk (Healy, Dunstan, Salmon, Shaw, et al., 2008; Loprinzi & Cardinal, 2013).

In addition to changes in PA, results for changes in QOL are still uncertain. Although participants began the study with relatively high QOL, marginal improvements, although insignificant, in overall QOL were observed over the course of the 12-week LIVESTRONG® at the YMCA group exercise program. Individual subscales showed little change throughout the program; however, a key finding suggests the greatest significant advancements in QOL reflect primarily physical well-being, thereby improving pain, nausea, energy level, ability to meet family needs, and side effects of treatment, as well as spending less time in bed and feeling ill less often. Overall, a lack of true baseline makes it difficult to identify any significant impacts participation in the 12-week LIVESTRONG® at the YMCA group exercise program may have had, and is something to be considered in future research.

While the majority of changes in this study were insignificant, there are some limitations that may be contributing factors. For one, there was a considerable dropout rate from week 1 to week 12. Although the dropout rate wasn't directly evaluated, PA and SED differences between those who completed only week 1, those who completed weeks 1 and 6, and those who completed all three time points were insignificant. Therefore, since only speculations can be made to explain the high dropout rate, this would be something to evaluate in future studies.

In addition to the dropout rate, there was no true baseline to compare direct changes within the program. The timeframe of when participants enrolled in the LIVESTRONG® at the

YMCA group exercise program made this factor difficult to control for, but is still something to consider. Furthermore, no control group was identified, which is necessary for future validation of the success of the program.

Conclusion

While it is difficult to determine whether or not the LIVESTRONG® at the YMCA group exercise program is effective in meeting its goals, research shows that participation in regular PA, whether it be individual- or group-based, is beneficial. Therefore, recommendations for future research in evaluating the effectiveness of the LIVESTRONG® at the YMCA group exercise program are as follow: 1) establish a baseline for both PA and QOL prior to week 1 of the LIVESTRONG® at the YMCA progam, 2) include a PA recall questionnaire to get a better understanding of the type of PA and perception of PA intensity, and 3) assess PA and QOL post-completion of the program to identify potential long-term impacts of participation in the LIVESTRONG® at the YMCA group exercise program.

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APPENDIX A. INFORMED CONSENT

NDSU   North Dakota State University

Health Nutrition and Exercise Sciences

1 Bentson Bunker Fieldhouse

Fargo, ND 58105

701-231-6737

Title of Research Study: Physical activity patterns and quality of life assessment of participants in a cancer survivor exercise program.

This study is being conducted by: Sarah Hilgers-Greterman: 701-231-8494 or sarah.greterman@ndsu.edu and Nick Redenius: 701-373-5712 or nicklaus.redenius@my.ndsu.edu

Why am I being asked to take part in this research study? You are being asked to participate in this study because you are participating in the YMCA Livestrong cancer survivor exercise program, over the age of 18, and have clearance from your physician to participate in the Livestrong program.   All individuals currently involved in the YMCA Livestrong cancer survivor program (about 24) will be asked to participate, and the choice to participate or not will have no bearing on your participation in the Livestrong program.

What is the reason for doing the study? The purpose of this research is to examine the physical activity patterns and quality of life of cancer survivor patients before, during and after participation in the elective YMCA Livestrong cancer survivor exercise program.

What will I be asked to do? Or What Information will be collected about me? You will partake in one week of evaluation during six separate sessions: one week prior to the start of the Livestrong program, at the midpoint (week 6) and endpoint (week 12) of the Livestrong program, and 3 months, 6 months and 9 months post-program. During the evaluation, you will wear an armband monitoring device around your upper left arm for one week (seven days) during each evaluation session. You will wear the armband monitoring device each day, while performing your normal activities. You will not be asked to perform any additional activities and this should not interfere with your daily living. The armband monitoring device will track your movements and physical activity throughout the day. Following the seven days, the monitoring device will be collected by the researchers and you will be asked to complete a FACT-G, quality of life, questionnaire and a physical activity recall questionnaire.

Where is the study going to take place, and how long will it take? The study will take place at the Fercho YMCA, downtown Fargo, ND and at your home. There will be six total evaluation sessions (one week prior to the start of the Livestrong program, midpoint (week 6) and endpoint (week 12) of the Livestrong program, and at 3 months, 6 months, and 9 months post-program) with each evaluation lasting one week (seven days).

What are the risks and discomforts? Wearing the armband monitoring device provides minimal risk and is adjustable to maximize comfort throughout the day. You will not wear the device while bathing, swimming, or partaking in any other activity involving water. General perspiration will not affect the device or cause any harm. Wear of the armband monitoring device outside the supervised exercise training Livestrong program will be advised and should not interfere with daily living and additional activities.

What are the benefits to me? There are no direct benefits to you as a participant, except to understand the amount of movement and physical activity you perform each day.

What are the benefits to other people? The evaluations used in this study are for enhancing knowledge on the effects, both physically and mentally, of those involved in a cancer survivor program. The results gained from this study will also provide insight to quality of life and physical activity participation throughout the duration of the Livestrong program and up to nine months following program completion.

Do I have to take part in the study? Your participation in this research is your choice. If you decide to participate in the study, you may change your mind and stop participating at any time with no bearing on your participation in the Livestrong program.

What will it cost me to participate? There is no cost to participate aside from any direct costs with participation in the Livestrong program.

What are the alternatives to being in this research study? Instead of being in this research study, you can choose not to participate.

Who will see the information that I give? All data will be collected by trained staff knowledge in the use of all evaluation techniques and questionnaires and kept completely confidential. In addition, only members of the research team will have access to the collected data at any point, and data will only be shared with individual participants at their own request. At no time will any participant have access to the data of another participant. Names will used for each participant to match their data at each time point of the study and to be able to report individually requested results; however, names will be removed prior to all data analysis. At the end of each data collection time period, all information will be transferred from a hard copy to an electronic spread sheet on one dedicated NDSU laptop that is password protected. Your information will be combined with information from other people taking part in the study. When we write about the study, we will write about the combined information that we have gathered. You will not be identified in these written materials. We may publish the results of the study; however, we will keep your name and other identifying information private. Upon completion of the study, all hardcopy sheets will be destroyed.

Can my taking part in the study end early? If you fail to complete all sessions, or a physician advises you to not partake in any physical activity you may be removed from the study.

Will I receive any compensation for taking part in this study? No compensation will be provided for this study.

What happens if I am injured because of this research? If you receive an injury in the course of

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taking part in the research, you should contact your physician and Sarah Hilgers-Greterman at the following phone number 701-231-8494. While participating in the Livestrong program, treatment for the injury will be available including first aid, emergency treatment and follow-up care as needed by the Livestrong staff. Payment for this treatment must be provided by you and your third party payer (such as health insurance or Medicare). This does not mean that you are releasing or waiving any legal right you might have against the researcher or NDSU as a result of your participation in this research.

What if I have questions?

Before you decide whether to accept this invitation to take part in the research study, please ask any questions that might come to mind now. Later, if you have any questions about the study, you can contact the researchers, Sarah Hilgers at 701-231-8494 or sarah.greterman@ndsu.edu or Nick Redenius at 701-373-5712 or nicklaus.redenius@my.ndsu.edu.

What are my rights as a research participant?

You have rights as a participant in research. If you have questions about your rights, or complaints about this research *or to report a research-related injury*, you may talk to the researcher or contact the NDSU Human Research Protection Program by:

- Telephone: 701.231.8908
- Email: ndsu.irb@ndsu.edu
- Mail: NDSU HRPP Office, NDSU Dept. 4000, PO Box 6050, Fargo, ND 58108-6050.

The role of the IRB is to see that your rights are protected in this research; more information about your rights can be found at: www.ndsu.edu/research/irb .

Documentation of Informed Consent:

You are freely making a decision whether to be in this research study. Signing this form means that

1. you have read and understood this consent form
2. you have had the consent form explained to you
3. you have had your questions answered, and
4. you have decided to be in the study.

You will be given a copy of this consent form to keep.

_____   _____

Your signature   Date

_____

Your printed name

_____   _____

Signature of researcher explaining study   Date

_____

Printed name of researcher explaining study

APPENDIX B. INTERNAL REVIEW BOARD APPROVAL

NDSU   NORTH DAKOTA STATE UNIVERSITY   701.231.8995
Fax 701.231.8098

Institutional Review Board   Federalwide Assurance #FWA00002439

Office of the Vice President for Research, Creative Activities and Technology Transfer
NDSU Dept. 4000
1735 NDSU Research Park Drive
Research 1, P.O. Box 6050
Fargo, ND 58108-6050

July 21, 2011

Gary Liguori
Dept. of Health, Nutrition & Exercise Sciences
EML 351

IRB Expedited Review of: "Physical activity patterns and quality of life assessmetn of participatns in a cancer survivor exercise program", Protocol #HE11305
Co-investigator(s) and research team: Sarah Hilgers, Jeremy Frost, Nick Redenius, John Schuna, Jr. Hanna Grinaker
Research site(s): Fercho YMCA, Fargo, ND   Funding: n/a

The protocol referenced above was reviewed under the expedited review process (category # 4, 7) on **6/29/2011**, and the IRB voted for: ☐ approval   ☒ approval, contingent on minor modifications. These modifications have now been accepted. IRB approval is based on the original submission, with revised: protocol and consent (received – 7/1/2011).
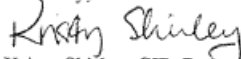
<p align="center">Approval expires: <u>6/28/2012</u>   Continuing Review Report Due: <u>5/1/2012</u></p>

Please note your responsibilities in this research:

- All changes to the protocol require approval from the IRB prior to implementation, unless the change is necessary to eliminate apparent immediate hazard to participants. Submit proposed changes using the *Protocol Amendment Request Form*.
- All research-related injuries, adverse events, or other unanticipated problems involving risks to participants or others must be reported in writing to the IRB Office within 72 hours of knowledge of the occurrence. All significant new findings that may affect risks to participation should be reported in writing to subjects and the IRB.
- If the project will continue beyond the approval period, a continuing review report must be submitted by the due date indicated above in order to allow time for IRB review and approval prior to the expiration date. The IRB Office will typically send a reminder letter approximately one month before the report due date; however, timely submission of the report is your responsibility. Should IRB approval for the project lapse, recruitment of subjects and data collection must stop.
- When the project is complete, a final project report is required so that IRB records can be inactivated. Federal regulations require that IRB records on a protocol be retained for three years following project completion. Both the continuing review report and the final report should be submitted according to instructions on the *Continuing Review/Completion Report Form*.
- Research records may be subject to a random or directed audit at any time to verify compliance with IRB regulations.

Thank you for cooperating with NDSU IRB policies, and best wishes for a successful study.

Sincerely,

Kristy Shirley

Kristy Shirley, CIP, Research Compliance Administrator

Last printed 7/21/2011 10:41:00 AM

NDSU is an EO/AA university.

APPENDIX C. SENSEWEAR ARMBAND MONITORING DEVICE AND

POSITIONING FOR PROPER WEAR

Anterior view of Sensewear armband

Demonstration of how
Sensewear armband attaches
to upper-arm.

APPENDIX D. DEMOGRAPHICS FORM

WEEK

NAME	GENDER	AGE	BIRTH-DATE	HEIGHT	WEIGHT	HANDED	SMOKER	BMI

APPENDIX E. FACT-G QUESTIONNAIRE

FACT-G (Version 4)

Below is a list of statements that other people with your illness have said are important. **Please circle or mark one number per line to indicate your response as it applies to the past 7 days.**

	PHYSICAL WELL-BEING	Not at all	A little bit	Some-what	Quite a bit	Very much
GP1	I have a lack of energy	0	1	2	3	4
GP2	I have nausea	0	1	2	3	4
GP3	Because of my physical condition, I have trouble meeting the needs of my family	0	1	2	3	4
GP4	I have pain	0	1	2	3	4
GP5	I am bothered by side effects of treatment	0	1	2	3	4
GP6	I feel ill	0	1	2	3	4
GP7	I am forced to spend time in bed	0	1	2	3	4

	SOCIAL/FAMILY WELL-BEING	Not at all	A little bit	Some-what	Quite a bit	Very much
GS1	I feel close to my friends	0	1	2	3	4
GS2	I get emotional support from my family	0	1	2	3	4
GS3	I get support from my friends	0	1	2	3	4
GS4	My family has accepted my illness	0	1	2	3	4
GS5	I am satisfied with family communication about my illness	0	1	2	3	4
GS6	I feel close to my partner (or the person who is my main support)	0	1	2	3	4
Q1	*Regardless of your current level of sexual activity, please answer the following question. If you prefer not to answer it, please mark this box* ☐ *and go to the next section.*					
GS7	I am satisfied with my sex life	0	1	2	3	4

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Please circle or mark one number per line to indicate your response as it applies to the <u>past 7 days</u>.

	EMOTIONAL WELL-BEING	Not at all	A little bit	Some-what	Quite a bit	Very much
GE1	I feel sad	0	1	2	3	4
GE2	I am satisfied with how I am coping with my illness	0	1	2	3	4
GE3	I am losing hope in the fight against my illness	0	1	2	3	4
GE4	I feel nervous	0	1	2	3	4
GE5	I worry about dying	0	1	2	3	4
GE6	I worry that my condition will get worse	0	1	2	3	4

	FUNCTIONAL WELL-BEING	Not at all	A little bit	Some-what	Quite a bit	Very much
GF1	I am able to work (include work at home)	0	1	2	3	4
GF2	My work (include work at home) is fulfilling	0	1	2	3	4
GF3	I am able to enjoy life	0	1	2	3	4
GF4	I have accepted my illness	0	1	2	3	4
GF5	I am sleeping well	0	1	2	3	4
GF6	I am enjoying the things I usually do for fun	0	1	2	3	4
GF7	I am content with the quality of my life right now	0	1	2	3	4

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