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Marian Luctkar-Flude

AUTEUR DE LA THÈSE / AUTHOR OF THESIS

M.Sc. (Nursing)

GRADE / DEGREE

School of Nursing

FACULTÉ, ÉCOLE, DÉPARTEMENT / FACULTY, SCHOOL, DEPARTMENT

**Fatigue, Physical Activity, Physical Functioning and
Quality of Life in Older Adults with Cancer**

TITRE DE LA THÈSE / TITLE OF THESIS

Dianne Groll

DIRECTEUR (DIRECTRICE) DE LA THÈSE / THESIS SUPERVISOR

CO-DIRECTEUR (CO-DIRECTRICE) DE LA THÈSE / THESIS CO-SUPERVISOR

EXAMINATEURS (EXAMINATRICES) DE LA THÈSE / THESIS EXAMINERS

Dave Holmes

Rama Nair

Gary W. Slater

Le Doyen de la Faculté des études supérieures et postdoctorales / Dean of the Faculty of Graduate and Postdoctoral Studies

**FATIGUE, PHYSICAL ACTIVITY, PHYSICAL FUNCTIONING AND
QUALITY OF LIFE IN OLDER ADULTS WITH CANCER**

by

Marian Luctkar-Flude

**Thesis submitted to the Faculty of Graduate and Postdoctoral Studies
in partial fulfillment of the requirements for the degree of
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Abstract

Cancer is predominantly a disease affecting older persons. 43% of new cancer cases in Canada occur among those who are at least 70 years old, while 25% occur in those aged 60-69 years. Cancer fatigue is the most common symptom associated with cancer and its treatment, and is often the most distressing symptom reported by cancer patients. Cancer fatigue adversely affects physical activity levels, physical function, and quality of life. Physical function is essential to older adults in maintaining independence and associated quality of life which is often more important to older adults than cancer survival. Recent research studies suggest that physical activity may reduce fatigue, and maintain or improve physical function levels and quality of life in cancer patients during and following treatment.

This thesis examines cancer fatigue and its relationship to physical activity, physical function, and quality of life in older adults with cancer. The results of a systematic review and the findings of a secondary analysis research study are presented. The systematic review provided evidence that physical activity may reduce fatigue in older cancer patients during and after cancer treatment and may help to maintain or improve physical function and quality of life in this population. Results of the secondary analysis indicated that cancer fatigue is prevalent and was the most frequently reported symptom at baseline, three months and six months post consultation for cancer treatment. Cancer fatigue was associated with lower levels of physical function and quality of life. Physical activity, a modifiable factor, was found to be significantly related to cancer fatigue at three months and six months, regardless of age, and was significantly related to physical function at six months.

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Chapter One

Introduction

Cancer is predominantly a disease affecting persons aged 65 and older, and as the North American population ages, the number of older adults diagnosed or living with cancer will increase (Canadian Cancer Society/National Cancer Institute of Canada, 2006; Yancik, 1997). Forty-three per cent of new cancer cases in Canada occur among those who are at least 70 years old, while 25% occur in those aged 60-69 years. The median age at cancer diagnosis is between 65 and 69 years (Canadian Cancer Society/National Cancer Institute of Canada, 2006).

Cancer fatigue is the most common symptom associated with cancer and its treatment, and is often the most distressing symptom reported by cancer patients (Cella, 1997; Curt, 2000; Curt et al., 2000; Rhodes, Watson, & Hanson, 1988; Stone, Richards, A'Hern, & Hardy, 2000; Winningham et al., 1994). Cancer fatigue adversely affects physical activity levels, physical function, and quality of life (Glaus, 1993; Mock et al., 1997; Nail, 2002; Nail & Jones, 1995; Winningham et al., 1994; Winningham, 1999), however cancer fatigue has historically been poorly recognized, poorly understood, and poorly managed (Stone et al., 2000). Recent interest in the subject of cancer fatigue has led to studies suggesting that physical activity can reduce fatigue in cancer patients during and following treatment, thus enhancing quality of life (Mock, 2001).

Cancer Fatigue

Attempts have been made to describe the specific experience of cancer fatigue. Cella, Peterman, Passik, Jacobsen, & Breitbart (1998, p.369) defined cancer fatigue as “significant tiredness, diminished energy or increased need to rest, disproportionate to any recent change in activity level”. Portenoy & Itri (1999, p.2) described cancer fatigue as a “multidimensional

phenomenon that develops over time, diminishing energy, mental capacity, and the psychologic condition of cancer patients”. Most recently, in 2004, the National Comprehensive Cancer Network (NCCN, p.310) developed Clinical Practice Guidelines in Oncology and suggested the following definition: “cancer-related fatigue is a persistent, subjective sense of tiredness related to cancer or cancer treatment that interferes with usual functioning”.

Cancer fatigue interferes with quality of life regardless of diagnosis, treatment or prognosis (Stone, Richards, A’Hern, & Hardy, 2001; Longman, Braden, & Mishel, 1999; Loge, Abrahamsen, Ekeberg & Kaasa, 2000). Fatigue is associated with all cancer treatment modalities: surgery, chemotherapy, radiation therapy and biotherapy (Irvine, Vincent, Bubela, Thompson & Graydon, 1991; Irvine, Vincent, Graydon, Bubela, & Thompson, 1994), however there remain significant gaps regarding the similarities and differences in fatigue among different age groups, with different types of cancer and/or comorbid conditions (Rieger, 2001).

Despite the recent development of multidisciplinary practice guidelines for the assessment and management of cancer fatigue, few practitioners are aware of research recommendations and practice guidelines (Mock, 2001; Mock, McCorkle, & Krumm, 2003), and patients remain uneducated about the problem and often do not report their fatigue to their physician (Stasi, Abriani, Beccaglia, Terzoli, & Amadori, 2003). This lack of awareness and lack of reporting is a significant problem, given that cancer fatigue is the most prevalent and distressing symptom associated with cancer and its treatment.

Untreated cancer fatigue may result in a decrease or discontinuation of normal physical and social activities, interpersonal interaction, recreational activity, and home and family care, and may affect all domains of quality of life: physical, psychosocial, social and spiritual well-being (Camarillo, 1991; Ferrell, Grant, Dean, Funk, & Ly, 1996; Nail & Jones, 1995). Patients

may also experience difficulty adhering to and completing treatment regimes, and may require delays in treatment, dose limitation or discontinuation of therapy, or may withdraw from clinical trials due to fatigue (Rosenthal & Oratz, 1998; Skalla & Rieger, 1995; Visovsky & Schneider, 2003; Whedon, Stearns, & Mills, 1995; Winningham et al., 1994).

Physical Function

Physical function can be defined as the ability to ambulate and to perform normal activities of daily living (Mock, 2001). Cancer fatigue has been found to have a significant effect on patients' abilities to function in usual roles and activities (Curt, 2000; Jacobsen et al., 1999; Akechi, Kugaya, Okamura, Yamawaki, & Uchitomi, 1999). Physical and functional well being are essential dimensions of overall quality of life (Cella & Tulsky, 1990). Higher levels of fatigue have been associated with lower levels of physical functioning (Berger & Farr, 1999). Patients advised to minimize daily activity to reduce fatigue may experience further impairment of physical capacity. Researchers have proposed that a cycle of decreasing activity and increasing fatigue leads to deconditioning, resulting in patients fatiguing more quickly when they participate in activity (Dimeo, 2001; Winningham et al., 1994). Exercise has been found to increase physical function in cancer patients during and following cancer treatment (Dimeo et al., 1997; Dimeo et al., 1998; MacVicar et al., 1989; Mock et al., 1997; Nail & Jones, 1995; Segal et al., 2003). Physical function is essential to older adults in maintaining independence and associated quality of life which is often more important to older adults than cancer survival (Garman & Cohen, 2002; Silliman, Balducci, Goodwin, Holmes & Leventhal, 1993).

Quality of Life

Quality of life is a subjective sense of well-being that can be difficult to define. It has been defined as patient satisfaction with their current level of functioning, compared to what they

perceive to be possible or ideal (Cella & Cherin, 1988). Quality of life is a multidimensional concept, entailing physical, psychological and social factors (Donovan, Sanson-Fisher, & Redman, 1989; Osoba, 1994; Olschewski, Schulgen, Schumacher, & Altman, 1994). Health related quality of life refers to those aspects of a person's life that impact directly upon their health, and encompasses the impact of a disease and its treatment on all aspects of a patient's life, including the impact of symptoms and the distress associated with functional limitations (American Society of Clinical Oncology, 1996; Gill & Feinstein, 1994; Patrick & Erickson, 1993).

Quality of life has been found to be negatively related to fatigue (Ashbury, Findlay, Reynolds, & McKerracher, 1998; Bower et al., 2000; Broekel, Jacobsen, Horton, Balducci, & Lyman, 1998; Ferrell et al., 1996; Fletcher et al., 1998; Holzner et al., 2003; Smets, Visser, Willems-Groot, & Garssen, 1998; Vogelzang et al., 1997,). Exercise during cancer treatment may improve quality of life (Headley, Ownby, & John, 2004; Mock, et al., 2003; Schwartz, 1999; Schwartz et al., 2001).

Physical Activity

Physical activity has been defined as "bodily movement produced by the contraction of skeletal muscle that increases energy expenditure above the basal level" (U.S. Department of Health & Human Services, 1996, p. 20). The terms physical activity and exercise are often used synonymously in the literature; however, exercise can be viewed as a subcategory of physical activity, and defined as "physical activity that is planned, structured, repetitive, and purposive in the sense that improvement or maintenance of one or more components of physical fitness is the objective" (Caspersen, Powell & Christensen, 1985, p. 128).

Cancer patients tend to decrease their physical activity levels after diagnosis and during treatment, and most do not return to pretreatment activity levels (Courneya & Friedenrich, 1997a, 1997b; Irwin et al., 2003). They are often advised to limit activity and get plenty of rest (Curt et al., 2000; Winningham, 1991). Decreased physical activity level during cancer treatment can result in weakness and immobility that can have a draining effect on energy level (Cella et al., 1998; Nail & Winningham, 1995). Higher fatigue levels are consistently associated with lower activity levels in cancer patients (Berger, 1998; Hickok, Roscoe, Morrow & Bushunow, 1998; Mock et al., 1994; Mock et al., 1997; Mock, 2001).

Of the nonpharmacologic interventions for fatigue during cancer treatment, physical activity has the strongest supporting evidence (Dimeo, 2001; NCCN, 2003). Several randomized clinical trials have demonstrated that physical activity decreases cancer fatigue (Dimeo, Stieglitz, Novelli-Fischer, Fetscher, & Keul, 1999; Mock et al., 1997, 2001; Oldervoll, L, Kaasa, Knobel, & Loge, 2003; Schwartz, 1998, 2000; Schwartz, Mori, Gao, Nail, & King, 2001; Segal et al., 2003). Aerobic exercise has been found to reduce fatigue during chemotherapy and radiation therapy, as well as decreasing fatigue in cancer survivors after cancer treatment has been completed (Dimeo et al., 1997; Dimeo, Rumberger, & Keul, 1998; MacVicar, Winningham, & Nickel, 1989; Mock et al., 1994; Mock et al., 1997). Some cancer patients have reported using exercise as a self-care strategy to reduce fatigue related to cancer treatment (Graydon, Bubela, Irvine, & Vincent, 1995; Richardson & Ream, 1997).

Cancer Fatigue in Older Adults

It has been reported that normal fatigue increases with age in healthy individuals (Schwarz & Hinz, 2001). Normal age-related changes include changes in stature and body composition, walking and cognitive function, sensory impairment and kidney and liver function,

and changes to the hematopoietic and immune systems (Baird, McCorkle, & Grant, 1991; Otto, 1993; Groenwald, Frogge, Goodman, & Yarbrow, 1997). The natural changes and comorbidities associated with aging may contribute to fatigue in older adults whether or not they are receiving treatment for an illness such as cancer. However, frail older persons may be unable to take measures to minimize treatment side effects and are susceptible to anemia (Baird et al., 1991; Groenwald et al., 1997).

There have been few studies that have looked at cancer fatigue in older persons, therefore it is difficult to ascertain whether the experience of cancer fatigue in older persons is similar to or differs from cancer fatigue in younger adults. Some of the factors that have been identified as contributing to cancer fatigue in older persons include immobility, deconditioning, insomnia and other sleep disorders, poor nutrition, use of centrally acting drugs, and decline in functional reserve of multiple organ systems (Curtis, Krech, & Walsh, 1991; Duthie, 2004; Portenoy & Itri, 1999). Pain and fatigue are also often linked with other symptoms in elderly cancer patients (Given, Given, Azzouz, Kozachik, & Stommel, 2001).

Treatment of Cancer Fatigue

Treatment of cancer fatigue in older adults has been poorly studied (Rao & Cohen, 2004). What we know about cancer fatigue has been studied in younger persons. Proposed interventions for cancer fatigue include both pharmacologic therapies and nonpharmacologic interventions such as activity enhancement, psychosocial interventions, nutrition consultation and sleep therapy (NCCN, 2003). It is not known whether or not treatments effective for younger persons will also be effective in older adults. Interventions have not been tested in older persons, and to date those developed for younger persons are used.

Most of the studies evaluating physical activity interventions have implemented exercise during treatment for breast cancer and few studies have assessed the efficacy of physical activity interventions in the elderly (Penedo, Schneiderman, Dahn, & Gonzalez, 2004). It has been proposed that physical activity interventions could help in preserving functional status in the elderly (Penedo et al, 2004; Rao & Cohen, 2004). However physical activity programs need to be tailored to meet the unique needs of older adults (King, Rejeski, & Buchner, 1998).

Despite the increasing prevalence of cancer in older adults, there is a limited understanding of the relationship between fatigue, physical activity, physical functioning and quality of life in older persons with cancer, and thus it is difficult to plan and provide strategies to reduce cancer fatigue, maintain or enhance physical function, and optimize quality of life in this population.

Purpose

The purpose of this thesis is to describe the relationships between fatigue, physical activity, physical functioning and quality of life in a cohort of older adults who are receiving active cancer treatment. This study is a secondary analysis of data gathered for a longitudinal, descriptive study entitled *Health and Well Being in Older Persons with Cancer* that was conducted by a multidisciplinary research team led by Dr. Joan Tranmer at Kingston General Hospital and the Cancer Centre of Southeastern Ontario.

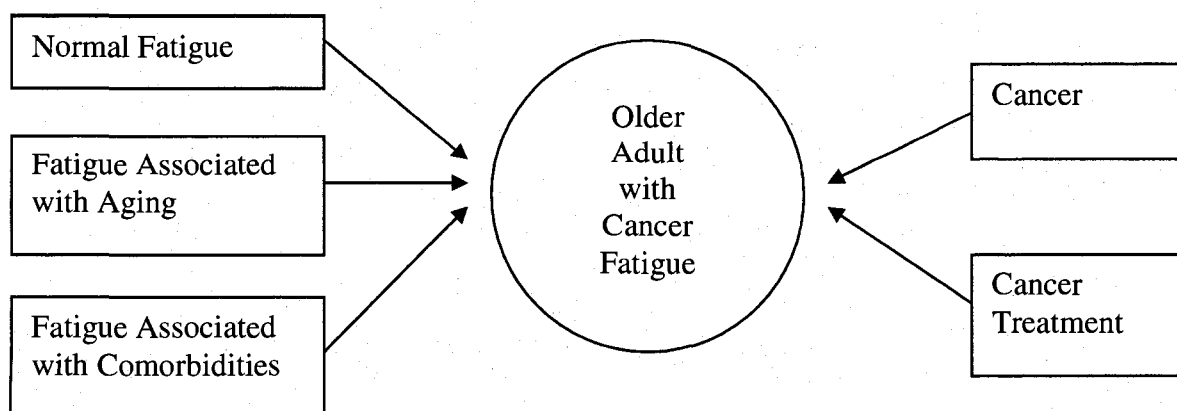
The prevalence of elderly patients living with cancer is increasing, and is expected to grow in the next decade. Emerging evidence shows that aggressive treatment of cancer in the elderly patient is safe and effective; however, there is a poor understanding of the influence of important factors such as fatigue and physical activity levels on physical functioning and quality of life in this population. Management of symptoms such as fatigue and improvement in

physical function and quality of life are important outcomes of nursing care. The proposed secondary analysis will explore the relationships between these variables and contribute to the growing knowledge of cancer fatigue. This study will be the first to profile and to describe the impact of cancer fatigue on the older adult with cancer. Given the importance of maintaining physical function for independent living and quality of life, it is critical to identify the impact of cancer fatigue on physical activity, physical functioning and quality of life and to identify how physical activity influences the impact of cancer fatigue on physical functioning and quality of life. This project may be the initial step towards the development of clinical guidelines and physical activity interventions to reduce cancer fatigue, enhance physical functioning and optimize quality of life in older adults during and following treatment for cancer.

Conceptual Framework

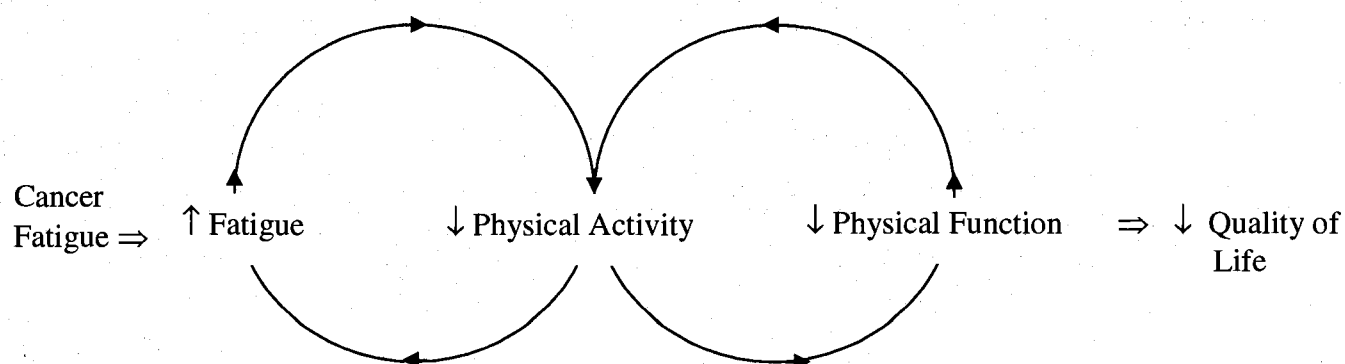
Cancer fatigue has been described as resulting from the effects of the cancer and its various treatment modalities. Fatigue in older adults has been associated with aging and with associated comorbidities. Thus fatigue in the older adult with cancer can be hypothesized to result from the combined effects of all of these factors in addition to the normal fatigue experienced by healthy individuals as depicted in Figure 1.

Figure 1: Proposed Conceptual Framework for Cancer Fatigue in the Older Adult:



The literature supports that there is a relationship between fatigue, physical activity, physical function and quality of life in cancer patients (Luctkar-Flude et al., in press). Researchers have proposed that a cycle of decreasing activity and increasing fatigue leads to deconditioning, resulting in patients fatiguing more quickly when they participate in activity (Dimeo, 2001; Winningham et al., 1994). The proposed cycle of increasing fatigue and decreasing physical activity resulting in declines in physical function and quality of life in cancer patients is depicted in Figure 2. The present study examined these relationships in a sample of older adults with cancer.

Figure 2: Conceptualization of Cycle of Fatigue, Physical Activity, Physical Function and Quality of Life in Older Adults with Cancer:



Physical activity is proposed as an intervention that may break or reverse this cycle by reducing fatigue and increasing or maintaining physical function. This may be achieved as increasing physical activity improves the muscle strength, stamina & joint flexibility necessary to perform activities of daily living (U.S. Department of Health and Human Services, 1996).

Research Objectives

Thus, the objective of this study was to explore the relationships between fatigue and physical activity, physical functioning and quality of life in older adults with cancer. The specific objectives of this thesis were to:

1. Synthesize the current research evidence related to the effectiveness of physical activity as an intervention to reduce fatigue in older adults with cancer during and following cancer treatment.
2. Describe the prevalence of cancer fatigue in a cohort of older adults with cancer at the time of consultation for treatment at a cancer centre, at three months, and at six months following the consultation.
3. Determine the relationships between fatigue and physical activity, in a cohort of older adults with cancer in the six months following consultation for treatment at a cancer centre.
4. Determine the relationships between fatigue and physical activity, and physical function and quality of life, in a cohort of older adults with cancer in the six months following consultation for treatment at a cancer centre.

In order to accomplish these objectives, the following research questions were addressed in a cohort of older adults (>65 years) referred to a regional cancer centre for treatment of their cancer condition:

1. Is there a relationship between physical activity levels at study enrolment (referral to cancer centre for cancer consultation and treatment) and fatigue at three months and six months post-enrolment?

2. Is there a relationship between physical activity at three months and fatigue levels at three months and six months post study enrolment?
3. Is there a relationship between physical activity levels at three months physical functioning at six month post study enrolment?
4. Is there a relationship between physical activity levels at three months and quality of life at six months post study enrolment?

The research hypothesis that was tested in this study was that higher physical activity levels were associated with lower fatigue levels, higher physical functioning scores and higher quality of life scores during and following cancer treatment.

In order to address the four research questions, correlations were calculated between each of the four variables at baseline, three months and six months, and between the three time periods. Controlling for demographic characteristics, disease site and treatment modality, the relationships between fatigue, physical activity, physical functioning and quality of life were described. Multivariate regression analysis was performed to control for demographic characteristics, disease site and treatment modality.

Self-reported symptom assessment data related to fatigue was collected using the Memorial Symptom Assessment Scale (MSAS)(Appendix A), a reliable and valid instrument for assessment of symptoms in cancer patients (Portenoy et al., 1994). Physical activity level was measured using the Physical Activity Scale for the Elderly (PASE) (Appendix B), which asks questions about leisure time activity, household activity and work-related activity, and was specifically designed to assess activities engaged in by older persons (Washburn, Smith, Jette, & Janney, 1993).

The Physical Component Summary (PCS) subscale of the Medical Outcome Short Form 12 General Health Questionnaire (SF 12) (Appendix C) was used to measure physical function. The SF 12 is a brief, self-administered instrument that measures functioning and well being in two health status domains: physical and emotional functioning. The SF12 is a reliable, valid measure of health in surgical and medical populations (Ware, Kosinski, & Keller, 1996). The European Organization for Research Treatment Quality of Life questionnaire (EORTC QLQ – C30) (Appendix D) was used to measure cancer related QOL. The EORTC QLQ – C30 is a 30 – item questionnaire designed to measure cancer patients’ physical, psychological and social functions, and is reported to be a reliable and valid measure of quality of life in cancer patients (Aaronson, et al., 1993).

Possible confounding variables were also measured. Factors likely to affect the prevalence of fatigue in cancer patients include stage of disease, site of cancer, treatment factors (Hotopf, 2004), demographic factors (De Jong, Courtens, Abu-Saad, Schouten, 2002), lifestyle factors (Bultmann, Kant, Kasl, Schroer, Swaen, & van den Brandt (2002), and comorbidities (Bower et al. 2000). Clinical measures of disease (cancer) severity and treatment factors were obtained through chart abstraction at baseline and at study completion. Measures of personal demographic characteristics were obtained through self-report on the baseline questionnaire. Measures of comorbidity were obtained by self-report at baseline through completion of the Functional Comorbidity Index (FCI)(Appendix E), an 18 item index that is correlated with physical function (Groll, Heyland, Caesar, & Wright, 2006; Groll, To, Bombardier, & Wright, 2005).

Given that the study is an observational study, causality was not inferred from the identified associations. However, confirmation of the proposed associations in older adults with

cancer will provide useful insight and hypothesis generation for the development and testing of physical activity interventions for cancer fatigue in this population.

Ethical Considerations

The Oncology Nursing Society-funded study received ethics approval from the Queen's University Research Ethics Board, and the University of Ottawa Research Ethics Board also approved the secondary analysis. The protection of human rights related to the recruitment, data collection and data analysis stages of the study are described in the study design sections of the third and fourth chapters. The consent form (Appendix F) outlines the risks and benefits to participation, confidentiality, and the freedom to withdraw or participate. Confidentiality will be protected and no identifying information will be revealed in the study results. Only anonymous statistical information will be published.

Format of Thesis

This manuscript-based thesis consists of three distinct papers prepared as submissions for publication. Chapter two (the first manuscript) addresses the first objective of the thesis which is to synthesize the current research evidence related to the effectiveness of physical activity as an intervention to reduce fatigue in older adults with cancer during and following cancer treatment. This manuscript has been accepted for publication in *Cancer Nursing* pending minimal revisions, which have been submitted.

Chapter three (the second manuscript) addresses the second objective of the thesis, which is to describe the prevalence of cancer fatigue in a cohort of older adults with cancer at the time of consultation for treatment at a cancer centre, at three months, and at six months following the consultation, and the third objective which is to determine the relationships between fatigue and physical activity, in a cohort of older adults with cancer in the six months following

consultation for treatment at a cancer centre. In addressing the third objective, the third chapter focuses on the first two research questions: “Is there a relationship between baseline physical activity levels and fatigue at three months and six months?” and “Is there a relationship between physical activity at three months and fatigue levels at three months and six months?”

Chapter four (the third manuscript) addresses the fourth objective which is to determine the relationships between fatigue and physical activity, and physical function and quality of life, in a cohort of older adults with cancer in the six months following consultation for treatment at a cancer centre. In addressing this final objective, the fourth chapter focuses on the third and fourth research questions: “Is there a relationship between physical activity levels at three months physical functioning at six months?” and “Is there a relationship between physical activity levels at three months and quality of life at six months?”

Chapter five consists of an integrative summary and describes the thesis contribution to knowledge. This chapter also discusses implications for practice, policy, education and future research.

Overview of Chapters

The second chapter, “Fatigue and Physical Activity in Older Adults with Cancer: A Systematic Review of the Literature,” outlines the methodology and results of a systematic review. Nine experimental studies and ten observational studies were synthesized in the review. An assessment of the methodological approach of each of the studies was conducted using the Queen’s Joanna Briggs Collaboration (QJBC) forms for critical appraisal for experimental and observational studies (Joanna Briggs Institute, 2005). This systematic review synthesizes current knowledge about the effectiveness of physical activity as an intervention to reduce fatigue in

older adults with cancer during and following cancer treatment. This analysis provides the foundation and direction for the remainder of the thesis.

The third and fourth chapters describe a secondary analysis of data collected for a prospective, longitudinal, descriptive study entitled *Health and Well Being in Older Persons with Cancer*. Data collection took place at the Cancer Centre of Southeastern Ontario. Patients were considered for inclusion in the study if they were 65 years of age or older, attended consultation at the cancer centre for treatment of cancer of the lung, breast, GU, GI, head or neck, lymphoma, leukemia, or skin cancer. Patients were excluded if they were currently referred to or receiving palliative care.

All patients who met the inclusion criteria were approached to participate in the study. Potential subjects were recruited by telephone by a research assistant. Consenting participants received a mailed questionnaire package and consent. Oncology and medical records were reviewed and appropriate clinical information was collected through chart review. Recruitment and enrollment of patients was conducted between October 2003 and April 2005, resulting in 440 subjects returning the baseline questionnaire. This study looked at data collected at baseline, three months and six months. A total of 328 subjects completed the six-month questionnaire and were included in the analysis (Appendix G). For regression analysis, the sample size needs to be at least 5-10 times the number of variables entered into the analysis (Norman & Streiner, 2000). This condition was met with the sample of 328 subjects who completed the six-month questionnaire

Standard descriptive univariate measures such as means, standard deviations, and frequencies were calculated to describe the patient characteristics, and outcome scores. In order to address the research questions, Pearson correlations were calculated between the outcome

variables at baseline, three months and six months, and between the three time periods.

Multivariate linear regression analysis was performed to control for demographic characteristics, disease site and treatment modality.

The third chapter, “Fatigue and Physical Activity in Older Adults with Cancer: A Six-Month Followup Study”, looks specifically at the relationship between fatigue and physical activity over a six-month period. The baseline demographic characteristics of the study participants are presented, along with data describing cancer site, cancer stage and treatment modality. The prevalence of the top ten symptoms reported by this cohort is presented along with the outcome scores and correlations between fatigue and physical activity. Results of the stepwise linear regression models predicting fatigue at 3 months and 6 months post study enrolment are presented and discussed.

The fourth chapter, “The Relationship of Fatigue and Physical Activity with Physical Function and Quality of Life in Older Adults with Cancer: A Six-Month Followup Study,” looks at the relationships between the four variables of interest and specifically the influence of physical activity levels during cancer treatment on physical function and quality of life outcomes following cancer treatment. Outcome scores and correlations between the four variables of interest are presented and discussed, along with the results of the stepwise linear regression models predicting physical function and quality of life at 6 months post study enrolment.

In the fifth chapter, the thesis summary, findings from the systematic review are integrated with the findings from the quantitative secondary analysis of the six-month data from the *Health and Well Being in Older Persons with Cancer* study. The contribution of this thesis to the knowledge of this patient population is identified, and implications for practice, policy, education and future research are presented.

Contributions to Manuscripts

Marian Luctkar-Flude is the primary author, and Dianne Groll, Joan Tranmer, Kirsten Woodend, and David Holmes are co-authors of all three manuscripts. Marian Luctkar-Flude was responsible for the conception and design of the study, analysis plan, analysis, interpretation of the data and drafting the manuscripts. Dianne Groll, Joan Tranmer, Kirsten Woodend and David Holmes made contributions to the conception and study design, analysis plan, and critically reviewed and suggested revisions to drafts of the manuscripts.

References

- Aaronson, N.K., Ahmedzai, S., Bergman, B., Bullinger, M., Cull, A., Duez, N.J., et al. (1993). The European Organization for Research And Treatment of Cancer QLQ-C30: A quality-of-life instrument for use in international clinical trials in oncology. *Journal of the National Cancer Institute*, 85(5), 365-376.
- Akechi, T., Kugaya, A., Okamura, H., Yamawaki, S., & Uchitomi, Y. (1999). Fatigue and its associated factors in ambulatory cancer patients: a preliminary study. *Journal of Pain and Symptom Management*, 17(1), 42-48.
- American Society of Clinical Oncology. (1996). Outcomes of cancer treatment for technology assessment and cancer treatment guidelines. *Journal of Clinical Oncology*, 14, 671-679.
- Ashbury, F.D., Findlay, H., Reynolds, B., & McKerracher, K. (1998). A Canadian survey of cancer patients' experiences: Are their needs being met? *Journal of Pain and Symptom Management*, 16(5), 298-306.
- Baird, S.B., McCorkle, R., & Grant, M. (1991). *Cancer nursing: a comprehensive textbook*. Philadelphia: W.B. Saunders.
- Berger, A. (1998). Patterns of fatigue and activity and rest during adjuvant breast cancer chemotherapy. *Oncology Nursing Forum*, 25, 51-62.
- Berger, A.M., & Farr, L. (1999). The influence of daytime inactivity and nighttime restlessness on cancer-related fatigue. *Oncology Nursing Forum*, 26, 1663-1671.
- Bower, J.E., Ganz, P.A., Desmond, K.A., Rowland, J.H., Meyerowitz, B.E., & Belin, T.R. (2000). Fatigue in breast cancer survivors: Occurrence, correlates, and impact on quality of life. *Journal of Clinical Oncology*, 18, 743-753.

- Broekel, J.A., Jacobsen, P.B., Horton, J., Balducci, L., & Lyman, G.H. (1998). Characteristics and correlates of fatigue after adjuvant chemotherapy for breast cancer. *Journal of Clinical Oncology, 16*, 1689-1696.
- Bultmann, U., Kant, I.J., Kasl, S.V., Schroer, K.A., Swaen, G.M., & van den Brandt, P.A. (2002). Lifestyle factors as risk factors for fatigue and psychological distress in the working population: Prospective results from the Maastricht Cohort Study. *Journal of Occupational and Environmental Medicine, 44*(2), 116-124.
- Camarillo, M.A. (1991). The oncology patient's experience of fatigue. *Quality of Life--A Nursing Challenge, 1*(1), 39-44.
- Canadian Cancer Society/National Cancer Institute of Canada (2006). *Canadian cancer statistics 2006*. Toronto: Canadian Cancer Society/National Cancer Institute of Canada.
- Caspersen, C.J., Powell, K.E., & Christenson, G.M. (1985). Physical activity, exercise, & physical fitness: Definitions and distinctions for health-related research. *Public Health Reports, 100*(2), 126-131.
- Cella, D.F., & Cherin, E.A. (1988). Quality of life during and after cancer treatment. *Comprehensive Therapy, 14*, 69-75.
- Cella, D.F., & Tulsky, D.S. (1990). Measuring quality of life today: Methodological aspects. *Oncology, 14*, 101-108.
- Cella (1997). The functional assessment of cancer therapy-anemia (FACT-An) scale: a new tool for the assessment of outcomes in cancer anemia and fatigue. *Seminars in Haematology, 34*, 13-19.
- Cella, D., Peterman, A., Passik, S., Jacobsen, P., & Breitbart, W. (1998). Progress toward guidelines for the management of fatigue. *Oncology, 12*(11A), 369-377.

- Courneya, K.S., & Friedenreich, C.M. (1997a). Relationship between exercise during treatment and current quality of life among survivors of breast cancer. *Journal of Psychosocial Oncology, 15*, 35-57.
- Courneya, K.S., & Friedenreich, C.M. (1997b). Relationship between exercise pattern across the cancer experience and current quality of life in colorectal cancer survivors. *Journal of Alternative and Complementary Medicine, 3*, 215-226.
- Curt, G.A. (2000). The impact of fatigue on patients with cancer: Overview of FATIGUE 1 and 2. *The Oncologist, 5*(suppl 2), 9-12.
- Curt, G., Breitbart, W., Cella, D., Groopman, J., Horning, S., Itri, L., et al. (2000). Impact of cancer-related fatigue on the lives of patients: New findings from the fatigue coalition. *Oncologist, 5*, 353-360.
- Curtis, E.B., Krech, R., & Walsh, T.D. (1991). Common symptoms in patients with advanced cancer. *Journal of Palliative Care, 7*(2), 25-29.
- De Jong, N., Courtens, A.M., Abu-Saad, H.H., & Schouten, H.C. (2002). Fatigue in patients with breast cancer receiving adjuvant chemotherapy: A review of the literature. *Cancer Nursing, 25*, 283-297.
- Dimeo, F.C. (2001). Effects of exercise on cancer-related fatigue. *Cancer, 15*(Suppl.6), 1689-1693.
- Dimeo, F., Rumberger, B., & Keul, J. (1998). Aerobic exercise as therapy for cancer fatigue. *Medicine and Science in Sports and Exercise, 30*, 475-478.
- Dimeo, F., Stieglitz, R.D., Novelli-Fischer, U., Fetscher, S., & Keul, J. (1999). Effects of physical activity on the fatigue and psychologic status of cancer patients during chemotherapy. *Cancer, 85*, 2273-2277.

- Dimeo, F., Stieglitz, R.D., Novelli-Fischer, U., Fetscher, S., Mertelsmann, R., & Keul, J. (1997). Correlation between physical performance and fatigue in cancer patients. *Annals of Oncology*, 8, 1251-1255.
- Donovan, K., Sanson-Fisher, R.W., & Redman, S. (1989). Measuring quality of life in cancer patients. *Journal of Clinical Oncology*, 7, 959-968.
- Duthie, E.H. (2004). Physiology of aging: Relevance to symptoms, perceptions, and treatment tolerance. In L. Balducci, G.H. Lyman, W.B. Ershler, & M. Extermann (Eds.), *Comprehensive Geriatric Oncology* (2nd ed., pp.208-222). New York: Taylor & Francis.
- Ferrell, B.R., Grant, M., Dean, G.E., Funk, B., & Ly, J. (1996). "Bone tired": the experience of fatigue and its impact on quality of life. *Oncology Nursing Forum*, 23, 1539-47.
- Fletcher, H., Rueffer, J.U., Nentry-Amar, M., Mellink, W.A., Sieber, M., Ferme, C., et al. (1998). Quality of life assessment in Hodgkin's disease: a new comprehensive approach. First Experience from the EORTC/GHSG trials. *Annals of Oncology*, 9, 147-154.
- Garman, K.S., & Cohen, H.J. (2002). Functional status and the elderly cancer patient. *Critical Reviews in Oncology/Hematology*, 43, 191-208.
- Gill, T.M., & Feinstein, A.R. (1994). A critical appraisal of the quality of quality-of-life measurements. *Journal of the American Medical Association*, 272, 619.
- Given, C.W., Given, B., Azzouz, F., Kozachik, S., & Stommel, M. (2001). Predictors of pain and fatigue in the year following diagnosis among elderly cancer patients. *Journal of Pain and Symptom Management*, 21, 456-466.
- Glaus, A. (1993). Assessment of fatigue in cancer and non-cancer patients and in healthy individuals. *Supportive Care in Cancer*, 1, 305-315.

- Graydon, J.E., Bubela, N., Irvine, D., & Vincent, L. (1995). Fatigue-reducing strategies used by patients receiving treatment for cancer. *Cancer Nursing, 18*, 23-28.
- Groenwald, S.L., Frogge, M.H., & Goodman, M., & Yarbro, C.H. (1997). *Cancer nursing: Principles and practice*. Garden City, New York: Doubleday.
- Groll, D.L., Heyland, D.K., Caesar, M., & Wright, J.G. (2006). Assessment of long-term physical function in acute respiratory distress syndrome (ARDS) patients: Comparison of the Charlson Comorbidity Index and the Functional Comorbidity Index. *American Journal of Physical Medicine & Rehabilitation, 85*(7), 1-8.
- Groll, D.L., To, T., Bombardier, C., & Wright, J.G. (2005). The development of a comorbidity index with physical function as the outcome. *Journal of Clinical Epidemiology, 58*, 595-602.
- Headley, J.A., Ownby, K.K., & John, L.D. (2004). The effect of seated exercise on fatigue and quality of life in women with advanced breast cancer. *Oncology Nursing Forum, 31*, 977-983.
- Hickok, J.T., Roscoe, J.A., Morrow, G.R., & Bushunow, P. (1998). Wrist actigraphy as a measure of fatigue (Abstract No. 231). *Proceedings of the American Society of Clinical Oncology, 17*, 60a.
- Holzner, B., Kemmler, G., Meraner, V., Maislinger, A., Kopp, M., Bodner, T., et al. (2003). Fatigue in ovarian carcinoma patients: a neglected issue? *Cancer, 15*, 1564-1572.
- Hotopf, M. (2004). Definitions, epidemiology, and models of fatigue in the general population and in cancer. In J. Arms, M. Krishnasamy, & I.J. Higginson (Eds.), *Fatigue in cancer* (pp. 3-27). Oxford: Oxford University Press.

- Irvine, D., Vincent, L., Bubela, N., Thompson, L., & Graydon, J. (1991). A critical appraisal of the research literature investigating fatigue in the individual with cancer. *Cancer Nursing, 14*, 188-199.
- Irvine, D., Vincent, L., Graydon, J., Bubela, N., & Thompson, L. (1994). The prevalence and correlates of fatigue in patients receiving treatment with chemotherapy and radiation therapy: a comparison with the fatigue experienced by healthy individuals. *Cancer Nursing, 17*, 367-378.
- Irwin, M., Crumley, D., McTiernan, A., Bernstein, L., Baumgartner, R., Gilliland, F., et al. (2003). Physical activity levels before and after a diagnosis of breast cancer: The Health, Eating, Activity, and Lifestyle (HEAL) Study. *Cancer, 97*, 1746-1757.
- Jacobsen, P.B., Hann, D.M., Azzarello, L.M., Horton, J., Balducci, L., & Lyman, G.H. (1999). Fatigue in women receiving adjuvant chemotherapy for breast cancer: characteristics, course, and correlates. *Journal of Pain and Symptom Management, 18*(4), 233-242.
- Joanna Briggs Institute. (2005). *Train the Trainer, Module 2* (pp.32-41). Adelaide: Joanna Briggs Institute.
- King, A.C., Rejeski, W.J., & Buchner, D.M. (1998). Physical activity interventions targeting older adults. *American Journal of Preventative Medicine, 15*, 316-333.
- Loge, J.H., Abrahamsen, A.F., Ekeberg, O., & Kaasa, S. (2000). Fatigue and psychiatric morbidity among Hodgkin's disease survivors. *Journal of Pain and Symptom Management, 19*(2), 91-99.
- Longman, A.J., Braden, C.J., Mishel, M.H. (1999). Side-effects burden, psychological adjustment, and life quality in women with breast cancer: pattern of association over time. *Oncology Nursing Forum, 26*, 909-915.

- MacVicar, M.G., Winningham, M.L., & Nickel, J.L. (1989). Effects of aerobic interval training on cancer patients' functional capacity. *Nursing Research* 38, 348-351.
- Mock, V. (2001). Fatigue management: Evidence and guidelines for practice. *Cancer Supplement*, 92, 1699-1707.
- Mock, V., Burke, M., Sheehan, P., Creaton, E., Winningham, M., McKenney-Tedder, S., et al. (1994). A nursing rehabilitation program for women with breast cancer receiving adjuvant chemotherapy. *Oncology Nursing Forum*, 21, 899-907.
- Mock, V., Hassey Dow, K., Meares, C.J., Grimm, P.M., Dienemann, J.A., Haisfield-Wolfe, M.E., et al. (1997). Effects of exercise on fatigue, physical functioning, and emotional distress during radiation therapy for breast cancer. *Oncology Nursing Forum*, 24, 991-1000.
- Mock, V., McCorkle, R., & Krumm, S. (2003). Clinical excellence through evidence-based practice: Fatigue management as a model. *Oncology Nursing Forum*, 30, 1-18.
- Mock, V., Pickett, M., Ropka, M.E., Lin, E.M., Stewart, K.J., Rhodes, V.A., et al. (2001). Fatigue and quality of life outcomes of exercise during cancer treatment. *Cancer Practice*, 9, 119-127.
- Nail, L.M. (2002). Fatigue in patients with cancer. *Oncology Nursing Forum*, 29, 537-46.
- Nail, L.M., & Jones, L.S. (1995). Fatigue as a side effect of cancer treatment: Impact on quality of life. *Quality of Life--A Nursing Challenge*, 4(1), 8-13.
- Nail, L.M., & Winningham, M.L. (1995). Fatigue and weakness in cancer patients: the symptom experience. *Seminars in Oncology Nursing*, 11(4), 272-278.

- National Comprehensive Cancer Network (NCCN). (2003). Cancer-related fatigue: Clinical practice guidelines in oncology. *Journal of the National Comprehensive Cancer Network*, 1, 308-331.
- Norman, G.R., & Streiner, D.L. (2000). *Biostatistics: The bare essentials*. Hamilton, ON: B.C. Decker Inc.
- Oldervoll, L.M., Kaasa, S., Knobel, H., & Loge, J.H. (2003). Exercise reduces fatigue in chronic fatigued Hodgkins disease survivors - Results from a pilot study. *European Journal of Cancer*, 39(1), 57-63.
- Olschewski, M., Schulgen, G., Schumacher, M., & Altman, D.G. (1994). Quality of Life Assessment in Clinical Cancer Research. *British Journal of Cancer*, 70, 1-5.
- Osoba, D. (1994). Lessons learned from measuring health-related quality of life in oncology. *Journal of Clinical Oncology*, 12, 608-616.
- Otto, S.E. (1993). *Oncology Nursing*. St. Louis: Mosby.
- Patrick, D.L., & Erickson, P. (1993). Assessing health-related quality of life for clinical decision making. In S.R. Walker & R.M. Rosser (Eds.), *Quality of Life Assessment. Key issues in the 1990s*. (pp. 11-64). Lancaster: Kluwer.
- Penedo, F.J., Schneiderman, N., Dahn, J.R., & Gonzalez, J.S. (2004). Physical activity interventions in the elderly: cancer and comorbidity. *Cancer Investigation*, 22(1), 51-67.
- Portenoy, R.K., & Itri, L.M. (1999). Cancer-related fatigue: Guidelines for evaluation and management. *The Oncologist*, 4, 1-10.
- Portenoy R.K., Thaler, H.T., Kornblith, A.B., McCarthy Lepore, J., Friedlander-Klar, H., Kiyasu, E., et al. (1994). The Memorial Symptom Assessment Scale: An instrument for

- the evaluation of symptom prevalence, characteristics and distress. *European Journal of Cancer*, 30A, 1326-1336.
- Rao, A., & Cohen, H.J. (2004). Symptom management in the elderly cancer patient: fatigue, pain, and depression. *Journal of the National Cancer Institute*, 32, 150-157.
- Rhodes, V.A., Watson, P.M., & Hanson, B.M. (1988). Patients' descriptions of the influence of tiredness and weakness on self-care abilities. *Cancer Nursing*, 11, 186-194.
- Richardson, A., & Ream, E.K. (1997). Self-care behaviors initiated by chemotherapy patients in response to fatigue. *International Journal of Nursing Studies*, 34, 35-43.
- Rieger, P.T. (2001). Assessment and epidemiologic issues related to fatigue. *Cancer*, 92(6 Suppl), 1733-1736.
- Rosenthal, M.A., & Oratz, R. (1998). Phase II clinical trial of recombinant alpha 2b interferon and 13 cis retinoic acid in patients with metastatic melanoma. *American Journal of Clinical Oncology*, 21, 352-354.
- Schwartz, A.L. (1998). Patterns of exercise and fatigue in physically active cancer survivors. *Oncology Nursing Forum*, 25, 485-491.
- Schwartz, A.L. (1999). Fatigue mediates the effects of exercise on quality of life in women with breast cancer. *Quality of Life Research*, 8, 529-538.
- Schwartz, A.L. (2000). Daily fatigue patterns and effect of exercise in women with breast cancer. *Cancer Practice*, 8(1), 16-24.
- Schwarz, R., & Hinz, A. (2001). Reference data for the quality of life questionnaire EORTC QLQ-C30 in the general German population. *European Journal of Cancer*, 37, 1345-1351.

- Schwarz, A.L., Mori, M., Gao, R., Nail, L.M., & King, M.E. (2001). Exercise reduces fatigue in women with breast cancer receiving chemotherapy. *Medicine and Science in Sports and Exercise, 33*, 718-723.
- Segal, R.J., Reid, R.D., Courneya, K.S., Malone, S.C., Parliament, M.B., Scott, C.G., et al. (2003). Resistance exercise in men receiving androgen deprivation therapy for prostate cancer. *Journal of Clinical Oncology, 21*, 1653-1659.
- Silliman, R.A., Balducci, L., Goodwin, J.S., Holmes, F.F., & Levanthal, E.A., (1993). Breast cancer in old age: What we know, don't know, and do. *Journal of the National Cancer Institute, 85* (3), 190-199.
- Skalla, K.A., & Rieger, P.T. (1995). Fatigue. In P.T. Rieger (Ed.), *Biotherapy: A comprehensive review* (pp. 221-242). Subury, MA: Jones and Bartlett.
- Smets, E.M.A., Visser, M., Willems-Groot, A., & Garssen, B. (1998). Fatigue and radiotherapy: experience in patients undergoing treatment. *British Journal of Cancer, 78*, 899-906.
- Stasi, R., Abriani, L., Beccaglia, P., Terzoli, E., & Amadori, S. (2003). Cancer-related fatigue: Evolving concepts in evaluation and treatment. *Cancer, 98*, 1786-1801.
- Stone, P., Richards, M., A'Hern, R., & Hardy, J. (2000). A study to investigate the prevalence, severity and correlates of fatigue among patients with cancer in comparison with a control group of volunteers without cancer. *Annals of Oncology, 11*, 561-567.
- Stone, P., Richards, M., A'Hern, R., & Hardy, J. (2001). Fatigue in patients with cancers of the breast or prostate undergoing radical radiotherapy. *Journal of Pain and Symptom Management, 22*, 1007-1015.
- U.S. Department of Health and Human Services. (1996). *Physical activity and health: A report of the Surgeon General*. Atlanta, GA: U.S. Department of Health and Human Services,

Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion.

Visovsky, C., & Schneider, S.M. (2003). Cancer-related fatigue. *Online Journal of Issues in Nursing*, 1-23.

Vogelzang, N., Breitbart, W., Cella, D., Curt, G.A., Groopman, J.E., Horning, S.J., et al. (1997). Patient, caregiver, and oncologist perceptions of cancer-related fatigue: results of a tripart assessment survey. *Seminars in Hematology*, 34(suppl 2), 4-12.

Ware, J.E., Kosinski M., & Keller S.D. (1996). A 12-item short-form Health Survey. Construction of scales and preliminary tests of reliability and validity. *Medical Care*. 34(3), 220-233.

Washburn, R.A., Smith, K.W., Jette, A.M., & Janney, C.A. (1993). The physical activity scale for the elderly (PASE): Development and evaluation. *Journal of Clinical Epidemiology*, 46(2), 153-162.

Whedon, M., Stearns, D., & Mills, L.E. (1995). Quality of life of long-term adult survivors of autologous bone marrow transplantation. *Oncology Nursing Forum*, 22, 1527-1535.

Winningham, M.L., (1991). Walking program for people with cancer: Getting started. *Cancer Nursing*, 14, 270-276.

Winningham, M.L. (1999). In: Yarbrow, C.H., Frogge, M.H., Goodman, M. eds. *Cancer Symptom Management*. 2nd ed. Boston, Mass: Jones & Bartlett.

Winningham, M.L., Nail, L.M., Burke, M.B., Brophy, L., Cimprich, B., Jones, L.S. et al. (1994). Fatigue and the cancer experience: The state of the knowledge. *Oncology Nursing Forum*, 21(1), 23-36.

Yancik, R. (1997). Cancer burden in the aged: an epidemiologic and demographic overview.

Cancer, 80, 1273-1283.

Chapter Two

**Fatigue and Physical Activity in Older Adults with Cancer:
A Systematic Review of the Literature****Marian Luctkar-Flude RN, BScN, MScN(c)**

Program Coordinator, Nursing Research Unit

Kingston General Hospital

76 Stuart Street

Kingston ON K7L 2V7

Canada

613-549-6666, Ext. 3321

Fax: 613-548-1381

luctkarm@kgh.kari.net

Dianne Groll, RN, PhD

Assistant Professor

Queen's University

Joan Tranmer, RN, PhD

Assistant Professor

Queen's University

Kirsten Woodend, RN, PhD

Assistant Professor

University of Ottawa

This project was supported in part by a research fellowship from the
Queen's Joanna Briggs Collaboration.

Marian Luctkar-Flude is a Program Coordinator in the Nursing Research Unit at Kingston General Hospital, and the Lab Coordinator for the new Faculty of Health Sciences Simulation Lab at Queen's University. She is currently working on her MScN through the University of Ottawa under the supervision of Dr. Dianne Groll and Dr. Kirsten Woodend. Dr. Joan Tranmer, an Assistant Professor at Queen's University is also a member of the thesis committee.

ABSTRACT

Cancer is a disease predominantly affecting older adults. Cancer fatigue is the most common and often most distressing symptom associated with cancer and its treatment, often persisting months to years after treatment. Untreated cancer fatigue may lead to significant reductions in physical activity, physical functioning and quality of life, and may interfere with patients' adherence to cancer treatment. Physical activity has the strongest supporting evidence as an intervention to reduce cancer fatigue, maintain physical function and optimize quality of life. This paper reviews the literature related to fatigue and physical activity in older adults with cancer. Nine experimental and ten observational studies that enrolled subjects 65 years or older were synthesized in the review and provided evidence that physical activity may be an effective intervention for cancer fatigue in older adults. The generalizability of the findings to older adults was limited by poor representation of this age group in the studies. Few studies provided an analysis of age-related effects of physical activity on fatigue, physical function and quality of life.

Introduction

Cancer is predominantly a disease affecting older persons, age 65 and older.¹⁻³ As the North American population ages, the number of older adults diagnosed or living with cancer will continue to increase. Cancer fatigue has been defined as “a persistent, subjective sense of tiredness related to cancer or cancer treatment that interferes with usual functioning.”⁴ Cancer fatigue has been poorly recognized, poorly understood and poorly managed.⁵ Research has associated cancer fatigue with decreases in physical activity levels and functional status^{6,7} and decreases in quality of life.^{8,9} Quality of life issues are significant considerations for older adults facing cancer treatment. Recent interest in cancer fatigue has led to studies that suggest that physical activity can reduce fatigue, improve physical functioning and enhance quality of life in cancer patients during and following cancer treatment.

Cancer Fatigue

Cancer fatigue is the most common and often the most distressing symptom associated with cancer and its treatment¹⁰⁻¹³, and is reported to affect 70 to 100% of patients receiving cancer treatment.^{14, 15} Fatigue is associated with all cancer treatment modalities: surgery, chemotherapy, radiation therapy, biotherapy and bone marrow transplantation.^{7, 16-19} However, the similarities and differences in fatigue associated with different age groups, cancer sites and comorbid conditions are poorly understood.²⁰

Research interest in cancer fatigue is a relatively recent development,²¹ lagging more than a decade behind similar research in cancer pain.²² Despite the recent development of multidisciplinary practice guidelines for the assessment and management of cancer fatigue,^{4, 23, 24} few practitioners, both medical and nursing, are aware of research recommendations and practice guidelines.²⁵ Patients often remain uneducated and do not report their fatigue to their physician.^{5,15}

Untreated cancer fatigue may result in a decrease or discontinuation of normal physical, social, interpersonal, and recreational activities, and interfere with home, family, work and educational role

performance.^{7, 26} Cancer fatigue may affect all domains of quality of life: physical, psychosocial, social and spiritual well-being,⁹ and may lead to loss of productivity and self-esteem,²⁷ and significant reductions in physical functioning and quality of life.²⁸⁻³⁰ Patients may also experience difficulty adhering to and completing treatment regimes, and may require delays in treatment, dose limitation or discontinuation of therapy, or may withdraw from clinical trials due to fatigue.^{31, 32}

Cancer Fatigue and Physical Activity

Cancer patients tend to decrease their physical activity levels after diagnosis, during and following treatment, and many do not return to their pretreatment activity levels.³³⁻³⁵ This trend is enforced as patients are often advised to limit activity and get plenty of rest.^{10, 11} However, immobility can have a draining effect on energy level²⁷ and higher fatigue levels are associated with lower activity levels.^{6, 36, 37} Researchers propose that decreased physical activity levels during cancer treatment can result in weakness and deconditioning, leading to a cycle of decreasing activity and increasing fatigue, as patients fatigue more quickly during activity.^{11, 38, 39}

Of the nonpharmacologic interventions for fatigue during cancer treatment, physical activity has the strongest supporting evidence.^{4, 39} Several randomized clinical trials have demonstrated that physical activity decreases cancer fatigue.^{6, 40-42} Aerobic exercise has been found to reduce fatigue during chemotherapy, radiation therapy^{6, 37} and after cancer treatment has been completed.⁴³

Physical function has been defined as the ability to ambulate and to perform normal activities of daily living⁴⁴. Cancer fatigue has been found to have a significant effect on patients' abilities to function in usual roles and activities.^{10, 28, 45} Higher fatigue has been associated with lower physical functioning.^{10, 46} Physical function may be improved by exercise both during and following cancer treatment.⁴⁷⁻⁵²

Physical and functional well-being are essential components for overall quality of life.⁵³ Quality of life is a multidimensional concept, entailing physical, psychological and social factors.⁵⁴ Health related quality of life considers the impact of symptoms and the distress associated with functional limitations.⁵⁵ Cancer fatigue has a negative effect on quality of life,^{7, 9, 56-58} and exercise during cancer treatment may improve quality of life.^{59, 60}

Cancer Fatigue in Older Persons

It has been reported that normal fatigue increases with age in healthy individuals⁶¹. Natural changes and comorbidities associated with aging may contribute to fatigue in older cancer patients. Few studies have looked at cancer fatigue in older persons or examined the similarities and differences with cancer fatigue in younger adults. Some factors identified as contributing to cancer fatigue in older persons include immobility, deconditioning, sleep disorders,⁶² use of centrally acting drugs,²⁴ anemia⁶³ and decline in functional reserve of organ systems.⁶⁴

Treatment of cancer fatigue in the elderly has been poorly studied.⁶⁵ Despite the higher prevalence of cancer in older adults, this age group remains underrepresented in clinical cancer treatment trials⁶⁶ and treatments for cancer fatigue have not addressed the specific concerns of older persons.

Physical Activity and Cancer Fatigue in Older Adults

Few studies have assessed the efficacy of physical activity interventions in the elderly.⁵² It has been proposed that physical activity interventions could help in preserving functional status,⁶⁵ a person's ability to physically perform tasks related to maintaining independence,⁶⁷ and could have physical and mental health benefits in older persons.⁵² Older cancer patients are often more concerned with quality of life issues related to treatment. However, proposed physical activity programs need to be tailored to meet the unique needs of older adults.⁶⁸

Physical activity interventions have shown effectiveness in reducing cancer fatigue, and improving or maintaining physical function and quality of life in younger patients. It is not known how effective these interventions would be in older adults. A systematic review of the literature was conducted to look at the effectiveness of physical activity as an intervention to reduce fatigue in older adults with cancer during and following cancer treatment.

REVIEW METHODOLOGY

A systematic review of the literature was initiated to determine if any research had been conducted answering any of the following primary research questions related to fatigue and physical activity in older persons with cancer:

1. Do older cancer patients with higher pretreatment physical activity levels experience lower levels of fatigue during and following cancer treatment?
2. Do older cancer patients with higher levels of physical activity during cancer treatment report lower levels of fatigue during and following cancer treatment?

Secondary research questions related to physical functioning, quality of life and physical activity were the following:

3. Do older cancer patients with higher levels of physical activity during treatment maintain higher levels of physical functioning?
4. Do older cancer patients with higher levels of physical activity during treatment report higher quality of life ratings during and following cancer treatment?

Inclusion Criteria

A literature search was conducted in July 2005 of all years using the following electronic databases:

Medline, CINAHL, HealthSTAR, AMED, EMBASE, All EBM Reviews (Cochrane DSR, ACP Journal

Club, DARE, CCTR), Dissertation Abstracts International, Grey Literature (New York Academy Internet Resources), Otseeker and PEDro.

Key words 'neoplasms' and 'fatigue' were combined using an 'and' statement. Key words related to physical activity were combined using an 'or' statement and then combined with the previous search using an 'and' statement. Physical activity keywords differed according to the database being searched and included 'motor activity', 'exercise', 'physical fitness', 'exercise therapy', 'activities of daily living', 'therapeutic exercise', 'functional status', 'rehabilitation'. The keyword 'cancer' was also used in searching EBM reviews, Grey Literature, Otseeker and PEDro and the keyword "tumor" was used to search EBM reviews. Where possible the searches were limited to 'English language,' 'humans' and 'all aged 65 and older'. This resulted in a total of 430 articles, which included many articles that were listed in two or more of the databases.

Abstracts of all of the articles were scanned online to identify studies meeting the inclusion criteria. None of the studies focused on fatigue and physical activity in older adults, therefore it was decided to include any studies that enrolled any subjects who were 65 years of age or older. Studies that did not measure either one or the other of the major outcomes of interest i.e. fatigue or physical activity, or the studies that did not include any subjects who were 65 years of age or older were excluded. A search of reference lists of relevant articles yielded two additional articles that were included in the review. A total of 24 articles were retrieved for review. Closer scrutiny of the articles revealed that there were several cases where two or three of the articles were reporting on the same research study. Therefore these articles were grouped together for analysis and a total of 19 studies were identified for review.

Critical Analysis

An assessment of the methodological approach of each of the studies was conducted using the Queen's Joanna Briggs Collaboration (QJBC) forms for critical appraisal for experimental and observational studies⁶⁹. The criteria for evaluating experimental studies were: adequate randomization, treatment allocation concealed, similar prognostic factors at baseline, eligibility criteria specified, outcome assessors blinded to treatment allocation, care provider blinded, patient blinded, point estimates and measure of variability presented for primary outcome measures, and inclusion of an intention to treat analysis. The criteria for evaluating observational studies were: sufficient description of groups and distribution of prognostic factors, groups assembled at similar point in their disease progression, intervention/treatment reliably ascertained, groups comparable on all important confounding factors, adequate adjustment for the effects of confounding variables, demonstrated dose-response relationship between intervention & outcome, outcome assessment blind to exposure status, follow-up long enough for outcomes to occur, what proportion of cohort followed-up, and drop-out rates and reasons for drop-out similar across intervention and unexposed groups.

The critical appraisal process continued with the completion of a data extraction sheet for each of the 24 articles retrieved. The data extraction form was a modified version of an abstract form template⁷⁰ provided in a QJBC systematic review workshop to summarize the pertinent details from each study. The modified data extraction sheet used in the present review included the following information: reference (title, authors, journal), study design, conceptual model, setting, population, sample size, sample age, sample disease site and stage, treatment type, timing of treatment, research objectives/questions, intervention, fatigue measurement, physical activity measurement, physical functioning measurement, quality of life measurement, other variables measured, findings related to

fatigue and physical activity, findings related to physical functioning and quality of life, other findings, methodological considerations and implications for current study.

The final step in the critical analysis process was to create a synopsis table to synthesize and compare relevant data extracted from the articles. The studies were subdivided into experimental and observational studies for comparison purposes. The synopsis tables included the following information: reference, study design, sample, intervention, measurement, findings and limitations.

FINDINGS

Nine experimental studies and ten observational studies were synthesized in the review.

Experimental Studies

The experimental studies consisted of nine Randomized Controlled Trials (RCTS), implementing aerobic and/or resistance exercise interventions. The study designs, interventions, measurement tools, findings and limitations are summarized in Table 1. Eligibility criteria were clearly specified for all of the studies, and all of these studies were published after the year 2000. Seven of the nine studies described adequate randomization procedures such as computer-generated random numbers or random numbers tables. Due to the nature of the exercise interventions it was impossible to conceal treatment allocations from the subjects. However, in the case where objective measures of physical function were taken, the assessors were blinded to the treatment allocations in four of the studies.

The studies were primarily small in size, and only three of the studies had over 100 subjects enrolled. Subjects were stratified by type of adjuvant treatment (2), treatment center (1), treatment intent (1), tumor site (1) and content of group psychotherapy classes (1). Cancer sites varied by study with breast (3), prostate (2), multiple myeloma (1), colorectal (1), lung (1) and mixed (1) cancer sites included. Treatment type varied by study with combined surgery, chemo, radiation and/or hormonal treatments (5), chemotherapy (2), radiation (1), androgen deprivation therapy (1) and stem cell

transplant (1) treatments included. Cancer stage also varied by study with any stage (5), early/local stage (3), and late/advanced or metastatic (1) stages included.

Observational Studies

The ten included observational studies were a mix of descriptive quantitative designs consisting of prospective longitudinal (4), retrospective (1), cross-sectional (2) and pre-test, post-test (2). The studies were published between 1995 and 2002 and are summarized in Table 2. Half of the studies (5) were small with less than 100 subjects enrolled. Cancer sites included in these studies were breast (3), colorectal (1), lung (1), leukemia/lymphoma (1) and mixed cancer sites (4). Cancer treatments included in these studies consisted of adjuvant chemotherapy (4), radiation therapy (1), chemotherapy or radiation therapy (1) or a combination of surgery, chemotherapy and/or radiation therapy (4), for early stage cancer (3), advanced stage cancer (1), Stage I-IV (1) or unspecified cancer stages (5).

All of the experimental studies and two of the observational studies included an exercise intervention. The majority of the studies (7) randomized subjects to an exercise group versus a usual care control group. One study randomized subjects to an exercise group versus a relaxation training group, and another study randomized subjects to a Group Psychotherapy (GP) group versus a GP plus exercise group. The majority of the exercise interventions were home-based (8) versus supervised exercise programs (3). The majority of the exercise interventions consisted of aerobic exercise (7) versus resistance/strength training (2) versus both (2). Six of the exercise interventions took place during adjuvant therapy, three took place during and after adjuvant therapy, and only two took place following completion of adjuvant therapy.

A variety of validated assessment tools were used in the various studies to measure fatigue, physical activity, physical function and quality of life. Fatigue was measured both multidimensionally and

unidimensionally. Physical activity intensity and duration were measured by self-reports for home-based exercise interventions and by objective attendance records for supervised exercise interventions.

The Relationship between Physical Activity, and Fatigue:

The review of the literature revealed a paucity of information regarding the relationship between pre-treatment physical activity levels and fatigue during cancer treatment (Research Question 2). However, the following studies address some aspect of the relationship between exercise, physical activity, physical function and quality of life during treatment for cancer (Research Questions 1, 3, and 4).

Results from the experimental studies were consistently positive regarding the relationship between physical activity and decreased fatigue during cancer treatment. Despite statistical limitations due to small sample size, an American study by Coleman et al.^{71, 72} suggest that an individualized, home-based aerobic and strength-training exercise program may be effective in decreasing fatigue and improving sleep during treatment for multiple myeloma. Headley et al.⁶⁰ reported that both exercise and control groups demonstrated increases in fatigue and decreases in physical well-being in a seated exercise program for stage IV breast cancer patients undergoing adjuvant chemotherapy. However, the intervention group experienced less of an increase in fatigue and a slower decrease in physical quality of life. Mock et al.⁷³ reported that moderate walking resulted in decreased fatigue and improved physical functioning and quality of life in early stage breast cancer patients being treated with adjuvant chemotherapy or radiation therapy.

A series of Canadian studies yielded similar results. In the GROUP-HOPE trial, Courneya et al.^{74,75} found significant beneficial effects for fatigue and functional well-being in cancer patients who participated in a home-based moderate intensity exercise program, during and after cancer treatment, and found that this exercise program may improve quality of life in these patients beyond the benefits of group psychotherapy alone. Courneya et al.^{76, 77} found evidence in the REHAB trial for beneficial

effects on changes in fatigue and overall quality of life and cardiopulmonary function in a group of early stage breast cancer patients participating in a supervised incremental aerobic exercise program post treatment. They found that changes in cardiopulmonary function were correlated with changes in quality of life.

The CAN-HOPE trial found borderline significant differences for fatigue, functional well-being and satisfaction with life as a result of a personalized, home-based exercise program.⁷⁷ This study found a significant association between increased fitness and improvements in quality of life. Courneya and others^{47,78-80} found that resistance training improved symptoms of fatigue and health-related quality of life in a group of men with locally advanced or metastatic prostate cancer during treatment with androgen deprivation therapy.

Two European studies were also reviewed. A German study by Dimeo et al.¹⁷ showed that an exercise group and a relaxation-training group both showed significant improvement in fatigue and that the exercise group showed a significant increase in physical performance that was not correlated with reduced fatigue. And finally, a Scottish study by Windsor et al.⁸¹ found that physically active patients participating in a home-based moderate-intensity walking program had lower fatigue levels before, during and after radiotherapy treatment for localized prostate cancer. The study also found a nonsignificant deterioration in physical functioning in the control group and a significant improvement in physical functioning in the exercise group.

Berger and Farr⁸² reported that daytime inactivity was associated with higher fatigue in a sample of women with early stage breast cancer during adjuvant chemotherapy. Berger and Higginbotham⁸³ reported that higher fatigue was correlated with lower activity, poorer health status and more symptom distress in a small sample of women with early stage breast during and following treatment with adjuvant chemotherapy.

A study comparing fatigue and fatigue relieving strategies among women with breast, ovarian, cervical or endometrial cancer undergoing either chemotherapy or radiation therapy found that the two groups did not differ significantly in level of fatigue or effectiveness of fatigue relieving strategies⁸⁴. Although few women chose exercise, it was found to be among the most effective strategies for relieving fatigue. Another study conducted by the same research group found that fatigue and alterations in functional activities increased over the course of radiation therapy in a mixed cancer site sample⁸⁵ and returned to pretreatment levels by three months post-treatment. Exercise was the least frequently used fatigue relieving strategy used by this sample of cancer patients. Sleep was the most effective strategy used, but exercise was effective for some subjects.

In a study of patients with metastatic colorectal cancer prior to treatment with chemotherapy, fatigue was associated with diminished mean activity.⁸⁶ Quality of life and physical function scores were correlated with circadian rest/activity levels but not to mean activity level. A retrospective study of athletic cancer survivors by Schwartz⁸⁷ found that a large percentage of the subjects used moderate exercise as an intervention to reduce fatigue, and that the majority of subjects decreased their usual exercise during treatment, despite positive effects of exercise on fatigue. An eight-week home-based aerobic exercise program was effective in reducing fatigue and maintaining functional ability in a group of women receiving chemotherapy treatment for Stage II breast cancer.⁸⁸ Exercise was consistently associated with reducing fatigue on the day of exercise and one day afterward.

A large study of advanced lung cancer patients reported that fatigue interfered with at least one daily life activity in over half of the subjects, and that fatigue predominantly interfered with physical activities⁸⁹. A pre-test, post-test six-week individualized exercise program with an education component resulted in subjects experiencing less general fatigue, physical fatigue and reduction in motivation, and showing significant improvement in physical functioning and positive effects on

quality of life after the program⁹⁰. Wang et al.⁹¹ found that over half of subjects in a sample of leukemia and lymphoma patients reported that severe fatigue severely interfered with normal function and fatigue had a substantially negative effect on general quality of life. Poor performance status correlated with higher mean “fatigue worst” scores in the study.

Age-Related Findings

Although none of the experimental or observational studies were focused on the older adult age group, a few of the studies reported conducting age-related analyses. Subanalysis of the GROUP-HOPE trial suggested that older participants derived less benefit from exercise than younger participants⁷⁴. Similarly, subanalysis of the REHAB trial also provided evidence that older participants may not have benefited as much from exercise during cancer treatment, although they did show some benefit⁷⁶. Due to insufficient numbers, the cut-off point used for older adults was 60 years of age instead of the usual 65 years of age. A significant age-related finding reported by Courneya and colleagues was that age was a negative predictor of exercise adherence for participants 75 and older⁷⁸.

The study by Berger and Farr excluded women over 70 years of age, and those with comorbid conditions, which likely may have included a large percentage of older adults⁸². Graydon et al. reported that fatigue scores were not correlated with age when measured with the Pearson Byars Fatigue Feeling Checklist, however on the Fatigue Relief Scale, older subjects had greater relief of fatigue at the 2nd time point⁸⁴. Irvine et al. found no relationship between fatigue scores and age using the same assessment tools⁸⁵ and Wang et al. found no differences in fatigue for any demographic variables including age⁹¹.

The remaining studies reported no subanalysis of older adults. This is likely due to the small enrollment numbers of older adults in these studies. Nineteen studies were reviewed that enrolled persons age 65 and over, however only two studies reported a mean subject age of 65 years or over^{78, 81}.

Only three studies reported mean subject ages between 60 and 64 years of age^{79,85,89} and the remaining studies reported mean subject ages less than 60 years of age. Thus older persons were not well represented in the majority of these studies.

Discussion

This review of the literature has provided evidence that exercise, both aerobic and strength training, may reduce fatigue in cancer patients during and after cancer treatment. This positive effect is consistent across various cancer sites, cancer stages and cancer treatment modalities. Exercise is also associated with improvements or slower declines in physical functioning and quality of life in the studies reviewed. The evidence from the nine randomized controlled trials is strong but limited by small sample sizes, use of self-report measures, high attrition rates and exercise contamination/diffusion of treatment effects. The studies did not report on the significance of pre-treatment exercise on fatigue during and after cancer treatment but one study reported that baseline physical activity level was highly correlated with exercise levels during treatment regardless of random group assignment.⁷³ This is consistent with the exercise contamination reported in many of the studies.

Although providing weaker evidence, the observational studies also consistently demonstrated lower fatigue levels being associated with higher activity levels, and supported the negative effects of fatigue on physical function and quality of life. The observational studies were limited by their descriptive and single-group designs, small sample sizes and use of self-report measures.

The greatest limitation of this review lies in the limited generalizability of the findings to the population of older adults with cancer. Although the studies enrolled older adults, this age group was poorly represented and few studies provided an analysis of age-related effects of physical activity on fatigue, physical function and quality of life in cancer patients.

In terms of addressing the research questions posed, the review did not provide an answer to the first question: Do older cancer patients with higher pretreatment physical activity levels experience lower levels of fatigue during and following cancer treatment? Most studies measured fatigue and physical activity levels during and following cancer treatment. With respect to the second, third and fourth questions, the findings from the review do support the conclusion that older cancer patients with higher levels of physical activity during treatment report lower levels of fatigue, higher levels of physical function, and higher quality of life ratings during and following cancer treatment.

The consistently positive results and lack of deleterious effects of exercise in cancer patients suggests that exercise may be beneficial to older adults with cancer. The finding that physical activity may provide less benefit to older adults⁸¹ demonstrates the need to conduct further research to determine the optimum levels of physical activity for older persons with cancer. Larger randomized controlled trials that enroll older adults or focus exclusively on this age group are necessary to provide significant results to guide clinical recommendations for physical activity in older cancer patients. The finding that advanced age is a negative predictor for exercise adherence demonstrates the need for research to identify strategies to facilitate exercise adherence in this age group in order to minimize the negative effects of fatigue due to cancer and cancer treatment, and to maintain physical function and optimize quality of life.

Reference List

1. Yancik R. Cancer burden in the aged: An epidemiologic and demographic overview. *Cancer*. 1997;80(7):1273-83.
2. National Cancer Institute of Canada. Canadian Cancer Statistics 2004. 2004. Toronto, National Cancer Institute of Canada.
3. *Cancer: Principles & Practice of Oncology*. 7th ed. Philadelphia: Lippincott Williams & Wilkins; 2005.
4. National Comprehensive Cancer Network. Cancer-related fatigue: clinical practice guidelines in oncology. *Journal of the National Comprehensive Cancer Network*. 2003;1(3):308-31.
5. Stone P, Richardson A, Ream E, Smith AG, Kerr DJ, Kearney N. Cancer-related fatigue: Inevitable, unimportant and untreatable? Results of a multi-centre patient survey. *Ann Oncol*. 2000;11:971-975.
6. Mock V, Dow KH, Meares CJ, et al. Effects of exercise on fatigue, physical functioning, and emotional distress during radiation therapy for breast cancer. *Oncol Nurs Forum*. 1997;24(6):991-1000.
7. Nail LM, Jones LS. Fatigue as a side effect of cancer treatment: Impact on quality of life. *Quality of Life--A Nursing Challenge*. 1995;4(1):8-13.
8. Longman AJ, Braden CJ, Mishel MH. Side-effects burden, psychological adjustment, and life quality in women with breast cancer: Pattern of association over time. *Oncol Nurs Forum*. 1999;26(5):909-15.
9. Ferrell BR, Grant M, Dean GE, Funk B, Ly J. "Bone tired": The experience of fatigue and its impact on quality of life. *Oncol Nurs Forum*. 1996;23(10):1539-47.
10. Curt GA, Breitbart W, Cella D et al. Impact of cancer-related fatigue on the lives of patients: New findings from the Fatigue Coalition. *Oncologist*. 2000; 5(5):353-60.
11. Winningham ML, Nail LM, Burke MB, et al. Fatigue and the cancer experience: The state of the knowledge. *Oncol Nurs Forum*. 1994;21(1):23-36.
12. Portenoy RK, Thaler HT, Kornblith AB, et al. Symptom problems, characteristics, and distress in a cancer population. *Qual Life Res*. 1994;3:183-189.
13. Glaus A. Assessment of fatigue in cancer and non-cancer patients and in healthy individuals. *Support Care Cancer*. 1993;1(6):305-315.
14. Ahlberg K, Ekman T, Gaston-Johansson F, Mock V. Assessment and management of cancer-related fatigue in adults. *Lancet*. 2003;362(9384):640-50.
15. Stasi R, Abriani L, Beccaglia P, Terzoli E, Amadori S. Cancer-related fatigue: Evolving concepts in evaluation and treatment. *Cancer*. 2003;98(9):1786-801.
16. Irvine DM, Vincent L, Bubela N, Thompson L, Graydon J. A critical appraisal of the research literature investigating fatigue in the individual with cancer. *Cancer Nurs*. 1991; 14(4):188-99.

17. Dimeo FC, Thomas F, Raabe-Menssen C, Propper F, Mathias M. Effect of aerobic exercise and relaxation training on fatigue and physical performance of cancer patients after surgery. A randomised controlled trial. *Support Care Cancer*. 2000;12(11):774-9.
18. Hacker ED, Ferrans C, Verlen E, et al. Fatigue and physical activity in patients undergoing hematopoietic stem cell transplant. *Oncol Nurs Forum*. 2006;33(3):614-24.
19. Whedon M, Stearns D, Mills LE. Quality of life of long-term adult survivors of autologous bone marrow transplantation. *Oncol Nurs Forum*. 1995;22(10):1527-37.
20. Rieger PT. Assessment and epidemiologic issues related to fatigue. *Cancer*. 2001; 92(6): 1733-6.
21. Fulton C, Knowles G. Cancer fatigue. *Eur J Cancer Care*. 2000;9:166-71.
22. Curt G, Johnston PG. Cancer fatigue: The way forward. *Oncologist*. 2003;8 Suppl 1:27-30.
23. Mock V. Fatigue management: Evidence and guidelines for practice. *Cancer*. 2001;92(6):1699-707.
24. Portenoy RK, Itri LM. Cancer-related fatigue: guidelines for evaluation and management. *Oncologist*. 1999;4(1):1-10.
25. Mock V. Clinical excellence through evidence-based practice: Fatigue management as a model. *Oncol Nurs Forum*. 2003;30(5):1-18.
26. Camarillo MA. The oncology patient's experience of fatigue. *Quality of Life--A Nursing Challenge* 1991;1(1):39-44.
27. Cella D, Peterman A, Passik S, Jacobsen P, Breitbart W. Progress toward guidelines for the management of fatigue. *Oncology*. 1998; 12(11A):369-77.
28. Jacobsen PB, Hann DM, Azzarello LM, Horton J, Balducci L, Lyman GH. Fatigue in women receiving adjuvant chemotherapy for breast cancer: Characteristics, course and correlates. *J Pain Symptom Manage*. 1999;18(4):233-42.
29. Nail LM. Fatigue in patients with cancer. *Oncol Nurs Forum*. 2002;29(3):537-46.
30. Mock V, McCorkle R, Ropka ME, Pickett M, Poniatowski B. Fatigue and physical functioning during breast cancer treatment. *Oncol Nurs Forum*. 2002;29:338.
31. Rosenthal MA, Oratz R. Phase II clinical trial of recombinant alpha 2b interferon and 13 cis retinoic acid in patients with metastatic melanoma. *Am J Clin Oncol*. 1998;21(4):352-4.
32. Visovsky C, Schneider SM. Cancer-related fatigue. *Online J Issues Nurs*. 2003;8(3):17p.
33. Irwin ML, Crumley D, McTiernan A et al. Physical activity levels before and after a diagnosis of breast carcinoma: The health, eating, activity and lifestyle (HEAL) study. *Cancer*. 2003;97(7):1746-57.
34. Courneya KS, Friedenreich CM. Relationship between exercise pattern across the cancer experience and current quality of life in colorectal cancer survivors. *J Alternative Complementary Med*. 1997;3:215-26.

35. Courneya KS, Friedenreich CM. Relationship between exercise during treatment and current quality of life among survivors of breast cancer. *J Psychosoc Oncol*. 1997;15:35-57.
36. Berger AM. Patterns of fatigue and activity and rest during adjuvant breast cancer chemotherapy. *Oncol Nurs Forum*. 1998;25(1):51-62.
37. Mock V. A nursing rehabilitation program for women with breast cancer receiving adjuvant chemotherapy. *Oncol Nurs Forum*. 1994;21(5):899-907.
38. Nail LM, Winningham ML. Fatigue and weakness in cancer patients: The symptoms experience. *Semin Oncol Nurs*. 1995;11(4):272-8.
39. Dimeo FC. Effects of exercise on cancer-related fatigue. *Cancer*. 2001;92(6):1689-93.
40. Schwartz AL. Daily fatigue patterns and effect of exercise in women with breast cancer. *Cancer Pract*. 2000; 8(1):16-24.
41. Dimeo FC, Stieglitz R-D, Novelli-Fischer U, Fetscher S, Keul J. Effects of physical activity on the fatigue and psychologic status of cancer patients during chemotherapy. *Cancer*. 1999; 85(10):2273-7.
42. Oldervoll LM, Kaasa S, Knobel H, Loge JH. Exercise reduces fatigue in chronic fatigued Hodgkin's disease survivors - Results from a pilot study. *Eur J Cancer*. 2003;39(1): 57-63.
43. Dimeo F, Fetscher S, Lange W, Mertelsmann R, Keul J. Effects of aerobic exercise on the physical performance and incidence of treatment-related complications after high-dose chemotherapy. *Blood*. 1997;90(9):3390-4.
44. Mock V. Fatigue and quality of life outcomes of exercise during cancer treatment. *Cancer Pract*. 9(3):119-27.
45. Akechi T, Kugaya A, Okamura H, Yamawaki S, Uchitomi Y. Fatigue and its associated factors in ambulatory cancer patients: A preliminary study. *J Pain Symptom Manage*. 1999;17(1):42-8.
46. Vogelzang NJ, Breitbart W, Cella D et al. Patient, caregiver, and oncologist perceptions of cancer-related fatigue: Results of a tripart assessment survey. *Semin Hematol*. 1997;34(3):4-12.
47. Segal RJ, Reid RD, Courneya KS et al. Resistance exercise in men receiving androgen deprivation therapy for prostate cancer. *J Clinical Oncol*. 2003;21(9) 1653-1659.
48. MacVicar MG, Winningham ML, Nickel JL. Effects of aerobic interval training on cancer patients' functional capacity. *Nurs Res*. 1989;38(6):348-51.
49. Dimeo F, Stieglitz RD, Novelli-Fischer U, Fetscher S, Mertelsmann R, Keul J. Correlation between physical performance and fatigue in cancer patients. *Ann Oncol*. 1997;8:1251-5.
50. Dimeo F, Rumberger BG, Keul J. Aerobic exercise as therapy for cancer fatigue. *Med Sci Sports Exerc*. 1998; 30(4):475-8.
51. Mock V. Effects of exercise on fatigue, physical functioning, and emotional distress during radiation therapy for breast cancer. *Oncol Nurs Forum*. 1997;24(6):991-1000.
52. Penedo FJ, Schneiderman N, Dahn JR, Gonzalez JS. Physical Activity Interventions in the Elderly: Cancer and Comorbidity. *Cancer Invest*. 2004;22(1):51-67.

53. Cella D, Tulskey D. Measuring quality of life today: Methodological aspects. *Oncology* 1990;14:101-8.
54. Olschewski M, Schulgen G, Schumacher M, Altman D. Quality of life assessment in clinical cancer research. *Brit J Cancer Care*. 1994;70:1-5.
55. Gill T, Feinstein A. A critical appraisal of the quality-of-life measurements. *JAMA*. 1994;272:619.
56. Smets EM, Visser MR, Willems-Groot AF et al. Fatigue and radiotherapy: (A) experience in patients undergoing treatment. *Brit J Cancer*. 1998;78(7):899-906.
57. Bower JE, Ganz PA, Desmond KA, Rowland JH, Meyerowitz BE, Belin TR. Fatigue in breast cancer survivors: occurrence, correlates, and impact on quality of life. *J Clin Oncol*. 2000;18(4):743-53.
58. Broekel J, Jacobsen P, Horton J, Balducci L, Lyman G. Characteristics and correlates of fatigue after adjuvant chemotherapy for breast cancer. *J Clin Oncol*. 1998;16(5):1689-96.
59. Schwartz AL. Fatigue mediates the effects of exercise on quality of life. *Qual Life Res*. 1999;8(6):529-38.
60. Headley JA, Ownby KK, John LD. The effect of seated exercise on fatigue and quality of life in women with advanced breast cancer. *Oncol Nurs Forum*. 2004;31(5):977-83.
61. Schwarz R, Hinz A. Reference data for the quality of life questionnaire EORTC QLQ-C30 in the general German population. *Eur J Cancer*. 2001;37:1345-51.
62. Curtis E, Krech R, Walsh T. Common symptoms in patients with advanced cancer. *J Palliat Care*. 1991;7(2):25-9.
63. Balducci L. Anemia, cancer, and aging. *Cancer Control*. 2003;10(6):478-86.
64. Duthie EH. Physiology of aging: Relevance to symptoms, perceptions, and treatment tolerance. In: Balducci L, Lyman GH, Ershler WB, Extermann M, editors. *Comprehensive Geriatric Oncology*. 2nd ed. New York: Taylor & Francis; 2004. p. 208-22.
65. Rao A, Cohen H. Symptom management in the elderly cancer patient. *J Natl Cancer Inst*. 2004;32:150-7.
66. Yee KWL, Pater JL, Pho L, Zee B, Siu LL. Enrollment of older patients in cancer treatment trials in Canada: Why is age a barrier? *J Clin Oncol*. 2003;21(8):1618-23.
67. Garman KS, Cohen HJ. Functional status and the elderly cancer patient. *Crit Rev Oncol Hematol*. 2002;43:191-208.
68. King A, Rejeski W, Buchner D. Physical activity interventions targeting older adults. *Am J Prevent Med*. 1998;15(4):316-33.
69. Joanna Briggs Institute. *Train the Trainer, Module 2*. Adelaide: The Joanna Briggs Institute;2005:32-41.
70. Harrison, M.B. Continuity of care for complex health populations: Effectiveness and efficiency of two models of hospital to home transfer. PhD Thesis, 1998.

71. Coleman EA, Hall-Barrow J, Coon S, Stewart CB. Facilitating exercise adherence for patients with multiple myeloma. *Clin J Oncol Nurs*. 2003;7(5):529-34.
72. Coleman EA, Coon S, Hall-Barrow J, Richards K, Gaylor D, Stewart B. Feasibility of exercise during treatment for multiple myeloma. *Cancer Nurs*. 2003;26(5):410-419.
73. Mock V, Pickett M, Ropka ME et al. Fatigue and quality of life outcomes of exercise during cancer treatment. *Cancer Pract*. 2001;9(3):119-27.
74. Courneya KS, Friedenreich CM, Sela RA, Quinney HA, Rhodes RE, Handman M. The group psychotherapy and home-based physical exercise (GROUP-HOPE) trial in cancer survivors: Physical fitness and quality of life outcomes. *Psychooncology*. 2003;12(4):357-74.
75. Courneya KS. Exercise in cancer survivors: An overview of research. *Med Sci Sports Exerc*. 2003;35(11):1846-52.
76. Courneya KS, Vallance JKH, McNeely ML, Karvinen KH, Peddle CJ, Mackey JR. Exercise issues in older cancer survivors. *Crit Revs Oncol Hematol*. 2004;51(3):249-61.
77. Courneya KS, Mackey JR, Bell GJ, Jones LW, Field CJ, Fairey AS. Randomized controlled trial of exercise training in postmenopausal breast cancer survivors: Cardiopulmonary and quality of life outcomes. *J Clin Oncol*. 2003;21(9):1660-8.
78. Courneya KS, Segal RJ, Reid RD, et al. Three independent factors predicted adherence in a randomized controlled trial of resistance exercise training among prostate cancer survivors. *J Clin Epidemiol*. 2004;57(6):571-9.
79. Courneya KS, Friedenreich CM, Quinney HA, Fields AL, Jones LW, Fairey AS. A randomized trial of exercise and quality of life in colorectal cancer survivors. *Eur J Cancer Care*. 2003;12(4):347-57.
80. Pickett M. Adherence to moderate-intensity exercise during breast cancer therapy. *Cancer Pract*. 2002;10(6):284-92.
81. Windsor PM, Nicol KF, Potter J. A randomized, controlled trial of aerobic exercise for treatment-related fatigue in men receiving radical external beam radiotherapy for localized prostate carcinoma. *Cancer*. 2004;101(3):550-7.
82. Berger AM, Farr L. The influences of daytime inactivity and nighttime restlessness on cancer-related fatigue. *Oncol Nurs Forum*. 1999;26(10):1663-71.
83. Berger AM, Higginbotham P. Correlates of fatigue during and following adjuvant breast cancer chemotherapy: A pilot study. *Oncol Nurs Forum*. 2000;27(9):1443-8.
84. Graydon JE, Bubela N, Irvine D, Vincent L. Fatigue-reducing strategies used by patients receiving treatment for cancer. *Cancer Nurs*. 1995;18(1):23-8.
85. Irvine DM, Vincent L, Graydon JE, Bubela N. Fatigue in women with breast cancer receiving radiation therapy. *Cancer Nurs*. 1998;21(2):127-35.
86. Mormont M-C, Waterhouse J, Bleuzen P et al. Marked 24-h rest/activity rhythms are associated with better quality of life, better response, and longer survival in patients with metastatic colorectal cancer and good performance status. *Clin Cancer Res*. 2000;6(8):3038-45.

87. Schwartz AL. Patterns of exercise and fatigue in physically active cancer survivors. *Oncol Nurs Forum*. 1998;25(3):485-91.
88. Schwartz AL, Mori M, Gao R, Nail LM, King ME. Exercise reduces daily fatigue in women with breast cancer receiving chemotherapy. *Med Sci Sports Exerc*. 2001;33(5):718-23.
89. Tanaka K, Akechi T, Okuyama T, Nishiwaki Y, Uchitomi Y. Impact of dyspnea, pain, and fatigue on daily life activities in ambulatory patients with advanced lung cancer. *J Pain Symptom Manage*. 2002; 23(5):417-23.
90. Van Weert E, Hoekstra-Weebers JEHM, Grol BMF et al. Physical functioning and quality of life after cancer rehabilitation. *Int J Rehabil Res*. 2004;27(1):27-35.
91. Wang XS, Giralt SA, Mendoza TR et al. Clinical factors associated with cancer-related fatigue in patients being treated for leukemia and non-Hodgkin's lymphoma. *J Clin Oncol*. 2002; 20(5):1319-28.

Table 1: Experimental Studies Enrolling Cancer Patients Aged 65 and Older

Reference	Study Design/ Sample	Intervention	Measurement	Findings and Limitations
Coleman, Hall- Barrow, Coon & Stewart (2003); ⁷¹	RCT, N=24, 42-74 yrs multiple myeloma,	Home-based individualized aerobic exercise & strength training, during treatment	Fatigue (F): Profile of Mood States (POMS) Physical Activity (PA): log tracking frequency, intensity	Exercise program may be effective in decreasing fatigue Small sample size High attrition rate
Coleman, Coon, et al. (2003) ⁷²	chemotherapy & stem cell transplant	during treatment	Physical Function (PF): strength tests, fitness level, body composition	Burden of exercise testing
Courneya, Friedenreich, et al. (2003); ⁷⁴	RCT, N=108, 25-74 yrs, breast & other, Stage I-IV, surgery	Home-based individualized aerobic exercise, during & after	F: Fatigue Scale (FS) of the FACT measurement system for cancer survivors PA: Leisure Score Index (LSI)	Significant beneficial effects found for fatigue & functional well-being; may improve QOL beyond benefits of group psychotherapy
Courneya (2003); ⁷⁵ Courneya, Vallance, et al. (2004) ⁷⁶ (GROUP-HOPE TRIAL)	(S), radiotherapy (RT), chemotherapy (CT)	treatment, in addition to group psychotherapy	PF: cardiovascular endurance, body composition, flexibility Quality of Life (QOL): FACT-G	Did not use full factorial design Exercise intervention not supervised Contamination of study groups Small number of older participants
Courneya, et al. (2003); ⁷⁷ Courneya (2003); ⁷⁵ Courneya, et al. (2004) ⁷⁶ (REHAB TRIAL)	RCT, N=52, 50-69 yrs, early breast, S with RT and/or CT and/or hormone therapy (HT)	Supervised incremental aerobic exercise post treatment (with or without HT)	F: FS of the FACT PA: LSI PF: FACT-B & Trial Outcome Index (TOI) & cycle ergometer QOL: Fact B & TOI	Evidence for beneficial effects on fatigue, overall QOL & cardiopulmonary functioning Low recruitment rate (14%)
Courneya, Segal, et al. (2004); ⁷⁸ Segal, Reid, et al.	RCT, N=155, M=68.2 yrs, prostate, androgen deprivation	Supervised resistance exercise training during treatment	F: FS of the FACT PA: LSI, objective attendance records PF: muscular strength	Improved symptoms of fatigue and health related QOL Exercise contamination

(2003) ⁴⁷	therapy		QOL: FACT-P	Attention effect for exercise group
Courneya et al. (2003); ⁷⁹	RCT, N=102, M=61.1 yrs, colorectal, S +/- RT/CT	Home-based personalized exercise program during treatment	F: FS of the FACT PA: LSI PF: cardiovascular, body composition & flexibility tests QOL: FACT-C & FACT-G, & Satisfaction with Life Scale (SWLS)	Significant association between change in fitness & change in QOL; borderline significant differences for fatigue & functional well-being Significant exercise contamination Unsupervised exercise intervention
Courneya (2003) ⁷⁵ (CAN-HOPE TRIAL)				
Dimeo, Thomas, Raabe-Menssen, Propper & Mathias (2004) ¹⁷	RCT, N=69, 32-74 yrs, lung & GI, Stages I-IV, S,RT or CT	Aerobic exercise vs. relaxation training, post treatment	F: European Organization for Research and Treatment of Cancer (EORTC) Quality of Life Questionnaire Core 30 (QLQ-C30) PA: Rating of Perceived Exertion Scale (RPE) PF: ergometer stress test, EORTC QLQ-C30 function scales QOL: EORTC QLQ-C30	Both groups showed improvement in fatigue; significant increase in physical performance in exercise group, not correlated with reduced fatigue No control group without therapy for fatigue
Headley, Ownby & John (2004) ⁶⁰	RCT, N=38, 37-73 yrs, breast, Stage IV, CT	Seated exercise program during treatment	F: Functional Assessment of Chronic Illness Therapy-Fatigue Version IV (FACIT-F) PA: RPE QOL: FACIT-F	Less increase in fatigue and slower decrease in QOL in exercise group Prior exercise program participation Adherence rate of 75% Inconsistent documentation of RPE
Mock, Pickett, et al. (2001); ⁷³ Pickett, Mock et al. (2002) ⁸⁰	RCT, N=50, 28-75 yrs, breast, Stage I-IV, S & CT or RT	Individualized home-based moderate walking exercise, during treatment	F: modified Piper Fatigue Scale (PFS) & investigator developed diary form PA: activity level rating scale PF: 12 minute walk test, & Medical Outcomes Study Short Health Form (MOS SF-36) physical function scale	Moderate walking resulted in decreased fatigue & improved physical functioning & QOL Diffusion of treatment effect Self-administered intervention & self report of activity

			QOL: MOS SF-36	Prior exercise participation
Windsor, Nicol & Potter (2004) ⁸¹	RCT, N=65, 52-82 yrs, M=68.8 yrs, prostate, RT	Home-based individualized moderate-intensity walking	F: Brief Fatigue Inventory (BFI) PA: wrist band heart rate monitor, Scottish Physical Activity Questionnaire, & activity diary PF: modified shuttle test, heart rate	Physically active patients had lower fatigue levels, pre, during & post treatment; significant improvement in physical functioning in exercise group

Table 2: Observational Studies Enrolling Cancer Patients Aged 65 and Older

Reference	Study Design/ Sample	Intervention or Measurement Timing	Measurement	Findings
Berger & Farr (1999) ⁸²	Prospective, descriptive, repeated measures, N=72, 33-69 years, breast, Stage I-II, surgery (S) & chemotherapy (CT)	Measurement during treatment	Fatigue (F): revised Piper Fatigue Scale (PFS) Physical Activity (PA): wrist actigraphs	Daytime inactivity associated with higher fatigue Excluded women over 70 and with comorbid conditions Incomplete data
Berger & Higginbotham (2000) ⁸³	Prospective, descriptive, repeated measures, N=14, 32-69 yrs, breast, Stage I-II, S & CT	Measurement during & after treatment	F: Morin sleep diary, Symptom Experience Scale, & PFS PA: wrist actigraphs Physical Function (PF): Medical Outcomes Study Short Health Form (MOS SF-36) physical function scale	Higher fatigue correlated with lower activity, poorer health status & more symptom distress Mean fatigue levels higher than previously reported Missing actigraph data
Graydon, Bubela, Irvine & Vincent (1995) ⁸⁴	Prospective, repeated measures, N=99, breast & other	Measurement during treatment	F: Pearson Byars Fatigue Feeling Checklist (PBFFC) & Fatigue Relief Scale	Exercise was one of the two most effective fatigue reducing strategies, but was chosen by only a few Fatigue Relief Scale was a new instrument
Irvine, et al. (1998) ⁸⁵	Longitudinal, prospective, N=121, 33-81 yrs, breast, prostate & other, RT	Measurement during & after treatment	F: PBFFC & Fatigue Relief Scale PF: Sickness Impact Profile (SIP)	Fatigue & alterations in functional activities increased over course of RT; no relationship between fatigue scores & age; exercise least frequently used strategy

Mormont, Waterhouse, et al. (2000) ⁸⁶	Prospective, N=192, 20-75 yrs, metastatic colorectal, CT	Measurement pre treatment	F: European Organization for Research and Treatment of Cancer (EORTC) Quality of Life Questionnaire Core 30 (QLQ-C30) PA: wrist actigraph PF: EORTC QLQ C-30 PF subscale QOL: EORTC QLQ C-30	Fatigue associated with diminished mean activity Global QOL & physical function not correlated with mean activity level
Schwartz (1998) ⁸⁷	Retrospective, cross-sectional, descriptive, N=192, 19-81 yrs, athletic cancer survivors	Self-report post treatment	F: rated most intense fatigue during treatment PA: self report	Fatigue rated most intense during treatment; most decreased usual exercise during treatment despite positive effects on fatigue; many used moderate exercise as an intervention to reduce fatigue
Schwartz, Mori, Gao, Nail, & King (2001) ⁸⁸	One group, pretest-posttest, N=61, 27-69 yrs, breast, Stage II, CT	8 week home-based aerobic exercise program, during treatment	F: Visual Analogue Scales (VAS-F), fatigue diary PA: diary of frequency, duration & calories expended (accelerometer) PF: 12 minute walking distance	Exercise effective in maintaining functional ability and reducing fatigue Single group design (minimized treatment diffusion)
Tanaka, et al. (2002) ⁸⁹	Cross-sectional, N=171, 27-80 yrs, M=63 yrs, lung, Stage III-IV, S and/or CT and/or RT		F: numerical scales from 0-10 PA: interference of daily activity PF: Eastern Cooperative Oncology Group (ECOG) performance status	Fatigue interfered with at least one daily life activity in over half of patients predominantly interfering with physical activities
Van Weert, et al. (2004) ⁹⁰	Prospective, pre-test-posttest, N=37, 43-67 yrs, breast & other, Stages I-IV, S and/or CT and/or RT	Individualized exercise program, psycho-education and information, post treatment	F: Multi Fatigue Index (MFI) PA: Rotterdam Symptom Check List (RSCL) activity level scores PF: bicycle ergometry test & muscle force test (dynamometer)	Experienced less general fatigue, physical fatigue & reduction in motivation following program; showed significant improvement in physical functioning & positive effects on QOL No control group

Wang, et al. (2002) ⁹¹	Cross-sectional, N=228, 18-84 years, leukemia & lymphoma, CT, RT or S	F: BFI PA: interference with general activity, walking & normal work using BFI PF: ECOG performance status QOL: BFI enjoyment of life scale	Severe fatigue interfered with normal function (50%); substantial negative effect of fatigue on QOL; poor performance status correlated with higher mean "fatigue worst" scores
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Chapter Three

Fatigue and Physical Activity in Older Adults with Cancer: A Six-Month Followup Study

Marian Luctkar-Flude RN, BScN, MScN(c)
Program Coordinator, Nursing Research
Kingston General Hospital
Kingston, Ontario
K7L 2V8
(613) 549-6666 Ext # 3321
Fax: (613) 548-1381

Dianne Groll RN, PhD
Assistant Professor
Queen's University, Department of Psychiatry
Kingston, Ontario

Kirsten Woodend RN, PhD
Associate Professor
University of Ottawa, School of Nursing
Ottawa, Ontario

Joan Tranmer RN, PhD
Assistant Professor
Queen's University, School of Nursing
Kingston, Ontario

David Holmes RN, PhD
Associate Professor
University of Ottawa, School of Nursing
Ottawa, Ontario

Abstract

Purpose: To determine the relationship between physical activity and fatigue in older adults with cancer.

Design: Longitudinal, prospective, cohort

Setting: A Canadian regional cancer centre

Sample: 440 adults aged 65 years and older seeking consultation for cancer treatment at a tertiary care regional cancer clinic.

Methods: Subjects completed self-report questionnaires at baseline, three and six months post consultation for cancer treatment, to rate fatigue (Memorial Symptom Assessment Scale), and physical activity (Physical Activity Scale for the Elderly).

Main Research Variables: Fatigue, Physical activity

Findings: Fatigue was the most prevalent symptom reported. Higher fatigue was associated with lower physical activity levels. Age and comorbidity were associated with higher fatigue and lower physical activity scores. Physical activity level significantly predicted fatigue level regardless of age.

Conclusions: Physical activity level is a modifiable factor significantly predicting cancer fatigue at 3 months and 6 months following consultation for cancer treatment. These results suggest that promoting physical activity may reduce fatigue in older adults with cancer.

Implications for Nursing: Physical activity interventions need to be developed and tested in older adults with cancer to reduce cancer fatigue.

Key Points

1. Cancer fatigue is the most prevalent symptom reported by older adults with cancer

2. Higher physical activity levels are associated with lower fatigue levels in older adults up to six months following consultation for cancer treatment.
3. Physical activity may be an effective intervention to treat cancer fatigue in older adults regardless of cancer site and treatment modality.

Introduction

Cancer is predominantly a disease affecting older persons. The increased number of new cases of cancer is primarily due to an increasing and aging population (Canadian Cancer Society/National Cancer Institute of Canada, 2006; Yancik, 1997). Forty-three percent of new cancer cases in Canada occur among those who are at least 70 years old, while 25% occur in those aged 60-69 years.

Cancer fatigue has been reported as a highly prevalent and distressing symptom that interferes with usual functioning and quality of life (Nail, 2002; Winningham, 1999; Winningham et al., 1994). The National Comprehensive Cancer Network (NCCN, 2003) has defined cancer fatigue as: "a persistent, subjective sense of tiredness related to cancer or cancer treatment that interferes with usual functioning" (p.310). Fatigue in cancer patients is associated with symptom distress, decreases in physical activity levels, and decreases in functional status (Glaus, 1993; Mock et al., 1997; Monga, Kerrigan, Thornby, & Monga, 1999; Nail & Jones, 1995). Cancer fatigue interferes with quality of life regardless of diagnosis, treatment or prognosis (Loge, Abrahamsen, Ekeberg & Kaasa, 2000; Longman, Braden, & Mishel, 1999; Stone, Richards, A'Hern, & Hardy, 2001).

It is estimated that cancer fatigue affects 70-100% of patients receiving cancer treatment (Ahlberg, Ekman, Gaston-Johansson, & Mock, 2003; Mock, McCorckle, & Krumm, 2003).

Fatigue is associated with all cancer treatment modalities: surgery, chemotherapy, radiation therapy and biotherapy (Irvine, Vincent, Bubela, Thompson & Graydon, 1991; Irvine, Vincent, Graydon, Bubela, & Thompson, 1994; Jacobsen & Stein, 1999). However, few healthcare practitioners are aware of recent research recommendations and practice guidelines (Mock, 2001; Mock et al., 2003). Patients remain uneducated about the problem and often do not report their fatigue to their physician (Donovan & Ward, 2005; Stasi, Abriani, Beccaglia, Terzoli, & Amadori, 2003). Untreated cancer fatigue may result in a decrease or discontinuation of normal physical, recreational and social activities (Camarillo, 1991; Ferrell, Grant, Dean, Funk & Ly, 1996; Nail & Jones, 1995). Patients may also experience difficulty adhering to and completing treatment regimes, and may require delays in treatment, dose limitation or discontinuation of therapy or may withdraw from clinical trials due to fatigue (Rosenthal & Oratz, 1998; Skalla & Rieger, 1995; Visovsky & Schneider, 2003; Whedon, Stearns, & Mills, 1995; Winningham et al., 1994).

Of the nonpharmacologic interventions for fatigue during cancer treatment, physical activity has the strongest supporting evidence (Dimeo, 2001; NCCN, 2003; Penedo, Schneiderman, Dahn, & Gonzalez, 2004). Physical activity has been defined as “bodily movement produced by the contracture of skeletal muscle that increases energy expenditure above the basal level” (U.S. Department of Health & Human Services, 1996, p. 20). The terms physical activity and exercise are often used synonymously in the literature; however, exercise can be viewed as a subcategory of physical activity, and defined as “physical activity that is planned, structured, repetitive, and purposive in the sense that improvement or maintenance of one or more components of physical fitness is the objective” (Caspersen, Powell & Christensen, 1985, p. 128).

Several randomized clinical trials have demonstrated that physical activity decreases cancer fatigue (Burnham & Wilcox, 2002; Dimeo, Stieglitz, Novelli-Fischer, Fetscher, & Keul, 1999; Mock et al., 1997; Oldervoll, Kaasa, Knobel, & Loge, 2003; Schwartz, 2000). These studies were conducted on cancer patients between the ages of 21 and 65 years. Aerobic exercise has been found to reduce fatigue during chemotherapy and radiation therapy as well as decreasing fatigue in cancer survivors after cancer treatment has been completed (Dimeo et al., 1997; Dimeo, Rumberger, & Keul, 1998; MacVicar, Winningham, & Nickel, 1989; Mock et al., 1994; Mock et al., 1997).

Few studies have looked at cancer fatigue in older persons (age 65 and older); therefore it is difficult to ascertain whether the experience of cancer fatigue in older persons is similar to or differs from cancer fatigue in younger adults. Some of the factors that have been identified as contributing to cancer fatigue in older persons include immobility, deconditioning, insomnia and other sleep disorders, poor nutrition, use of centrally acting drugs, decline in functional reserve of multiple organ systems, and the presence of pain or other symptoms (Curtis, Krech, & Walsh, 1991; Duthie, 2004; Portenoy & Itri, 1999; Given, Given, Azzouz, Kozachik, & Stommel, 2001). Older patients have been underrepresented in clinical trials due to physician and patient bias, and exclusion due to age, comorbidities or perceived lack of compliance (Hutchins, Unger, Crowley, Coltman, & Albain, 1999; Mitka, 2003; Repetto et al. 1998; Unger, Hutchins, & Albain, 2004). Our knowledge of cancer fatigue is based predominantly on studies conducted in younger persons. It is not known whether or not treatments effective for younger persons will also be effective in older adults. Interventions have not been tested in older persons, and to date those developed for younger persons are used.

It has been proposed that physical activity interventions could help in preserving functional status and improve physical and mental health in the elderly (Penedo et al., 2004; Rao & Cohen, 2004) however physical activity programs need to be tailored to meet the unique needs of older adults (King, Rejeski, & Buchner, 1998). Therefore, the purpose of this study was to describe the relationship between fatigue and physical activity in a cohort of older adults who are receiving cancer treatment.

Purpose

As the primary objective of this study was to determine the relationships between fatigue and physical activity in older adults with cancer the following research questions were addressed:

1. Is there a relationship between physical activity levels at study enrolment (referral to cancer centre for cancer consultation and treatment) and fatigue at 3 months and 6 months post-enrolment?
2. Is there a relationship between physical activity at 3 months and fatigue levels at 3 months and 6 months post study enrolment?

It was hypothesized that higher physical activity levels would be associated with lower fatigue levels in older adults during and following cancer treatment.

Methods

Design

This study was a secondary analysis of data collected for a prospective, longitudinal, descriptive study entitled *Health and Well Being in Older Persons with Cancer*. The primary study was conducted by a team of investigators, led by Dr. Joan Tranmer, and was funded by the Oncology Nursing Society.

Setting and Sample

Data collection took place at the Cancer Centre of Southeastern Ontario. Patients were considered for inclusion in the study if they were 65 years of age or older, attended consultation at the cancer centre for treatment of cancer of the lung, breast, GU, GI, head or neck, lymphoma, leukemia, or skin cancer. Patients were excluded if they were currently referred to or receiving palliative care

All patients who met the inclusion criteria were approached to participate in the study. Potential subjects were recruited by telephone by a research assistant. Consenting participants received a mailed questionnaire package and consent. If questionnaires were not returned within 2 weeks, the research assistant contacted the participant to encourage completion, to determine if there were any questions regarding the questionnaire, and to resend another package if required. Oncology and medical records were reviewed and a trained research assistant collected appropriate clinical information through chart review. Recruitment and enrollment of patients was conducted between October 2003 and April 2005, resulting in 440 subjects returning the baseline questionnaire. This study looked at data collected at baseline, 3-months and 6-months. A total of 328 subjects completed the 6-month questionnaire and were included in the analysis.

Outcome Variables

Fatigue.

Self-reported symptom assessment data related to fatigue was collected using the Memorial Symptom Assessment Scale (MSAS), a multidimensional, reliable and valid instrument for assessment of symptoms in cancer patients. Fatigue (lack of energy) was one item of the 32 item scale. Internal consistency (Cronbach's alpha) for the scales ranges from 0.58 to 0.88 (Portenoy et al., 1994). Scores were also highly correlated with clinical status and quality of

life measures. The MSAS asks participants to rate how often they experienced the symptom (rarely, occasionally, frequently or almost constantly), how severe the symptom usually was (slight, moderate, severe or very severe), and how much the symptom distressed or bothered them (not at all, a little bit, somewhat, quite a bit or very much). Symptom scores were calculated as the mean of the frequency, severity and distress scores (Tranmer et al., 2003).

Physical activity.

Physical activity level was measured using the Physical Activity Scale for the Elderly (PASE), which asks questions about leisure time activity (including exercise), household activity and work-related activity, and was specifically designed to assess activities engaged in by older persons (Washburn, Smith, Jette, & Janney, 1993). As older persons may be less likely to participate in formal exercise programs (U.S. Department of Health and Human Services, 1996), it is important to use a physical activity assessment tool that incorporates all of the subcategories of physical activity, including exercise. The PASE correlates well with other performance based and self-report measures (Harada, Chiu, King, & Stewart, 2001; Washburn & Ficker, 1999; Washburn, McAuley, Katula, Mihalko, & Boileau, 1999), with good internal consistency (Cronbach's alpha of 0.69), and test-retest reliability ($r = 0.60$) (Washburn et al., 1993).

Independent variables

Factors likely to affect the prevalence of fatigue in cancer patients include stage of disease, site of cancer, treatment factors (Hotopf, 2004), demographic factors (De Jong, Courtens, Abu-Saad, Schouten, 2002), lifestyle factors (Bultmann et al., 2002), and comorbidities (Bower et al. 2000). Clinical measures of disease (cancer site) severity (stage) and treatment (modality) factors were obtained through chart abstraction at baseline and at study completion. Measures of personal demographic characteristics (age, gender, marital status, education, income & living

arrangement) were obtained through self-report on the baseline questionnaire. Measures of comorbidity were obtained by self-report at baseline through completion of the Functional Comorbidity Index (FCI), which contains 18 common diagnoses (see Appendix G) associated with poorer physical function (Groll, Heyland, Caesar, & Wright, 2006; Groll, To, Bombardier, & Wright, 2005). A summary of all the variables collected is presented in Table 1.

Data Analysis

All questionnaire and chart abstraction data were entered into a Microsoft Access database and verified by a second person. Data were analyzed using SPSS Version 12.0 for Windows. Standard descriptive univariate measures such as means, standard deviations, medians and frequencies were calculated to describe the patient characteristics, fatigue scores, and physical activity scores. When the assumptions of correlation and multiple regression analysis were tested, several of the continuous variables did not meet the assumption of normality. A natural log transformation of these variables was performed and the analysis was run using both the transformed and untransformed data. The results were the same and thus the results using the untransformed data are presented.

In order to address the research questions, Pearson correlations were calculated between the outcome variables at baseline, 3 months and 6 months, and between the three time periods. Multivariate linear regression analysis was performed to control for demographic characteristics, disease site and treatment modality.

For regression analysis, the sample size needs to be at least 5-10 times the number of variables entered into the analysis (Norman & Streiner, 2000). This condition was met with the sample of 328 subjects who completed the six-month questionnaire.

Ethics

The study received ethics approval from the Queen's University Research Ethics Board, and the University of Ottawa Research Ethics Board also approved the secondary analysis.

Results

Sample Characteristics

A total of 440 subjects consented to participate and completed the baseline questionnaire. Of these, 328 (75%) completed the six-month questionnaire and 112 (25%) did not. Of these, 76 (17%) withdrew, 28 (6%) died, and 8 (2%) were lost to followup. Table 2 summarizes the demographic characteristics of the population at baseline. The mean age of the subjects was 72.6 years (range = 65-90 years) and 56% of the subjects were male. Subjects self-reported an average of 2.9 comorbidities (range = 1-12).

Most of the subjects were treated for early stage cancer of the breast, prostate, colon/rectum or lung. Subjects were treated with radiotherapy (62%), surgery (55%), chemotherapy (34%) and or hormones (21%) (Table 3).

Prevalence and Outcome Scores

Fatigue (lack of energy) was the most prevalent symptom reported at baseline (68.6%), 3 months (70.7%) and 6 months (67.9%). The related symptoms of difficulty sleeping and feeling drowsy were among the top four symptoms reported at each time point (see Table 4). Outcome scores and ranges are reported in Table 5. Mean fatigue scores (MSAS) decreased from 1.31 (SD = 1.13) at baseline to 1.13 (SD = 1.14) at 3 months, and decreased further to 0.96 (SD = 1.12) at 6 months. The changes in fatigue scores were statistically significant between baseline and three months, between baseline and six months, and between three months and six months ($p < 0.01$). Due to the skewness of the distributions, medians were also calculated. The decrease in the

median scores was even greater, from 1.33 at baseline to 0.25 at 6 months. Higher scores on the MSAS are indicative of increased frequency, intensity and/or distress of fatigue.

Physical activity scores increased from 93.3 (SD = 66.2) at baseline to 110.3 (SD = 72.3) at 3 months, and increased further to 119.7 (SD = 70.6) at 6 months. Again median scores showed a greater change from 78.93 at baseline to 111.36 at 6 months. The changes in physical activity scores were statistically significant between baseline and three months and between baseline and six months ($p < 0.01$). Higher physical activity scores on the PASE are indicative of increased frequency and/or intensity of physical activity.

Correlational Analysis

Fatigue and physical activity were negatively correlated at all time periods (Table 6). Baseline fatigue levels were positively correlated with fatigue levels at 3 months and six months, and baseline physical activity levels were positively correlated with physical activity levels at 3 months and 6 months. All correlations were statistically significant ($p < 0.001$).

Predictors of Fatigue at Three and Six Months

The dependent variables for the regression analysis were fatigue outcome scores at three months and six months post study enrolment. Physical activity scores at baseline and 3 months were entered as independent variables into two separate stepwise regression models along with the measured demographic variables, cancer site, stage and treatment modality, and self-reported functional comorbidity.

As hypothesized, baseline physical activity was significantly related to fatigue at 3 months ($\beta = -0.294$, $p = 0.018$) and 6 months ($\beta = -0.208$, $p = 0.001$). Surgery, housing arrangement, chemotherapy, and sex (female) were also significantly related to fatigue at 3 months (see Table 7); chemotherapy and radiotherapy were significantly related to fatigue at 6

months. The standardized beta values reflect the relative importance of each of the independent variables in predicting the dependent variable, thus, physical activity was the variable in the model most strongly related to fatigue.

The adjusted R^2 for the model predicting fatigue at 3 months was 0.135, and the R^2 for the model predicting fatigue at 6 months was 0.078. Both models were significant ($p < 0.001$). The adjusted R^2 is the proportion of the variation in the dependent variable explained by the regression model. Thus, the regression models using baseline physical activity level as an independent variable explain 13.5% of the variance in fatigue at 3 months and 7.8% of the variance in fatigue at 6 months.

Similarly, physical activity at 3 months was a significant predictor of fatigue at 3 months ($\beta = -0.317$, $p < 0.001$) and 6 months ($\beta = -0.177$, $p < 0.010$). Chemotherapy, functional comorbidity and housing arrangement were also significant predictors of fatigue at 3 months, and chemotherapy and functional comorbidity significantly predicted fatigue at 6 months. Again, physical activity was the strongest predictor of fatigue in each model. Physical activity level at 3 months accounted for 31.7% of the variance attributed to the model predicting fatigue at 3 months, and 17.7% of the variance attributed to the model predicting fatigue at 6 months. Adjusted R^2 for the models were 0.175 and 0.087 respectively, and both models were significant ($p < 0.001$). The regression models using physical activity level at 3 months as an independent variable explain 17.5% of the variance in fatigue at 3 months and 8.7% of the variance in fatigue at 6 months.

Discussion

The current study found that fatigue was the most prevalent symptom reported by a cohort of older adults with cancer at the time of consultation at a cancer centre and continued to be up to

six months following the consultation for treatment. This is comparable with other recent studies. Esbensen, Osterlind & Hallberg (2006) found that fatigue was the most common symptom reported at baseline and 3 months in a study of older persons with mixed cancer diagnoses, and Kenefick (2006) found that fatigue remained a primary source of symptom distress throughout six months of observation in a group of older women after surgical treatment for breast cancer.

Fatigue scores were highest at baseline when many subjects (most of the breast and colon cancer subjects) had just completed their surgery and were attending consultations at the cancer center for further adjuvant treatment. It has been reported that cancer fatigue may be present even before treatment begins (Cimprich, 1999; Morrow, Andrews, Hickok, Roscoe, & Matteson, 2002; Piper et al., 1989). Post-surgery fatigue improves with time (Tavio, Milan & Tirelli, 2002). Fatigue scores declined at 3 months and declined further at 6 months when most subjects had completed their cancer treatment. These results are also consistent with past studies that have reported that fatigue levels are highest during and immediately following cancer treatment (Headley, 1997; Janda et al., 2000; Monga et al., 1999; Truong et al., 2006; Wengstrom, Haggmark, Strander, & Forsberg, 2000; Woo, Dibble, Piper, Keating, & Weiss, 1998) however, fatigue continued to be the most prevalent symptom at 6 months, consistent with other research findings that fatigue persists beyond completion of cancer treatment (Andrykowski, Curran & Lightner, 1998; Broekel, Jacobsen, Horton, Balducci, & Lyman, 1998; Jacobsen et al., 1999; Jereczek-Fossa, Marsiglia, & Orecchia, 2002; Kaasa, Knobel, Loge, & Hjermsstad, 1998; Kenefick, 2006; Loge, Abrahamsen, Ekeberg, & Kaasa, 1999; Smets, Visser, Willems-Groot & Garssen, 1998).

Physical activity scores gradually increased over the six-month period. Some patients in our study would have had surgery prior to their consultation at the cancer centre; therefore their baseline scores may be low. In one study, surgery alone accounted for a 24% decline in physical activity (Irwin et al, 2003). As time from surgery increased, physical activity scores may be expected to increase as this has been reported in previous studies (Berger, 1998; Courneya & Friedenreich, 1997).

As hypothesized, higher physical activity levels were associated with lower fatigue levels in older adults during and following cancer treatment. Results from this study are encouraging because they are based on older cancer patient's reported physical activity levels as measured by the PASE, which reflect leisure time activity (including formal exercise), household activity and work-related activity engaged in by older persons. These results suggest that increasing physical activity further through exercise interventions may have additional benefits in reducing cancer fatigue. Recent studies and reviews of exercise interventions in cancer patients have consistently reported a negative association between physical activity and fatigue (Culos-Reed, Robinson, Lau, O'Connor, & Keats, 2007; Galvao & Newton, 2005; Luctkar-Flude et al, in press; McNeely et al., 2006; Pedersen & Saltin, 2006; Pinto, Frierson, Rabin, Trunzo, & Marcus, 2005) and provide evidence that both aerobic and resistance exercises may be effective in reducing cancer fatigue.

Results of the regression analysis indicated that having cancer surgery was associated with lower levels of fatigue at three months post study enrolment. Most of these patients had had surgery several months prior to their consultation at the cancer centre. The lower fatigue levels would be expected as post-surgery fatigue is reported to improve with time (Tavio et al., 2002).

The positive association between comorbidity and fatigue is of particular significance to the older cancer patient because older cancer patients report more comorbidities than younger cancer patients (Kurtz, Kurtz, Stommel, Given & Given, 1999; Townsley et al., 2006; Yancik et al., 2001). In this study, comorbidity and fatigue were associated regardless of age; however this study was conducted only on older persons. A study that included younger participants may have revealed that age was a more important factor. In other studies, comorbidities were associated with higher fatigue levels in women with breast cancer (Bower et al., 2000), higher symptom severity (Kurtz et al., 1999), and older women in particular were more likely to experience fatigue related to concurrent illness (Mast, 1998).

Baseline comorbidity was a significant predictor of fatigue at the 3 month and 6 month periods of this study. There is similar evidence that physical activity may also be effective in reducing the fatigue associated with comorbid conditions such as chronic obstructive pulmonary disease, chronic heart failure, fibromyalgia, chronic fatigue syndrome, and multiple sclerosis (Pedersen & Saltin, 2006; Mostert & Kesselring, 2002). In this study, treatment with chemotherapy was also associated with higher levels of fatigue. Chemotherapy has previously been associated with long-term fatigue. (Payne, 2002). The combination of chemotherapy and comorbidity appears to put older women at particular risk for cancer fatigue (Mast, 1998).

Limitations of the Study

Given that the study was an observational study, causality cannot be inferred from the identified associations. However, confirmation of the proposed associations in older adults with cancer may provide useful insight and hypothesis generation for the development and testing of physical activity interventions for cancer fatigue in this population.

This study is limited by the single study centre, which reduces the generalizability of the results to older cancer patients in general. Similarly, the heterogeneity of this sample of cancer patients in terms of cancer site, stage, treatment modality and the timing of the treatment in relation to survey completion also limits the generalizability of the findings to specific populations of cancer patients. Many subjects were late returning their baseline questionnaires and had already begun adjuvant chemotherapy or radiation treatment by the time the surveys were completed, which may have reduced the magnitude of the change in scores between the baseline and three month surveys.

Another potential limitation of this study is participation bias. It is possible that cancer patients experiencing the most fatigue were less likely to enroll in the study, and more likely to withdraw before completing all of the questionnaires. This would actually make the findings stronger, as the bias is in the correct direction. It has also been reported that older cancer patients are less likely to consent to participate in research studies (Koval et al., 1992; Neumark, Stommel, Given & Given, 2001; Tennstedt, Dettling & McKinlay, 1992). Attrition was fairly high (25%) but comparable with other studies enrolling older cancer patients. Attrition rates in longitudinal studies have been reported to range from 16 to 50% (McMillan & Weitzner, 2003; Moser, Dracup, & Doering, 2000; Motzer, Moseley, & Lewis, 1997).

Conclusions

Physical activity level is a modifiable factor that significantly predicted cancer fatigue in this cohort of older adults at three months and six months following consultation for cancer treatment. These results suggest that the inverse relationship between fatigue and physical activity that has previously been reported in younger cancer patients is also present in older adults with cancer. Thus it would be reasonable to hypothesize that physical activity interventions for

fatigue that are effective in younger cancer patients might also be effective in older cancer patients.

Further research utilizing randomized controlled trials to test these interventions in older populations is needed to identify the optimal levels and types of physical activity to treat cancer fatigue in older adults. Results from this study suggest that older cancer patients with low baseline physical activity levels, comorbidities, and/ or treatment with chemotherapy may be at greater risk for fatigue. Identifying patients at risk for cancer fatigue should be a priority so that support can be provided and promising interventions such as physical activity may be implemented. At this point it would be reasonable to encourage cancer patients of all ages to participate in regular physical activity during and following cancer treatment in consultation with their oncologist.

References

- Ahlberg, K., Ekman, T., Gaston-Johansson, F., & Mock, V. (2003). Assessment and management of cancer-related fatigue in adults. *The Lancet*, *362*, 640-650.
- Andrykowski, M. A., Curran, S. L., & Lightner, R. (1998). Off-treatment fatigue in breast cancer survivors: A controlled comparison. *Journal of Behavioral Medicine*, *21*, 1-18.
- Berger, A. M. (1998). Patterns of fatigue and activity and rest during adjuvant breast cancer chemotherapy. *Oncology Nursing Forum*, *25*, 51-62.
- Bower, J.E., Ganz, P.A., Desmond, K.A., Rowland, J.H., Meyerowitz, B.E., & Belin, T.R. (2000). Fatigue in breast cancer survivors: Occurrence, correlates, and impact on quality of life. *Journal of Clinical Oncology*, *18*, 743-753.
- Broekel, J.A., Jacobsen, P.B., Horton, J., Balducci, L., & Lyman, G.H. (1998). Characteristics and correlates of fatigue after adjuvant chemotherapy for breast cancer. *Journal of Clinical Oncology*, *16*, 1689-1696.
- Bultmann, U., Kant, I.J., Kasl, S.V., Schroer, K.A., Swaen, G.M., & van den Brandt, P.A. (2002). Lifestyle factors as risk factors for fatigue and psychological distress in the working population: Prospective results from the Maastricht Cohort Study. *Journal of Occupational and Environmental Medicine*, *44*, 116-124.
- Burnham, T.R., & Wilcox, A. (2002). Effects of exercise on physiological and psychological variables in cancer survivors. *Medicine & Science in Sports & Exercise*, *34*, 1863-1867.
- Camarillo, M.A. (1991). The oncology patient's experience of fatigue. *Quality of Life--A Nursing Challenge*, *1*(1), 39-44.
- Canadian Cancer Society/National Cancer Institute of Canada (2006). *Canadian cancer statistics 2006*. Toronto: Canadian Cancer Society/National Cancer Institute of Canada.

- Caspersen, C. J., Powell, K. E., & Christensen, G. M. (1985). Physical activity, exercise, and physical fitness: Definitions and distinctions for health-related research. *Public Health Reports, 100*(2), 126-131.
- Cimprich, B. (1999). Pretreatment symptom distress in women newly diagnosed with breast cancer. *Cancer Nursing, 22*(3), 185-194.
- Courneya, K. S. & Friedenreich, C. M. (1997). Relationship between exercise during treatment and current quality of life among survivors of breast cancer. *Journal of Psychosocial Oncology, 15*, 35-57.
- Culos-Reed, S.N., Robinson, J.L., Lau, H., O'Connor, K., & Keats, M.R. (2007). Benefits of a physical activity intervention for men with prostate cancer. *Journal of Sport & Exercise Psychology, 29*(1), 118-127.
- Curtis, E.B., Krech, R., & Walsh, T.D. (1991). Common symptoms in patients with advanced cancer. *Journal of Palliative Care, 7*, 25-29.
- De Jong, N., Courtens, A.M., Abu-Saad, H.H., & Schouten, H.C. (2002). Fatigue in patients with breast cancer receiving adjuvant chemotherapy: A review of the literature. *Cancer Nursing, 25*, 283-297.
- Dimeo, F.C. (2001). Effects of exercise on cancer-related fatigue. *Cancer, 15*(Suppl.6), 1689-1693.
- Dimeo, F., Rumberger, B., & Keul, J. (1998). Aerobic exercise as therapy for cancer fatigue. *Medicine and Science in Sports and Exercise, 30*, 475-478.
- Dimeo, F., Stieglitz, R.D., Novelli-Fischer, U., Fetscher, S., & Keul, J. (1999). Effects of physical activity on the fatigue and psychologic status of cancer patients during chemotherapy. *Cancer, 85*, 2273-2277.

- Dimeo, F., Stieglitz, R.D., Novelli-Fischer, U., Fetscher, S., Mertelsmann, R., & Keul, J. (1997). Correlation between physical performance and fatigue in cancer patients. *Annals of Oncology*, 8, 1251-1255.
- Donovan, H. S. & Ward, S. (2005). Representations of fatigue in women receiving chemotherapy for gynecologic cancers. *Oncology Nursing Forum*, 32, 113-116.
- Duthie, E.H. (2004). Physiology of aging: Relevance to symptoms, perceptions, and treatment tolerance. In L. Balducci, G.H. Lyman, W.B. Ershler, & M. Extermann (Eds.), *Comprehensive Geriatric Oncology* (2nd ed., pp.208-222). New York: Taylor & Francis.
- Esbensen, B. A., Osterlind, K., & Hallberg, I. R. (2006). Quality of life of elderly persons with cancer: A 3-month follow-up. *Cancer Nursing*, 29, 214-224.
- Ferrell, B.R., Grant, M., Dean, G.E., Funk, B., & Ly, J. (1996). "Bone tired": the experience of fatigue and its impact on quality of life. *Oncology Nursing Forum*, 23, 1539-47.
- Galvao, D. A. & Newton, R. U. (2005). Review of exercise intervention studies in cancer patients. *Journal of Clinical Oncology*, 23, 899-909.
- Given, C.W., Given, B., Azzouz, F., Kozachik, S., & Stommel, M. (2001). Predictors of pain and fatigue in the year following diagnosis among elderly cancer patients. *Journal of Pain and Symptom Management*, 21, 456-466.
- Glaus, A. (1993). Assessment of fatigue in cancer and non-cancer patients and in healthy individuals. *Supportive Care in Cancer*, 1, 305-315.
- Groll, D.L., Heyland, D.K., Caeser, M., & Wright, J.G. (2006). Assessment of long-term physical function in acute respiratory distress syndrome (ARDS) patients: Comparison of the

- Charlson Comorbidity Index and the Functional Comorbidity Index. *American Journal of Physical Medicine & Rehabilitation*, 85(7), 1-8.
- Groll, D. L., To, T., Bombardier, C., & Wright, J. G. (2005). The development of a comorbidity index with physical function as the outcome. *Journal of Clinical Epidemiology*, 58, 595-602.
- Harada, N.D., Chiu, V., King, A.C., & Stewart, A.L. (2001). An evaluation of three self-reported physical activity instruments for older adults. *Medicine and Science in Sports and Exercise*, 33, 962-970.
- Headley, J.A. (1997). Chemotherapy-induced ovarian failure in women with breast cancer. *Dissertation Abstracts International*, 58(08), 4139. (UMI No. 9804903)
- Hotopf, M. (2004). Definitions, epidemiology, and models of fatigue in the general population and in cancer. In J. Arms, M. Krishnasamy, & I.J. Higginson (Eds.), *Fatigue in cancer* (pp. 3-27). New York: Oxford University Press.
- Hutchins, L. F., Unger, J. M., Crowley, J. J., Coltman, C. A., & Albain, K. S. (1999). Underrepresentation of patients 65 years of age or older in cancer-treatment trials. *The New England Journal of Medicine*, 341, 2061-2067.
- Irvine, D., Vincent, L., Bubela, N., Thompson, L., & Graydon, J. (1991). A critical appraisal of the research literature investigating fatigue in the individual with cancer. *Cancer Nursing*, 14, 188-199.
- Irvine, D., Vincent, L., Graydon, J., Bubela, N., & Thompson, L. (1994). The prevalence and correlates of fatigue in patients receiving treatment with chemotherapy and radiation therapy: a comparison with the fatigue experienced by healthy individuals. *Cancer Nursing*, 17, 367-378.

- Irwin, M., Crumley, D., McTiernan, A. Bernstein, L., Baumgartner, R., Gilliland, F., et al. (2003). Physical activity levels before and after a diagnosis of breast cancer: The Health, Eating, Activity, and Lifestyle (HEAL) Study. *Cancer, 97*, 1746-1757.
- Jacobsen, P. B. & Stein, K. (1999). Is fatigue a long-term side effect of breast cancer treatment. *Cancer Control, 6*, 256-263.
- Jacobsen, P.B., Hann, D.M., Azzarello, L.M., Horton, J., Balducci, L., & Lyman, G.H. (1999). Fatigue in women receiving adjuvant chemotherapy for breast cancer: Characteristics, course, and correlates. *Journal of Pain and Symptom Management, 18*, 233-242.
- Janda, M., Gerstner, N., Obermair, A., Fuerst, A., Wachter, S., Dieckmann, K. et al. (2000). Quality of life changes during conformal radiation therapy for prostate carcinoma. *Cancer, 89*, 1322-1328.
- Jerezek-Fossa, B. A., Marsignlia, H. R., & Orecchia, R. (2002). Radiotherapy-related fatigue. *Critical Reviews in Oncology/Hematology, 41*, 317-325.
- Kaasa, S., Knobel, H., Loge, J. H., & Hjermstad, M. J. (1998). Hodgkin's disease: Quality of life in future trials. *Annals of Oncology, 9*(Suppl 5),137-145.
- Kenefick, A. L. (2006). Patterns of symptom distress in older women after surgical treatment for breast cancer. *Oncology Nursing Forum, 33*, 327-335.
- King, A.C., Rejeski, W.J., & Buchner, D.M. (1998). Physical activity interventions targeting older adults. *American Journal of Preventative Medicine, 15*, 316-333.
- Koval, J. J., Ecclestone, N. A., Paterson, D. H., Brown, B., Cunningham, D. A., & Rechnitzer, P. A. (1992). Response rates in a survey of physical capacity among older persons. *Journal of Gerontology: Social Sciences, 47*, S140-147.

- Kurtz, M. E., Kurtz, J. C., Stommel, M., Given, C. W., & Given, B. (1999). The influence of symptoms, age, comorbidity and cancer site on physical functioning and mental health of geriatric women patients. *Women & Health, 29*, 1-12.
- Loge, J. H., Abrahamsen, A. F., Ekeberg, O., & Kaasa, S. (1999). Hodgkin's disease survivors more fatigued than the general population. *Journal of Clinical Oncology, 17*, 253-261.
- Loge, J.H., Abrahamsen, A.F., Ekeberg, O., & Kaasa, S. (2000). Fatigue and psychiatric morbidity among Hodgkin's disease survivors. *Journal of Pain and Symptom Management, 19*, 91-99.
- Longman, A.J., Braden, C.J., Mishel, M.H. (1999). Side-effects burden, psychological adjustment, and life quality in women with breast cancer: Pattern of association over time. *Oncology Nursing Forum, 26*, 909-915.
- Luctkar-Flude, M.F., Groll, D., Tranmer, J.E., & Woodend, K. (in press). *Fatigue and physical activity in older adults with cancer: A systematic review of the literature.*
- MacVicar, M.G., Winningham, M.L., & Nickel, J.L. (1989). Effects of aerobic interval training on cancer patients' functional capacity. *Nursing Research 38*, 348-351.
- Mast, M. (1998). Correlates of fatigue in survivors of breast cancer. *Cancer Nursing, 21*, 136-142.
- McMillian, S.C., & Weitzner, M.A. (2003). Methodologic issues in collecting data from debilitated patients with cancer near end of life. *Oncology Nursing Forum, 30*, 123-129.
- McNeely, M.L., Campbell, J.R., Rowe, B.H., Klassen, T.P., Mackey, J.R., & Courneya, K.S. (2006). Effects of exercise on breast cancer patients and survivors: A systematic review and meta-analysis. *CMAJ: Canadian Medical Association Journal, 175*(1), 34-41.

- Mitka, M. (2003). Too few older patients in cancer trials: Expert says disparity affects research results and care. *JAMA: The Journal of the American Medical Association*, 290, 27-28.
- Mock, V. (2001). Fatigue management: Evidence and guidelines for practice. *Cancer Supplement*, 92, 1699-1707.
- Mock, V., Burke, M., Sheehan, P., Creaton, E., Winningham, M., McKenney-Tedder, S., Powel, L., & Liebman, M. (1994). A nursing rehabilitation program for women with breast cancer receiving adjuvant chemotherapy. *Oncology Nursing Forum*, 21, 899-907.
- Mock, V., Hassey Dow, K., Meares, C.J., Grimm, P.M., Dienemann, J.A., Haisfield-Wolfe, M.E., et al. (1997). Effects of exercise on fatigue, physical functioning, and emotional distress during radiation therapy for breast cancer. *Oncology Nursing Forum*, 24, 991-1000.
- Mock, V., McCorkle, R., & Krumm, S. (2003). Clinical excellence through evidence-based practice: Fatigue management as a model. *Oncology Nursing Forum*, 30, 1-18.
- Monga, U., Kerrigan, A. J., Thornby, J., & Monga, T. N. (1999). Prospective study of fatigue in localized prostate cancer patients undergoing radiotherapy. *Radiation Oncology Investigations*, 7, 178-185.
- Morrow, G. R., Andrews, P. L. R., Hickok, J. T., Roscoe, J. A., & Matteson, S. (2002). Fatigue associated with cancer and its treatment. *Supportive Care in Cancer*, 10, 389-398.
- Moser, D. K., Dracup, K., & Doering, L. V. (2000). Factors differentiating dropouts from completers in a longitudinal, multicenter clinical trial. *Nursing Research*, 49, 109-116.
- Mostert, S., & Kesselring, J. (2002). Effects of a short-term exercise training program on aerobic fitness, fatigue, health perception and activity level of subjects with multiple sclerosis. *Multiple Sclerosis*, 8, 161-168.

- Motzer, S. A., Moseley, J. R., & Lewis, F. M. (1997). Recruitment and retention of families in clinical trials with longitudinal designs. *Western Journal of Nursing Research, 19*, 314-333.
- Nail, L.M. (2002). Fatigue in patients with cancer. *Oncology Nursing Forum, 29*, 537-46.
- Nail, L.M., & Jones, L.S. (1995). Fatigue as a side effect of cancer treatment: Impact on quality of life. *Quality of Life--A Nursing Challenge, 4*(1), 8-13.
- National Comprehensive Cancer Network (NCCN). (2003). Cancer-related fatigue: Clinical practice guidelines in oncology. *Journal of the National Comprehensive Cancer Network, 1*, 308-331.
- Neumark, D. E., Stommel, M., Given, C. W., & Given, B. A. (2001). Research design and subject characteristics predicting nonparticipation in a panel survey of older families with cancer. *Nursing Research, 50*, 363-368.
- Norman, G.R., & Streiner, D.L. (2000). *Biostatistics: The bare essentials*. Hamilton, ON: B.C. Decker Inc.
- Oldervoll, L.M., Kaasa, S., Knobel, H., & Loge, J.H. (2003). Exercise reduces fatigue in chronic fatigued Hodgkins disease survivors - Results from a pilot study. *European Journal of Cancer, 39*, 57-63.
- Payne, J.K. (2002). The trajectory of fatigue in adult patients with breast and ovarian cancer receiving chemotherapy. *Oncology Nursing Forum, 29*(9), 1334-1340.
- Pedersen, B.K., & Saltin, B. (2006). Evidence for prescribing exercise as therapy in chronic disease. *Scandinavian Journal of Medicine and Science in Sports, 16*(Suppl 1), 3-63.
- Penedo, F.J., Schneiderman, N., Dahn, J.R., & Gonzalez, J.S. (2004). Physical activity interventions in the elderly: cancer and comorbidity. *Cancer Investigation, 22*, 51-67.

- Pinto, B.M., Frierson, G.M., Rabin, C., Trunzo, J.J., & Marcus, B.H. (2005). Home-based physical activity intervention for breast cancer patients. *Journal of Clinical Oncology*, 23(15), 3577-3587.
- Piper, B.G., Lindsey, A.M., Dodd, M.J., Ferketich, M.J., Paul, S.M., & Weller, S. (1989). The development of an instrument to measure the subjective dimension of fatigue. In S.G. Funk, E.M. Tourquist, M. Champagne, L. Archer Copp, & R.A. Wiese (Eds), *Key aspects of comfort: Management of pain and nausea* (pp. 199-208). New York: Springer.
- Portenoy, R.K., & Itri, L.M. (1999). Cancer-related fatigue: Guidelines for evaluation and management. *The Oncologist*, 4, 1-10.
- Portenoy R.K., Thaler, H.T., Kornblith, A.B., McCarthy Lepore, J., Friedlander-Klar, H., Kiyasu, E., et al. (1994). The Memorial Symptom Assessment Scale: An instrument for the evaluation of symptom prevalence, characteristics and distress. *European Journal of Cancer*, 30A, 1326-1336.
- Rao, A., & Cohen, H.J. (2004). Symptom management in the elderly cancer patient: Fatigue, pain, and depression. *Journal of the National Cancer Institute*, 32, 150-157.
- Repetto, L., Venturino, A., Vercelli, M., Gianni, W., Biancardi, V., Casella, C. et al. (1998). Performance status and comorbidity in elderly cancer patients compared with young patients with neoplasia and elderly patients without neoplastic conditions. *Cancer*, 82, 760-765.
- Rosenthal, M.A., & Oratz, R. (1998). Phase II clinical trial of recombinant alpha 2b interferon and 13 cis retinoic acid in patients with metastatic melanoma. *American Journal of Clinical Oncology*, 21, 352-354.

- Schwartz, A.L. (2000). Daily fatigue patterns and effect of exercise in women with breast cancer. *Cancer Practice*, 8, 16-24.
- Skalla, K.A., & Rieger, P.T. (1995). Fatigue. In P.T. Rieger (Ed.), *Biotherapy: A comprehensive review* (pp. 221-242). Subury, MA: Jones and Bartlett.
- Smets, E.M.A., Visser, M., Willems-Groot, A., & Garssen, B. (1998). Fatigue and radiotherapy: Experience in patients undergoing treatment. *British Journal of Cancer*, 78, 899-906.
- Stasi, R., Abriani, L., Beccaglia, P., Terzoli, E., & Amadori, S. (2003). Cancer-related fatigue: Evolving concepts in evaluation and treatment. *Cancer*, 98, 1786-1801.
- Stone, P., Richards, M., A'Hern, R., & Hardy, J. (2001). Fatigue in patients with cancers of the breast or prostate undergoing radical radiotherapy. *Journal of Pain & Symptom Management*, 22, 1007-1015.
- Tavio, M., Milan, I., & Tirelli, U. (2002). Cancer-related fatigue. *International Journal of Oncology*, 21, 1093-1099.
- Tennstedt, S.L., Dettling, U., & McKinlay, J.B. (1992). Refusal rates in a longitudinal study of older people: Implications for field methods. *Journal of Gerontology*, 47, S313-S318.
- Townsley, C.A., Pond, G.R., Oza, A.M., Hirte, H.W., Winqvist, E., Glenwood, G., et al. (2006). Evaluation of adverse events experienced by older patients participating in studies of molecularly targeted agents alone or in combination. *Clinical Cancer Research*, 12(7), 2141-2149.
- Tranmer, J.E., Heyland, D., Dudgeon, D., Groll, D., Squires-Graham, M., & Coulson, K. (2003). Measuring the symptom experience of seriously ill cancer and noncancer hospitalized patients near the end of life with the Memorial Symptom Assessment Scale. *Journal of Pain and Symptom Management*, 25, 420-429.

Truong, P.T., Berthelet, E., Lee, J.C., Petersen, R., Lim, J.T.W., Gaul, C.A., et al. (2006).

Prospective evaluation of the prevalence and severity of fatigue in patients with prostate cancer undergoing radical external beam radiotherapy and neoadjuvant hormone therapy.

The Canadian Journal of Urology, 13(3), 3139-3146.

Unger, J. M., Hutchins, L. F., & Albain, K. S. (2004). Under-representation of elderly patients in

cancer clinical trials: Causes and remedial strategies. In L. Balducci, G. H. Lyman, W. B.

Ershler, & M. Extermann (Eds.), *Comprehensive Geriatric Oncology* (2nd ed., pp. 259-

274). New York: Taylor & Francis.

U.S. Department of Health and Human Services. (1996). *Physical activity and health: A report of*

the Surgeon General. Atlanta, GA: U.S. Department of Health and Human Services,

Centers for Disease Control and Prevention, National Center for Chronic Disease

Prevention and Health Promotion.

Visovsky, C., & Schneider, S.M. (2003). Cancer-related fatigue. *Online Journal of Issues in*

Nursing, 1-23.

Washburn, R.A., & Ficker, J.L. (1999). Physical Activity Scale for the Elderly (PASE): The

relationship with activity measured by a portable accelerometer. *Journal of Sports*

Medicine & Physical Fitness, 39(4), 336-340.

Washburn, R.A., McAuley, E., Katula, J., Mihalko, S.L., & Boileau, R.A. (1999). The Physical

Activity Scale for the Elderly (PASE): Evidence for validity. *Journal of Clinical*

Epidemiology, 52(7), 643-651.

Washburn, R.A., Smith, K.W., Jette, A.M., & Janney, C.A. (1993). The physical activity scale for

the elderly (PASE): Development and evaluation. *Journal of Clinical Epidemiology*, 46,

153-162.

- Wengstrom, Y., Haggmark, C., Strander, H., & Forsberg, C. (2000). Perceived symptoms and quality of life in women with breast cancer receiving radiation therapy. *European Journal of Oncology Nursing*, 4(2), 78-88.
- Whedon, M., Stearns, D., & Mills, L.E. (1995). Quality of life of long-term adult survivors of autologous bone marrow transplantation. *Oncology Nursing Forum*, 22, 1527-1535.
- Winningham, M.L. (1999). In: Yarbro, C.H., Frogge, M.H., Goodman, M. eds. *Cancer Symptom Management*. 2nd ed. Boston, Mass: Jones & Bartlett.
- Winningham, M.L., Nail, L.M., Burke, M.B., Brophy, L., Cimprich, B., Jones, L.S. et al. (1994). Fatigue and the cancer experience: The state of the knowledge. *Oncology Nursing Forum*, 21, 23-36.
- Woo, B., Dibble, S. L., Piper, B. F., Keating, S. B., & Weiss, M. C. (1998). Differences in fatigue by treatment methods in women with breast cancer. *Oncology Nursing Forum*, 25, 915-920.
- Yancik, R. (1997). Cancer burden in the aged: An epidemiologic and demographic overview. *Cancer*, 80, 1273-1283.
- Yancik, R., Wesley, M.N., Ries, L.A.G., Havlik, R.J., Edwards, B.K., Yates, J.W. (2001). Effects of age and comorbidity in postmenopausal breast cancer patients aged 55 years and older. *JAMA: The Journal of the American Medical Association*, 285(7), 885-892.

Table 1

Table of Variables

Variable	Type of Variable	Source
Fatigue	Outcome	Memorial Symptom Assessment Scale (MSAS), Lack of energy score: self-report at baseline, 3 months & six months
Physical Activity	Outcome	Physical Activity Scale for the Elderly (PASE), Physical activity score: self-report at baseline, 3 months & six months
Functional Comorbidity	Independent	Functional Comorbidity Index (FCI): self report and chart abstraction at baseline
Cancer site	Independent	Baseline chart abstraction
Cancer stage	Independent	Baseline chart abstraction
Treatment modalities	Independent	Followup chart abstraction
Personal Demographic Characteristics	Independent	Self-report at baseline
a) Age		
b) Gender		
c) Marital status		
d) Educational status		
e) Household income		
f) Living arrangements		
g) Geographical distance from cancer centre		
h) Height and weight		
i) Smoking and alcohol intake		

Table 2

Baseline Demographic Characteristics (N=440)

Variable	Category	Mean (range)	SD	n	%
Age (years)		72.6 (65-90)	5.6		
BMI		27 (15-43)	4.8		
Self-reported functional comorbidity (FCI)		2.9 (1-12)	1.8		
Sex	Female			192	43.6
	Male			248	56.4
Marital status	Single/widowed			88	20.0
	Married/common law			323	73.4
	Divorced/separated			27	6.1
Education	Did not complete public school			2	0.5
	Completed high school			306	69.5
	Completed college or university			80	18.2
	Completed postgraduate			42	9.5
Income	< \$20000			67	15.2
	\$21000-\$40000			173	39.3
	\$41000-\$60000			83	18.9
	>\$60000			61	13.9
Living arrangement	Lives alone			87	19.8
	Lives with spouse or partner			326	74.1
	Lives with family member			14	3.2
	Lives with other			11	2.5

Note. FCI = Functional Comorbidity Index

Table 3

Cancer Site, Stage and Treatment (N=440)

Cancer Site	<i>n</i>	%
Breast	110	25.0
Prostate	107	24.3
Colorectal	70	15.9
Lung	42	9.5
Other	111	25.3

Cancer Stage	<i>n</i>	%
I	157	35.7
II	88	20.0
III	77	17.5
IV	24	5.5
Missing/cannot assess	94	21.3

Treatment Modality	<i>n</i>	%
Chemotherapy	150	34.2
Radiotherapy	270	61.5
Surgery	241	54.9
Hormones	92	21.0
Biotherapy	3	0.7
Observation	19	4.3

Note: Cancer Stage I=localized, Stage II & III=locally advanced (depends on cancer site), Stage IV=metastatic

Table 4

Prevalence of Top Ten Symptoms (MSAS) Reported by a Cohort of Older Adults with Cancer at Baseline, 3 Months and 6 Months

Symptom	Baseline			3 Months			6 Months		
	Rank	N	%	Rank	N	%	Rank	N	%
Lack of energy (fatigue)	1	302	68.6	1	258	70.7	1	220	67.9
Difficulty sleeping	2	248	56.4	4	173	47.4	4	171	52.8
Worrying	3	238	54.1	5	152	41.6	5	146	45.1
Feeling Drowsy	4	235	53.4	2	211	57.8	2	181	55.9
Pain	5	231	52.5	3	174	47.7	3	175	54.0
Dry mouth	6	184	41.8	6	145	39.7	7	139	42.9
Cough	7	183	41.6	9	132	36.2	8	130	40.1
Feeling nervous	8	179	40.7	10	112	30.7	9	120	37.0
Feeling irritable	9	176	40.0	8	133	36.4	10	120	37.0
Difficulty concentrating	10	175	39.8	7	139	38.1	6	142	43.8

Note. MSAS = Memorial Symptom Assessment Scale symptom scores

Table 5

Outcome Scores

<u>Variable</u>	<u>Mean</u>	<u>Standard Deviation</u>	<u>Median</u>	<u>Range</u>
<u>Fatigue (MSAS)</u>				
Baseline	1.31	1.13	1.33	0-4
3 months	1.13	1.14	1.00	0-4
6 months	0.96	1.12	0.25	0-4
<u>Physical Activity (PASE)</u>				
Baseline	93.3	66.2	78.93	0-335.3
3 months	110.3	72.3	101.15	0-474
6 months	119.7	70.6	111.36	0-401.1

Note. MSAS = Memorial Symptom Assessment Scale lack of energy score, PASE = Physical Activity Scale for the Elderly physical activity score

Table 6

Pearson Correlations Between Outcome Scores at Baseline, 3 Months and 6 Months*

	Fatigue		Physical Activity		
	3 Month	6 Month	Baseline	3 Month	6 Month
<u>Fatigue (MSAS)</u>					
Baseline	.362	.258	-.394	-.314	-.319
3 Month		.536	-.252	-.400	-.367
6 Month			-.190	-.228	-.427
<u>Physical Activity (PASE)</u>					
Baseline				.631	.483
3 Month					.624

*All correlations are significant at $p < 0.01$ (2-tailed)

Note. MSAS = Memorial Symptom Assessment Scale lack of energy score, PASE = Physical Activity Scale for the Elderly physical activity score

Table 7

Significant Results of Stepwise Linear Regression Models Related to Research HypothesesRelationship between Physical Activity at Baseline and Fatigue (MSAS) at 3 Months*

Independent Variable	Standardized Beta	Sig
Physical Activity Baseline (PASE)	-0.294	0.001
Chemotherapy	0.143	0.018
Housing Arrangement	0.157	0.010
Surgery	-0.189	0.004
Sex	0.136	0.041

*Adjusted R Square = 0.135, Sig = 0.001

Relationship between Physical Activity at Baseline and Fatigue (MSAS) at 6 Months*

Independent Variable	Standardized Beta	Sig
Physical Activity Baseline (PASE)	-0.208	0.001
Chemotherapy	0.164	0.009
Radiotherapy	0.126	0.042

*Adjusted R Square = 0.078, Sig = 0.001

Relationship between Physical Activity at 3 Months and Fatigue (MSAS) at 3 Months*

Independent Variable	Standardized Beta	Sig
Physical Activity 3 Month (PASE)	-0.317	0.001
Housing Arrangement	0.153	0.015
Chemotherapy	0.160	0.012
Comorbidity (FCI)	0.157	0.015

*Adjusted R Square = 0.175, Sig = 0.001

Relationship between Physical Activity at 3 Months and Fatigue (MSAS) at 6 Months*

Independent Variable	Standardized Beta	Sig
Physical Activity 3 Month (PASE)	-0.177	0.010
Chemotherapy	0.169	0.012
Comorbidity (FCI)	0.148	0.028

*Adjusted R Square = 0.087, Sig = 0.001

Note. MSAS = Memorial Symptom Assessment Scale lack of energy score, PASE = Physical Activity Scale for the Elderly physical activity score, FCI = Functional Comorbidity Index

Chapter Four

The Relationship of Fatigue and Physical Activity with Physical Function and Quality of Life in
Older Adults with Cancer:
A Six-Month Followup Study

Marian Luctkar-Flude RN, BScN, MScN(c)
Program Coordinator, Nursing Research
Kingston General Hospital
Kingston, Ontario
(613) 549-6666 Ext # 3321
Fax: (613) 548-1381

Dianne Groll RN, PhD
Associate Professor
Queen's University, Department of Psychiatry
Ottawa, Ontario
K1H 8M5

Kirsten Woodend RN, PhD
Associate Professor
University of Ottawa, School of Nursing
Ottawa, Ontario
K1H 8M5

Joan Tranmer RN, PhD
Associate Professor
Queen's University, School of Nursing
Kingston, Ontario

David Holmes RN, PhD
Associate Professor
University of Ottawa, School of Nursing
Ottawa, Ontario
K1H 8M5

Abstract

Purpose: To determine the relationship of fatigue and physical activity with physical function and quality of life in older adults with cancer.

Design: Longitudinal, prospective, cohort.

Setting: A regional Canadian cancer centre.

Sample: 440 adults aged 65 years and older seeking consultation for cancer treatment at a tertiary care regional cancer centre

Methods: Subjects completed self-report questionnaires at baseline, three and six months post consultation for cancer treatment, to rate fatigue (Memorial Symptom Assessment Scale), physical activity (Physical Activity Scale for the Elderly), physical function (Physical Component Summary subscale of the Medical Outcome Short Form 12 General Health Questionnaire) and quality of life (European Organization for Research Treatment Quality of Life questionnaire).

Main Research Variables: Fatigue, physical activity, physical function, and quality of life.

Findings: Higher fatigue levels were associated with lower levels of physical function and quality of life. Higher physical activity levels were associated with higher levels of physical function and quality of life. Physical activity was a significant predictor of physical function at six months, but not a significant predictor of quality of life at six months. Demographics, cancer site and treatment variables contributed inconsistently as predictors of the outcome variables.

Conclusions: Physical activity level is a modifiable factor significantly predicting physical function in older adults at 3 months and 6 months following consultation for cancer treatment.

These results suggest that participating in physical activity may help older adults with cancer maintain physical function during cancer treatment.

Implications for Nursing: Physical activity interventions need to be developed and tested in older adults with cancer to maintain physical function during treatment.

Key Points

1. Cancer fatigue is associated with lower levels of physical function and quality of life in older adults with cancer.
2. Higher physical activity levels are associated with higher physical function scores in older adults up to six months following consultation for cancer treatment.
3. Physical activity may be an effective intervention to maintain physical function in older adults regardless of cancer site and treatment modality.

Introduction

Cancer is predominantly a disease affecting older persons. The increased number of new cases of cancer is primarily due to an increasing and aging population (Canadian Cancer Society/National Cancer Institute of Canada, 2006; Yancik, 1997). 43% of new cancer cases in Canada occur among those who are at least 70 years old, while 25% occur in those aged 60-69. The median age at cancer diagnosis is between 65 and 69 years of age (Canadian Cancer Society/National Cancer Institute of Canada, 2006).

Cancer diagnosis and cancer treatment have been associated with declines in physical function and quality of life. Physical function can be defined as the ability to ambulate and to perform normal activities of daily living (Mock, 2001). Older persons and older cancer patients

have been found to have poorer functioning (Deimling, 2005; Hewitt, Rowland & Yancik, 2003; Pleis & Lethbridge-Cejku, 2006). Physical function is essential to older adults in maintaining independence and associated quality of life which is often more important to older adults than cancer survival (Garman & Cohen, 2002; Harlacher & Fusgen, 2006; Silliman, Balducci, Goodwin, Holmes & Leventhal, 1993).

Quality of life is a subjective sense of well-being that may be defined as patient satisfaction with their current level of functioning, compared to what they perceive to be possible or ideal (Cella & Cherin, 1988). Quality of life is a subjective, multidimensional concept, entailing physical, psychological and social factors (Donovan, Sanson-Fisher, & Redman, 1989; Osoba, 1994; Olschewski, Schulgen, Schumacher, & Altman, 1994). Health related quality of life refers to those aspects of a person's life that impact directly upon their health, and encompasses the impact of a disease and its treatment on all aspects of a patient's life, including the impact of symptoms and the distress associated with functional limitations (American Society of Clinical Oncology, 1996; Gill & Feinstein, 1994; Patrick & Erickson, 1993).

Cancer fatigue is a highly prevalent and distressing symptom that interferes with usual functioning and quality of life (Nail, 2002; Winningham et al., 1994; Winningham, 1999). Quality of life has consistently been found to be negatively related to fatigue (Ashbury, Findlay, Reynolds, & McKerracher, 1998; Bower et al., 2000; Broekel, Jacobsen, Horton, Balducci, & Lyman, 1998; Ferrell et al., 1996; Fletcher et al., 1998; Holzner et al., 2003; Smets, Visser, Willems-Groot, & Garssen, 1998; Vogelzang et al., 1997,); however, recent studies suggest that physical activity interventions may reduce fatigue and improve physical function in cancer patients (Wagner & Cella, 2004). Physical activity during cancer treatment may also improve

quality of life (Headley, Ownby, & John, 2004; Mock, et al., 2003; Schwartz, 1999; Schwartz et al., 2001).

Physical activity has been defined as “bodily movement produced by the contracture of skeletal muscle that increases energy expenditure above the basal level” (U.S. Department of Health & Human Services, 1996, p. 20). The terms physical activity and exercise are often used synonymously in the literature; however, exercise can be viewed as a subcategory of physical activity, and defined as “physical activity that is planned, structured, repetitive, and purposive in the sense that improvement or maintenance of one or more components of physical fitness is the objective” (Caspersen, Powell & Christensen, 1985, p. 128).

Therefore, the purpose of this study was to describe the relationship of fatigue and physical activity with physical functioning and quality of life in a cohort of older adults who are receiving cancer treatment. This manuscript addresses the relationships between fatigue and physical activity, and physical function and quality of life in older adults with cancer.

Literature Review

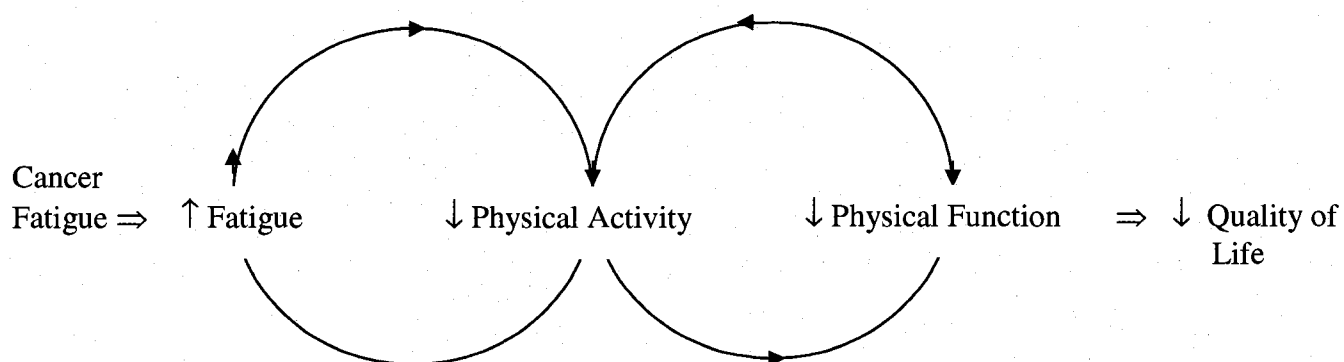
Most of the studies evaluating exercise interventions have implemented exercise during treatment for breast cancer and few studies have assessed the efficacy of physical activity interventions in the elderly (Penedo et al., 2004). It has been proposed that exercise could help in preserving functional status in the elderly and that physical activity interventions could have physical and mental health benefits in the elderly (Penedo et al, 2004; Rao & Cohen, 2004). However physical activity programs need to be tailored to meet the unique needs of older adults (King, Rejeski, & Buchner, 1998).

A systematic review of the literature was conducted to look at the effectiveness of physical activity as an intervention to reduce fatigue, and maintain physical function and quality

of life in older adults with cancer during and following cancer treatment (Luctkar-Flude, Groll, Tranmer & Woodend, in press). Nine experimental studies and ten observational studies were synthesized in the review that provided evidence that exercise, both aerobic and strength training, may reduce fatigue in cancer patients during and after cancer treatment. Exercise was also associated with improvements or slower declines in physical functioning and quality of life in the studies reviewed.

The literature supports that there is a relationship between fatigue, physical activity, physical functioning and quality of life in cancer patients. Researchers have proposed that a cycle of decreasing activity and increasing fatigue leads to deconditioning, resulting in patients fatiguing more quickly when they participate in activity (Dimeo, 2001; Winningham et al., 1994). The proposed cycle of increasing fatigue and decreasing physical activity resulting in declines in physical function and quality of life in cancer patients is depicted in Figure 1. The present study examined these relationships in a sample of older adults with cancer.

Figure 1: Conceptualization of Cycle of Fatigue, Physical Activity, Physical Function and Quality of Life in Older Adults with Cancer:



Physical activity is proposed as an intervention that may break or reverse this cycle by reducing fatigue and increasing or maintaining physical function. This may be achieved as increasing physical activity improves the muscle strength, stamina & joint flexibility necessary to perform activities of daily living (U.S. Department of Health and Human Services, 1996).

The prevalence of elderly patients living with cancer is increasing, and is expected to grow in the next decade. Management of symptoms such as fatigue and improvement in physical function and quality of life are important outcomes of oncology care. Given the importance of maintaining physical function for independent living and quality of life, it is critical to identify the impact of cancer fatigue on physical functioning and quality of life and to identify how physical activity influences the impact of cancer fatigue on physical functioning and quality of life. This project may be the initial step towards the development of clinical guidelines and physical activity interventions to reduce cancer fatigue enhance physical functioning and optimize quality of life in older adults during and following treatment for cancer.

Purpose

The objective of this study was to determine the relationship of fatigue and physical activity with physical function and quality of life in older adults with cancer. The relationship between fatigue and physical activity in this population was described in chapter three. The following research questions were addressed in this manuscript:

1. Is there a relationship between physical activity levels at 3 months and physical functioning at 6 months post study enrolment?
2. Is there a relationship between physical activity levels at 3 months and quality of life at 6 months post study enrolment?

It was hypothesized that higher physical activity levels during cancer treatment would be associated with higher levels of physical functioning and quality of life in older adults during and following cancer treatment.

Methods

Design

This study was a secondary analysis of data collected for a prospective, longitudinal, descriptive study entitled *Health and Well Being in Older Persons with Cancer*. The primary study was conducted by a team of investigators, led by Dr. Joan Tranmer, and was funded by the Oncology Nursing Society.

Setting and Sample

Data collection took place at the Cancer Centre of Southeastern Ontario. Patients were considered for inclusion in the study if they were 65 years of age or older, attended consultation at the cancer centre for treatment of cancer of the lung, breast, GU, GI, head or neck, lymphoma, leukemia, or skin cancer. Patients were excluded if they were currently referred to or receiving palliative care

All patients who met the inclusion criteria were approached to participate in the study. Potential subjects were recruited by telephone by a research assistant. Consenting participants received a mailed questionnaire package and consent. If questionnaires were not returned within 2 weeks, the research assistant contacted the participant to encourage completion, to determine if there were any questions regarding the questionnaire, and to resend another package if required. Oncology and medical records were reviewed and a trained research assistant collected appropriate clinical information through chart review. Recruitment and enrollment of patients was conducted between October 2003 and April 2005, resulting in 440 subjects returning the

baseline questionnaire. This study looked at data collected at baseline, 3-months and 6-months. A total of 328 subjects completed the 6-month questionnaire and were included in the analysis.

Outcome variables

Fatigue.

Self-reported symptom assessment data related to fatigue was collected using the Memorial Symptom Assessment Scale (MSAS), a multidimensional, reliable and valid instrument for assessment of symptoms in cancer patients. Fatigue (lack of energy) was one item of the 32 item scale. Internal consistency (Cronbach's alpha) for the scales ranges from 0.58 to 0.88 (Portenoy et al., 1994). Scores were also highly correlated with clinical status and quality of life measures. The MSAS asks participants to rate how often they experienced the symptom (rarely, occasionally, frequently or almost constantly), how severe the symptom usually was (slight, moderate, severe or very severe), and how much the symptom distressed or bothered them (not at all, a little bit, somewhat, quite a bit or very much). Symptom scores were calculated as the mean of the frequency, severity and distress scores (Tranmer et al., 2003).

Physical activity.

Physical activity level was measured using the Physical Activity Scale for the Elderly (PASE), which asks questions about leisure time activity (including exercise), household activity and work-related activity, and was specifically designed to assess activities engaged in by older persons (Washburn, Smith, Jette, & Janney, 1993). As older persons may be less likely to participate in formal exercise programs (U.S. Department of Health and Human Services, 1996), it is important to use a physical activity assessment tool that incorporates all of the subcategories of physical activity, including exercise. The PASE correlates well with other performance based and self-report measures (Harada, Chiu, King, & Stewart, 2001; Washburn & Ficker, 1999;

Washburn, McAuley, Katula, Mihalko, & Boileau, 1999), with internal consistency (Cronbach's alpha) of 0.69, and test-retest reliability ($r = 0.60$) (Washburn et al., 1993).

Physical function.

The Physical Component Summary (PCS) subscale of the Medical Outcome Short Form 12 General Health Questionnaire (SF 12) was used to measure physical function. The SF 12 is a brief, 12-item, self-administered instrument that measures functioning and well being in two health status domains: physical and emotional functioning. The SF12 is a reliable, valid measure of health in surgical and medical populations. In 14 validity tests involving physical criteria, relative validity estimates for the PCS ranged from 0.43 to 0.93 (median = 0.67) in comparison with the best 36-item short-form scale, and test-retest (2-week) correlations of 0.89 and 0.76 were observed for the 12-item Physical Component Summary (Ware, Kosinski, & Keller, 1996).

Quality of life.

The European Organization for Research Treatment Quality of Life questionnaire (EORTC QLQ – C30) global health and quality of life (QOL) scale was used to measure cancer related QOL. The EORTC QLQ – C30 is a 30 – item questionnaire designed to measure cancer patients' physical, psychological and social functions. The questionnaire is composed of 5 multiitem functional scales (physical, role, social, emotional and cognitive function), 3 symptom scales (fatigue, nausea and vomiting, and pain), a global health status/QOL and 5 single items assessing additional symptoms. This questionnaire has been widely used to measure HRQL in a variety of cancer conditions at various stages of the illness. The EORTC QLQ – C30 is reported to be a reliable and valid measure of quality of life in cancer patients. The reliability coefficients for the global health and quality of life scale were reported as .86 before treatment and .89 during treatment, with mean scores of 56.7 (SD=23.5) before treatment and 55.2 (SD=23.3) during

treatment (Aaronson, et al., 1993). Scores range from 0 to 100, with a higher score representing a higher level of functioning.

Independent variables.

Factors likely to affect the prevalence of fatigue in cancer patients include stage of disease, site of cancer, treatment factors (Hotopf, 2004), demographic factors (De Jong, Courtens, Abu-Saad, Schouten, 2002), lifestyle factors (Bultmann, Kant, Kasl, Schroer, Swaen, & van den Brandt (2002), and comorbidities (Bower et al. 2000). Clinical measures of disease (cancer site) severity (stage) and treatment (modality) factors were obtained through chart abstraction at baseline and at study completion. Measures of personal demographic characteristics (age, gender, marital status, education, income & living arrangement) were obtained through self-report on the baseline questionnaire. Measures of comorbidity were obtained by self-report at baseline through completion of the Functional Comorbidity Index (FCI), which contains 18 common diagnoses associated with poorer physical function (Groll, Heyland, Caesar, & Wright, 2006; Groll, To, Bombardier, & Wright, 2005). A summary of all the variables collected is presented in Table 1.

Data Analysis

All questionnaire and chart abstraction data were entered into a Microsoft Access database. All of the data entered was verified by a second person. Data were analyzed using SPSS Version 12.0 for Windows. Standard descriptive univariate measures such as means, standard deviations, medians and frequencies were calculated to describe the patient characteristics, and outcome scores. When the assumptions of correlation and multiple regression analysis were tested, several of the continuous variables did not meet the assumption of normality. A natural log transformation of these variables was performed and the analysis was

run using both the transformed and untransformed data. The results were the same and thus the results using the untransformed data are presented.

In order to address the research questions, Pearson correlations were calculated between the outcome variables at baseline, 3 months and 6 months, and between the three time periods. Multivariate regression analysis was performed to control for demographic characteristics, disease site and treatment modality.

For regression analysis, the sample size needs to be at least 5-10 times the number of variables entered into the analysis (Norman & Streiner, 2000). This condition was met with the sample of 328 subjects who completed the six-month questionnaire.

Ethics

The study received ethics approval from the Queen's University Research Ethics Board, and the University of Ottawa Research Ethics Board also approved the secondary analysis.

Results

Sample Characteristics

A total of 440 subjects consented to participate and completed the baseline questionnaire (see Figure 1). Of these, 328 (75%) completed the six-month questionnaire and 112 (25%) did not. Of these, 76 (17%) withdrew, 28 (6%) died, and 8 (2%) were lost to followup. Table 2 summarizes the demographic characteristics of the population at baseline.

The mean age of the subjects was 72.6 years (range = 65-90 years) and 56% of the subjects were male. Subjects self-reported an average of 2.9 comorbidities (range = 1-12).

Table 3 summarizes the cancer site, stage and treatment modalities in the study population. Most of the subjects were treated for early stage cancer of the breast, prostate,

colon/rectum or lung. Subjects were treated with radiotherapy (62%), surgery (55%), chemotherapy (34%) and or hormones (21%).

Outcome Scores

Fatigue and physical activity scores were reported in chapter three and are summarized in Table 4 along with physical function and quality of life scores. There was minimal change in all of the outcome scores across the three time periods. Mean physical function scores decreased from 41.8 (SD = 11.7) at baseline to 41.2 (SD = 11) at 3 months. Mean scores then increased to 42 (11.2) at 6 months. Due to the skewness of the distributions, medians were also calculated. The decrease in the median scores was even greater, from 42.64 at baseline to 41.34 at 3 months; however the changes in physical function scores were not statistically significant. Higher physical function scores on the SF-12 PCS are indicative of higher levels of physical function.

Mean quality of life scores increased from 70.4 (SD = 22.3) at baseline, to 72 (SD = 20.4) at 3 months, and increased further to 72.7 (SD = 21) at 6 months however, there was no change in the median scores (75.0) across the 6-month time period. Higher quality of life scores on the EORTC QLQ-30 are indicative of higher levels of quality of life.

Correlational Analysis

The Pearson correlations between fatigue and physical activity and physical function and quality of life are presented in Table 5. Fatigue was negatively correlated with physical function and quality of life at all time periods. Physical activity was positively correlated with physical function and quality of life at all time periods. All correlations were statistically significant ($p < 0.001$). The strength of the correlations ranged from small to large, where according to Cohen (1988), a small effect size is $r = 0.10$, a medium effect is $r = 0.30$ and a large effect is $r = 0.50$.

Predictors of Physical Function and Quality of Life at Six Months

Results of the regression analysis are presented in Table 6. The dependent variables for the regression analysis were physical function and quality of life outcome scores at six months post study enrolment. Physical activity scores at 3 months were entered as independent variables into a series of stepwise linear regression models along with the measured demographic variables, cancer site, stage and treatment modality, and self-reported functional comorbidity. As hypothesized, physical activity level at 3 months were significantly related to physical function at 6 months ($\beta = 0.155$, $p = 0.032$). The standardized beta values reflect the relative importance of each of the independent variables in predicting the dependent variable, thus, physical activity was not the strongest predictor of fatigue in the model.

Diagnosis of prostate cancer, functional comorbidity, and age were also significantly related to physical function at 6 months. Higher levels of physical activity and diagnosis of prostate cancer were associated with higher levels of physical function, whereas higher comorbidity and older age were associated with lower levels of physical function. Prostate cancer and comorbidity had stronger relationships with physical function than did physical activity and age. The adjusted R^2 for the model predicting physical function at 6 months was 0.256 and the model was significant ($p < 0.001$). The adjusted R^2 is the proportion of the variation in the dependent variable explained by the regression model. Thus, the regression model using physical activity level at 3 months as an independent variable explains 25.6% of the variance in physical function at 6 months.

Physical activity level at 3 months was not significantly related to quality of life at 6 months ($\beta = 0.129$, $p = 0.785$) and the variable was dropped from the model. The diagnosis of prostate cancer or colorectal cancer, and female gender were associated with higher quality of life scores at 6 months. Functional comorbidity and treatment with chemotherapy were associated

with lower quality of life scores at 6 months. The model was significant ($p < 0.001$) and the adjusted R^2 for the model was 0.172. Thus, the regression model using physical activity level at 3 months as an independent variable explains 17.2% of the variance in quality of life at 6 months.

Discussion

It is proposed that physical activity reduces fatigue and enhances physical function by improving fitness and muscle strength (Pedersen & Saltin, 2006). The current study found that physical function scores decreased at three months when most subjects were undergoing cancer treatment and improved at six months when most subjects had completed their treatment. Wyatt and Friedman (1998) found that middle-aged and older women with breast cancer reported a significant decrease in functional status at six weeks after surgery that was never fully regained by six months after surgery. In a study looking at quality of life in old people with and without cancer, Thome, Dykes & Hallberg (2004) found that the older persons with cancer had lower physical function scores than those without. These declines in physical function are important considerations for health care providers as they relate to maintenance of independence and quality of life in older persons with cancer.

In this study, quality of life scores did not exhibit much change over the six-month period. Subjects in this study reported higher quality of life scores than did cancer patients in a study by Aaronson and colleagues (1993) in which mean scores decreased during treatment. Other studies have found that quality of life scores improve as treatment progresses from baseline to post-treatment (Wengstrom, Haggmark, Strander, & Forsberg, 2000). Similar to findings in the current study, other researchers have found that quality of life in elderly persons with cancer did not improve or deteriorate significantly from baseline to three months (Esbensen, Osterlind & Hallberg, 2006). Further research has found quality of life scores in women with breast cancer

to be lower in older women (Cimprich, Ronis & Martinez-Ramos, 2002), and that elderly women with cancer report poorer quality of life than women without cancer (Thome et al., 2004).

The current study found that higher fatigue levels were associated with lower physical function and quality of life scores in a cohort of older adults during and following cancer treatment. Cancer fatigue has been found to have a significant effect on patients' abilities to function in usual roles and activities (Curt, 2000; Jacobsen et al., 1999; Akechi, Kugaya, Okamura, Yamawaki, & Uchitomi, 1999). Higher levels of fatigue have been associated with lower levels of physical functioning (Ahlberg, Ekman, & Gaston-Johansson, 2005; Bennett, Stewart, Kayser-Jones & Glaser, 2002; Berger & Farr, 1999; Dodd, Miaskowski, & Paul, 2001; Monga, Kerrigan, Thornby & Monga, 1999), and lower quality of life scores (Byar, Berger, Bakken, & Cétak, 2006).

As hypothesized, correlational analysis found that higher physical activity levels were associated with higher physical function and quality of life scores in this cohort of older adults during and following cancer treatment. This was expected as increasing physical activity improves the muscle strength, stamina & joint flexibility necessary to perform activities of daily living (U.S. Department of Health and Human Services, 1996).

Physical activity has been found to increase physical function in cancer patients during and following cancer treatment (Campbell, Mutrie, White, McGuire, & Kearney, 2005; Culos-Reed, Robinson, Lau, O'Connor & Keats, 2007; Dimeo et al., 1997; Dimeo, Rumberger, & Keul, 1998; Drouin et al., 2005; MacVicar, Winningham, & Nickel, 1989; Mock et al., 1997; Mock et al., 2005; Nail & Jones, 1995; Pinto, Trunzo, Reiss, & Shiu, 2002; Segal et al., 2003). Reviews of physical activity intervention studies in cancer patients have consistently reported a positive association between physical activity and physical function (Galvao & Newton, 2005; Luctkar-

Flude et al, in press; Pedersen & Saltin, 2006; Penedo, Schneiderman, Dahn & Gonzalez, 2004). These provide evidence that both aerobic and resistance exercises may be effective in maintaining physical function. Although these studies did not focus on older adults, physical activity is reported to enhance physical function in older adults in general (Berkman et al., 1993; Latham, Bennett, Stretton, & Anderson, 2004; Mazzeo et al., 1998; Mor et al., 1989; Pescatello & DiPietro, 1993; Simonsick et al., 1993; Stewart & King, 1991; U.S. Department of Health and Human Services, 1996).

Subjects in this study with higher levels of fatigue reported lower quality of life scores. Researchers have reported a negative relationship between fatigue and quality of life in cancer patients (Ashbury, Findlay, Reynolds, & McKerracher, 1998; Bower et al., 2000; Broekel, Jacobsen, Horton, Balducci, & Lyman, 1998; Byar et al., 2006; Ferrell et al., 1996; Fletcher et al., 1998; Holzner et al., 2003; Lilleby, Fossa, Haehre, & Olsen, 1999; Porock, Beshears, Hinton, & Anderson, 2005; Smets, Visser, Willems-Groot, & Garssen, 1998; Vogelzang et al., 1997,). Research also suggests that exercise during cancer treatment may improve quality of life (Durak & Lilly, 1998; Headley, Ownby, & John, 2004; Mock, McCorkle, & Krumm, 2003; Schwartz, 1999; Schwartz, Mori, Gao, Nail, & King, 2001; Turner, Hayes, & Reul-Hirche, 2004; Young-McCaughan, & Sexton, 1991). Reviews of exercise intervention studies in cancer patients have consistently reported a positive association between physical activity and quality of life (Galvao & Newton, 2005; Luctkar-Flude et al, in press). Results of the correlational analysis from this study also found a positive association between physical activity and quality of life in this cohort of older cancer patients.

Physical activity level at 3 months, when most subjects were undergoing cancer treatment was found to be a significant predictor of physical function at 6 months, when most subjects had

completed their treatment. Physical activity contributes to physical function by improving muscle strength, stamina and joint flexibility (U.S. Department of Health and Human Services, 1996). Inactivity is reported to be a risk factor for functional decline in older adults in general (Avlund, Vass, & Hendriksen, 2003). Several studies have indicated that most cancer patients are not physically active or reduce physical activity levels during and after cancer treatment (Courneya & Friedenreich, 1997a & 1997b; Pinto et al., 2002; Porock et al., 2005). Physical activity levels in women with cancer have been reported to be lower than in women without cancer, and lowest in women aged 65 years and older (Kroenke et al., 2004). Thus cancer treatment may contribute to declines in physical function as cancer patients reduce their physical activity levels. Physical activity levels are generally reported to decrease with age, and older persons are less likely to engage in formal exercise (U.S. Department of Health and Human Services, 1996; Wagner, Lacroix, Buchner, & Larson, 1992), thus older cancer patients may be at greater risk for declines in physical function.

Other factors associated with lower physical function in this study were higher number of comorbid conditions and older age. Recent studies of older adults have associated comorbidity with decreased physical function (Bennett et al., 2002; Given, Given, Azzouz, Stommel, & Kozachik, 2001; Hodgson & Given, 2004; Kurtz et al., 1999). Cancer survivors are more likely to report having three or more other chronic medical conditions and more likely to report functional limitations than those without cancer (Hewitt et al., 2003). Penedo and colleagues (2004) suggested that physical activity might reduce the disease burden conveyed by comorbid conditions among cancer patients, by improving physical function. Results have been similar in patients with other chronic conditions such as arthritis, chronic obstructive pulmonary disease, heart disease, fibromyalgia, chronic fatigue syndrome, and multiple sclerosis (Bennett et al.,

2002; Lin, Davey & Cochrane, 2004; Mostert & Kesselring, 2002; Panton, Golden, Brooder et al., 2004; Pedersen & Saltin, 2006; Schulz et al., 2004). Older age has been reported to be associated with lower levels of physical function in cancer patients, (Deimling, 2005; Kurtz et al., 1999), in older cancer patients (Given et al., 2000; Hewitt et al., 2003), and in older persons in general (Kaplan, Strawbridge, Camacho, & Cohen, 1993; Pleis & Lethbridge-Cejku, 2006). Thus the development of physical activity interventions for older cancer patients, and particularly for those with other comorbid conditions, may help to maintain or improve physical function in these patients.

In this study, physical activity level at 3 months was not found to be a significant predictor of quality of life at 6 months. This may be due to the small changes in physical activity and quality of life scores between 3 months and 6 months, which may indicate that participants may have attained their maximum functioning within a short period of time. This finding is not consistent with studies conducted with younger cancer patients that found quality of life was significantly improved by exercise (Burnham & Wilcox, 2002; Campbell et al., 2005; Courneya & Friedenreich, 1997a & 1997b; Durak & Lilly, 1998; Headley et al., 2004; Kolden et al., 2002; MacVicar & Winningham, 1986; Schwartz, 1999; Young-McCaughan, & Sexton, 1991; Young-McCaughan et al., 2003). The difference may be due to the fact that physical activity was measured in this study, but in the literature physical activity was often increased by the introduction of an exercise intervention that may account for greater changes in physical activity and associated quality of life scores. It is also proposed in the literature that physical activity may improve quality of life in older adults in general (Cress et al., 2005; Pescatello & DiPietro, 1993; Stewart & King, 1991).

Factors associated with lower quality of life scores in this study were functional comorbidity and treatment with chemotherapy. The presence of comorbid conditions has been reported to adversely affect the quality of life of older women with breast cancer (Lickley, 1997). Other studies have found that adjuvant treatment and chemotherapy in particular have been associated with poorer physical functioning and quality of life (Broeckel, Jacobsen, Balducci, Horton, & Lyman, 2000; Ganz, Rowland, Meyerowitz, & Desmond, 1998). The symptom burden associated with comorbid conditions and adjuvant treatment may contribute to increased levels of fatigue and reduced physical activity levels in cancer patients, in turn contributing to poorer physical functioning and quality of life, as proposed in this thesis.

Limitations of the Study

Given that the study was an observational study, causality was not inferred from the identified associations. However, confirmation of the proposed associations in older adults with cancer may provide useful insight and hypothesis generation for the development and testing of physical activity interventions to promote physical function in this population. Using an experimental study design in the future that introduces a physical activity intervention may provide stronger associations between the study variables and result in significant findings with respect to physical activity during cancer treatment predicting quality of life following treatment. The self-report measure of physical activity level may not accurately reflect this variable and may have contributed to the lack of significance detected.

The single study centre limits the generalizability of the results to older cancer patients in general. The heterogeneous sample of cancer patients in terms of cancer site, stage, and treatment modality limit the conclusions and generalizability of the results of this study to specific cancer patient populations. Another limitation is the timing of the treatment in relation to survey

completion. Many subjects were late returning their baseline questionnaires and had already begun adjuvant chemotherapy or radiation treatment by the time the surveys were completed. Also, many patients had had cancer surgery prior to their consultation at the cancer centre for adjuvant treatment.

Another potential limitation of this study is participation bias. It is possible that cancer patients experiencing the most fatigue were less likely to enroll in the study, and more likely to withdraw before completing all of the questionnaires. It has also been reported that older cancer patients are less likely to consent to participate in research studies (Koval et al., 1992; Neumark, Stommel, Given & Given, 2001; Tennstedt, Dettling & McKinlay, 1992), and are less likely to be compliant with quality of life questionnaires (Di Maio & Perrone, 2003; Langer et al, 1992). Attrition was fairly high (25%) but comparable with other studies enrolling older cancer patients. Attrition rates in longitudinal studies have been reported to range from 16 to 50% (McMillan & Weitzner, 2003; Moser, Dracup, & Doering, 2000; Motzer, Moseley, & Lewis, 1997).

Conclusions

Results of this study suggest that higher levels of cancer fatigue and lower levels of physical activity are associated with lower levels of physical function and quality of life in a cohort of older adults during and following cancer treatment. Lower physical activity levels, higher comorbidity and older age are factors contributing to lower physical function in older adults following cancer treatment. Higher comorbidity and treatment with chemotherapy are factors contributing to lower quality of life in older adults following cancer treatment.

Physical activity level during cancer treatment is a modifiable factor that significantly predicted physical function in this cohort of older adults at six months following consultation for cancer treatment. These results suggest that the positive relationship between physical activity

and physical function that has previously been reported in younger cancer patients is also present in older adults with cancer. Thus it would be reasonable to hypothesize that physical activity interventions promoting physical function that are effective in younger cancer patients might also be effective in older cancer patients. Further research utilizing randomized controlled trials to test these interventions in older populations is needed to confirm this hypothesis and to identify the optimal levels and types of physical activity to maintain physical function in older adults. Longitudinal studies that include measures of fatigue, physical activity, physical function and quality of life prior to surgery would add to the generalizability of these findings by providing true baseline measures.

After ruling out contraindications to physical activity, it would be reasonable to encourage cancer patients of all ages to participate in regular physical activity during and following cancer treatment. Older adults should be encouraged to speak to their oncologists about appropriate types and levels of physical activity before engaging in a new exercise program.

References

- Aaronson, N.K., Ahmedzai, S., Bergman, B., Bullinger, M., Cull, A., Duez, N.J., et al. (1993). The European Organization for Research And Treatment of Cancer QLQ-C30: A quality-of-life instrument for use in international clinical trials in oncology. *Journal of the National Cancer Institute*, 85(5), 365-376.
- Ahlberg, K., Ekman, T., Gaston-Johansson, F., & Mock, V. (2003). Assessment and management of cancer-related fatigue in adults. *The Lancet*, 362, 640-650.
- Ahlberg, K., Ekman, T., & Gaston-Johansson, F. (2005). Fatigue, psychological distress, coping resources, and functional status during radiotherapy for uterine cancer. *Oncology Nursing Forum*, 32(3), 633-640.
- Akechi, T., Kugaya, A., Okamura, H., Yamawaki, S., & Uchitomi, Y. (1999). Fatigue and its associated factors in ambulatory cancer patients: a preliminary study. *Journal of Pain and Symptom Management*, 17(1), 42-48.
- American Society of Clinical Oncology. (1996). Outcomes of cancer treatment for technology assessment and cancer treatment guidelines. *Journal of Clinical Oncology*, 14, 671-679.
- Ashbury, F.D., Findlay, H., Reynolds, B., & McKerracher, K. (1998). A Canadian survey of cancer patients' experiences: Are their needs being met? *Journal of Pain and Symptom Management*, 16(5), 298-306.
- Avlund, K., Vass, M., & Hendriksen, C. (2003). Onset of mobility disability among community-dwelling old men and women. The role of tiredness in daily activities. *Age and Ageing*, 32(6), 579-584.
- Baird, S.B., McCorkle, R., & Grant, M. (1991). *Cancer nursing: a comprehensive textbook*. Philadelphia: W.B. Saunders.

- Bennett, J.A., Stewart, A.L., Kayser-Jones, H., & Glaser, D. (2002). The mediating effect of pain and fatigue on level of functioning in older adults. *Nursing Research, 51*(4), 254-265.
- Berger, A. (1998). Patterns of fatigue and activity and rest during adjuvant breast cancer chemotherapy. *Oncology Nursing Forum, 25*, 51-62.
- Berger, A.M., & Farr, L. (1999). The influence of daytime inactivity and nighttime restlessness on cancer-related fatigue. *Oncology Nursing Forum, 26*, 1663-1671.
- Berger, A.M., & Higginbotham, P. (2000). Correlates of fatigue during and following adjuvant breast cancer chemotherapy: A pilot study. *Oncology Nursing Forum, 27*, 1443-1448.
- Berkman, L. F., Seeman, T.E., Albert, M., Blazer, D., Kahn, R., Mohs, R., et al. (1993). High, usual and impaired functioning in community-dwelling older men and women: Findings from the MacArthur Foundation Research Network on Successful Aging. *Journal of Clinical Epidemiology, 46*(10), 1129-1140.
- Bower, J.E., Ganz, P.A., Desmond, K.A., Rowland, J.H., Meyerowitz, B.E., & Belin, T.R. (2000). Fatigue in breast cancer survivors: Occurrence, correlates, and impact on quality of life. *Journal of Clinical Oncology, 18*, 743-753.
- Broeckel, J.A., Jacobsen, P.B., Balducci, L., Horton, J., & Lyman, G.H. (2000). Quality of life after adjuvant chemotherapy for breast cancer. *Breast Cancer Research and Treatment, 62*, 141-150.
- Broeckel, J.A., Jacobsen, P.B., Horton, J., Balducci, L., & Lyman, G.H. (1998). Characteristics and correlates of fatigue after adjuvant chemotherapy for breast cancer. *Journal of Clinical Oncology, 16*, 1689-1696.
- Bultmann, U., Kant, I.J., Kasl, S.V., Schroer, K.A., Swaen, G.M., & van den Brandt, P.A. (2002). Lifestyle factors as risk factors for fatigue and psychological distress in the working

- population: Prospective results from the Maastricht Cohort Study. *Journal of Occupational and Environmental Medicine*, 44(2), 116-124.
- Burnham, T.R., & Wilcox, A. (2002). Effects of exercise on physiological and psychological variables in cancer survivors. *Medicine & Science in Sports & Exercise*, 34(12), 1863-1867.
- Byar, K.L., Berger, A.M., Bakken, S.L., & Cetak, M.A. (2006). Impact of adjuvant breast cancer chemotherapy on fatigue, other symptoms, and quality of life. *Oncology Nursing Forum*, 33(1), E18-E26.
- Camarillo, M.A. (1991). The oncology patient's experience of fatigue. *Quality of Life--A Nursing Challenge*, 1(1), 39-44.
- Campbell, A., Mutrie, N., White, F., McGuire, F., & Kearney, N. (2005). A pilot study of a supervised group exercise programme as a rehabilitation treatment for women with breast cancer receiving adjuvant treatment. *European Journal of Oncology Nursing*, 9, 56-63.
- Carr, J.L., Moffett, J.A.K., Howarth, E., Richmond, S.J., Torgerson, D.J., Jackson, D.A., et al. (2005). A randomized trial comparing a group exercise programme for back pain patients with individual physiotherapy in a severely deprived area. *Disability and Rehabilitation*, 27, 929-937.
- Cella, D.F., & Cherin, E.A. (1988). Quality of life during and after cancer treatment. *Comprehensive Therapy*, 14, 69-75.
- Cella, D.F., & Tulsky, D.S. (1990). Measuring quality of life today: Methodological aspects. *Oncology*, 14, 101-108.

- Cella (1997). The functional assessment of cancer therapy-anemia (FACT-An) scale: a new tool for the assessment of outcomes in cancer anemia and fatigue. *Seminars in Haematology*, 34, 13-19.
- Cella, D., Peterman, A., Passik, S., Jacobsen, P., & Breitbart, W. (1998). Progress toward guidelines for the management of fatigue. *Oncology*, 12(11A), 369-377.
- Cimprich, B., Ronis, D.L., & Martinez-Ramos, G. (2002). Age at diagnosis and quality of life in breast cancer survivors. *Cancer Practice*, 10(2), 85-93.
- Cohen, J. (1992). A power primer. *Psychological Bulletin*, 112(1), 155-159.
- Cohen, J. (1998). *Statistical power analysis for the behavioral sciences*. Hillsdale, NJ: Lawrence Erlbaum Associates.
- Coleman, E.A., Coon, S., Hall-Barrow, J., Richards, K., Gaylor, D., Stewart, B. (2003). Feasibility of exercise during treatment for multiple myeloma. *Cancer Nursing*, 26, 410-419.
- Coleman, E.A., Hall-Barrow, J., Coon, S., & Stewart, C.B. (2003). Facilitating exercise adherence for patients with multiple myeloma. *Clinical Journal of Oncology Nursing*, 7, 529-534.
- Courneya, K.S. (2003). Exercise in cancer survivors: An overview of research. *Medicine and Science in Sports and Exercise*, 35, 1846-1852.
- Courneya, K.S., & Friedenreich, C.M. (1997a). Relationship between exercise during treatment and current quality of life among survivors of breast cancer. *Journal of Psychosocial Oncology*, 15, 35-57.

- Courneya, K.S., & Friedenreich, C.M. (1997b). Relationship between exercise pattern across the cancer experience and current quality of life in colorectal cancer survivors. *Journal of Alternative and Complementary Medicine*, 3, 215-226.
- Courneya, K.S., Friedenreich, C.M., Quinney, H.A., Fields, A.L., Jones, L.W., & Fairey, A.S. (2003). A randomized trial of exercise and quality of life in colorectal cancer survivors. *European Journal of Cancer Care*, 12, 347-357.
- Courneya, K.S., Friedenreich, C.M., Sela, R.A., Quinney, H.A., Rhodes, R.E., & Handman, M. (2003). The group psychotherapy and home-based physical exercise (GROUP-HOPE) trial in cancer survivors: Physical fitness and quality of life outcomes. *Psychooncology*, 12, 357-374.
- Courneya, K.S., Mackey, J.R., Bell, G.J., Jones, L.W., Field, C.J., & Fairey, A.S. (2003). Randomized controlled trial of exercise training in postmenopausal breast cancer survivors: Cardiopulmonary and quality of life outcomes. *Journal of Clinical Oncology*, 21, 1660-1668.
- Courneya, K.S., Segal, R.J., Reid, R.D., Jones, L.W., Malone, S.C., Venner, P.M., et al. (2004). Three independent factors predicted adherence in a randomized controlled trial of resistance exercise training among prostate cancer survivors. *Journal of Clinical Epidemiology*, 57, 571-579.
- Courneya, K.S., Vallance, J.K.H., McNeely, ML, Karvinen, K.H., Peddle, C.J., & Mackey, J.R. (2004). Exercise issues in older cancer survivors. *Critical Reviews in Oncology/Hematology*, 51, 249-261.

- Cress, M.E., Buchner, D.M., Prohaska, T., Rimmer, J., Brown, M., Macera, C., et al. (2005). Best practices for physical activity programs and behavior counseling in older adult populations. *Journal of Aging and Physical Activity, 13*, 61-74.
- Culos-Reed, S.N., Robinson, J.L., Lau, H., O'Connor, K., & Keats, M.R. (2007). Benefits of a physical activity intervention for men with prostate cancer. *Journal of Sport and Exercise Psychology, 29*, 118-127.
- Curt, G.A. (2000). The impact of fatigue on patients with cancer: Overview of FATIGUE 1 and 2. *The Oncologist, 5*(suppl 2), 9-12.
- Curt, G., Breitbart, W., Cella, D., Groopman, J., Horning, S., Itri, L., et al. (2000). Impact of cancer-related fatigue on the lives of patients: New findings from the fatigue coalition. *Oncologist, 5*, 353-360.
- Curt, G., & Johnston, P.G. (2003). Cancer fatigue: the way forward. *Oncologist, 8* (suppl 1), 27-30.
- Curtis, E.B., Krech, R., & Walsh, T.D. (1991). Common symptoms in patients with advanced cancer. *Journal of Palliative Care, 7*(2), 25-29.
- De Jong, N., Courtens, A.M., Abu-Saad, H.H., & Schouten, H.C. (2002). Fatigue in patients with breast cancer receiving adjuvant chemotherapy: A review of the literature. *Cancer Nursing, 25*, 283-297.
- Di Maio, M., & Perrone, F. (2003). Quality of life in elderly patients with cancer. *Health and Quality of Life Outcomes, 1*(44).
- Dimeo, F.C. (2001). Effects of exercise on cancer-related fatigue. *Cancer, 15*(Suppl.6), 1689-1693.

- Dimeo, F., Rumberger, B., & Keul, J. (1998). Aerobic exercise as therapy for cancer fatigue. *Medicine and Science in Sports and Exercise, 30*, 475-478.
- Dimeo, F., Stieglitz, R.D., Novelli-Fischer, U., Fetscher, S., & Keul, J. (1999). Effects of physical activity on the fatigue and psychologic status of cancer patients during chemotherapy. *Cancer, 85*, 2273-2277.
- Dimeo, F., Stieglitz, R.D., Novelli-Fischer, U., Fetscher, S., Mertelsmann, R., & Keul, J. (1997). Correlation between physical performance and fatigue in cancer patients. *Annals of Oncology, 8*, 1251-1255.
- Dimeo, F.C., Thomas, F., Raabe-Menssen, C., Propper, F., & Mathias, M. (2004). Effect of aerobic exercise and relaxation training on fatigue and physical performance of cancer patients after surgery. A randomised controlled trial. *Supportive Care in Cancer, 12*, 774-779.
- Dodd, M.J., Miaskowski, C., & Paul, S.M. (2001). Symptom clusters and their effect on the functional status of patients with cancer. *Oncology Nursing Forum, 28*(3), 465-470.
- Donovan, K., Sanson-Fisher, R.W., & Redman, S. (1989). Measuring quality of life in cancer patients. *Journal of Clinical Oncology, 7*, 959-968.
- Drouin, J.S., Armstrong, H., Krause, S., Orr, J., Birk, T.J., Hryniuk, W.M., & Hryniuk, I.R. (2005). Effects of aerobic exercise training on peak aerobic capacity, fatigue, and psychological factors during radiation for breast cancer. *Rehabilitation Oncology, 23*(1), 11-17.
- Durak, E.P., & Lilly, P.C. (1998). The application of an exercise and wellness program for cancer patients: A preliminary outcomes report. *Journal of Strength and Conditioning Research, 12*(1), 3-6.

- Duthie, E.H. (2004). Physiology of aging: Relevance to symptoms, perceptions, and treatment tolerance. In L. Balducci, G.H. Lyman, W.B. Ershler, & M. Extermann (Eds.), *Comprehensive Geriatric Oncology* (2nd ed., pp.208-222). New York: Taylor & Francis.
- Esbensen, B.A., Osterlind, K., & Hallberg, I.R. (2006). Quality of life of elderly persons with cancer: A 3-month follow-up. *Cancer Nursing*, 29(3), 214-224.
- Ferrell, B.R., Grant, M., Dean, G.E., Funk, B., & Ly, J. (1996). "Bone tired": the experience of fatigue and its impact on quality of life. *Oncology Nursing Forum*, 23, 1539-47.
- Fletcher, H., Rueffer, J.U., Nenry-Aimar, M., Mellink, W.A., Sieber, M., Ferme, C., et al. (1998). Quality of life assessment in Hodgkin's disease: a new comprehensive approach. First Experience from the EORTC/GHSG trials. *Annals of Oncology*, 9, 147-154.
- Fulton, C., & Knowles, G. (2000). Focus for applied cancer education and training: cancer fatigue. *European Journal of Cancer Care*, 9(3), 167-8.
- Galvao, D.A., & Newton, R.U. (2005). Review of exercise intervention studies in cancer patients. *Journal of Clinical Oncology*, 23(4), 899-909.
- Ganz, P.A., Rowland, J.H., Meyerowitz, B.E., & Desmond, K.A. (1998). Impact of different adjuvant therapy strategies on quality of life in breast cancer survivors. *Recent Results in Cancer Research*, 152, 396-411.
- Garman, K.S., & Cohen, H.J. (2002). Functional status and the elderly cancer patient. *Critical Reviews in Oncology/Hematology*, 43, 191-208.
- Gill, T.M., & Feinstein, A.R. (1994). A critical appraisal of the quality of quality-of-life measurements. *Journal of the American Medical Association*, 272, 619.

- Given, C.W., Given, B., Azzouz, F., Kozachik, S., & Stommel, M. (2001). Predictors of pain and fatigue in the year following diagnosis among elderly cancer patients. *Journal of Pain and Symptom Management, 21*, 456-466.
- Given, C.W., Given, B., Azzouz, F., Stommel, M., & Kozachik, S. (2000). Comparison of changes in physical functioning of elderly patients with new diagnoses of cancer. *Medical Care, 38*(5), 482-493.
- Glaus, A. (1993). Assessment of fatigue in cancer and non-cancer patients and in healthy individuals. *Supportive Care in Cancer, 1*, 305-315.
- Graydon, J.E., Bubela, N., Irvine, D., & Vincent, L. (1995). Fatigue-reducing strategies used by patients receiving treatment for cancer. *Cancer Nursing, 18*, 23-28.
- Groenwald, S.L., Frogge, M.H., & Goodman, M., & Yarbrow, C.H. (1997). *Cancer nursing: Principles and practice*. Garden City, New York: Doubleday.
- Groll, D.L., Heyland, D.K., Caeser, M., & Wright, J.G. (2006). Assessment of long-term physical function in acute respiratory distress syndrome (ARDS) patients: Comparison of the Charlson Comorbidity Index and the Functional Comorbidity Index. *American Journal of Physical Medicine & Rehabilitation, 85*(7), 1-8.
- Groll, D. L., To, T., Bombardier, C., & Wright, J. G. (2005). The development of a comorbidity index with physical function as the outcome. *Journal of Clinical Epidemiology, 58*, 595-602.
- Harada, N.D., Chiu, V., King, A.C., & Stewart, A.L. (2001). An evaluation of three self-reported physical activity instruments for older adults. *Medicine and Science in Sports and Exercise, 33*, 962-970.

- Harrison, M.B. (1998). Continuity of care for complex hospital populations: Effectiveness and efficiency of two models of hospital to home transfer (Doctoral dissertation, McMaster University, 1998). *Dissertation Abstracts International*, 60(9), 4520.
- Headley, J.A., Ownby, K.K., & John, L.D. (2004). The effect of seated exercise on fatigue and quality of life in women with advanced breast cancer. *Oncology Nursing Forum*, 31, 977-983.
- Hewitt, M., Rowland, J.H., & Yancik, R. (2003). Cancer survivors in the United States: Age, health and disability. *The Journals of Gerontology: Medical Sciences*, 58A (1), 82-91.
- Hickok, J.T., Roscoe, J.A., Morrow, G.R., & Bushunow, P. (1998). Wrist actigraphy as a measure of fatigue (Abstract No. 231). *Proceedings of the American Society of Clinical Oncology*, 17, 60a.
- Hilfinger, D.K., Yeager, K.A., Dibble, S.L., & Dodd, M.J. (1997). Patients' perspectives of fatigue while undergoing chemotherapy. *Oncology Nursing Forum*, 24, 43-48.
- Hodgson, N.A., & Given, C.W. (2004). Determinants of functional recovery in older adults surgically treated for cancer. *Cancer Nursing*, 27(1), 10-16.
- Holzner, B., Kemmler, G., Meraner, V., Maislinger, A., Kopp, M., Bodner, T., et al. (2003). Fatigue in ovarian carcinoma patients: a neglected issue? *Cancer*, 15, 1564-1572.
- Hotopf, M. (2004). Definitions, epidemiology, and models of fatigue in the general population and in cancer. In J. Arms, M. Krishnasamy, & I.J. Higginson (Eds.), *Fatigue in cancer* (pp. 3-27). Oxford: Oxford University Press.
- Irvine, D., Vincent, L., Bubela, N., Thompson, L., & Graydon, J. (1991). A critical appraisal of the research literature investigating fatigue in the individual with cancer. *Cancer Nursing*, 14, 188-199.

- Irvine, D.M., Vincent, L., Graydon, J.E., & Bubela, N. (1998). Fatigue in women with breast cancer receiving radiation therapy. *Cancer Nursing, 21*, 127-135.
- Irvine, D., Vincent, L., Graydon, J., Bubela, N., & Thompson, L. (1994). The prevalence and correlates of fatigue in patients receiving treatment with chemotherapy and radiation therapy: a comparison with the fatigue experienced by healthy individuals. *Cancer Nursing, 17*, 367-378.
- Irwin, M., Crumley, D., McTiernan, A. Bernstein, L., Baumgartner, R., Gilliland, F., et al. (2003). Physical activity levels before and after a diagnosis of breast cancer: The Health, Eating, Activity, and Lifestyle (HEAL) Study. *Cancer, 97*, 1746-1757.
- Jacobsen, P.B., Hann, D.M., Azzarello, L.M., Horton, J., Balducci, L., & Lyman, G.H. (1999). Fatigue in women receiving adjuvant chemotherapy for breast cancer: characteristics, course, and correlates. *Journal of Pain and Symptom Management, 18*(4), 233-242.
- Joanna Briggs Institute. (2005). *Train the Trainer, Module 2* (pp.32-41). Adelaide: Joanna Briggs Institute.
- Kaplan, G.A., Strawbridge, W.J., Camacho, T., & Cohen, R.D. (1993). Factors associated with change in physical functioning in the elderly: A six-year prospective study. *Journal of Aging and Health, 5*(1), 140-153.
- King, K.B., Nail, L.M., Kreamer, K., Strohl, R.A., & Johnson, J.E. (1985). Patients' descriptions of the experience of receiving radiation therapy. *Oncology Nursing Forum, 12*, 55-61.
- King, A.C., Rejeski, W.J., & Buchner, D.M. (1998). Physical activity interventions targeting older adults. *American Journal of Preventative Medicine, 15*, 316-333.
- Kolden, G.G., Strauman, T.J., Ward, A., Kuta, J., Woods, T.E., Schneider, K.L., et al. (2002). *Psycho-Oncology, 11*, 447-456.

- Koval, J.J., Ecclestone, N.A., Paterson, D.H., Brown, B., Cunningham, D.A., Rechnitzer, P.A. (1992). Response rates in a survey of physical capacity among older persons. *Journal of Gerontology: Social Sciences*, 47(3), S140-147.
- Kroenke, C.H., Rosner, B., Chen, W.Y., Kawachi, I., Colditz, G.A., Holmes, M.D. (2004). Functional impact of breast cancer by age at diagnosis. *Journal of Clinical Oncology*, 22(10), 1849-1856.
- Kurtz, M.E., Kurtz, J.C., Stommel, M., Given, C.W., Given, B. (1999). The influence of symptoms, age, comorbidity and cancer site on physical functioning and mental health of geriatric women patients. *Women & Health*, 29(3), 1-12.
- Langer, C.J., Manola, J., Bernardo, P., Kugler, J.W., Bonomi, P., Cella, D., et al. (2002). Cisplatin-based therapy for elderly patients with advanced non-small-cell lung cancer: Implications of Eastern Cooperative Oncology Group 5592, a randomized trial. *Journal of the National Cancer Institute*, 94(3), 173-181.
- Latham, N.K., Bennett, D.A., Stretton, C.M., & Anderson, C.S. (2004). Systematic review of progressive resistance strength training in older adults. *Journal of Gerontology: Medical Sciences*, 59A(1), 48-61.
- Lickley, H.L.A. (1997). Primary breast cancer in the elderly. *Canadian Journal of Surgery*, 40(5), 341-351.
- Lilleby, W., Fossa, S.D., Waehre, H.R., & Olsen, D.R. (1999). Long-term morbidity and quality of life in patients with localized prostate cancer undergoing definitive radiotherapy or radical prostatectomy. *International Journal of Radiation Oncology Biology Physics*, 43(4), 735-743.

- Lin, S.Y., Davey, R.C., & Cochrane, T. (2004). Community rehabilitation for older adults with osteoarthritis of the lower limb: A controlled clinical trial. *Clinical Rehabilitation, 18*, 92-101.
- Loge, J.H., Abrahamsen, A.F., Ekeberg, O., & Kaasa, S. (2000). Fatigue and psychiatric morbidity among Hodgkin's disease survivors. *Journal of Pain and Symptom Management, 19*(2), 91-99.
- Longman, A.J., Braden, C.J., Mishel, M.H. (1999). Side-effects burden, psychological adjustment, and life quality in women with breast cancer: pattern of association over time. *Oncology Nursing Forum, 26*, 909-915.
- Luctkar-Flude, M.F., Groll, D., Tranmer, J.E., & Woodend, K. (in press). *Fatigue and physical activity in older adults with cancer: A systematic review of the literature.*
- MacVicar, M.G., & Winningham, M.L. (1986). Promoting the functional capacity of cancer patients. *The Cancer Bulletin, 38*(5), 235-239.
- MacVicar, M.G., Winningham, M.L., & Nickel, J.L. (1989). Effects of aerobic interval training on cancer patients' functional capacity. *Nursing Research 38*, 348-351.
- Mazzeo, R.S., Cavanagh, P., William, J., Fiatarone, M., Hagberg, J., McAuley, E., et al. (1998). ACSM position stand: Exercise and physical activity for older adults. *Medicine & Science in Sports & Exercise, 30*(6), 992-1008.
- Mock, V. (2001). Fatigue management: Evidence and guidelines for practice. *Cancer Supplement, 92*, 1699-1707.
- Mock, V., Burke, M., Sheehan, P., Creaton, E., Winningham, M., McKenney-Tedder, S., Powel, L., & Liebman, M. (1994). A nursing rehabilitation program for women with breast cancer receiving adjuvant chemotherapy. *Oncology Nursing Forum, 21*, 899-907.

- Mock, V., Frangakis, C., Davidson, N.R., Ropka, M.E., Pickett, M., Poniatowski, B. et al. (2005). Exercise manages fatigue during breast cancer treatment: A randomized controlled trial. *Psycho-Oncology*, 14, 464-477.
- Mock, V., Hassey Dow, K., Meares, C.J., Grimm, P.M., Dienemann, J.A., Haisfield-Wolfe, M.E., et al. (1997). Effects of exercise on fatigue, physical functioning, and emotional distress during radiation therapy for breast cancer. *Oncology Nursing Forum*, 24, 991-1000.
- Mock, V., McCorkle, R., & Krumm, S. (2003). Clinical excellence through evidence-based practice: Fatigue management as a model. *Oncology Nursing Forum*, 30, 1-18.
- Mock, V., McCorkle, R., Ropka, M.E., Pickett, M., & Poniatowski, B. (2002). Fatigue and physical functioning during breast cancer treatment. *Oncology Nursing Forum*, 29, 338.
- Mock, V., Pickett, M., Ropka, M.E., Lin, E.M., Stewart, K.J., Rhodes, V.A., et al. (2001). Fatigue and quality of life outcomes of exercise during cancer treatment. *Cancer Practice*, 9, 119-127.
- Monga, U., Kerrigan, A.J., Thornby, J., Monga, T.N. (1999). Prospective study of fatigue in localized prostate cancer patients undergoing radiotherapy. *Radiation Oncology Investigations*, 7, 178-185.
- Mor, V., Murphy, J., Masterson-Allen, S., Willey, C., Razmpour, A., Jackson, E., et al. (1989). Risk of functional decline among well elders. *Journal of Clinical Epidemiology*, 42(9), 895-904.
- Mormont, M-C., Waterhouse, J., Bleuzen, P., Giacchetti, S., Jami, A., Bogdan, A., et al. (2000). Marked 24-h rest/activity rhythms are associated with better quality of life, better

- response, and longer survival in patients with metastatic colorectal cancer and good performance status. *Clinical Cancer Research*, 6, 3038-3045.
- Mostert S. & Kesselring J. (2002). Effects of a short-term exercise training program on aerobic fitness, fatigue, health perception and activity level of subjects with multiple sclerosis. *Multiple Sclerosis*, 8(2),161-168.
- Nail, L.M. (2002). Fatigue in patients with cancer. *Oncology Nursing Forum*, 29, 537-46.
- Nail, L.M., & Jones, L.S. (1995). Fatigue as a side effect of cancer treatment: Impact on quality of life. *Quality of Life--A Nursing Challenge*, 4(1), 8-13.
- Nail, L.M., & Winningham, M.L. (1995). Fatigue and weakness in cancer patients: the symptom experience. *Seminars in Oncology Nursing*, 11(4), 272-278.
- National Cancer Institute of Canada. (2004). *Canadian cancer statistics 2004*. Toronto: National Cancer Institute of Canada.
- National Comprehensive Cancer Network (NCCN). (2003). Cancer-related fatigue: Clinical practice guidelines in oncology. *Journal of the National Comprehensive Cancer Network*, 1, 308-331.
- Neumark, D.E., Stommel, M., Given, C.W., & Given, B.A. (2001). Research design and subject characteristics predicting nonparticipation in a panel survey of older families with cancer. *Nursing Research*, 50(6), 363-368.
- Norman, G.R., & Streiner, D.L. (2000). *Biostatistics: The bare essentials*. Hamilton, ON: B.C. Decker Inc.
- Oldervoll, L.M., Kaasa, S., Knobel, H., & Loge, J.H. (2003). Exercise reduces fatigue in chronic fatigued Hodgkins disease survivors - Results from a pilot study. *European Journal of Cancer*, 39(1), 57-63.

- Olschewski, M., Schulgen, G., Schumacher, M., & Altman, D.G. (1994). Quality of Life Assessment in Clinical Cancer Research. *British Journal of Cancer*, 70, 1-5.
- Osoba, D. (1994). Lessons learned from measuring health-related quality of life in oncology. *Journal of Clinical Oncology*, 12, 608-616.
- Otto, S.E. (1993). *Oncology Nursing*. St. Louis: Mosby.
- Panton, L.B., Golden, J., Broeder, C.E., Browder, K.D., Cestaro-Seifer, D.J., & Seifer, F.D. (2004). The effects of resistance training on functional outcomes in patients with chronic obstructive pulmonary disease. *European Journal of Applied Physiology*, 91, 443-449.
- Pedersen, B.K., & Saltin, B. (2006). Evidence for prescribing exercise as therapy in chronic disease. *Scandinavian Journal of Medicine and Science in Sports*, 16(Suppl 1), 3-63.
- Penedo, F.J., Schneiderman, N., Dahn, J.R., & Gonzalez, J.S. (2004). Physical activity interventions in the elderly: cancer and comorbidity. *Cancer Investigation*, 22(1), 51-67.
- Pescatello, L.S., & DiPietro, L. (1993). Physical activity in older adults. *Sports Medicine*, 15(6), 353-364.
- Pickett, M., Mock, V., Ropka, M.E., Cameron, L., Coleman, M. & Podewils, L. (2002). Adherence to moderate-intensity exercise during breast cancer therapy. *Cancer Practice*, 10, 284-292.
- Pinto, B.M., Trunzo, J.J., Reiss, P., & Shiu, S-Y. (2002). Exercise participation after diagnosis of breast cancer: Trends and effects on mood and quality of life. *Psycho-Oncology*, 11, 389-400.
- Pleis, J.R., & Lethbridge-Cejku, M. (2006). Summary health statistics for U.S. adults: National health interview survey, 2005. National Center for Health Statistics. *Vital Health Statistics*, 10(232).

- Porock, D., Beshears, B., Hinton, P., & Anderson, C. (2005). Nutritional, functional, and emotional characteristics related to fatigue in patients during and after biochemotherapy. *Oncology Nursing Forum, 32*(3), 661-667.
- Portenoy, R.K., & Itri, L.M. (1999). Cancer-related fatigue: Guidelines for evaluation and management. *The Oncologist, 4*, 1-10.
- Portenoy R.K., Thaler, H.T., Kornblith, A.B., McCarthy Lepore, J., Friedlander-Klar, H., Kiyasu, E., et al. (1994). The Memorial Symptom Assessment Scale: An instrument for the evaluation of symptom prevalence, characteristics and distress. *European Journal of Cancer, 30A*, 1326-1336.
- Rao, A., & Cohen, H.J. (2004). Symptom management in the elderly cancer patient: fatigue, pain, and depression. *Journal of the National Cancer Institute, 32*, 150-157.
- Rhodes, V.A., Watson, P.M., & Hanson, B.M. (1988). Patients' descriptions of the influence of tiredness and weakness on self-care abilities. *Cancer Nursing, 11*, 186-194.
- Richardson, A., & Ream, E.K. (1997). Self-care behaviors initiated by chemotherapy patients in response to fatigue. *International Journal of Nursing Studies, 34*, 35-43.
- Rieger, P.T. (2001). Assessment and epidemiologic issues related to fatigue. *Cancer, 92*(6 Suppl), 1733-1736.
- Rosenthal, M.A., & Oratz, R. (1998). Phase II clinical trial of recombinant alpha 2b interferon and 13 cis retinoic acid in patients with metastatic melanoma. *American Journal of Clinical Oncology, 21*, 352-354.
- Schulz, K-H., Gold, S.M., Witte, J., Bartsch, K., Lang, U.E., Hellweb, R., et al. (2004). Impact

- of aerobic training on immune-endocrine parameters, neurotrophic factors, quality of life and coordinative function in multiple sclerosis. *Journal of the Neurological Sciences*, 225, 11-18.
- Schwartz, A.L. (1998a). Patterns of exercise and fatigue in physically active cancer survivors. *Oncology Nursing Forum*, 25, 485-491.
- Schwartz, A.L. (1998b). The Schwartz Cancer Fatigue Scale: Testing reliability and validity. *Oncology Nursing Forum*, 25, 711-717.
- Schwartz, A.L. (1999). Fatigue mediates the effects of exercise on quality of life in women with breast cancer. *Quality of Life Research*, 8, 529-538.
- Schwartz, A.L. (2000). Daily fatigue patterns and effect of exercise in women with breast cancer. *Cancer Practice*, 8(1), 16-24.
- Schwarz, R., & Hinz, A. (2001). Reference data for the quality of life questionnaire EORTC QLQ-C30 in the general German population. *European Journal of Cancer*, 37, 1345-1351.
- Schwarz, A.L., Mori, M., Gao, R., Nail, L.M., & King, M.E. (2001). Exercise reduces fatigue in women with breast cancer receiving chemotherapy. *Medicine and Science in Sports and Exercise*, 33, 718-723.
- Segal, R.J., Reid, R.D., Courneya, K.S., Malone, S.C., Parliament, M.B., Scott, C.G., et al. (2003). Resistance exercise in men receiving androgen deprivation therapy for prostate cancer. *Journal of Clinical Oncology*, 21, 1653-1659.
- Sheehan, D.C., & Forman, W.B. (1997). Symptomatic management of the older person with cancer. *Clinics in Geriatric Medicine*, 13, 203-219.

- Silliman, R.A., Balducci, L., Goodwin, J.S., Holmes, F.F., & Levanthal, E.A., (1993). Breast cancer in old age: What we know, don't know, and do. *Journal of the National Cancer Institute*, 85 (3), 190-199.
- Simonsick, E.M., Lafferty, M.E., Phillips, C.L., Mendes de Leon, C.R., Kasl, S.V., Seeman, T.E., et al. (1993). Risk due to inactivity in physically capable older adults. *American Journal of Public Health*, 83(10), 1443-1450.
- Skalla, K.A., & Rieger, P.T. (1995). Fatigue. In P,T. Rieger (Ed.), *Biotherapy: A comprehensive review* (pp. 221-242). Subury, MA: Jones and Bartlett.
- Smets, E.M.A., Visser, M., Willems-Groot, A., & Garssen, B. (1998). Fatigue and radiotherapy: experience in patients undergoing treatment. *British Journal of Cancer*, 78, 899-906.
- Stasi, R., Abriani, L., Beccaglia, P., Terzoli, E., & Amadori, S. (2003). Cancer-related fatigue: Evolving concepts in evaluation and treatment. *Cancer*, 98, 1786-1801.
- Stewart, A.L., & King, A.C. (1991). Evaluating the efficacy of physical activity for influencing quality-of-life outcomes in older adults. *Annals of Behavioral Medicine*, 13(3), 108-116.
- Stone, P., Richards, M., A'Hern, R., & Hardy, J. (2000). A study to investigate the prevalence, severity and correlates of fatigue among patients with cancer in comparison with a control group of volunteers without cancer. *Annals of Oncology*, 11, 561-567.
- Stone, P., Richards, M., A'Hern, R., & Hardy, J. (2001). Fatigue in patients with cancers of the breast or prostate undergoing radical radiotherapy. *Journal of Pain and Symptom Management*, 22, 1007-1015.
- Tanaka, K., Akechi, T., Okuyama, T., Nishiwaki, Y., & Uchitomi, Y. (2002). Impact of dyspnea, pain, and fatigue on daily life activities in ambulatory patients with advanced lung cancer. *Journal of Pain and Symptom Management*, 23, 417-23.

- Tennstedt, S.L., Dettling, U., & McKinlay, J.B. (1992). Refusal rates in a longitudinal study of older people: Implications for field methods. *Journal of Gerontology: Social Sciences*, 47(6), S313-S318.
- Thome, B., Dykes, A-K., & Hallberg, I.R. (2004). Quality of life in old people with and without cancer. *Quality of Life Research*, 13, 1067-1080.
- Tranmer, J.E., Heyland, D., Dudgeon, D., Groll, D., Squires-Graham, M., & Coulson, K. (2003). Measuring the symptom experience of seriously ill cancer and noncancer hospitalized patients near the end of life with the Memorial Symptom Assessment Scale. *Journal of Pain and Symptom Management*, 25, 420-429.
- Turner, J., Hayes, S., & Reul-Hirche, H. (2004). Improving the physical status and quality of life of women treated for breast cancer: A pilot study of a structured exercise intervention. *Journal of Surgical Oncology*, 86, 141-146.
- U.S. Department of Health and Human Services. (1996). *Physical activity and health: A report of the Surgeon General*. Atlanta, GA: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion.
- Van Weert, E., Hoekstra-Weeber, J.E., Grol, B.M., Otter, R., Arendzen, J.H., Postema, K., et al. (2004). Physical functioning and quality of life after cancer rehabilitation. *International Journal of Rehabilitation Research*, 27(1), 27-35.
- Visovsky, C., & Schneider, S.M. (2003). Cancer-related fatigue. *Online Journal of Issues in Nursing*, 1-23.

- Vogelzang, N., Breitbart, W., Cella, D., Curt, G.A., Groopman, J.E., Horning, S.J., et al. (1997). Patient, caregiver, and oncologist perceptions of cancer-related fatigue: results of a tripart assessment survey. *Seminars in Hematology*, 34(suppl 2), 4-12.
- Wagner, E.H., LaCroix, A.Z., Buchner, D.M., & Larson, E.B. (1992). Effects of physical activity on health status in older adults I: Observational studies. *Annual Reviews in Public Health*, 13, 451-468.
- Wang, X.S., Giralt, S.A., Mendoza, T.R., Engstrom, M.C., Johnson, B.A., Peterson, N., et al. (2002). Clinical factors associated with cancer-related fatigue in patients being treated for leukemia and non-Hodgkin's lymphoma. *Journal of Clinical Oncology*, 20, 1319-1328.
- Ware, J.E., Kosinski M., & Keller S.D. (1996). A 12-item short-form Health Survey. Construction of scales and preliminary tests of reliability and validity. *Medical Care*. 34(3), 220-233.
- Washburn, R.A., Smith, K.W., Jette, A.M., & Janney, C.A. (1993). The physical activity scale for the elderly (PASE): Development and evaluation. *Journal of Clinical Epidemiology*, 46(2), 153-162.
- Wengstrom, Y., Haggmark, C., Strander, H., & Forsberg, C. (2000). Perceived symptoms and quality of life in women with breast cancer receiving radiation therapy. *European Journal of Oncology Nursing*, 4(2), 78-88.
- Whedon, M., Stearns, D., Y Mills, L.E. (1995). Quality of life of long-term adult survivors of autologous bone marrow transplantation. *Oncology Nursing Forum*, 22, 1527-1535.
- Windsor, P.M., Nicol, K.F., & Potter, J. (2004). A randomized, controlled trial of aerobic exercise for treatment-related fatigue in men receiving radical external beam radiotherapy for localized prostate carcinoma. *Cancer*, 101, 550-557.

- Winningham, M.L., (1991). Walking program for people with cancer: Getting started. *Cancer Nursing, 14*, 270-276.
- Winningham, M.L. (1999). In: Yarbro, C.H., Frogge, M.H., Goodman, M. eds. *Cancer Symptom Management*. 2nd ed. Boston, Mass: Jones & Bartlett.
- Winningham, M.L., Nail, L.M., Burke, M.B., Brophy, L., Cimprich, B., Jones, L.S. et al. (1994). Fatigue and the cancer experience: The state of the knowledge. *Oncology Nursing Forum, 21*(1), 23-36.
- Wyatt, G.K., & Friedman, L.L. (1998). Physical and psychosocial outcomes of midlife and older women following surgery and adjuvant therapy for breast cancer. *Oncology Nursing Forum, 25*(4), 761-768.
- Yancik, R. (1997). Cancer burden in the aged: an epidemiologic and demographic overview. *Cancer, 80*, 1273-1283.
- Young-McCaughan, S., & Sexton, D. (1991). A retrospective investigation of the relationship between aerobic exercise and quality of life in women with breast cancer. *Oncology Nursing Forum, 18*(4), 751-757.
- Young-McCaughan, S., Mays, M.Z., Arzola, S.M., Yoder, L.H., Dramiga, S.A., Leclerc, K.M. et al. (2003). Changes in exercise tolerance, activity and sleep patterns, and quality of life in patients with cancer participating in a structured exercise program. *Oncology Nursing Forum, 30*(3), 441-454.

Table 1

Table of Variables

Variable	Type of Variable	Source
Fatigue	Outcome	Memorial Symptom Assessment Scale (MSAS): self-report -lack of energy score
Physical Activity	Outcome	Physical Activity Scale for the Elderly (PASE): self-report -physical activity score
Physical Function	Outcome	Medical Outcome Short Form 12 General Health Questionnaire (SF 12): self-report -Physical Component Score (PCS)
Quality of Life	Outcome	European Organization for Research Treatment Quality of Life Questionnaire (EORTC QLQ – C30): self-report -global quality of life score
Functional Comorbidity	Independent	Functional Comorbidity Index (FCI): self report and chart abstraction at baseline
Cancer site	Independent	Baseline chart abstraction
Cancer stage	Independent	Baseline chart abstraction
Treatment modalities	Independent	Followup chart abstraction
Personal Demographic Characteristics	Independent	Self-report at baseline
a) Age		
b) Gender		
c) Marital status		
d) Educational status		
e) Household income		
f) Living arrangements		
g) BMI		

Table 2

Baseline Demographic Characteristics (N=440)

Variable	Category	Mean (range)	SD	n	%
Age (years)		72.6 (65-90)	5.6		
BMI		27 (15-43)	4.8		
Self-reported functional comorbidity (FCI)		2.9 (1-12)	1.8		
Sex	Female			192	43.6
	Male			248	56.4
Marital status	Single/widowed			88	20.0
	Married/common law			323	73.4
	Divorced/separated			27	6.1
	Missing			2	0.01
Education	Did not complete public school			2	0.5
	Completed high school			306	69.5
	Completed college or university			80	18.2
	Completed postgraduate			42	9.5
	Missing			10	0.02
Income	< \$20000			67	15.2
	\$21000-\$40000			173	39.3
	\$41000-\$60000			83	18.9
	>\$60000			61	13.9
	Missing			56	0.1
Living arrangement	Lives alone			87	19.8
	Lives with spouse or partner			326	74.1
	Lives with family member			14	3.2
	Lives with other			11	2.5
	Missing			2	0.01

Table 3

Cancer Site, Stage and Treatment (N=440)

Cancer Site	<i>n</i>	%
Breast	110	25.0
Prostate	107	24.3
Colorectal	70	15.9
Lung	42	9.5
Other	111	25.3

Cancer Stage	<i>n</i>	%
I	157	35.7
II	88	20.0
III	77	17.5
IV	24	5.5
Missing/cannot assess	94	21.3

Treatment Modality	<i>n</i>	%
Chemotherapy	150	34.2
Radiotherapy	270	61.5
Surgery	241	54.9
Hormones	92	21.0
Biotherapy	3	0.7
Observation	19	4.3

Note: Cancer Stage I=localized, Stage II & III=locally advanced (depends on cancer site), Stage IV=metastatic

Table 4

<i>Outcome Scores</i>				
Variable	Mean	Standard Deviation	Median	Range
<u>Fatigue (MSAS)</u>				
Baseline	1.31	1.13	1.33	0-4
3 months	1.13	1.14	1.00	0-4
6 months	0.96	1.12	0.25	0-4
<u>Physical Activity (PASE)</u>				
Baseline	93.3	66.2	78.93	0-335.3
3 months	110.3	72.3	101.15	0-474
6 months	119.7	70.6	111.36	0-401.1
<u>Physical Function (SF-12 PCS)</u>				
Baseline	41.8	11.7	42.64	0-52.7
3 months	41.2	11	41.34	0-43.7
6 months	42	11.2	42.01	0-46.9
<u>Quality of Life (EORTC QLQ-C30)</u>				
Baseline	70.4	22.3	75.00	0-100
3 months	72	20.4	75.00	0-100
6 months	72.7	21	75.00	0-100

Note. MSAS = Memorial Symptom Assessment Scale lack of energy score, PASE = Physical Activity Scale for the Elderly physical activity score, SF 12 PCS = Medical Outcome Short Form 12 General Health Questionnaire Physical Component summary subscale, EORTC QLQ-C30 + European Organization for Research Treatment Quality of Life Questionnaire global QOL score

Table 5

*Pearson correlations between outcome scores at baseline, 3 months and 6 months**

	Physical Function (SF12 PCS)			Quality of Life (EORTC QLQ-C30)		
	Baseline	3 Months	6 Months	Baseline	3 Months	6 Months
Fatigue (MSAS)						
Baseline	-0.657	-0.492	-0.483	-0.630	-0.451	-0.372
3 Months		-0.614	-0.470		-0.647	-0.374
6 Months			-0.664			-0.674
Physical Activity (PASE)						
Baseline	0.468	0.399	0.375	0.402	0.337	0.295
3 Months		0.442	0.359		0.375	0.280
6 Months			0.455			0.408
Physical Function (SF12 PCS)						
Baseline		0.660	0.698	0.612	0.487	0.430
3 Months			0.700		0.650	0.512
6 Months						0.655
Quality of Life (EORTC QLQ-C30)						
Baseline	0.612	0.476	0.499		0.546	0.511
3 Months		0.650	0.560			0.620
6 Months						

*All correlations were significant ($p < 0.001$)

Note. MSAS = Memorial Symptom Assessment Scale lack of energy score, PASE = Physical Activity Scale for the Elderly physical activity score, SF 12 PCS = Medical Outcome Short Form 12 General Health Questionnaire Physical Component summary subscale, EORTC QLQ-C30 + European Organization for Research Treatment Quality of Life Questionnaire global QOL score

Table 6

Significant Results of Stepwise Linear Regression Models Related to Research HypothesesRelationship between Physical Activity at 3 Months and Physical Function (SF 12 PCS) at 6 Months *

Independent Variable	Standardized Beta	Sig
Physical Activity (PASE) 3 Months	0.155	0.032
Prostate	0.285	0.001
Comorbidity (FCI)	-0.240	0.001
Age	-0.147	0.031

*Adjusted R Square = 0.256, Sig = 0.001

Relationship between Physical Activity at 3 Months and Quality of Life(EORTC QLQ-C30) at 6 Months *

Independent Variable	Standardized Beta	Sig
Comorbidity (FCI)	-0.222	0.001
Chemotherapy	-0.241	0.003
Colorectal	0.288	0.001
Prostate	0.337	0.001
Gender	0.190	0.031

*Adjusted R Square = 0.172, Sig = 0.001

Note. PASE = Physical Activity Scale for the Elderly physical activity scale, SF 12 PCS = Medical Outcome Short Form 12 General Health Questionnaire Physical Component summary subscale, EORTC QLQ-C30 + European Organization for Research Treatment Quality of Life Questionnaire Global QOL score

Chapter Five

Thesis Summary

This thesis was undertaken to increase the understanding about cancer fatigue and its relationship to physical activity, physical function and quality of life in older adults with cancer. It synthesized the current research evidence related to the effectiveness of physical activity as an intervention to reduce fatigue in older adults with cancer during and following cancer treatment. It explored the relationship of the research variables of interest through a secondary analysis of data collected in the *Health and Well Being in Older Persons with Cancer* study and compared these findings to the literature.

Approximately 43% of new cancer cases in Canada occur among those who are at least 70 years old, while 25% occur in those aged 60-69. The median age at cancer diagnosis is between 65 and 69 years of age (Canadian Cancer Society/National Cancer Institute of Canada, 2006). Cancer fatigue is reported to affect 70 to 100% of patients receiving cancer treatment (Ahlberg, Ekman, Gaston-Johansson, & Mock, 2003; Stasi, Abriani, Beccaglia, Terzoli, & Amadori, 2003). Thus it can be expected that cancer fatigue is a significant problem for older persons with cancer and their families.

This thesis consists of two major research components. The first component synthesizes research to establish the 'state of knowledge' from the research related to the effectiveness of physical activity as an intervention to reduce fatigue in older adults with cancer during and following cancer treatment. The second component consists of a quantitative secondary analysis of the six-month data collected for the *Health and Well Being in Older Persons with Cancer* study. Data for the study was collected through a series of self-report questionnaires at baseline, three months and six months, and chart abstraction at baseline and followup. The specific

outcome variables that were measured were fatigue (MSAS score), physical activity (PASE score), physical function (SF-12 PCS subscale score), and quality of life (EORTC QLQ-30 score). Clinical measures of disease (cancer) severity and treatment factors were obtained through chart abstraction at baseline and at study completion. Measures of personal demographic characteristics were obtained through self-report on the baseline questionnaire. Measures of comorbidity were obtained by self-report at baseline through completion of the Functional Comorbidity Index (FCI).

In order to address the four research questions, correlations were calculated between each of the four variables at baseline, three months and six months, and between the three time periods. Controlling for demographic characteristics, disease site and treatment modality, the relationships between fatigue, physical activity, physical functioning and quality of life were described. Multivariate regression analysis was performed to control for demographic characteristics, disease site and treatment modality.

Summary of Findings

Systematic Review

The first objective of this thesis was to synthesize the current research evidence related to the effectiveness of physical activity as an intervention to reduce fatigue in older adults with cancer during and following cancer treatment. A systematic review of the literature was conducted and provided the foundation and direction for the remainder of the thesis. The systematic review included a rigorous search and retrieval process and critical assessment of the methodological approach of each of the studies using the Queen's Joanna Briggs Collaboration (QJBC) forms for critical appraisal for experimental and observational studies (Joanna Briggs

Institute, 2005). The review was conducted to look at the effectiveness of physical activity as an intervention to reduce fatigue in older adults with cancer during and following cancer treatment.

Although none of the studies focused exclusively on older cancer patients, nine experimental studies and ten observational studies that enrolled persons aged 65 and older were synthesized in the review and provided evidence that exercise, both aerobic and strength training, may reduce fatigue in older cancer patients during and after cancer treatment. The review also provided evidence that physical activity may help to maintain or improve physical function and quality of life in this population. The major limitations of the review are that older adults were poorly represented in the studies, and that few of the studies provided analysis of age-related effects. The systematic review process and results are described in the first manuscript (Chapter two).

Secondary Analysis

The secondary analysis builds on the results of the systematic review. To date, most of the literature related to cancer fatigue has been conducted on younger cancer patients. This study may be the first to examine the relationships between fatigue, physical activity, physical function and quality of life in older persons with cancer. The secondary analysis was conducted to address the remaining thesis objectives.

The second objective of this thesis was to describe the prevalence of cancer fatigue in a cohort of older adults with cancer at the time of consultation for treatment at a cancer centre, at three months, and at six months following the consultation. Results of the univariate analysis indicated that cancer fatigue is prevalent in this population and that it was indeed the most frequently reported symptom at baseline, three months, and six months post consultation for treatment at the cancer centre. These results are consistent with the literature.

The third objective of this thesis was to determine the relationship between fatigue and physical activity, in a cohort of older adults with cancer in the six months following consultation for treatment at a cancer centre. Results of the correlational analysis indicated that fatigue was negatively correlated with physical activity at all time periods. These findings are consistent with the results of studies conducted with younger cancer patients. Multivariate linear regression analysis was used to specifically answer the following research questions:

1. Is there a relationship between baseline physical activity levels and fatigue at three months and six months?
2. Is there a relationship between physical activity at three months and fatigue levels at three months and six months?

The results of the regression analysis indicated that physical activity levels at both baseline and three months were significantly related to cancer fatigue at three months and six months post consultation for cancer treatment regardless of age. As hypothesized higher physical activity levels were associated with lower fatigue levels. Baseline and 3-month physical activity levels were the strongest predictors of fatigue at both 3 months and 6 months. Since physical activity is a modifiable factor, increasing physical activity levels may improve fatigue levels. Thus physical activity during treatment may be an effective strategy for managing fatigue during and following cancer treatment in older cancer patients.

The fourth and final objective of this thesis was to determine the relationships between fatigue and physical activity, and physical function and quality of life in a cohort of older adults with cancer in the six months following consultation for treatment at a cancer centre. Results of the correlational analysis indicated that fatigue was negatively correlated with both physical function and quality of life scores at all time periods. These findings are consistent with the

results of studies conducted with younger cancer patients. Physical activity scores were positively correlated with physical function and quality of life scores at all time periods. Multivariate linear regression analysis was used to specifically answer the following research questions:

3. Is there a relationship between physical activity levels at three months and physical functioning at six months?
4. Is there a relationship between physical activity levels at three months and quality of life at six months?

The results of the regression analysis indicated that physical activity levels at three months were significantly related to physical functioning at six months as hypothesized, with higher physical activity levels predicting higher physical function scores. Increased comorbidities and higher age were predictive of lower physical function scores. Again, since physical activity is a modifiable variable, increasing physical activity levels may help older cancer patients to maintain or improve their physical function during cancer treatment.

Physical activity levels at three months were not significantly related to quality of life scores at six months and it was dropped from the regression model. Increased comorbidities and treatment with chemotherapy were both predictive of poorer quality of life scores. Thus results from this study were not significant with respect to a relationship between physical activity and quality of life, however, the association was in a positive direction and further research with randomized controlled trials may yield significant results.

Contribution to Knowledge

Most of the previous research on cancer fatigue has been conducted on younger cancer patients. The results of this study partially support the conceptualization of the proposed conceptual framework for cancer fatigue in the older adult as depicted in figure 1. Factors such

as age (higher), comorbidities (higher number), cancer site (lung), and cancer treatment modality (chemotherapy) were associated with cancer fatigue at baseline. The additional factors of income (lower) and gender (female) were also associated with baseline fatigue. Treatment modality (chemotherapy) was also associated with cancer fatigue at three months, and comorbidity was associated with cancer fatigue at six months. These findings contribute to the knowledge of factors associated with cancer fatigue in older adults and may contribute to the identification of similarities and differences between cancer fatigue in younger and older cancer patients.

The results of this study also partially support the conceptualization of the cycle of cancer fatigue, physical activity, physical function and quality of life as depicted in figure 2. Correlational analysis supports these relationships, however, causality cannot be inferred from the identified associations. Multivariate linear regression analysis found that physical activity levels during treatment were predictive of fatigue levels and physical function scores, but not predictive of quality of life scores. Again, much of the research looking at the relationships between cancer fatigue, physical activity, physical function and quality of life has been conducted in younger cancer patients. This study suggests that similar relationships exist in older cancer patients and that the potential benefits of physical activity that have been found in younger cancer patients may help older cancer patients reduce cancer fatigue and maintain or improve physical function during cancer treatment. Further research utilizing randomized controlled trials of physical activity interventions are needed to further evaluate this hypothesis and the conceptualization of the cycle of fatigue and physical activity.

Implications

Based on the findings of this thesis, there are several implications for nursing practice, education, further research, and for policy.

Implications for Practice

Recently published cancer fatigue guidelines have recognized the significance of cancer fatigue and support the utilization of physical activity and exercise as an intervention to treat cancer fatigue. Telephone nursing practice and symptom management guidelines by Cancer Care Ontario (2004) include a fatigue guideline that recognizes changes in activity or exercise patterns as a risk factor/possible cause for cancer fatigue and recommends encouraging cancer patients to increase physical activity/exercise as able. The National Cancer Institute (2006) recommends specific techniques for the management of fatigue including the encouragement of activity/planned exercise programs within individual limitations; making goals realistic by keeping in mind the state of disease and treatment regimens. And the National Comprehensive Cancer Network (NCCN) (2007) stresses the importance of the assessment of treatable contributing factors such as activity level (decreased activity/decreased physical fitness) and recommends activity enhancement for patients on active treatment and long-term followup. Specific interventions recommended by the NCCN are to maintain optimal level of activity, to consider initiation of exercise program, and to consider referral to physical therapy/physical medicine & rehabilitation therapy as appropriate.

Findings from this thesis support the application of these general clinical practice guideline recommendations in older adults with cancer; however there is a need to develop more specific guidelines for the older cancer population. Results from this study suggest that older cancer patients with low baseline physical activity levels, comorbidities, and/ or treatment with chemotherapy may be at greater risk for fatigue. Identifying patients at risk for cancer fatigue should be a priority so that support can be provided and promising interventions such as physical activity may be implemented. Management of comorbidities in cancer patients, and in older

cancer patients in particular must be optimized to reduce fatigue and to enable participation in physical activity. After identifying and treating other treatable contributing factors to cancer fatigue, it may be reasonable to encourage older adults with cancer to participate in regular physical activity during and following cancer treatment in consultation with their oncologist.

Implications for Education

Education of patients, as well as their support persons may help older cancer patients to manage cancer fatigue. Patients should be encouraged to report their fatigue and should be made aware that they do not just have to live with cancer fatigue, because many patients and health care professionals still believe there is no treatment for it. Education of patients regarding the benefits of physical activity during and following cancer treatment may be challenging, as it may be difficult to convince fatigued individuals to engage in exercise to improve their fatigue. It may be best to encourage low levels of activity, which can be gradually increased over time, particularly if the patient has already experienced some decline in physical function. Older patients with comorbidities should be educated regarding the importance of managing these other disease conditions because they may contribute to cancer fatigue and may interfere with the ability and desire to exercise.

Oncology nursing education at the undergraduate and graduate level, as well as ongoing education programs for practicing oncology nurses needs to include current clinical practice guidelines for the assessment and treatment of cancer fatigue. The importance and effectiveness of physical activity as a treatment for cancer fatigue should be stressed. Age-related factors that contribute to cancer fatigue in older adults should also be included, as well as the important relationships between cancer fatigue, physical activity level, physical function and quality of life, due to the implications of reduced physical activity levels on the older cancer patient's ability to

perform activities of daily living, maintain independence, participate in social activities, and complete cancer treatment regimes.

Implications for Further Research

The results of this thesis have several implications for further research. The consistently positive results and lack of deleterious effects of exercise in cancer patients demonstrated by the systematic review suggests that exercise may be beneficial to older adults with cancer. The general lack of studies enrolling older cancer patients and the lack of age-related analysis in those that did indicates a need for more research involving this population. The finding that physical activity may provide less benefit to older adults demonstrates the need to conduct further research to determine the optimum types and levels of physical activity for older persons with cancer. The finding that advanced age is a negative predictor for exercise adherence demonstrates the need for research to identify strategies to motivate participation and facilitate exercise adherence in this age group in order to minimize the negative effects of fatigue due to cancer and cancer treatment, and to maintain physical function and optimize quality of life.

Results of the secondary analysis are encouraging in that the associations between fatigue, physical activity, physical function and quality of life that have been demonstrated in younger populations of cancer patients also exist in older patients with cancer. Longitudinal studies that include measures of fatigue, physical activity, physical function and quality of life prior to surgery would add to the generalizability of these results by providing true baseline measures. Further research utilizing larger randomized controlled trials that enroll older adults or focus exclusively on this age group to test physical activity interventions in older populations is needed to identify the optimal levels and types of physical activity to treat cancer fatigue and to maintain

physical function in older adults with cancer, as well as to guide clinical recommendations for physical activity in older cancer patients.

Implication of Policy

Strategies to increase the awareness of clinical practice guidelines for the management of cancer fatigue for all health care professionals are necessary. Increased support of services such as cancer fatigue management clinics and cancer rehabilitation programs are necessary to help older cancer patients to manage cancer fatigue, and to maintain or improve physical function and quality of life during and following cancer treatment, in a similar fashion to the support provided by cardiac rehabilitation centres.

References

Ahlberg K, Ekman T, Gaston-Johansson F, Mock V. Assessment and management of cancer-related fatigue in adults. *Lancet*. 2003;362(9384):640-50.

Cancer Care Ontario (2004). *Telephone nursing practice and symptom management guidelines*.

Retrieved March 17, 2007, from

<http://www.cancercare.on.ca/documents/NursingTelephonePracticeGuidelines.pdf>

Joanna Briggs Institute. (2005). *Train the Trainer, Module 2* (pp.32-41). Adelaide: Joanna Briggs Institute.

National Comprehensive Cancer Network (NCCN). (2003). Cancer-related fatigue: Clinical practice guidelines in oncology. *Journal of the National Comprehensive Cancer Network*, 1, 308-331.

National Comprehensive Cancer Network (NCCN). (2007). *NCCN Clinical practice guidelines in oncology: Cancer-related fatigue*. Retrieved March 17, 2007, from

http://www.nccn.org/professionals/physician_gls/PDF/fatigue.pdf

Stasi R, Abriani L, Beccaglia P, Terzoli E, Amadori S. Cancer-related fatigue: Evolving concepts in evaluation and treatment. *Cancer*. 2003;98(9):1786-801.

Appendix A – Memorial Symptom Assessment Scale (MSAS)

SYMPTOM ASSESSMENT

We have listed 24 symptoms below. Read each one carefully. If you have had the symptom during this past week let us know how OFTEN you had it, how SEVERE it was usually, and how much it DISTRESSED or BOTHERED you, by circling the appropriate number. If you DID NOT HAVE the symptom, make an X in the box marked “DID NOT HAVE.”

During the past week: Did you have any of the following symptoms:	DID NOT HAVE	IF YES: How OFTEN did you have it?				IF YES: How SEVERE was it usually?				IF YES: How much did it DISTRESS or BOTHER you?				
		Rarely	Occasionally	Frequently	Almost Constantly	Slight	Moderate	Severe	Very Severe	Not at all	A Little Bit	Somewhat	Quite a Bit	Very much
Difficulty concentrating		1	2	3	4	1	2	3	4	0	1	2	3	4
Pain		1	2	3	4	1	2	3	4	0	1	2	3	4
Lack of energy		1	2	3	4	1	2	3	4	0	1	2	3	4
Cough		1	2	3	4	1	2	3	4	0	1	2	3	4
Feeling nervous		1	2	3	4	1	2	3	4	0	1	2	3	4
Dry mouth		1	2	3	4	1	2	3	4	0	1	2	3	4
Nausea		1	2	3	4	1	2	3	4	0	1	2	3	4
Feeling drowsy		1	2	3	4	1	2	3	4	0	1	2	3	4
Numbness/tingling in hands/feet		1	2	3	4	1	2	3	4	0	1	2	3	4
Difficulty sleeping		1	2	3	4	1	2	3	4	0	1	2	3	4
Feeling bloated		1	2	3	4	1	2	3	4	0	1	2	3	4
Problems with urination		1	2	3	4	1	2	3	4	0	1	2	3	4
Vomiting		1	2	3	4	1	2	3	4	0	1	2	3	4
Shortness of breath		1	2	3	4	1	2	3	4	0	1	2	3	4
Diarrhea		1	2	3	4	1	2	3	4	0	1	2	3	4
Feeling sad		1	2	3	4	1	2	3	4	0	1	2	3	4
Sweats		1	2	3	4	1	2	3	4	0	1	2	3	4
Worrying		1	2	3	4	1	2	3	4	0	1	2	3	4

During the past week: Did you have any of the following symptoms:	DID NOT HAVE	IF YES: How OFTEN did you have it?				IF YES: How SEVERE was it usually?				IF YES: How much did it DISTRESS or BOTHER you?				
		Rarely	Occasionally	Frequently	Almost Constantly	Slight	Moderate	Severe	Very Severe	Not at all	A Little Bit	Somewhat	Quite a Bit	Very much
Problems with sexual interest or activity		1	2	3	4	1	2	3	4	0	1	2	3	4
Itching		1	2	3	4	1	2	3	4	0	1	2	3	4
Lack of appetite		1	2	3	4	1	2	3	4	0	1	2	3	4
Dizziness		1	2	3	4	1	2	3	4	0	1	2	3	4
Difficulty swallowing		1	2	3	4	1	2	3	4	0	1	2	3	4
Feeling irritable		1	2	3	4	1	2	3	4	0	1	2	3	4

We have listed 8 symptoms below. Read each one carefully. If you have had the symptom during this past week let us know how SEVERE it was usually, and how much it DISTRESSED or BOTHERED you, by circling the appropriate number. If you DID NOT HAVE the symptom, make an X in the box marked "DID NOT HAVE."

During the past week: Did you have any of the following symptoms:	DID NOT HAVE	IF YES: How SEVERE was it usually?				IF YES: How much did it DISTRESS or BOTHER you?				
		Slight	Moderate	Severe	Very Severe	Not at all	A Little Bit	Somewhat	Quite a Bit	Very much
Mouth sores		1	2	3	4	0	1	2	3	4
Change in the way food tastes		1	2	3	4	0	1	2	3	4
Weight loss		1	2	3	4	0	1	2	3	4
Hair loss		1	2	3	4	0	1	2	3	4
Constipation		1	2	3	4	0	1	2	3	4
Swelling of arms or legs		1	2	3	4	0	1	2	3	4
"I don't look like myself"		1	2	3	4	0	1	2	3	4
Changes in skin		1	2	3	4	0	1	2	3	4

Appendix B - Physical Activity Scale for the Elderly (PASE)
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PHYSICAL ACTIVITY

Please circle the correct response or fill in the blank for the following:

LEISURE TIME ACTIVITY

1. Over the past 7 days, how often did you participate in **sitting activities** such as reading, watching TV or doing handcrafts?

(0.) NEVER



GO TO Q. #2

(1.) SELDOM

(1-2 DAYS)



(2.) SOMETIMES

(3-4 DAYS)



(3.) OFTEN

(5-7 DAYS)



1a. What were these activities?

1b. On average, how many hours per day did you engage in these **sitting activities**?

(1.) LESS THAN 1 HOUR

(2.) 1 BUT LESS THAN 2 HOURS

(3.) 2-4 HOURS

(4.) MORE THAN 4 HOURS

2. Over the past 7 days, how often did you take a **walk outside your home or yard** for any reason? For example, for fun or exercise, walking to work, walking the dog, etc?

(0.) NEVER



GO TO Q. #3

(1.) SELDOM

(1-2 DAYS)



(2.) SOMETIMES

(3-4 DAYS)



(3.) OFTEN

(5-7 DAYS)



2a. On average, how many hours per day did you spend **walking**?

(1.) LESS THAN 1 HOUR

(2.) 1 BUT LESS THAN 2 HOURS

(3.) 2-4 HOURS

(4.) MORE THAN 4 HOURS

3. Over the past 7 days, how often did you engage in **light sport or recreational activities** such as bowling, golf with a cart, shuffleboard, fishing from a boat or pier, or other similar activities?

(0.) NEVER



GO TO Q. #4

(1.) SELDOM

(1-2 DAYS)



(2.) SOMETIMES

(3-4 DAYS)



(3.) OFTEN

(5-7 DAYS)



3a. What were these activities?

3b. On average, how many hours per day did you engage in these **light sport or recreational activities**?

(1.) LESS THAN 1 HOUR

(2.) 1 BUT LESS THAN 2 HOURS

(3.) 2-4 HOURS

(4.) MORE THAN 4 HOURS

4. Over the past 7 days, how often did you engage in **moderate sport and recreational activities** such as doubles tennis, ballroom dancing, hunting, ice skating, golf without a cart, softball or other similar activities?

(0.) NEVER



GO TO Q. #5

(1.) SELDOM

(1-2 DAYS)



(2.) SOMETIMES

(3-4 DAYS)



(3.) OFTEN

(5-7 DAYS)



4a. What were these activities?

4b. On average, how many hours per day did you engage in these **moderate sport or recreational activities**?

(1.) LESS THAN 1 HOUR

(2.) 1 BUT LESS THAN 2 HOURS

(3.) 2-4 HOURS

(4.) MORE THAN 4 HOURS

5. Over the past 7 days, how often did you engage in **strenuous sport and recreational activities** such as jogging, swimming, cycling, singles tennis, aerobic dance, skiing (downhill or cross-country) or other similar activities?

(0.) NEVER



GO TO Q. #6

(1.) SELDOM

(1-2 DAYS)



(2.) SOMETIMES

(3-4 DAYS)



(3.) OFTEN

(5-7 DAYS)



5a. What were these activities?

5b. On average, how many hours per day did you engage in these **strenuous sport or recreational activities**?

(1.) LESS THAN 1 HOUR

(2.) 1 BUT LESS THAN 2 HOURS

(3.) 2-4 HOURS

(4.) MORE THAN 4 HOURS

6. Over the past 7 days, how often did you do any **exercises specifically to increase muscle strength and endurance**, such as lifting weights or pushups, etc?

(0.) NEVER



GO TO Q. #7

(1.) SELDOM

(1-2 DAYS)



(2.) SOMETIMES

(3-4 DAYS)



(3.) OFTEN

(5-7 DAYS)



6a. What were these activities?

6b. On average, how many hours per day did you engage in **exercises to increase muscle strength and endurance**?

(1.) LESS THAN 1 HOUR

(2.) 1 BUT LESS THAN 2 HOURS

(3.) 2-4 HOURS

(4.) MORE THAN 4 HOURS

HOUSEHOLD ACTIVITY

7. During the past 7 days, have you done any light housework, such as dusting or washing dishes?

(1.) NO (2) YES

8. During the past 7 days, have you done any heavy housework or chores, such as vacuuming, scrubbing floors, washing windows, or carrying wood?

(1.) NO (2.) YES

9. During the past 7 days, did you engage in any of the following activities?

Please answer YES or NO for each item.

	<u>NO</u>	<u>YES</u>
a. Home repairs like painting, wallpapering electrical work etc.	1	2
b. Lawn work or yard care, including snow Or leaf removal, wood chopping etc.	1	2
c. Outdoor gardening	1	2
d. Caring for another person, such as children, dependent spouse or another adult	1	2

WORK-RELATED ACTIVITY

10. During the past 7 days, did you work for pay or as a volunteer?

(1.) NO (2.) YES



10a. How many hours per week did you work for pay and/or as a volunteer?

_____ HOURS

10b. Which of the following categories best describes the amount of physical activity required on your job and/or volunteer work?

- (1) Mainly sitting with slight arm movements.
(Examples: office worker, watchmaker, seated assembly line worker, bus driver, etc.)
- (2) Sitting or standing with some walking.
(Examples: cashier, general office worker, light tool and machinery worker.)
- (3) Walking, with some handling of materials generally weighing less than 50 pounds.
(Examples: mailman, waiter/waitress, construction worker, heavy tool and machinery worker.)
- (4) Walking and heavy manual work often requiring handling of materials weighing over 50 pounds. (Examples: lumberjack, stone mason, farm or general labor)

Appendix C

Medical Outcome Short Form 12 General Health Questionnaire (SF 12)

SF-12™ - © Medical Outcomes Trust and John E. Ware, Jr. - All Rights Reserved - Page 1 of 2

The SF-12™ Health Survey**Instructions for Completing the Questionnaire**

Please answer every question. Some questions may look like others, but each one is different. Please take the time to read and answer each question carefully by filling in the bubble that best represents your response.

EXAMPLE

This is for your review. Do not answer this question. The questionnaire begins with the section ***Your Health in General*** below.

For each question you will be asked to fill in a bubble in each line:

1. How strongly do you agree or disagree with each of the following statements?

	Strongly Agree	Agree	Uncertain	Disagree	Strongly disagree
a) I enjoy listening to music.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
b) I enjoy reading magazines.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

Please begin answering the questions now.

Your Health in General

1. In general, would you say your health is:

Excellent Very good Good Fair Poor

2. The following items are about activities you might do during a typical day. Does your health now limit you in these activities? If so, how much?

	Yes, Limited A Lot	Yes, Limited A Little	No, Not Limited At All
a. Moderate activities , such as moving a table, pushing a vacuum cleaner, bowling, or playing golf	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
b. Climbing several flights of stairs	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

Please turn the page to continue.

3. During the **past 4 weeks**, have you had any of the following problems with your work or other regular daily activities as a result of your physical health?

YES	NO
------------	-----------

a. **Accomplished less** than you would like

b. Were limited in the **kind** of work or other activities

4. During the **past 4 weeks**, have you had any of the following problems with your work or other regular daily activities as a result of any emotional problems (such as feeling depressed or anxious)?

YES	NO
------------	-----------

a. **Accomplished less** than you would like

b. Didn't do work or other activities as **carefully** as usual

5. During the **past 4 weeks**, how much did pain interfere with your normal work (including both work outside the home and housework)?

Not at all	A little bit	Moderately	Quite a bit	Extremely
<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

6. These questions are about how you feel and how things have been with you during the **past 4 weeks**. For each question, please give the one answer that comes closest to the way you have been feeling. How much of the time during the **past 4 weeks** . . .

All of the Time	Most of the Time	A Good Bit of the Time	Some of the Time	A Little of the Time	None of the Time
------------------------	-------------------------	-------------------------------	-------------------------	-----------------------------	-------------------------

a. Have you felt calm and peaceful?

b. Did you have a lot of energy?

c. Have you felt downhearted and blue?

7. During the **past 4 weeks**, how much of the time has your physical health or emotional problems interfered with your social activities (like visiting with friends, relatives, etc.)?

All of the time	Most of the time	Some of the time	A little of the time	None of the time
------------------------	-------------------------	-------------------------	-----------------------------	-------------------------

THANK YOU FOR COMPLETING THIS QUESTIONNAIRE!

Appendix D – European Organization for Research Treatment Quality of Life Questionnaire
(EORTC QLQ-C30)

HEALTH RELATED QUALITY OF LIFE

We are interested in looking at your health and your quality of life.

Please answer all of the questions by circling the number that best applies to you.

	Not at all	A little	Quite a bit	Very much
1. Do you have any trouble doing strenuous activities like carrying a heavy shopping bag or suitcase?	1	2	3	4
2. Do you have any trouble taking a long walk?	1	2	3	4
3. Do you have any trouble taking a short walk outside of the house?	1	2	3	4
4. Do you need to stay in bed or a chair during the day?	1	2	3	4
5. Do you need help with eating, dressing, washing yourself or using the toilet?	1	2	3	4
During the past week:	Not at all	A little	Quite a bit	Very much
6. Were you limited in doing either your work or other daily activities?	1	2	3	4
7. Were you limited in pursuing your hobbies or other leisure time activities?	1	2	3	4
8. Were you short of breath?	1	2	3	4
9. Have you had pain?	1	2	3	4
10. Did you need to rest?	1	2	3	4
11. Have you had trouble sleeping?	1	2	3	4
12. Have you felt weak?	1	2	3	4
13. Have you lacked appetite?	1	2	3	4
14. Have you felt nauseated?	1	2	3	4
15. Have you vomited?	1	2	3	4
16. Have you been constipated?	1	2	3	4
17. Have you had diarrhea?	1	2	3	4
18. Were you tired?	1	2	3	4
19. Did pain interfere with your daily activities?	1	2	3	4

	Not at all	A little	Quite a bit	Very much
20. Have you had difficulty in concentrating on things, like reading a newspaper or watching TV?	1	2	3	4
21. Did you feel tense?	1	2	3	4
22. Did you worry?	1	2	3	4
23. Did you feel irritable?	1	2	3	4
24. Did you feel depressed?	1	2	3	4
25. Have you had difficulty remembering things?	1	2	3	4
26. Has your physical condition or medical treatment interfered with your family life?	1	2	3	4
27. Has your physical condition or medical treatment interfered with your social activities?	1	2	3	4
28. Has your physical condition or medical treatment caused you financial difficulties?	1	2	3	4

For the following questions please circle the number between 1 and 7 that best applies to you:

29. How would you rate your overall health during the past week?

1 2 3 4 5 6 7

Very poor

Excellent

30. How would you rate your overall quality of life during the past week?

1 2 3 4 5 6 7

Very poor

Excellent

Appendix E

FUNCTIONAL COMORBIDITY INDEX:

1	Arthritis (rheumatoid and osteoarthritis)
2	Osteoporosis
3	Asthma
4	Chronic Obstructive Pulmonary Disease (COPD), acquired respiratory distress syndrome, or emphysema
5	Angina (or chest pain)
6	Congestive Heart Failure (or heart disease)
7	Heart Attack (Myocardial Infarct)
8	Neurological Disease (such as Multiple Sclerosis or Parkinson's)
9	Stroke or TIA
10	Peripheral Vascular Disease (claudication)
11	Diabetes Types I and II
12	Gastrointestinal Disease (ulcer, hernia, reflux).
13	Depression
14	Anxiety or Panic Disorders
15	Visual Impairment (such as cataracts, glaucoma, macular degeneration)
16	Hearing Impairment (very hard of hearing, even with hearing aids)
17	Degenerative disc disease (back disease, spinal stenosis, or severe chronic back pain)
18	<p>Body Mass Index >30 (weight in kg / (height in meters)²)</p> <p>height _____ (cm or inches?)</p> <p>weight _____ (kg or lbs?) BMI =</p>

Appendix F

Study No. _____

Patient Information and Consent

A description of cardiovascular health, symptom burden, social support and physical and emotional well being in older persons with cancer

**Investigative Team: Dr. J.E. Tranmer^{1,3}, E. Green², L. Robb-Blenderman¹, Dr. P.A. Groome³, D. Groll^{1,3}, A. Day¹, Dr. D. Ginsburg³, Dr. J. McCans^{1,3}
Kingston Regional Cancer Centre/Kingston General Hospital¹, Cancer Care Ontario²,
Faculty of Health Sciences Queen's University³**

You are being invited to participate in a research study led by a team of investigators from the Kingston Regional Cancer Centre/Kingston General Hospital, Cancer Care Ontario and the Faculty of Health Sciences at Queen's University. In this study we are looking at cardiovascular health, symptoms, social supports and physical and emotional well being in cancer patients who are 65 years of age and older.

Background and Purpose of the Study

The number of older persons living with both cancer and cardiovascular illness is increasing and is expected to grow in the next decade. The purpose of this study is collect information about the cardiovascular health status, symptoms, social supports, and levels of physical and emotional well being of persons aged 65 and older receiving cancer treatment, to understand how cancer and other issues influence physical and emotional well being in cancer patients who are 65 years of age and older. We hope that the information obtained from this study will help us to plan ways to improve the delivery of health services for older persons who are receiving treatment for cancer.

Inclusion and Exclusion Criteria

You are being considered for this study because you are 65 years of age or older and are referred to KRCC for consultation for treatment for your cancer and can participate in the questionnaire for this study.

Details of this Study:

If you consent to participate in the study you will be asked to complete five questionnaire packages, three months apart, for a one-year period. The questionnaire packages will be mailed to you to be completed at your convenience. The questions will ask you to rate aspects of your health, quality of life, physical activity level, symptoms, the types of supports you have available as well as some general questions. A research assistant will also obtain information about your health history and health from your medical chart.

Study No. _____

Each questionnaire will take you between 20 and 30 minutes to complete. A self-addressed, stamped envelope will be provided for you to mail the questionnaire back to us at Kingston General Hospital. If you consent to participate, a research assistant may telephone you at home to remind you to send back your completed questionnaire or to help you, as needed, with completion of the questionnaire.

Risks and Benefits:

There are no anticipated risks to this study. While you may not benefit directly, the results from this study may improve the care of other patients receiving cancer treatment.

Confidentiality:

All information for this study obtained from the questionnaire or your patient record is strictly confidential and your identity will be protected at all times. Your name will not be used in any discussion or final report for this study. Your answers will not be shared with any of the doctors, nurses or clinic staff involved in your treatment. All information will be stored in locked files and will only be available to members of the investigative team.

Freedom to Withdraw or Participate:

Whether you take part in this study is up to you. Your decision regarding whether or not to participate in the study will not affect the care that you receive at KRCC/KGH now or at any time in the future. If you do decide to participate, you are free to change your mind and withdraw from the study or to refuse to answer any of the questions without jeopardizing your care.

Participant's Statement and Signature:

I have read and understand the information provided about this study. The purpose and requirements for this study have been explained to me. I have been given enough time to think about the information and to ask for advice if I need it. I have had a chance to ask questions which have been answered to my satisfaction.

I know that if I choose not to participate or choose to withdraw at any time, it will not affect the quality of care I will receive. I understand that I may not benefit directly from this study, but hopefully the information obtained will benefit future patients.

I understand that I will receive five questionnaire packages that ask me questions about my symptoms, quality of life and health status. I understand that my questionnaire answers are completely confidential, and that my name will not be identified in any report that may be published.

I am voluntarily signing this form. I will receive a copy of this consent form for my records.
Study No. _____

If at any time I have further questions or problems I will contact:

Dr. Joan Tranmer, Principal Investigator
Director, Nursing Research (613) 549-6666 extension 4952

Dr. Sam Ludwin, Vice President Research Development, Kingston General Hospital,
(613) 549-6666 extension 4287

Dr. Albert F. Clark, Chair, Research Ethics Board, Queen's University, Office
Research Services, (613) 533-6081

By signing this consent form, I am indicating that I agree to participate in this study.

Signature of Patient

Date

Signature of Witness

Date

I, or one of my colleagues, have carefully explained to the subject, the nature of the above research study. I certify that to the best of my knowledge, the subject understands clearly the nature of the study and the demands, benefits and risk involved in participating in this study.

Signature of Research Assistant

Date

Appendix G

Study Participants Flow Chart

