INCORPORATING EXERCISE EVIDENCE INTO BREAST CANCER CARE

BRIDGING THE GAP: INCORPORATING EXERCISE EVIDENCE INTO CLINICAL PRACTICE IN BREAST CANCER CARE

By JENNA SMITH, H.B. Kinesiology, M.Sc. (Physiotherapy)

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AUTHOR: Jenna Smith H.B. Kinesiology (McMaster University), M.Sc. (Physiotherapy) (McMaster University)

SUPERVISOR: Dr. Julie Richardson, PhD

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LAY ABSTRACT

Breast cancer survivors live with treatment-related side effects for years after their cancer treatments have ended. Regular participation in exercise can help to manage these side effects and improve quality of life in survivors. However, only small portions of breast cancer survivors take part in regular exercise. Many survivors are not aware of the benefits of exercise, how to exercise safely, or where exercise related services are available. There is a large gap between the research evidence supporting the use of exercise for women with breast cancer, and actual clinical practice. This thesis includes four papers aimed at devising and implementing a knowledge translation strategy in order to close this knowledge to practice gap in Ontario. Results suggest that an innovate program including exercise and self-management education run by a physiotherapist within the cancer institution is feasible and safe for women with breast cancer during chemotherapy.

ABSTRACT

This thesis includes four manuscripts with an overarching objective to develop, implement, and evaluate strategies to close the current knowledge to practice gap in the field of cancer rehabilitation. The overall goal of this objective is to provide a strategy to increase exercise knowledge and behaviour in women with breast cancer. The theory of planned behavior and knowledge-to-action cycle were used across these manuscripts in order to create and implement meaningful, easy-to-access, and effective interventions for women with breast cancer during chemotherapy treatment.

The first manuscript presents a qualitative descriptive study outlining the barriers and facilitators to exercise promotion by health care professionals for women with breast cancer. Results found barriers to exercise promotion exist at the institutional, health care professional, and patient level. Patient complexity and availability of services and resources were found to influence exercise promotion in conjunction with the described barriers.

The second manuscript presents a qualitative descriptive study using a focus group. The purpose of this study was to bring together a multi-disciplinary group of health care professionals who work with women with breast cancer to determine novel exercise intervention strategies to implement within the cancer care institution in Ontario. Results found that an on-site exercise program, an on-site rehabilitation professional, and more effective self-management educational

strategies describing the benefits of exercise during and after breast cancer treatment were needed for women with breast cancer.

The third manuscript presents a study protocol for the final thesis chapter. The purpose of this protocol was to describe a pilot study that would assess the feasibility and effectiveness of conducting an innovative knowledge translation intervention for breast cancer survivors using exercise and self-management versus usual care. The intervention was to be considered feasible if the recruitment rate reached >50%, adherence rate >75%, and retention rate >75%.

The fourth manuscript presents the preliminary results of the pilot randomized controlled trial. The overall purpose of this study was to determine the feasibility of providing a complex knowledge translation intervention designed specifically for women with breast cancer using technology. This study also set out to explore preliminary estimates of effects of the knowledge translation intervention on physical activity level, exercise knowledge and behaviour, health related quality of life, overall health status, and resource utilization among breast cancer survivors. Results found the intervention to be feasible (recruitment rate of 96%, intervention retention rate of 100%, and intervention adherence rate of 89%). The exploratory findings of secondary outcomes found a significant between group difference in physical activity levels post intervention (mean difference= 25.38, 95%CI= (9.35, 41.42), p=0.003) as measure by the Godin Leisure-Time Exercise Questionnaire. No significant between group differences

were found for exercise knowledge scores, health related quality of life, or overall health status.

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I would also like to extend my appreciation to my committee members, Dr. Margaret McNeely, Dr. Lehana Thabane, and Dr. Richard Tozer for encouraging me to pursue this research program and sharing your knowledge and expertise. Your guidance and feedback has helped my growth as a clinical researcher and challenged me to think critically.

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LIST OF ABBREVIATIONS

AC = anthracycline

AI = aromatase inhibitor

BC = breast cancer

CI = confidence interval

CID = cumulative incidence difference

EQ-5D = EuroQol-five dimension measure of health status

EQ-5D-3L = EuroQol-five dimension, three level measure of health status

FACT-B = functional assessment of cancer therapy-breast

FITT = frequency, intensity, type, time (exercise principles)

GPO = general practitioner in oncology

HCP = health care professional

HRmax = heart rate max

HrQOL = health related quality of life

IGF-1 = insulin-like growth factor 1

JCC = Juravinski Cancer Centre

JR = Julie Richardson

JST = Jenna Smith-Turchyn

KM = kilometer

KT = knowledge translation

MO = medical oncologist

n = number

N = nurse

OPA = Ontario Physiotherapy Association

PSM = prospective surveillance model

PTs = physiotherapists

PYLL = potential years of life lost

QOL = quality of life

RCT = randomized control trial

RO = radiation oncologist

RT = radiation therapist

SD = standard deviation

SERM = selective estrogen receptor modulator

SM = self-management

SMD = standard mean difference

T = taxane

TPB = theory of planned behaviour

VAS = visual analogue scale

WMD = weighted mean difference

Y = year

LIST OF SYMBOLS

X^2 = chi squared

$>$ = greater than

$<$ = less than

k = test-retest reliability coefficient

r = correlation

α = alpha

DECLARATION OF ACADEMIC ACHIEVEMENT

Jenna Smith conceptualized the purpose and research questions for all chapters included in this thesis. Jenna led the collection of data, implementation of interventions, and led the analysis of data where appropriate (Chapters 2 and 3). The contributions of other authors to the published or prepared manuscripts are presented below.

CHAPTER 2:

Dr. Julie Richardson, Dr. Margaret McNeely, Dr. Richard Tozer, and Dr. Lehana Thabane all reviewed and helped to refine the research question, objectives, and provided feedback on the manuscript. Dr. Tozer assisted with recruitment of health care professional to interview for this study and Dr. Richardson assisted with qualitative analysis of the interview manuscripts.

CHAPTER 3:

Dr. Julie Richardson, Dr. Margaret McNeely, Dr. Richard Tozer, and Dr. Lehana Thabane all reviewed and helped to refine the research question and objectives for this study. They also edited the manuscript prior to submission for publication. Dr. Richardson assisted by co-leading the focus group in this study and assisted with qualitative analysis of the focus group transcript. Dr. Tozer was a participant in the focus group and assisted in facilitating organization of this focus group at the Juravinski Cancer Centre.

CHAPTER 4 & 5:

Dr. Richardson, Dr. McNeely, Dr. Tozer, and Dr. Thabane all reviewed and helped to refine the research question and objectives for this study. They all reviewed the manuscript prior to journal submission. Dr. McNeely assisted in providing specific strategies to enhance recruitment for this study and in refining the interventions provided within these manuscripts. Dr. Tozer assisted in locating a space for the intervention at the Juravinski Cancer Centre and assisted with recruitment. Dr. Thabane provided assistance with setting up and running the analyses throughout this project. Dr. Richardson provided blinded analysis of the study results, worked closely to refine the specific interventions and the content provided within the self-management modules used in this study.

CHAPTER 1: INTRODUCTION

The Burden of Breast Cancer in Canada

Breast cancer is a form of cancer that initiates in the cells of the breast. These cancer cells divide quickly and destroy surrounding cells, forming a cancerous tumor (Canadian Cancer Society (CCS), 2017-1). The two most common forms of breast cancer are termed ductal carcinoma and lobular carcinoma (CCS, 2017-1). Ductal carcinoma initiates in the cells that line the ducts, which carry milk from mammary glands (CCS, 2017-1). Lobular carcinoma initiates in the lobules of the breast (CCS, 2017-1). Lobules are groups of mammary glands that make milk. The severity and aggressiveness of breast cancer is classified based on its stage and grade. Higher stages represent more advanced cases (in relation to tumor size and spread of the cancer to loco-regional lymph nodes or other tissues) and a higher grade represents more aggressive behaviour (CCS, 2017-2; CCS, 2017-3).

Canadian women are more likely to develop breast cancer than any other form of cancer; over the course of a woman's lifetime, she has a one in nine chance of developing this condition (Canadian Cancer Society's Advisory Committee on Cancer Statistics (CCSACCS), 2016). In 2017 alone, it was anticipated there would be over 26,000 new cases of breast cancer diagnosed (CCSACCS, 2017). The majority (51%) of breast cancers are diagnosed in women between the ages of 50 and 69 with an equal distribution of incidence rates across the country (CCSACCS, 2016). Potential years of life lost (PYLL) is a measure of premature death and accounts for deaths that occur to people at younger than expected ages (CCSACCS, 2016). The PYLL for breast cancer is approximately 137,000, showing that females die from breast cancer at a younger age (CCSACCS, 2016).

Since the 1980's the breast cancer mortality rate has been steadily declining due to improved treatment (Edwards et al., 2005) and screening techniques (Shields & Williams, 2009). Today, breast cancer mortality rates are the lowest they have been in many decades; the current five-year survival rate is 87% (CCSACCS, 2016). However, survivors of breast cancer are now living with physical and emotional sequelae of the disease and its treatments for many years after their cancer treatments have ended. Management of these sequelae cause a burden, both in resources and finances, on the Canadian health care system (CCSACCS, 2011). In 2008, cancer accounted for approximately $4.4 billion dollars in health care spending; $3.8 billion in direct healthcare costs, including physician and hospital expenses, and $586 million in indirect costs from lost productivity and premature death (CCSACCS, 2015). As breast cancer is the most prevalent form of cancer in Canadian women, it accounts for a large percentage of these costs. With our aging Canadian population these costs are only expected to increase (CCSACCS, 2011).

Side Effects of Breast Cancer Treatment

Treatment regimens for breast cancer can vary depending on specific tumor biology, however, they usually include a combination of surgery, chemotherapy, radiation, and/or hormone therapy (CCS, 2017-4). It is these treatments, rather than the actual cancer, which often cause side effects in patients with breast cancer, both during and after treatment (Canadian Breast Cancer Foundation (CBCF), 2017). A short list of physical side effects include cancer related fatigue, muscle weakness, decreased range of motion, bone weakness, joint pain, lymphedema, nausea/vomiting, hot flushes, peripheral neuropathy, and dizziness (Cella & Fallowfield, 2008; Ewertz & Jensen, 2011; CBCF, 2017). The specific treatments given, along with individual factors such as age, other medical conditions, and pre-treatment fitness level, will determine the side effects that a woman with breast cancer experiences during and after cancer treatments.

Surgery for breast cancer is often completed early in the course of treatment to remove the cancer and assess the axillary lymph nodes for loco-regional metastases (National Comprehensive Cancer Network (NCCN), 2016). Surgery for breast cancer usually includes a lumpectomy or mastectomy and lymph node sampling (NCCN, 2016). The goal of a lumpectomy is to remove the cancer in the breast while sparing healthy breast tissue (NCCN, 2016). A mastectomy removes the entire breast with or without damage to the chest muscles (NCCN, 2016). Axillary lymph nodes are removed via a sentinel lymph node biopsy or a level I to III axillary lymph node dissection (NCCN, 2016). In the sentinel lymph node biopsy a radioactive tracer and/or dye is injected into the breast (NCCN, 2016). This tracer drains into the lymphatic vessels and marks the sentinel nodes (the first lymph nodes that the cancer is likely to have spread to) (NCCN, 2016). In this surgery it is this sentinel node, and sometimes one or two surrounding nodes, which is removed (NCCN, 2016). Alternatively, a level I to III axillary lymph node dissection can remove ten or more axillary lymph nodes (NCCN, 2016). These surgical procedures can cause shoulder pain, shoulder movement restrictions, upper extremity weaknesses, upper extremity lymphedema, and neurological dysfunction (Devoogdt et al., 2011; Yang et al., 2010; Hayes, Rye, Battistutta & Newman, 2010). Along with this, many women who receive a mastectomy opt for breast reconstruction (National Cancer Institute (NCI), 2017). This can cause further physical side effects away from the primary surgical site. For example, with disruption of the latissimus dorsi (latissimus dorsi flap) or transverse rectus abdominus (TRAM flap) muscles, trunk and core instability and weakness can occur (Monterio, 1997; McAnaw & Harris, 2002).

Chemotherapy is a treatment mode given before or after surgery (termed neo-adjuvant or adjuvant chemotherapy respectively). The goal of adjuvant chemotherapy is to kill any cancer cells that may have metastasized elsewhere after surgery and to prevent local or distant recurrences later (American Cancer Society (ACS), 2016). The goal of neo-adjuvant chemotherapy is to reduce the size of the tumor before surgery (NCI, 2017-1). A variety of drug combinations are offered during chemotherapy. A common combination in early stage breast cancer is termed “AC/T” (NCCN, 2015). This regime includes an anthracycline (topoisomerase II inhibitor), an alkylating agent and a taxane (anti-microtubule agent). In this regimen, doxorubicin and cyclophosphamide are administered together for four cycles followed by paclitaxel for an additional four cycles (ACS, 2016). On a basic level, these drugs work by damaging the DNA of the cancer cells or disrupting the mitotic spindle and thus preventing the growth and division of these cells (ACS, 2016). While chemotherapy acts upon the cancer cells, it also damages other fast-growing healthy cells (CCS, 2017-5). This leads to common side effects such as alopecia, mucositis and bone marrow suppression. Other side effects include fatigue, nausea/vomiting, neuropathy, inducement of menopause, and muscle and bone pain (ACS, 2016; National Cancer Institute (NCI), 2017).

Radiation is another form of treatment received by women with breast cancer. Radiation therapy is often given by a linear accelerator which delivers radiation through a high-energy beam to the breast and lymph node bearing areas (NCCN, 2016). Radiation works to kill cancer cells locally by damaging their DNA (NCCN, 2016). While radiation protocols vary on an individual basis, they are often given daily for multiple weeks (NCCN, 2016). Side effects of radiation treatment for breast cancer can include fatigue, skin irritation (radiation dermatitis) and pain in the chest and the axilla (CCS, 2017-6), which can lead to decreased shoulder range of motion.

Hormonal therapy for breast cancer is often given as a further form of treatment for breast cancers that are hormone receptor positive (CCS, 2017-7). In these types of cancers, hormones can bind to the hormone receptors and stimulate cancer growth (Eisen et al., 2015). There are two main classes of drugs given as hormonal therapy; selective estrogen receptor modulators (SERMs) and aromatase inhibitors. SERMs work by blocking the breast cancer estrogen receptors on cancer cells so that estrogen cannot stimulate growth (CCS, 2017-7). Tamoxifen is currently the only SERM used as adjuvant treatment in pre-menopausal women and some post-menopausal women. Aromatase inhibitors (AIs) are drugs that block the production of estrogen by inhibiting the enzyme aromatase, which produces estrogen (CCS, 2017-7). AIs are used most commonly in post-menopausal women and the most common drugs are anastrozole, letrozole and exemestane. Women often take these drugs for five to ten years (CBCF, 2017-1). Common side effects of this form of treatment include menopausal symptoms, weight gain, bowel changes, nausea, and fatigue (CBCF, 2017). Tamoxifen has an increased risk of thromboembolic events and risk of developing uterine cancer (CBCF, 2017). AIs can lead to accelerated bone density loss and arthralgia (CBCF, 2017).

The physical side effects of treatment, as described above, are only part of the burden faced by women with breast cancer. Emotionally, a diagnosis of breast cancer and its treatments cause anxiety and depression for patients (Lim, Devi & Ang, 2011; Brown et al., 2012). Anxiety occurs independently of treatment type or stage of breast cancer. Anxiety is commonly reported to be caused by beginning cancer treatment, while later is due to worry about symptom management, disease recurrence and mortality (Lim, Devi & Ang, 2011). Depressive symptoms due to these same concerns are said to occur in approximately 60% of cancer survivors (Brown et al., 2012). Together the physical and emotional effects of breast cancer and its treatments can prevent survivors from returning to their pre-cancer lifestyle at home and at work (Ewertz & Jensen, 2011).

Benefits of Exercise for Women with Breast Cancer

The benefits of exercise for women with breast cancer have been well documented in many high quality research studies (Schmitz et al., 2010; Cramp & Byron-Daniel, 2012; Shobeiri, Masoumi, Nikravesh, Moghadam & Karami, 2016; Murtezani et al., 2014; Blacklock, Rhodes, Blanchard & Gaul, 2010; Schmitz et al., 2010-2; Winters-Stone et al., 2013; McNeely et al., 2010; Cramer et al., 2017; Cramer, Lange, Klose, Paul & Dobos, 2012; Mustian, Palesh & Flecksteiner, 2008). Research has indicated that exercise is an effective way to manage the side effects of breast cancer treatment, improve overall functioning and quality of life, improve chemotherapy completion rates, and decrease cancer recurrence and mortality rates for this patient population (Cormie, Zopf, Zhang & Schmitz, 2017; CCSACCS 2016). These benefits apply to various forms of exercise including aerobic exercise, resistance training, weight bearing exercise, and alternate forms of exercise (Schmitz et al., 2010).

Aerobic Exercise:

Aerobic exercise is defined as a dynamic activity that depends largely on oxygen to meet the energy demands of large muscle groups (Canadian Society of Exercise Professionals (CSEP), 2016). This type of exercise causes an increase in participant's heart rate and often includes activities of lower intensity, but longer duration (CSEP, 2016). A Cochrane Review (2012) indicated that aerobic exercise was beneficial for individuals with cancer-related fatigue both during and after cancer treatment (Cramp & Byron-Daniel, 2012). Other reported beneficial effects of aerobic exercise for women with breast cancer include improved quality of life (Shobeiri et al, 2016; Murtezani et al., 2014), psychosocial factors (Blacklock, Rhodes, Blanchard & Gaul, 2010), and improvements in hemoglobin and red blood cell count (Mohamady, Elsisi & Aneis, 2017). Optimal guidelines suggest a gradual increase of moderate-intensity aerobic exercise (50-70% heart rate max) to obtain the greatest effect (Schmitz et al, 2010; Segal et al., 2015). Guidelines suggest completing at least 150 minutes of aerobic exercise per week in 30-minute sessions (Schmitz et al, 2010; Segal et al., 2015).

Resistance Training:

Resistance training is a form of exercise that causes the muscles to move against external resistance in order to improve muscle fitness (American College of Sport Medicine (ACSM), 2013). A recent randomized controlled trial found that a twice-weekly slowly progressive strength training program is safe and effective for managing common side effects of breast cancer treatment (Schmitz et al., 2010-2). Specifically, the intervention included twice-weekly supervised resistance training with a certified fitness professional at a community gym for 13 weeks followed by twice-weekly unsupervised resistance exercise for the remaining year (Schmitz et al., 2010-2). Resistance training included exercise for the major muscle groups of the upper and lower extremities (Schmitz et al., 2010-2). The results showed that this training regime decreased the overall risk of lymphedema by 50% and among high-risk women (those who had greater than five lymph nodes removed) this strengthening program decreased their lymphedema risk by 70% (Schmitz et al., 2010-2). Other beneficial effects of resistance training reported in the literature for women with breast cancer include improvements in fatigue and quality of life (Hagstrom et al., 2016-1; Steindorf et al., 2014), and improvements in the inflammatory profile of participants (Hagstrom et al., 2016-2). Optimal guidelines for this population include two, moderate intensity strength training sessions per week for all major muscle groups (Schmitz et al., 2010-1).

Weight-bearing Exercise:

Weight-bearing exercise is another important form of exercise for breast cancer survivors in order to prevent fractures. This type of exercise includes any movement in which a person's body has to bear a load. The load could be an individual's body weight or an external load. Post treatment, survivors have a high risk of fracture secondary to the various treatments they receive (Winters-Stone et al., 2013). This occurs because bone loss is expedited by the treatments for breast cancer. For example, chemotherapy leads to early ovarian failure which decreases hormone production and can lead to a 5-8% loss in bone in one year (Shapiro, Manola & Leboff, 2001; Vehmanen et al., 2001). Aromatase inhibition, which patients can receive for five to ten years after finishing chemotherapy treatment, leads to a further 2-3% loss in bone per year (Santen, 2011). A study which included resistance and impact training found that the program significantly prevented bone loss at the spine and improved bone mineral density at the hip in prematurely menopausal breast cancer survivors (Winters-Stone et al., 2013).

Other forms of Exercise:

Alternate forms of exercise, including stretching and flexibility exercises, have also been shown to be beneficial in symptom management for women with upper extremity dysfunction, such as movement restrictions post breast cancer surgery (McNeely et al., 2010). Implementing exercise early post-surgery appears to enhance these benefits (McNeely et al., 2010). Yoga and Tai Chi have also shown beneficial effects for both the physical and emotional consequences of breast cancer (Cramer et al., 2017; Cramer, Lange, Klose, Paul & Dobos, 2012; Mustian, Palesh & Flecksteiner, 2008). Together, this evidence shows that there are a wide variety of exercise options available to patients and survivors of breast cancer in order to improve their cancer treatment related side effects and improve their function and quality of life.

Mechanism of Exercise for Symptom Management:

The literature proposes many mechanisms by which exercise works to minimize side effects, improve recurrence rates and mortality in women diagnosed with early stage breast cancer. Preliminary evidence suggests that these include biological mechanisms, functional mechanisms and mechanisms to prevent comorbid conditions (Ballard-Barbash et al., 2012).

In terms of biological mechanisms, exercise has been purported to positively change markers of inflammation and immunity, as well as levels of metabolic and sex hormones (Ballard-Barbash et al., 2012; Cormie, Zopf, Zhang & Schmitz, 2017; Pedersen, Christensen & Hojman, 2015). For example, the review done by Ballard-Barbash et al., (2012) showed that exercise may result in improvements in circulating insulin levels, IGF-1 and IGF-1 binding proteins in breast cancer survivors. Circulating IGF-1 levels are positively correlated with breast cancer risk in estrogen receptor positive tumors, independent of menopausal status (Endogenous Hormones and Breast Cancer Collaborative

Group, Key, Appleby, Reeves & Roddam, 2010) as well as all cause mortality in women with a diagnosis of breast cancer (Duggan et al., 2013). Exercise can also manage levels of insulin (Ballard-Barbash et al., 2012). Women with higher insulin levels have poorer prognoses post cancer treatment (Provinciali et al., 2015). Exercise also decreases levels of c-reactive protein, which indicates the presence of inflammation in the body (Ballard-Barbash et al., 2012). Survivors with higher levels of c-reactive protein are at higher risk for recurrence, metabolic disturbances, and cardiotoxicity (Asegaonkar, Asegaonkar, Takalkar, Advani & Thorat, 2015). Acute bouts of exercise also lead to increases in immune cell circulation with improved mobilization of natural killer cells, T cells and B cells (Pedersen, Christensen & Hojman, 2015). This is important as the immune system is known to be the first line of defense to fight tumor growth (Pedersen, Christensen & Hojman, 2015).

Functional mechanisms of exercise for women with breast cancer include increased overall levels of fitness, often measured by functional capacity. Previous recommendations to patients have been to rest during treatment, however we now know that this advice leads to muscle wasting, decreased cardiorespiratory fitness, and therefore physical symptoms like fatigue and weakness (Cramp & Byron-Daniel, 2012). Increases in functional capacity leads to better outcomes post-surgery (Santa Mina, Scheede-Bergdahl, Gillis & Carli, 2015) and allows for a higher tolerance of chemotherapy treatments (Courneya et al., 2007; van Waart et al., 2015). This has led to higher chemotherapy completion rates, which improves the overall effectiveness of the therapies provided (Courneya et al., 2007; van Waart et al., 2015). In addition, exercise has been purported to increase the transportation of systemic therapies, such as chemotherapy, to the cancer cells through improved oxygen function (Pedersen, Christensen & Hojman, 2015).

Together, these biologic and functional benefits of exercise not only prevent side effects, recurrence rates, and mortality in breast cancer survivors, but also help prevent many other comorbid chronic conditions (Cormie, Zopf, Zhang & Schmitz, 2017). For example, cardiotoxicity, which is a common side effect of some breast cancer treatments (Yu & Jones, 2016), can lead to heart disease (coronary artery disease with radiation, cardiomyopathy with drugs such as anthracyclines and trastuzumab). After nine years of survivorship, women are more likely to die of heart disease, than a recurrence of cancer (Patnaik, Byers, DiGuiseppi, Dabelea & Denberg, 2011). This shows the importance of participating in regular exercise on multiple systems throughout the body.

When to Introduce Exercise?: The Prospective Surveillance Model:

There is ample evidence to support the use of exercise for women with breast cancer at various time points during their cancer treatment; pre-treatment, during adjuvant therapies, and post treatment into survivorship (Schmitz et al., 2010; Segal et al., 2015). When overall fitness is maintained and potential impairments prevented, function and quality of life can be maintained. The Prospective Surveillance Model for Rehabilitation for Women with Breast Cancer (PSM) is a comprehensive model of survivorship care that focuses on improving the physical function of women living with breast cancer (Stout et al., 2012). Prospective surveillance has been defined by Stout (2009) as “a proactive approach to periodically examining patients and providing ongoing assessment during and after disease treatment, often in the absence of impairment, in an effort to enable early detection of and intervention for physical impairments known to be associated with cancer treatment.” The goals of the PSM are to (1) promote surveillance for common physical impairments and functional limitations associated with breast cancer treatment (2) provide education to reduce the risk and prevent adverse events while facilitating early identification of physical impairments and functional limitations (3) to introduce rehabilitation and exercise early when physical impairments are identified and (4) to promote exercise, physical activity and weight management through the trajectory of disease treatment and survivorship (Stout et al., 2012). The model outlines a process whereby physical impairments, function and exercise levels are assessed and managed proactively and periodically throughout the course of treatment for breast cancer and throughout survivorship to expedite the implementation of rehabilitation if necessary (Stout et al., 2012).

The design of the PSM spans the entire cancer trajectory including pre-operative rehabilitation, evaluation and education through to breast cancer diagnosis and treatment planning (Stout et al., 2012). During the pre-operative phase the goal is to establish baseline measures of individual function (Campbell et al., 2012). This gives the health care team personalized functional values to refer to at future assessments and which can be used as a foundation for post-operative rehabilitation (Campbell et al., 2012). In the early post-operative phase, re-assessment and safe exercise prescription are the focus of care (Stout et al., 2012). During adjuvant treatment and survivorship trajectories the patient continues with ongoing physical activity and exercise and is monitored for overall function, physical symptoms and side effects (Stout et al., 2012). Each stage incorporates valid and reliable outcome measures to assess a person's impairments and overall level of functioning (Stout et al., 2012). Therefore, it is clear that in this model rehabilitation is incorporated as a process across the entire cancer trajectory. Desired outcomes are not accomplished in a single visit, but using this model would enable rehabilitation to be included throughout the course of a person's cancer journey to maintain function and prevent disease sequela (Stout et al., 2012).

Function is the outcome of focus within the PSM. It was recognized within the creation of this model that functional outcomes relate to a person's ability to partake in meaningful and productive activities after their cancer treatment

(Campbell et al., 2012). It has been suggested within this model that measures of function be assessed in the pre-operative and early post-operative phases as well as at regular intervals throughout and after treatment (Campbell et al., 2012). Suggested measures for functional capacity include the 6 or 12-minute walk test, handgrip, gait speed and chair stand (Campbell et al., 2012). Suggested measures for upper extremity function include the Patient Specific Functional Scale, Disabilities of the Arm, Shoulder and Hand self-report measure, the Upper Extremity Functional Index, and the BREAST-Q (Campbell et al., 2012). The Functional Assessment of Cancer Therapy-Breast, the European Organization for Research and Treatment of Cancer-Quality of Life Questionnaire and the Short Form-36 have been suggested for general function measures (Campbell et al., 2012).

The rationale for the PSM is in its potential to reduce the incidence and severity of the broad range of physical and functional impairments experienced by breast cancer survivors (Cheville, Nyman, Pruthi & Basford, 2012). By reducing the incidence and severity of these impairments it is expected that the health care costs to treat these issues will decrease (Cheville et al., 2012; Schmitz, DiSipio, Gordon & Hayes, 2015).

Knowledge to Practice Gap

Despite the high quality evidence described above showing the benefits of exercise for women with breast cancer, few breast cancer survivors participate in regular physical activity. The literature consistently states that less than 30% of cancer survivors self-report meeting the recommended guidelines for exercise participation (Courneya, Katzmarzyk & Bacon, 2008; Fernandez et al., 2015; Schmidt, Wiskemann, Ulrich, Schneeweiss & Steindorf, 2017). Studies also consistently show that exercise levels decrease during chemotherapy (Fernandez et al., 2015; Schmidt et al., 2017) with a recent study showing that over 77% of breast cancer patients receiving usual care did not engage in *any* exercise during chemotherapy (Schmidt et al., 2017). These statistics are disappointing considering the researched benefits, relatively low costs of participating in these programs, and low risk of injury compared to the costs of dealing with lingering treatment-related side effects medically. An evident knowledge to practice gap exists.

Barriers to Exercise from the Patients Perspective

In order to understand why this knowledge to practice gap exists, the barriers to exercise participation for this population must be explored. A recent study reported that the top three barriers to exercise participation during cancer treatment were lack of energy (reported by 81.5% of participants), physical symptoms (74.1%) and a lack of awareness of available programs (51.9%) (Fernandez et al., 2015). Other barriers included physical challenges, belief that exercise would make them feel worse and a lack of awareness of the need to exercise during treatment (37%, 25.9%, 22.2% respectively) (Fernandez et al., 2015). These findings are in accordance with other barriers to exercise previously reported in the literature (Blaney et al., 2010; Sander, Wilson, Izzo, Mountford & Hayes, 2012; Brunet, Taran, Burke & Sabiston, 2013). For example, a qualitative study by Blaney et al. (2010) found that the side effects of cancer treatment, specifically lack of energy and symptoms of fatigue, were central barriers to exercise and led to further complications such as deconditioning and lack of motivation. In another qualitative study, Saunder et al. (2012) found that patients with breast cancer reported a fear of exercising because they did not know which exercises were safe to perform. Other barriers reported for this population include lack of time, lack of willpower, weather constraints, feeling self-conscious, lack of access to exercise equipment, and a lack of knowledge on proper exercise prescription (Fernandez et al., 2015).

One of the most startling observations made in the literature is that there is a lack of education that is being provided to patients with all types of cancer on the benefits of exercise during and after treatment (Fernandez et al., 2015). In southwestern Ontario it was reported that 83.3% of patients had no education from their oncologist about any form of physical activity at any point of their treatment and 86.7% of patients received no information about physical activity from their primary nurse (Fernandez et al., 2015). For those who did receive advice on physical activity, this was said to come from an outpatient physiotherapist, family member or friend who had previous experience with cancer (Fernandez et al., 2015). Four individuals reported that they had received education about physical activity, but were unfamiliar with the positive influences of exercise for people with cancer (Fernandez et al., 2015). This lack of information provided to patients is a common theme in the literature (Ottenbacher et al., 2011; Cummins et al., 2016; Smith et al., 2017). Finally, participants commonly listed an unawareness of programming and limited accessibility to programs in their area as barriers to participation (Fernandez et al., 2015). Refer to **Table 1** for a summary of common barriers to exercise participation for this population. Together these barriers have been one reason why the research evidence has been difficult to translate into clinical practice. However, even with this in-depth knowledge and the implementation of interventions to try and overcome patient related barriers, there remains a large gap in the provision of exercise programming specifically 'tailored' to patient's needs. This requires further exploration.

Table 1: Barriers to Exercise Participation

Barrier	Percentage (%) Reported
Lack of energy	81.5
Physical symptoms	74.1
Unawareness of available programs	51.9
Physical challenges	37
Poor perceptions of exercise	25.9

Unawareness of need to exercise	22.2

Thesis Objectives

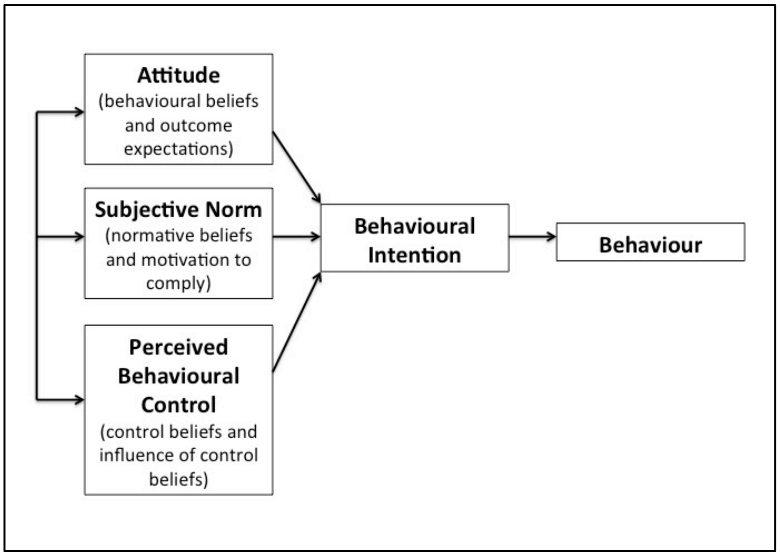
The overall objective of this thesis was to develop, implement, and evaluate strategies to close the current knowledge to practice gap in the field of cancer rehabilitation. To do this three distinct projects were completed. The overall goal of this objective is to provide a strategy to increase exercise knowledge and behaviour in women with breast cancer. The hope was to provide an easy-to-access, effective intervention to improve the lives of women with breast cancer.

In order to achieve this overarching objective, theoretical foundations were used in the developments of the intervention components. Behavioural change theories are a tool that researchers can apply to study the various concepts associated with change in behaviour for any population. Many behavioural change theories are described in the literature. The Theory of Planned Behaviour (TPB) is one theory that aims to explain and predict successful behavioural change (Ajzen, 1991; Godin & Kok, 1996). It has been suggested as one of the most influential theoretical models of behavioural change over the past decade as it accurately explains and predicts health related behaviours, including exercise (Manstead, 2011; Godin & Kok, 1996). It was developed in 1985, by Ajzen, as an extension of the Theory of Reasoned Action (Kraft, Rise, Sutton & Roysamb, 2005). See **Figure 1** for a pictorial representation of the Theory of Planned

Behaviour. The central concept of the TPB is the individuals' intention to perform a behaviour (Ajzen, 1991). This theory suggests that individuals with stronger intentions to perform a behaviour are more likely to actually complete the behaviour (Ajzen, 1991). Another important concept in the Theory of Planned Behaviour is perceived behavioural control. This is defined as a person's perception of the level of difficulty to perform the behaviour of interest (Ajzen, 1991). An assumption of the theory of planned behaviour is that perceived behavioural control can be used to directly predict behaviour or to indirectly predict behaviour through altering a person's intention (Ajzen, 1991).

Two other concepts identified in this theory include attitudes and subjective norms. Attitude is the degree that a person has a favourable, or unfavourable, evaluation of the behavior in question and is determined by a person's behavioural beliefs and outcome expectations (Ajzen, 1991). Subjective norms are the perceived social pressure to perform a behavior and are determined by the person's normative beliefs and motivation to comply (Ajzen, 1991). These two concepts can have a direct effect on each other and perceived behavioural control, and are direct determinants of intention (Ajzen, 1991). The importance of each of these single concepts in predicting behaviour is situation dependent (Ajzen, 1991). Throughout this project, the theory of planned behaviour was referenced in an attempt to provide interventions that would lead to sustained behaviour change in participants.

Figure 1: Theory of Planned Behaviour



With this overall objective and theoretical considerations in mind, the specific objectives of this project were:

1. To determine the **barriers and facilitators to promoting exercise** for women with breast cancer from the perspective of the health care professional (Chapter 2).
2. To determine **novel exercise intervention strategies to implement within the cancer care institution** in Ontario in order to overcome barriers to exercise participation and promotion for women with breast cancer (Chapter 3).
3. To **implement a novel knowledge translation strategy**, focusing on accessible exercise locations and self-management education, within the cancer institution in Ontario (Chapter 4).

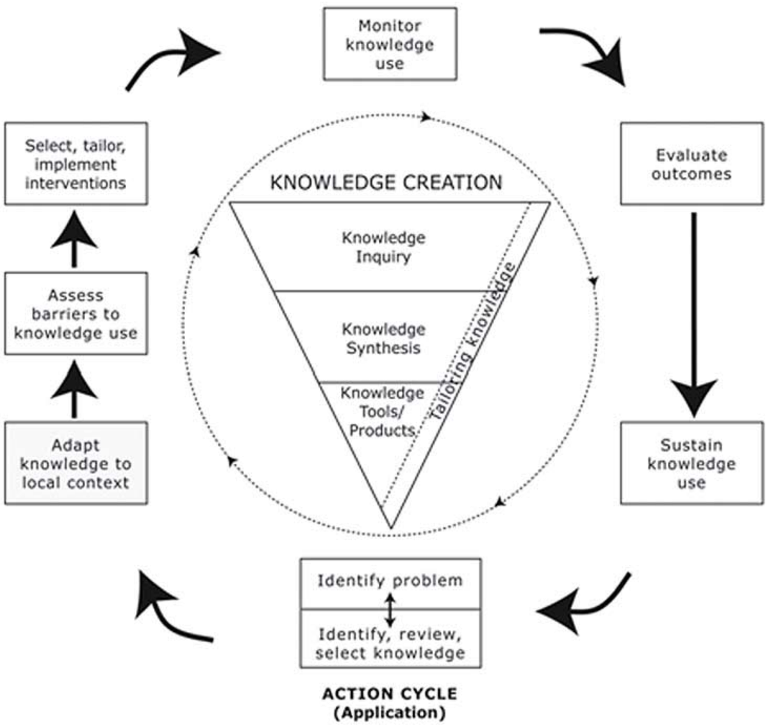
4. To **evaluate the feasibility** (through recruitment, retention and adherence rates) of providing a complex knowledge translation intervention for women with breast cancer (Chapter 5).
5. To **evaluate preliminary estimates of effects** of the knowledge translation intervention on physical activity levels, levels of exercise knowledge, health related quality of life, and resource utilization among breast cancer survivors (Chapter 5).

Outline of Included Manuscripts

The knowledge to action model (Graham et al., 2006) has been used to guide the creation and implementation of this knowledge translation project. See **Figure 2**. This model includes a knowledge funnel and action cycle (Graham et al., 2006). The knowledge funnel represents the process that knowledge is refined, distilled, and tailored to the needs of the knowledge end users (KT Clearinghouse, 2014). The funnel includes three steps: knowledge inquiry, knowledge synthesis, and knowledge tools/products (KT Clearinghouse, 2014).

The action cycle is used to describe the phases of activities that are needed for knowledge applications to lead to actual behavioural change (KT Clearinghouse, 2014). The seven phases of the action cycle include: identify the knowledge-to-action gaps, adapt knowledge to local context, assess the barriers to knowledge use, select/tailor/implement interventions, monitor knowledge use, evaluate outcomes, and sustain knowledge use (KT Clearinghouse, 2014). This thesis uses the third (assess the barriers to knowledge use) to sixth (evaluate outcomes) phases of the action cycle.

Figure 2: Knowledge to Action Cycle



The first manuscript (Chapter 2) “Physical Activity and Breast Cancer: A Qualitative Study on the Barriers to and Facilitators of Exercise Promotion from the Perspective of Health Care Professionals” relates to the third phase of the action cycle (assess the barriers to knowledge use). As stated in the introduction, a large knowledge to practice gap exists in using exercise to treat common side effects of breast cancer treatment. Despite the fact that the barriers to exercise participation from the patient’s perspective have been explored and interventions tested to overcome these barriers, a large knowledge to practice gap continues to exist. One of the main “patient described” barriers is that oncologists and other health care providers are not educating patients about the importance of remaining physically active during and after treatments. No research is available to determine ***why*** this education is not being provided. Therefore, this study investigated *why* this education does not occur and determines specific barriers and facilitators to exercise promotion from the perspective of various health care professionals.

The second manuscript (Chapter 3) relates to the forth phase of the action cycle (select/tailor interventions) and is titled, “Physical Activity and Breast Cancer: Results of a Focus Group to Devise Novel Exercise Interventions for Women with Breast Cancer.” Using the results from the first manuscript and the researched barriers to exercise participation for women with breast cancer, the purpose of this study was to bring together a multi-disciplinary group of health care professionals who work with women with breast cancer to determine novel exercise intervention strategies to implement within the cancer care institution in Ontario. The goal was to come to a consensus on novel approaches to implement to overcome the described barriers to exercise participation and promotion.

The third manuscript (Chapter 4) describes the implementation plan for the final trial intervention and is titled, “Bridging the Gap: Incorporating Exercise Evidence into Clinical Practice in Breast Cancer Care in Ontario-A Pilot Trial

Protocol”. This protocol outlines the methodology, outcomes, and projected timeline of the study presented in Chapter 5.

The final manuscript (Chapter 5) relates to the fourth (implement interventions), fifth (monitor knowledge use), and sixth (evaluate outcomes) phases of the action cycle. This manuscript is titled, “Bridging the Gap: Incorporating Exercise Evidence into Clinical Practice in Breast Cancer Care-A Pilot Randomized Controlled Trial.” This project implemented the intervention determine in the focus group in Chapter 3. The intervention included a multidimensional knowledge translation intervention including an aerobic exercise component, housed within the cancer institution, and a self-management component, using technology, for women receiving chemotherapy for stage 1 to 3 breast cancer. The main objective of this study was to evaluate the feasibility of implementing this knowledge translation strategy (measured through recruitment, retention, and adherence rates). Secondary objectives included evaluating preliminary estimates of effect for physical activity level, exercise knowledge and behaviour, health related quality of life, and resource utilization between the intervention and control group. For this project, a pilot study was needed as the first step in order to assess process and resource variables before implementation of a large-scale intervention (Thabane et al., 2010). Process variables include measuring recruitment rate, retention rate, and adherence rates to the intervention provided (Thabane et al., 2010). Resource variables include determining the centers willingness and capacity to house a specific intervention, equipment availability, intervention location, and budget concerns (Thabane et al., 2010). There is currently a lack of pilot trials for a novel KT intervention of this sort and therefore this pilot study will aid in shaping and guiding a larger trial.

Together these four manuscripts provide background knowledge on *why* the current knowledge to practice gap exists in breast cancer rehabilitation and provides suggestions to close this gap. Overall, this project highlights one way to include exercise as a regular component of breast cancer care within the institution in Ontario. This is one step on the road to including rehabilitation and physiotherapy as a regular component of breast cancer treatment and has the potential to affect all levels of breast cancer prevention; secondary and tertiary prevention of treatment related side effects and primary prevention of breast cancer recurrence through sustained behaviour change.

Readers may notice overlap within these chapters in respect to the background information presented. This includes the description of breast cancer, its prevalence in Canadian society, and the benefits of exercise for this population. While repetitive within this thesis document, this information supports each article in order to justify each specific research study and was used as a basis to build upon and progress the research findings across this entire thesis project. Along with this, repetition in regards to the methodology presented in Chapter 4 (pilot RCT protocol) and Chapter 5 (pilot RCT) is acknowledged, as

Chapter 5 builds on the protocol by dissemination specific results of the pilot RCT. The Discussion section (Chapter 6) will bring together each manuscript and discuss how they built on one another to try and bridge the gap in this area of breast cancer rehabilitation.

CHAPTER 2: PHYSICAL ACTIVITY AND BREAST CANCER: A QUALITATIVE STUDY ON THE BARRIERS TO AND FACILITATORS OF EXERCISE PROMOTION FROM THE PERSPECTIVE OF HEALTH CARE PROFESSIONALS

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TITLE

Physical Activity and Breast Cancer: A Qualitative Study on the Barriers to and Facilitators of Exercise Promotion from the Perspective of Health Care Professionals

AUTHORS

Jenna Smith-Turchyn;* Julie Richardson;* Richard Tozer;[†] Margaret McNeely;[‡] Lehana Thabane[§]

From the: *School of Rehabilitation Science, McMaster University, Hamilton, ON; †Juravinski Cancer Centre, Department of Oncology, Hamilton, ON; ‡School of Rehabilitation Medicine, University of Alberta, Edmonton, AB; §Department of Clinical Epidemiology & Biostatistics, McMaster University, Hamilton, ON.

Correspondence to: Jenna Smith-Turchyn, School of Rehabilitation Science, McMaster University, IAHS Rm 403, 1400 Main Street West, Hamilton, ON L8S 1C7; smithjf@mcmaster.ca.

ABSTRACT

Purpose: To determine the barriers to and facilitators of exercise promotion by health care professionals (HCPs) for women with breast cancer (BC). ***Methods:*** Subjects: HCPs who treat individuals with BC in Ontario. Design: Qualitative descriptive study. Procedure: Semi-structured interviews were conducted with participants. The interviews were recorded and transcribed. Two reviewers independently used content analysis to determine codes and themes developed in the interviews. NVivo 10 was used during the coding process. ***Results:*** A total of 24 HCPs participated in this study. The data from the interviews were grouped into five main categories: (1) institutional barriers, (2) HCP barriers, (3) perceived patient barriers, (4) facilitators: resource and service needs, and (5) patient characteristics. A graphic depiction of the interaction was created of these categories and how they affect the promotion of exercise for women with BC. ***Conclusions:*** Participants in this study identified a number of barriers to exercise promotion at the institutional, professional, and patient levels and suggested a number of strategies to facilitate exercise promotion. These findings can inform future exercise interventions to increase exercise adherence and engagement in this population.

Key Words: breast neoplasm; exercise; health promotion; physical therapy; rehabilitation.

Breast cancer (BC) is the most prevalent form of cancer in women in North America:[1,2] one in eight women is expected to develop BC in their lifetime.[1–3] In addition, the projected burden of this disease continues to increase with the aging population, and it is predicted that, by 2032, the number of new BC cases in women will increase by 55%.[4] BC and the associated treatments result in numerous side effects, including pain, fatigue, nausea, weakness, lymphedema, and decreased range of motion,[5–11] and these side effects affect a person's quality of life and overall functioning.

Recent research has shown that regular moderate-intensity exercise of various forms can improve many of these physical side effects.[9,12–27] Despite this evidence, only 30% of individuals with cancer take part in regular physical activity.[28–31] Therefore, to enhance quality-of-life outcomes, strategies in the clinical setting that support changing physical activity behaviour are paramount. The literature has thoroughly explored the barriers to and facilitators of exercise participation from the patient's perspective.[28,32–34] Known barriers include individual factors, such as physical symptoms and fatigue, as well as educational barriers resulting from a lack of general knowledge about the need to stay physically active during and after treatment, about proper exercise prescriptions, and about available exercise programs.[28] One of the most startling findings is that there is a lack of education being provided to patients on the benefits of exercise during and after treatment.[28] In Ontario, it was reported that 83% of patients had no form of education from their oncologist about exercise, and 88% had no education from their primary care nurse about physical activity or exercise at any point in their cancer treatment.[28] Physiotherapists are currently not a usual part of the health care team that treats and manages women with BC in Ontario.

Since these educational and knowledge barriers are common, and since past research has shown the significant influence of the health care team in changing lifestyle behaviours for women with BC,[35-36] it is important to examine the barriers to and facilitators of exercise promotion from the perspective of HCPs.[35]

METHODS

Study design

This study used a descriptive qualitative design. In descriptive qualitative studies, the researcher deliberately chooses to describe an event in terms of a conceptual or philosophical framework and descriptive qualitative studies are therefore not highly interpretive.[37] These types of qualitative studies are the method of choice when clear descriptions of phenomena are desired.[37] In this form of research, participants' perspectives and ideas are processed by generating codes, which are then grouped into thematic categories.[37] The Hamilton Integrated Research Ethics Board in Hamilton, Ontario, approved this study.

Participant recruitment

We recruited English-speaking HCPs who work with women with BC who are treated as outpatients at cancer centres in southwestern Ontario. The HCPs recruited included oncologists, general practitioners in oncology, nurses, radiation therapists, social workers, and dieticians. We sought a diversity of HCPs in our sampling.

Participants were recruited through a combination of purposive and snowball sampling.[38] First, a recruitment letter was sent by email to members of a cancer centre's "breast disease" team. Interested respondents were contacted to schedule an interview date. Participants also suggested other potential participants for the study, and these individuals were sent a follow-up email to request an interview. The sample size for this study was determined based on the need to recruit participants until saturation of the interview data was achieved.[38–40]

Data collection

Semi-structured interviews were conducted by one researcher (JST) with participants, one on one, in person (*n* = 21), by telephone (*n* = 2), or by videoconference (*n* = 1). An interview guide was created based on the purpose of the study and the results of a literature review. The interview guide was pilot-tested on the first two participants, and minor revisions were made before implementing the final version (see Table 1). Additional probing questions were used when necessary to ensure that the participants understood what we were asking or to elicit more information when needed. Before each interview, informed consent was obtained. Each interview lasted approximately 30 minutes, and all interviews were audio-recorded. After each interview, the interviewer made field notes to record her overall impression of the participant in regard to mood, gestures, and other noteworthy occurrences. (Notes on gestures could not be completed for telephone interviews.)

[Table 1 here.]

Data analysis

The analyses and reporting were performed according to conventional methods for descriptive qualitative studies.[38] After the interviews had been conducted, the audio recordings were transcribed verbatim by an independent transcriptionist; the transcripts were then checked for accuracy and completeness by the interviewer. The first five transcripts were coded independently using line-by-line analysis by two researchers (JST, JR), who then met to discuss the emerging themes and develop a coding manual for subsequent analysis. After the coding manual was developed, one researcher (JST) independently coded the remaining transcripts as they were completed. All transcripts were uploaded to NVivo 10 (qualitative analysis software from QSR International Pty Ltd., Doncaster, Australia), and the coded data were aggregated into nodes and grouped into meaningful categories based on the patterns that emerged. Discussions between the researchers occurred periodically during the transcription to consider how well the developing codes addressed the research question. See Table 2 for an example of the coding process for the parent node “Barriers”.

[Table 2 here.]

RESULTS

Description of participants

A total of 24 HCPs from four urban cancer centres agreed to participate in this study. (See Table 3 for participant details.) The participants were knowledgeable about the benefits of exercise for this population; however, they gave a range of responses about how much they actually knew. All but one participant had a positive response toward the use of exercise for BC survivors. The majority of HCPs acknowledged that they discussed physical activity and exercise with their patients, but most admitted that they did so inconsistently (data not shown).

[Table 3 here.]

Findings

Overall, the HCPs interviewed in this study were supportive of the use of exercise for women with BC. Interestingly, when we compared how the health professions perceived the benefits of exercise, we found that physicians related the benefits and importance of exercise to recurrence risk and mortality, whereas non-physicians (nurses and other HCPs) related the benefits and importance of exercise to symptom management and quality of life. Neither focus is suggested to be better, but this comparison reveals a difference in the treatment these professionals offer and the emphasis of their training.

To determine the barriers to and facilitators of promoting exercise for this population, the data from the interviews were coded and grouped into five main categories: (1) institutional barriers, (2) HCP barriers, (3) perceived patient barriers, (4) facilitators: resource and service needs, and (5) patient characteristics. (See Table 4.)

[Table 4 here.]

Institutional barriers

Institutional barriers reported by HCPs in relation to promoting exercise for women with BC include (1) time with each patient, (2) a lack of identification of who should be discussing exercise, and (3) a lack of funding for exercise interventions and for the role of rehabilitation professionals in an institution. Lack of time and the higher priority of other issues related to their own profession was the most commonly mentioned barrier preventing HCPs from discussing exercise with their patients. The need to discuss so many issues in such a short time meant that HCPs had to prioritize.

> Sometimes it's just, you've got a fifteen-minute appointment. In that fifteen-minute appointment, you're expected to do so much … you just can't get it all in.… It's not because people don't want to, it's just – the reality is that there isn't time. (General practitioner in oncology [GPO])

Another barrier commonly mentioned was a lack of definition of whose job it was to discuss exercise and physical activity levels in an institution.

> I see it as partly my role, my responsibility, but I can't pinpoint one group of people right now who I think it's their duty and role to consistently do that. (Medical oncologist [MO])

A lack of available funding for new programs in Ontario was also mentioned repeatedly.

> [The] challenge in introducing supports that deal with exercise … is not in convincing those with the ability to make (funding) decisions that these are worthwhile causes; everyone is going to agree to that.… The problem is there are a lot of [issues] that are [seen as] a higher priority in the view of those that are making [funding] decisions." (Radiation oncologist [RO])

Health care professional barriers

HCP barriers identified by participants include (1) lacking specific exercise knowledge, (2) seeing exercise as a low priority in relation to their other professional responsibilities, (3) forgetting to discuss physical activity, and (4) having personal limitations – for example, not exercising themselves. The most commonly reported HCP barrier reported by participants was lacking specific knowledge about exercise so as to educate patients effectively and with details. This was seen repeatedly in statements such as:

> There is evidence that exercise is beneficial.… I can't quote the evidence.… I think strengthening as well as a little bit of aerobic. (Nurse [N])

Many also commented that although they appreciated the benefits of exercise for symptom management, it was a low priority on their list of things to discuss with their patients (a list that includes topics such as treatment/medication regimes, possible side effects, side effect management, and prognosis), especially at initial diagnosis.

> There's a lot going on when you first see a patient, and … telling a patient about chemotherapy for the first time, right before they're about to start.… I'm not sure how effective it is to talk about exercise at that point. (MO)

It was also noted that although they thought it was important, many simply forgot to talk about exercise because it hasn't been a part of their regular daily practice.

Perceived patient barriers

HCPs also reported perceived barriers on the part of their patients that prevented them from promoting exercise. These perceived barriers included patients: (1) having a negative attitude toward exercise, (2) lacking accessibility to exercise programs (due to cost and transportation), (3) experiencing weather constraints, (4) experiencing side effects, and (5) having little time to commit to exercise. The most commonly reported perceived patient barrier was a negative attitude toward exercise. This was expressed by HCPs in many ways, including that their patients are afraid to exercise, doubt their exercise capability, have misconceptions about what exercise is, and think that exercise will make them feel worse. For example, one HCP said,

> I think that people are still under the impression it means that you've got to go work out … you've got to lift weights … and then I think that sort of stops a lot of people. They think, "I can't ever do that" or "I've never done that," and I think that's a psychological barrier on how … they … view the exercise because even walking around the block is a form of exercise. Taking the stairs at work is a form of exercise. (N)

Many HCPs were also concerned about their patients' ability to access exercise programs. This came up in relation to describing a patient's ability to pay for both exercise programs and transportation to the programs.

> I've had lots of patients who just … don't have money to pay for joining a program. (N)

Facilitators: Resource and service needs

Many participants suggested that having facilitators (in the form of additional resources and services) would aid in promoting exercise for individuals with BC; these included an increase in both institutional supports (services needed in a cancer centre) and individual supports (resources needed by patients). In regard to institutional supports, four main suggestions were made: (1) including a rehabilitation professional on the team that works with individuals with BC, (2) housing exercise interventions in the institution, (3) creating content-specific education for HCPs, and (4) using “champion leaders.” Many participants acknowledged that referring patients to exercise programs would be easier if exercise programs were run in house. For example,

> You know, we have often mentioned that, especially in [the] chemo [waiting rooms], that we should have an area that’s got some stationary bikes … because people do a lot of waiting – you know, to have something that is accessible. (N)

They also acknowledged the importance of having someone in house to refer patients to for exercise education.

> In an ideal world, if someone were here that we could actually just send (patients to) in the supportive care department, having a person to connect them with. That would be nice. (MO)

Numerous individual supports for patients were also suggested. These included educational resources that HCPs could give patients, such as pamphlets, posters, prescription pads, or handouts.

Patient characteristics

While discussing the barriers to and facilitators of exercise promotion, many HCPs highlighted the complexity of this patient group and the numerous variables that needed to be considered when discussing exercise. More specifically, they highlighted the various risk groups in this population (from estrogen receptor status to age), the various comorbidities that many of these patients have (from obesity to cardiovascular disease), the high prevalence of psychosocial issues to consider (self-image, anxiety, depression), and the variability in pre-cancer fitness levels and BC treatments received (a combination of surgery, chemotherapy, radiation therapy, hormone replacement). In fact, these factors could increase the complexity for HCP's when promoting exercise, and could itself be a barrier to promoting. One participant described patient complexity by saying,

> Take a young lady…. Everything's good … she has a young family … she's just been shocked by having this diagnosis of breast cancer; it's the first major illness of her life. She's thinking, "I'm going to die," and the next thing she starts to realize is the cancer's got control of her life…. She gets depressed…. Then we make her physically sick with the chemotherapy, screw up her sex life…. It's almost like we've created an illness…. She becomes very dependent, and then we finish our treatment and try to get the patient integrated back into normal life. The patient is a changed patient, and we've created a psychological and emotional wreck….

> Now she's wondering, when's the cancer going to come back.… So now, try to put into that whole scenario, introducing exercise. (MO)

This type of patient complexity will increase the difficulty of promoting exercise. One participant highlighted this, saying,

> A lot of the times, they have concerns that are more pressing than exercise, and so what time you do have with them, you devote to whatever their [main] physical … or emotional concerns are. (Radiation therapist [RT])

Putting it all together: A graphic depiction of the determinants of exercise promotion

Figure 1 describes the likelihood of HCPs promoting exercise for women with BC. It depicts the three categories of barriers mentioned in the interviews and the interaction of each with one another. In addition to these established barriers, two other components (patient complexity and availability of resources and services) have an effect on the consequences that these barriers will have on the likelihood of a HCP promoting exercise. A patient that is highly complex would enhance the barriers described and decrease the likelihood of exercise promotion, whereas a patient who is less complex would have the opposite effect, minimizing the barriers and increasing the likelihood of exercise promotion. In addition, a low availability of resources and services would enhance the described barriers and diminish the likelihood of exercise promotion by HCPs, whereas having resources and services available would minimize these barriers. Accordingly, HCPs working with an individual who is highly complex and who does not have easy access to resources and services have a low likelihood of promoting exercise and vice versa. A continuum exists between these two extremes. Therefore, to increase the likelihood of exercise promotion by HCPs for women with BC, rehabilitation professionals not only have to create interventions to minimize the barriers but also consider the complexity of this patient group and provide, or facilitate easy access to, sustainable resources and services.

DISCUSSION

To our knowledge, this is the first qualitative study to examine the barriers to and facilitators of promoting exercise for women with BC from the perspective of HCPs. While HCPs were knowledgeable about the benefits of exercise for this population, their exercise advice was general. For example, some would recommend that patients "stay active," but they did not give specific details (e.g., following the FITT principles of frequency, intensity, time, and type) to encourage patients to follow them. This is important because research shows that patients' adherence to exercise is improved when the instructions they receive are specific and understandable.[41] This finding is also interesting as it relates to previous research on patient barriers to exercise participation, which found that both a lack of knowledge of the sort of exercise being prescribed and fear of doing unsuitable exercises were barriers to participation.[28,32–24]

While conducting this study, it became clear that how individuals in the same profession promote exercise is inconsistent. Also, it is unclear whose role it is to discuss exercise with patients; many HCPs assume that someone else is doing it. This lack of role definition is likely preventing HCPs from giving patients a detailed and consistent message in regards to the importance of regular exercise. A possible solution would be to include physiotherapists (PTs) on the health care team to fill this role at institutions across Ontario because PTs specialize in prescribing exercise for individuals with chronic conditions. It has been reported that only 17 oncology rehabilitation programs across all of Canada employ a PT; this shows a lack of access to physiotherapy for Canadians undergoing cancer treatment, despite the evidence on the benefits of rehabilitation for cancer survivors.[42]

Due to financial constraints in Ontario hospitals, it may not be feasible to incorporate PTs into all cancer institutions. An alternative solution is to have PTs act in consultation roles in institutions, providing education to HCPs employed in this setting so that they can act as the knowledge translators on this topic. This would allow the information given to patients to be more specific, and the delivery of exercise promotion to be more efficient, while the role of other HCPs would simply be to reinforce the message.

Another question raised in these interviews was, when is the right time to promote exercise with these patients? There is evidence to support the use of exercise interventions both during and after cancer treatment.[16,43–45] However, many HCPs suggested that it was inappropriate in the beginning stages of treatment (before and during chemotherapy) because of the volume of information being given at that time and because of the physical and emotional changes the individual is going through. We acknowledge this difficulty, but based on the benefits shown in the research,[16,43–45] it is necessary to incorporate this education into all stages of cancer treatment. The challenge will be to devise ways to frame the interventions at each stage in order to be sensitive to the challenges the individual is experiencing.

Future directions

Future research should take these findings, together with the previous research on the barriers to and facilitators of exercise participation from the perspective of BC patients, and suggest novel interventions in cancer institutions in Ontario. These interventions should consist of exercise programs run by PTs and include effective educational strategies to promote exercise with this population. As the number of individuals surviving BC is expected to increase substantially in the next decade,[4] promoting healthy behavioural change is important to decrease the individual and societal burden of the disease and return survivors to at least their pre-cancer levels of functioning at work and at home.

Our study had several limitations. First, all participants were from southwestern Ontario. Participants from other parts of Canada may have other important perspectives on this topic due to variations in provincial and territorial health care systems and funding of rehabilitation professionals, so this will be important to explore in future research. Second, no PTs were interviewed as part of this study because there are currently no PTs who are part of the “breast disease” teams at the participating institutions. However, given PTs’ expertise in therapeutic exercise, their perspectives are important to consider in determining future needs and ideas for promoting exercise interventions for this population. Finally, including participants who responded to the recruitment email may have led us to recruit individuals who were especially interested in the topic or who supported the content of this research study.

CONCLUSION

The aim of this study was to describe the barriers to and facilitators of exercise promotion for women with BC from the perspective of HCPs. Participants identified a number of barriers at the institutional, professional, and patient levels and suggested a number of strategies to facilitate exercise promotion. These findings can inform future interventions to make them more meaningful for this population.

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KEY MESSAGES

What is already known on this topic

BC and its treatments result in many physical and psychological side effects that affect survivors for many years after their cancer diagnosis. Exercise has been shown to mitigate many of these side effects, but only a very small percentage of women with BC take part in regular exercise. Barriers from a patient's perspective include physical symptoms, a lack of education about the need to stay physically active, and a lack of awareness of available exercise programs.

What this study adds

This is the first study to describe the barriers to and facilitators of exercise promotion by HCPs for women with BC. Results show that there are barriers at the institutional, professional, and patient levels that need to be overcome before incorporating this effective form of treatment into the cancer care continuum for women with BC.

REFERENCES

1. Canadian Cancer Society's Advisory Committee on Cancer Statistics. Canadian Cancer Statistics 2014. Toronto, ON: Canadian Cancer Society; 2014.
2. American Cancer Society. Cancer Facts & Figures 2014. Atlanta: American Cancer Society; 2014.
3. American Cancer Society. Breast Cancer Facts & Figures 2013–2014. Atlanta: American Cancer Society, Inc. 2013.
4. Canadian Cancer Society's Advisory Committee on Cancer Statistics. Canadian Cancer Statistics 2015. Toronto, ON: Canadian Cancer Society; 2015.
5. Shapiro SL, Lopez AM, Schwartz GE, et al. Quality of life and breast cancer: relationship to psychosocial variables. J Clin Psychol. 2001;57(4):501-19.
6. Wengstrom Y, Haggmark C, Strander H, et al. Perceived symptoms and quality of life in women with breast cancer receiving radiation therapy. Eur J Oncol Nurs. 2000;4(2):78-88.
7. Ganz PA. Monitoring the physical health of cancer survivors: a survivorship-focused medical history. J Clin Oncol. 2006;24(32):5105-5111.
8. Stava CJ, Jimenez C, Hu MI, et al. Skeletal sequelae of cancer and cancer

treatment. J Cancer Surviv. 2009;3:75–88.

9. Cella D, Fallowfield LJ. Recognition and management of treatment-related side effects for breast cancer patients receiving adjuvant endocrine therapy. Breast Cancer Res Treat. 2009;107:167–180.
10. Ewertz M, Jensen AB. Late effects of breast cancer treatments and potentials for rehabilitation. Acta Oncol. 2011;50:187-93.
11. Knobf MF, Sun Y. A longitudinal study of symptoms and self-care activities in women treated with primary radiotherapy for breast cancer. Cancer Nurs. 2005;28(3):210-18.
12. Cormie P, Pumpa K, Galvao D, et al. Is it safe and efficacious for women with lymphedema secondary to breast cancer to lift heavy weights during exercise: a randomized controlled trial. J Cancer Surviv. 2013;7(3):413-424.
13. Pastakia K, Kumar S. Exercise parameters in the management of breast cancer: a systematic review of randomized controlled trials. Physiother Res Int. 2011;16(4):237-244.
14. Chan D, Lui L, So W. Effectiveness of exercise programmes on shoulder mobility and lymphedema after axillary lymph node dissection for breast cancer: systematic review. J Adv Nurs. 2010;66(9):1902-1914.
15. Bicego D, Brown K, Ruddick M, et al. Effects of exercise on quality of life in women living with breast cancer: a systematic review. Breast J.

2009;15(1):45-51.

16. McNeely M, Campbell K, Rowe B, et al. Effects of exercise on breast cancer patients and survivors: a systematic review and meta-analysis. CMAJ. 2009;175(1):34.41.
17. Schmitz KH, Courneya KS, Matthews C, et al. American College of Sports Medicine roundtable on exercise guidelines for cancer survivors. Med Sci Sports Exerc. 2010;42(7):1409-1426.
18. Schmitz KH, Holtzman J, Courneya KS, et al. Controlled physical activity trials in cancer survivors: a systematic review and meta-analysis. Cancer Epidem Biomar. 2005;14:1588–1595.
19. Courneya K, Friedenreich C. Physical exercise and quality of life following cancer diagnosis: a literature review. Ann Behav Med. 1999;21(2):171-179.
20. Cramp F, Byron-Daniel J. Exercise for the management of cancer-related fatigue in adults. Cochrane Database Syst Rev. 2012;11.
21. Courneya KS, Segal RJ, McKenzie DC. Effects of exercise during adjuvant chemotherapy on breast cancer outcomes. Med Sci Sports Exerc. 2014;46(9):1744-1751.
22. McNeely M, Campbell K, Ospina M. Exercise interventions for upper-limb dysfunction due to breast cancer treatment. Cochrane Db Syst Rev. 2010;16(6):CD005211

23. Tomlinson D, Diorio C, Beyene J. Effect of exercise on cancer-related fatigue: A meta—analysis. Am J Phys Med Rehabil. 2014;93(8):675-686.
24. Zou LY, Yang L, He XL, et al. Effects of aerobic exercise on cancer-related fatigue in breast cancer patients receiving chemotherapy: A meta-analysis. Tumour Biol 2014;35(6):5659-5667.
25. Schmitz K, Ahmed R, Troxel A, et al. Weight lifting for women at risk of breast cancer-related lymphedema. A randomized trial. JAMA. 2010;304(24):2699-2705.
26. Cramer H, Lange S, Klose P, et al. Yoga for breast cancer patients and survivors: A systematic review and meta-analysis. BMC Cancer. 2012;18(12):412.
27. Mustian KM, Palesh OG, Flecksteiner SA. Tai Chi Chuan for breast cancer survivors. Med Sport Sci. 2008;52:209-217.
28. Fernandez S, Franklin J, Amlani N, et al. Physical activity and cancer: A cross-sectional study on the barriers and facilitators to exercise during cancer treatment. Canadian Oncology Nursing Journal. 2015;25(1):37-42.
29. GW Cancer Institute. (2013, June 25). Cancer rehabilitation: a critical component of survivorship care [Webinar]. In GW Cancer Institute Webinar Series.
30. Courneya KS, Katzmarzyk PT, Bacon E. Physical activity and obesity in Canadian cancer survivors. Cancer. 2008;112(11):2475-82.

31. Cheifetz O. Clinicians commentary on Sing et al. Physiother Can. 2013;65(2):192-3.
32. Blaney JM, Lowe-Strong A, Rankin J, et al. The cancer rehabilitation journey: barriers to and facilitators of exercise among patients with cancer-related fatigue. Phys Ther. 2010;90:1135-47.
33. Sander AP, Wilson J, Izzo N, et al. Factors that affect decisions about physical activity and exercise in survivors of breast cancer: a qualitative study. Phys Ther. 2012;92:525-36.
34. Brunet J, Taran S, Burke S, et al. A qualitative exploration of barriers and motivators to physical activity participation in women treated for breast cancer. Disabil Rehabil 2013;35(24):2038-2045.
35. Jones LW, Courneya KS, Fairey AS, et al. Effects of an oncologist's recommendation to exercise on self-reported exercise behavior in newly diagnosed breast cancer survivors: A single blind, randomized controlled trial. Ann Behav Med. 2004;28(2):105-113.
36. Courneya KS, Friedenreich CM. Utility of the theory of planned behavior for understanding exercise during breast cancer treatment. Psycho-oncol. 1999;8(2):112-122.
37. Sandelowski M. Focus on research methods: Whatever happened to qualitative description? Res Nurs Health. 2000;23:334-340.
38. Creswell JW. Qualitative inquiry & research design: Choosing among five

approaches. SAGE Publications Inc; 2013.

39. Corbin J, Strauss A. Basics of qualitative research: techniques and procedures for developing grounded theory. SAGE Publications Inc.; 2015.
40. Richards L. Handling qualitative data: a practical guide. SAGE Publications Inc.; 2009.
41. Taylor D. Physical activity is medicine for older adults. Postgrad Med J. 2014;90(1059):26-32.
42. Canestraro A, Nakhle A, Stack M, et al. Oncology rehabilitation provision and practice patterns across Canada. Physiother Can. 2013;65(1):94-102.
43. Van Waart H, Stuiver M, Van Harten W, et al. Effect of low-intensity physical activity and moderate-to high-intensity physical exercise during adjuvant chemotherapy on physical fitness, fatigue, and chemotherapy completion rates: Results of the PACES randomized clinical trial. J Clin Oncol. 2015;33(17):1918-1927.
44. Hwang J, Chang H, Shim Y, et al. Effects of supervised exercise therapy in patients receiving radiotherapy for breast cancer. Yonsei Med J. 2008;49(3):443-450.
45. Hojan K, Milecki P, Molinska-Glura M. Effect of physical activity on bone strength and body composition in breast cancer premenopausal women during endocrine therapy. Eur J Phys Rehabil Med. 2013;49(3):331-339.

TABLES

Table 1: Interview Guide:

Interview questions
1. Can you tell me what you know about exercise for individuals with breast cancer?
2. Is there anything more you want to add?
3. What do you think that most of your patients know about exercise during cancer treatment?
4. In your interactions with your patients, do you discuss their physical activity levels?
5. What do you find are the barriers to discussing physical activity and exercise with your patients?
6. Do you think there are certain groups of patients who would benefit from this discussion more than others?
7. What would help to facilitate this discussion?
8. Do you think any other member of your team discusses physical activity with their patients? Who?
9. What are your (and the institution's) future needs in relation to promoting exercise with your patients?
10. Do you have any other thoughts/comments on this topic?

Table 2: Example of Coding/Category Formation for Parent node of "Barriers":

Parent node	Category	Codes
Barriers	Institutional barriers	Time with patients
		Lack of role definition
		Lack of funding
	Health care professional barriers	Lack of knowledge about exercise
		Negative view toward exercise (it is not important)
		Forget to discuss exercise
		Personal limitations (don't exercise themselves)
	Perceived patient barriers	Negative attitude toward exercise
		Lack of accessibility of programs
		Weather
		Physical side effects
		Patient time

Table 3: Participant Characteristics:

Characteristic	No.	%
Health care professional		
Medical oncologist	7	29.2
Primary care nurse	5	20.8
Radiation oncologist	4	16.7
Surgeon	2	8.3
Radiation therapist	2	8.3
General practitioner in oncology	1	4.2
Nurse practitioner	1	4.2
Social worker	1	4.2
Dietician	1	4.2
Sex		
Female	16	66.7
Male	8	33.3
Location		
Juravinski Cancer Centre (JCC)	21*	87.5
Joseph Brant Hospital	2*	8.3
St. Joseph's Hospital Hamilton	1	4.2
Niagara Health System	1	4.2

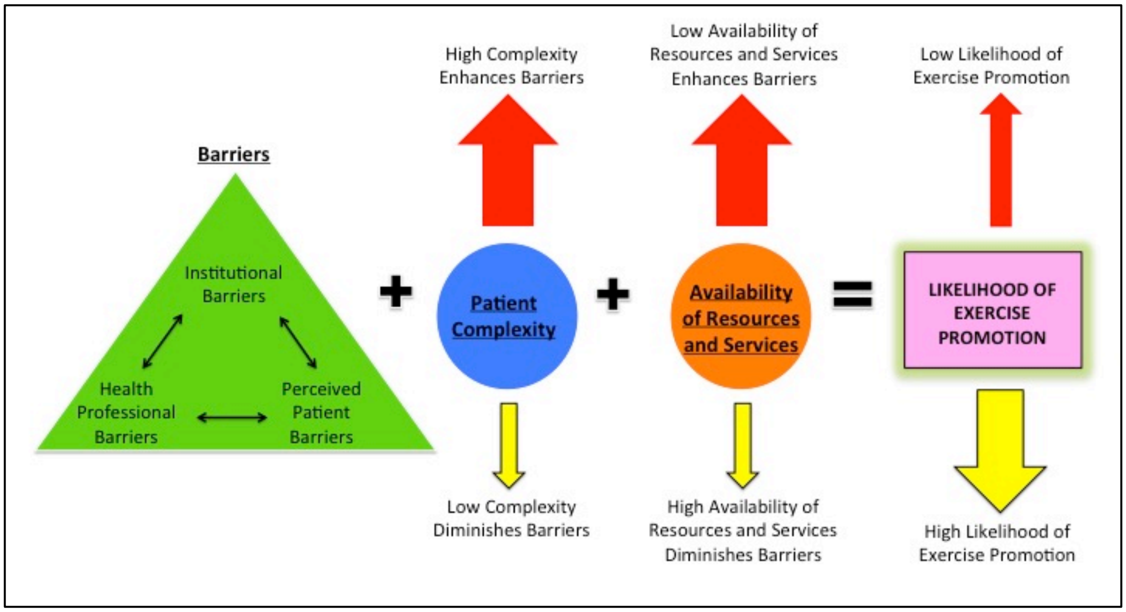
*One participant worked at both the JCC and the Joseph Brant Hospital and was thus included twice.

Table 4: Barriers to and Facilitators of Exercise Promotion:

Barriers	
Institutional barriers	Time with each patient
	So many issues to discuss
	Lack of identification of who in the institution should be discussing exercise
	Lack of funding for exercise interventions and/or rehabilitation professionals
Health care professional barriers	Lack of specific knowledge about exercise
	Discussion of exercise is a low priority
	Forget to discuss exercise
	Personal limitations
Perceived patient barriers	Negative attitude towards exercise
	Lack of accessibility
	Cost
	Transportation
	Weather constraints
	Patient side effects and symptoms
	Patient time
Facilitators: Resource and Service Needs	
Institutional supports	Inclusion of a rehabilitation professional as part of the breast disease site team
	Exercise programs housed at the institutional level
	Health care professional education
	Champion leaders
Individual supports	Patient education materials:
	Pamphlets
	Posters
	Prescription pad
	Handouts
Other Considerations	
Patient Characteristics	Risk Groups
	Comorbidities
	Psychosocial Issues
	Pre-cancer fitness level
	Treatments received

FIGURES

Figure 1: Determinants of exercise promotion:



CHAPTER 3: PHYSICAL ACTIVITY AND BREAST CANCER: RESULTS OF A FOCUS GROUP TO DEVISE NOVEL EXERCISE INTERVENTION FOR WOMEN WITH BREAST CANCER

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TITLE

Physical Activity and Breast Cancer: Results of a Focus Group to Devise Novel Exercise Interventions for Women with Breast Cancer

AUTHORS

Jenna Smith-Turchyn PT, PhD(c) (Corresponding Author):

McMaster University, School of Rehabilitation Science, 1400 Main Street W., Hamilton, ON, Phone: 905-869-0599, Fax: 905-524-0069, Email: smithjf@mcmaster.ca

Julie Richardson PT, PhD:

McMaster University, School of Rehabilitation Science, 1400 Main Street W., Hamilton, ON, Phone: 905-525-9140 x27811, Fax: 905-524-0069, Email: jrichard@mcmaster.ca

Richard Tozer MD, PhD:

Juravinski Cancer Centre, Department of Oncology, 699 Concession St., Hamilton, ON,

Phone: 905-387-9711 x67658, Fax: 905-575-6326, Email: tozer@hhsc.ca

Lehana Thabane MSc, PhD:

McMaster University, Department of Health Research Methods, Evidence and Impact, St. Joseph's Healthcare Hamilton, 50 Charlton Ave. E., Hamilton, ON, Phone: 905-522-1155 x33720, Fax: 905-308-7386, Email: thabanl@mcmaster.ca

Margaret McNeely PT, PhD:

School of Rehabilitation Medicine, University of Alberta, 8205 114 St., 3-48 Corbett Hall, Edmonton, AB, Phone: 780-248-1531, Fax: N/a, Email: mmcneely@ualberta.ca

ABSTRACT

Purpose: To determine, from the diverse perspective of vested members of the health care team, novel exercise intervention strategies to implement within the cancer care institution in order to overcome barriers to exercise participation and promotion for women with breast cancer (BC).

Methods: *Design:* Qualitative descriptive study. *Setting:* Cancer care institution. *Participants:* Health care professionals who work with women with BC. *Intervention:* A focus group was used to answer the research question. A moderator guided the focus group using a semi-structured script. *Measurements:* The focus group was recorded and transcribed. The transcript was coded independently using topic and analytical coding.

Results: Three main issues came forth during analysis. These included a lack of (1) exercise programming and equipment available within the cancer care institution (2) communication with rehabilitation professionals, and (3) effective exercise education strategies available for patients with BC. Specific strategies were suggested to overcome each issue.

Limitations: As purposeful sampling was used for recruitment, it is possible that participants agreed to be in this study because they had positive views on the need to incorporate exercise more effectively into practice.

Conclusions: To our knowledge this is the first study to include a multidisciplinary team to come to a consensus on a knowledge translation exercise strategy. Findings show that future exercise interventions should implement active interventions within the cancer institution, include rehabilitation professionals as part of the health care team, and use technology to educate patients.

Keywords: Breast neoplasms, exercise, translational medical research, qualitative research

INTRODUCTION

Breast Cancer (BC) is the most frequently diagnosed cancer in North American women.[1] The prognosis for this disease has improved significantly in the last decade, with a five year survival rate around 90%.[1] However, women with BC live with many physical and psychological side effects for many years after their cancer treatments have ended.[2-4] These side effects manifest into various functional limitations.[2-4] Moderate intensity exercise of various forms has been shown to mitigate many of these side effects,[5-16] however, it has been found that less than 30% of the population takes part in the recommended level of exercise.[17-18]

Barriers to exercise participation for women with BC have been studied thoroughly in the literature.[17,19-21] Results have found both individual factors and educational factors to limit participation.[17] Individual factors include physical symptoms and fatigue, whereas educational factors relate to a lack of general knowledge on the need to stay physically active during and after treatment, proper exercise prescriptions, and available exercise programs.[17] One of the most startling findings is that there is a lack of education being provided to patients on the benefits of exercise during and after BC treatment.[17]

Barriers to exercise promotion from the perspective of the health care professional (HCP) are not as well documented in the literature. However, recent research in Ontario has found that barriers at the institutional level, HCP level, and patient level may all contribute to a lack of exercise promotion.[22] For example, institutionally a lack of time with each patient, a lack of defined role for who should be discussing exercise, and a lack of funding for the inclusion of rehabilitation professionals and exercise programs were stated barriers to exercise promotion.[22] Professionally, HCPs commonly described a lack of their own specific exercise knowledge and a vast number of competing priorities needed to discuss with their patients as barriers to exercise promotion.[22] Finally, professionals also perceived patients with BC as having poor attitudes towards exercise, lacking accessibility to exercise resources, and having complex medical needs as patient barriers to promoting the recommended levels of exercise.[22] Both the patient and the HCP reported that barriers to exercise participation and promotion respectively have limited the implementation of this effective, low-cost, low-risk management strategy.

Due to the gap between the research evidence, supporting the use of regular, moderate intensity exercise to manage the side effects of cancer treatment, and actual clinical practice, there is growing demand to develop novel knowledge translation exercise strategies and to incorporate exercise into the regular cancer care continuum. With evidenced based guidelines from organizations such as the American Congress of Sports Medicine[10] and Cancer Care Ontario[23] summarizing the benefit of and need for exercise interventions, future work is needed to implement these strategies effectively.

The purpose of this qualitative study is to determine, from the diverse perspective of vested members of the health care team, novel exercise intervention strategies to implement within the cancer care institution to overcome the described barriers to exercise participation and promotion for women with BC.

METHODS

Study Design:

A qualitative descriptive design using a focus group to collect data from HCPs who treat women with BC was used in this study. Qualitative descriptive studies are the method of choice when clear descriptions of a problem or event are desired.[24] In this study we sought to describe strategies to overcome the barriers to exercise implementation, therefore a qualitative descriptive study was the method of choice. Focus groups are a technique that involves the use of in-depth group interviews with purposively recruited participants who have expertise on a given topic.[25,26] This methodology has been found to be a useful vehicle for involving users in care management and strategy development techniques.[27] The Hamilton Integrated Research Ethics Board approved this study (#0552).

Participants:

Participants included in this study were English-speaking HCPs working with women with BC in southwestern Ontario. We sought to recruit between six to ten participants for this focus group as this number has been shown in the literature to be a manageable number to gain a variety of perspectives while still allowing all participants to engage in the discussion.[25,28,29] In order to answer the study question participants were recruited from a multidisciplinary team of HCPs. Health professionals included oncologists, nurses, dieticians, and physiotherapists. Participants were recruited through a combination of purposive and snowball sampling. Firstly a recruitment email was sent to members of the breast disease site team at the Juravinski Cancer Centre (JCC) in Hamilton, Ontario. This team includes oncologists, surgeons, primary care nurses, social workers, and dieticians. Individuals from the JCC who agreed to participate in the focus group also suggested other potential participants for the study and these individuals were sent a personalized email to request their participation. All participants were within a similar age range (40-65 years) and had similar socio-economic characteristics and educational levels (master's level or greater). Similarity in these characteristics is suggested in the literature to ensure all members of a focus group are comfortable talking to each other and sharing ideas.[25,28,30] Participants had met the primary researcher (JST) during a previous study and were aware that the moderators (JST & JR) were physiotherapists with an interest in promoting exercise in women with BC.

Data Collection:

Focus group data was collected in November 2015 in a private conference room at the JCC. Participants were offered a light breakfast during the session. The focus group was moderated by the first author (JST), trained in qualitative research methods, with assistance from another researcher (JR). The moderator guided the focus group using a semi-structured script while the assistant made field notes on participant's moods and gestures and summarized major discussion points on a flip chart, giving the participants an opportunity to clarify anything they felt was missing or misunderstood by the research team. To begin, the participants were asked to provide written informed consent. They were then given a brief introduction to the literature on the benefits of exercise for women with BC, as well as the researched barriers to exercise participation and promotion from both the patients and HCPs perspective. After each of these topics the participant's were given time to ask clarification questions and to voice their opinions about the research findings. Following this the participants were asked to suggest exercise intervention strategies based on their professional needs, the institutions needs in order to provide quality care, and the barriers discussed. Open-ended questions were used initially to facilitate the group discussion and ease the participants into the discussion.[31] Additional probing questions were used when necessary to ensure comprehension or to elicit more information. Discussion was facilitated until saturation of the responses between participants was evident. The focus group lasted approximately one hour and was audio recorded using two recorders.

Data Analysis:

Following the focus group the audio recording was transcribed verbatim with all identifiers removed. The transcript was then checked for accuracy and completeness by the moderator. Two researchers (JST and JR) simultaneously coded the transcripts independently prior to discussing results. Content analysis used topic and analytical coding. Topic coding refers to labeling the text according to its subject.[32] This is often the initial stage of identification and labeling.[33] Analytical coding is coding that comes from interpretation and reflection on meaning.[32] This is often the second stage of coding, used to refine and interpret meaning in the transcripts.[33] In this project, topic coding dominated, especially early on, and was the first step in allowing more interpretive work using analytical coding. After coding the transcript, the researchers met to discuss the emerging themes and develop a final coding scheme. The transcript and field notes were then uploaded into NVivo v10.2 (qualitative analysis software) and the coded data was aggregated into nodes and grouped into categories based on the patterns that arose from the data. The coded data was reviewed periodically in order to ensure comprehensive analysis.[32] Saturation of themes was ensured between various professions and participants during analysis. To determine saturation authors ensured that no new themes were developed for continued analysis of information. Discussions between researchers occurred periodically during transcription to consider how the developing codes addressed the research question. Memos were completed throughout the coding process to track changes in processes and analytical momentum, determine the importance of specific codes, associations between codes or categories, and questions that arose from the coded data.[32,33] Frequencies and percentages were calculated for demographic data. The results were summarized and sent to participants for member checking and feedback after analysis was completed.

RESULTS

Ten participants agreed to be in the study. One participant had to cancel the day of the focus group due to family illness, leaving nine participants. No other individuals were present. The participants varied in health profession and gender. See **Table 1** for participant characteristics.

After discussing the researched barriers to exercise participation and exercise promotion for patients and HCPs, three major challenges currently present for this population were identified in the discussion and came forth during analysis. These challenges were grouped into three categories: (1) a lack of exercise programming and exercise equipment available within the cancer care institution, (2) a lack of communication with rehabilitation professionals within the institution and externally, and (3) a lack of effective education strategies available for patients with BC and their families. The intervention strategies suggested to address each of these challenges are described below.

Category 1: There is currently a lack of exercise programming and equipment available within the cancer care institution in Ontario:

There was mutual agreement from all participants that an on-site exercise program was needed for this patient population. This was suggested in a variety of ways, from exercise equipment being available within waiting rooms, to having designated exercise rooms within the cancer centre, or having a walking track throughout the hospital. Having an exercise program available on site was thought to have the potential to decrease patient accessibility problems (with regard to costs of existing programs and transportation barriers) and increase exercise awareness, by having patients and their families see others in similar situations participating safely in exercise. See **Table 2** for specific examples of suggestions for this category.

Category 2: There is currently a lack of communication with rehabilitation professionals:

Three participants described situations where they needed information from rehabilitation resources, and sought out resources for advice on rehabilitation within the institution, but could not find the information they needed or did not know who to talk to within or outside of the cancer centre. This resulted in them not knowing what to tell the patient about their current problem. All participants agreed, that having a rehabilitation professional on site would allow them to give their patients better information to support their rehabilitation needs. This professional could be used as an individual referral for the patient or as a support/information service for the HCPs. Suggested ways that a rehabilitation professional could be used within the institution varied from having physiotherapists perform pre-treatment functional assessments and triaging patients based on their needs, to providing general education on physical activity and exercise, or providing exercise interventions on site. **Table 2** gives specific examples of suggested strategies for this category.

Category 3: There is currently a lack of effective exercise education strategies available for patients with breast cancer and their families:

All participants agreed that more effective educational strategies on the benefits of exercise during and after BC treatment are needed for patients and their families within the institution. If effectively implemented, participants thought that patients would be less apprehensive of their ability to exercise during treatment and their families would be more encouraging of maintaining physical activity levels and less fearful of safety concerns. The majority of focus group participants thought this should be done through the use of technology. There was a variety of suggested ways to implement educational interventions using technology, including (1) using computer programs currently available within patient waiting rooms, (2) creating and showing educational programs on television screens currently in patient waiting rooms, and (3) providing patients with activity trackers to make them aware of their own physical activity levels compared to the recommended guidelines. See **Table 2** for examples of these educational strategies.

Other Considerations:

While participants suggested these exercise intervention strategies, they also voiced many points that need consideration before successful implementation would occur. This included the need to specify the disease severity of patients who were provided exercise interventions; to make the interventions accessible for all patients with BC who want to participate within the cancer centre (regardless of socioeconomic status or education level); to make the interventions financially manageable for the patient and the institution; to consider the psychological aspects of the disease and how this may affect successful behavioural change; and the need to include ‘important others’ (families and the patients’ health care team) of patients within the provided interventions.

Figure 1 summarizes the results of the focus group. The algorithm on the left side of the figure describes the main challenges related to exercise and rehabilitation. These challenges result in decreased physical activity levels in patients and survivors, which result in adverse physical side effects and functional limitations during and after their BC treatment. The circle on the right side of the figure summarizes the suggested interventions to overcome these challenges. The three main strategies (having both rehabilitation specialists and exercise interventions on site, together with using current technology to educate patients) are presented in the central yellow ovals, while special considerations are represented outside of these central strategies, but are shown to be necessary in each strategy for successful behavioural change within this population.

DISCUSSION

The aim of this study was to determine novel exercise intervention strategies to implement within the cancer care institution in Ontario in order to overcome the described barriers to exercise participation and promotion for women with BC. To our knowledge this is the first study to include a multidisciplinary team of HCPs in the development of novel exercise strategies to implement for this population. The depth of research over the past decade on the benefits of exercise for women with BC both during and after treatment has grown substantially. There is convincing evidence of symptom management at various points throughout the cancer trajectory and decreased recurrence rates post treatment.[3,8-14,34] Because of these demonstrated benefits, it is recommended that exercise interventions be incorporated at various points during the patients' care.[35] This includes pre-treatment, at various points during active treatment, and post treatment.[35] Having the patient monitored at various points by a rehabilitation professional, has been shown to prevent long-term side effects (such as lymphedema incidence and upper extremity morbidity) and improve health care costs related to these side effects, therefore benefiting all stakeholders.[34-39]

However, cancer rehabilitation programs remain the exception, rather than the norm for individuals with BC in Ontario.[40] There is now a need for research that pertains to the development of novel and effective delivery models to change patient behaviour, improve exercise adherence, and translate the knowledge into clinical practice at the systems level.[40] Research projects, such as this study, which incorporate stakeholders in the development of these needed interventions, is one approach to ensure the collegial support of various HCPs within the institution to drive these programs.[40,41] With the support of various stakeholders within institutions the sustainability and effectiveness of promoting behavioural change is likely to be enhanced.

Numerous implementation strategies were suggested within this research study to engage patients with BC in exercise. An important consideration is to determine who should be providing this intervention for this population. Certain aspects of scope of practice do overlap for HCPs such as primary care nurses, physiotherapists, and kinesiologists. The necessary skills for providing these intervention strategies include: (1) adequate knowledge of the disease process, treatments given and physiological responses of treatment, (2) adequate knowledge on exercise parameters and the physiological responses of exercise, (3) adequate knowledge of safe practices in regards to exercise and emergency response skills, and (4) the ability to accommodate/tailor exercise programs to suite the needs of ill populations. Based on these skills, we propose that the best suited to take on this role be a rehabilitation professional who is an exercise specialists trained in working with people with chronic conditions. This professional could also act as a facilitator to train other professions on how to work effectively with this population on this intervention.[42,43]

While support was evident within this focus group for the implementation of exercise interventions within the cancer centre, it came up repeatedly that a major focus must also be on producing successful and sustainable behaviour change with this population and that research must include an assessment of program sustainability within the institution. In order to do this, the literature highlights the need for theory-based interventions in BC rehabilitation.[44,45] Specifically, in order for behavioural change to happen for women with BC, evidence shows a person's attitudes and subjective norms (ideas of important others such as family, friends, fellow patients, and the health care team) have high levels of association with an individual's intention to exercise, and therefore actual exercise behaviour.[45] These concepts were all represented in the suggestions of the focus group members, which shows consistency with the current theory based literature on this topic. Therefore, while being implemented, the suggested exercise interventions must take theoretical considerations into account in order to ensure sustainable behaviour change for this patient group.

Limitations:

The results of this study should be interpreted with an understanding of its limitations. One limitation of this study was that all participants in this study are employed in one area of Ontario. Therefore, the generalizability of these results to various areas within and outside of Canada should be within the context under consideration. However, this treatment centre is part of a larger regional treatment program which follows similar practice guidelines and has similar program funding allocations. Therefore, while certain details of these interventions may need to be adapted to specific settings, translation of the larger issues and ideas brought forth in this study can occur. Also, purposive sampling was used to recruit the participants to this study. It is possible that these participants agreed to be in this study because they had positive ideas on the current barriers to exercise for this population and understood the need to incorporate exercise more effectively into clinical practice.

CONCLUSION

In conclusion, this study was novel in that it brought together HCPs to discuss and suggest strategies to implement “real life” exercise interventions within institutions as part of the acute management for patients with BC to close the knowledge to practice gap. Findings show that future interventions should focus on implementing exercise interventions within the cancer care institution, including rehabilitation professionals as part of the team of HCPs who work with this patient population, and using technology to educate patients and families on the need to exercise during and after treatment. The next step is to design and implement these interventions and then to assess their effectiveness in overcoming the barriers to exercise for women with BC.

REFERENCES

1. Canadian Cancer Society's Advisory Committee on Cancer Statistics (2015) Canadian Cancer Statistics 2015. Toronto, ON. https://www.cancer.ca/~/media/cancer.ca/CW/cancer%20information/cancer%20101/Canadian%20cancer%20statistics/Canadian-Cancer-Statistics-2015-EN.pdf. Accessed 01 February 2016.
2. Shapiro SL, Lopez AM, Schwartz GE, Bootzin R, Figueredo AJ, Braden CJ, Kurker SF. Quality of life and breast cancer: relationship to psychosocial variables. *J Clin Psychol.* 2001;57(4):501-19.
3. Cella D, Fallowfield LJ. Recognition and management of treatment-related side effects for breast cancer patients receiving adjuvant endocrine therapy. *Breast Cancer Res Treat*. 2009;107:167–180.
4. Ewertz M, Jensen AB. Late effects of breast cancer treatments and potentials for rehabilitation. *Acta Oncol*. 2011;50:187-93.
5. Cormie P, Pumpa K, Galvao D, Turner E, Spry N, Saunders C, Zissiadis Y, Newton RU. Is it safe and efficacious for women with lymphedema secondary to breast cancer to lift heavy weights during exercise: a randomized controlled trial. *J Cancer Surviv*. 2013;7(3):413-424.
6. Pastakia K, Kumar S. Exercise parameters in the management of breast cancer: a systematic review of randomized controlled trials. *Physiother Res Int*. 2011;16(4):237-244.

7. Chan D, Lui L, So W. Effectiveness of exercise programmes on shoulder mobility and lymphedema after axillary lymph node dissection for breast cancer: systematic review. *J Adv Nurs*. 2010;66(9):1902-1914.
8. Bicego D, Brown K, Ruddick M, Storey D, Wong C, Harris SR. Effects of exercise on quality of life in women living with breast cancer: a systematic review. *Breast J*. 2009;15(1):45-51.
9. McNeely M, Campbell K, Rowe B, Klassen TP, Mackey JR, Courneya KS. Effects of exercise on breast cancer patients and survivors: a systematic review and meta-analysis. *CMAJ*. 2009;175(1):34.41.
10. Schmitz KH, Courneya KS, Matthews C, Demark-Wahnefried W, Galvao DA, Pinto BM, Irwin ML, Wolin KY, Segal RJ, Lucia A, Schneider CM, von Gruenigen VE, Schwartz AL. American College of Sports Medicine roundtable on exercise guidelines for cancer survivors. *Med Sci Sports Exerc*. 2010;42(7):1409-1426.
11. Courneya KS, Segal RJ, McKenzie DC. Effects of exercise during adjuvant chemotherapy on breast cancer outcomes. *Med Sci Sports Exerc*. 2014;46(9):1744-1751.
12. McNeely M, Campbell K, Ospina M. Exercise interventions for upper-limb dysfunction due to breast cancer treatment. *Cochrane Db Syst Rev*. 2010;16(6):CD005211

13. Zou LY, Yang L, He XL, Xu JJ. Effects of aerobic exercise on cancer-related fatigue in breast cancer patients receiving chemotherapy: A meta-analysis. *Tumour Biol*. 2014;35(6):5659-5667.
14. Schmitz K, Ahmed R, Troxel A, Cheville A, Lewis-Grant L, Smith R, Bryan CJ, Williams-Smith CT, Chittams J. Weight lifting for women at risk of breast cancer-related lymphedema. A randomized trial. *JAMA*. 2010;304(24):2699-2705.
15. Cramer H, Lange S, Klose P, Paul A, Dobos G. Yoga for breast cancer patients and survivors: A systematic review and meta-analysis. *BMC Cancer*. 2012.18(12):412.
16. Mustian KM, Palesh OG, Flecksteiner SA. Tai Chi Chuan for breast cancer survivors. *Med Sport Sci*. 2008;52:209-217.
17. Fernandez S, Franklin J, Amlani N, DeMilleVille C, Lawson D, Smith J. Physical activity and cancer: A cross-sectional study on the barriers and facilitators to exercise during cancer treatment. *Canadian Oncology Nursing Journal.* 2015;25(1):37-42.
18. Courneya KS, Katzmarzyk PT, Bacon E . Physical activity and obesity in Canadian cancer survivors. *Cancer*. 2008;112(11):2475-82.
19. Blaney JM, Lowe-Strong A, Rankin J, Campbell A, Allen J, Gracey J. The cancer rehabilitation journey: barriers to and facilitators of exercise among patients with cancer-related fatigue. *Phys Ther*. 2010;90:1135-47.

20. Sander AP, Wilson J, Izzo N, Mountford SA, Hayes KW. Factors that affect decisions about physical activity and exercise in survivors of breast cancer: a qualitative study. *Phys Ther.* 2012;92:525-36.
21. Brunet J, Taran S, Burke S, Sabiston CM. A qualitative exploration of barriers and motivators to physical activity participation in women treated for breast cancer. *Disabil Rehabil*. 2013;35(24):2038-2045.
22. Smith-Turchyn J, Richardson J, Tozer R, McNeely M, Thabane L. Physical activity and breast cancer: A qualitative study on the barriers to and facilitators of exercise promotion from the perspective of health care professionals. *Physiother Can*. 2016;68(4):383-390.
23. Segal R, Zwaal C, Green E, Tomasone J, Loblaw A, Petrella T. 2015. Exercise for people with cancer: A quality initiative of the program in evidence-based care, Cancer Care Ontario. https://www.cancercare.on.ca/common/pages/UserFile.aspx?fileId=342807. Accessed 15 January 2016.
24. Sandelowski M. Focus on research methods: Whatever happened to qualitative description? *Res Nurs Health*. 2000;23:334-340.
25. Rabiee F. Focus-group interview and data analysis. *Proceedings of the Nutrition Society.* 2004;63:655-660.
26. Thomas L, MacMillian J, McColl E, Hall C, Bond S. Comparison of focus group and individual interview methodology in examining patient

satisfaction with nursing care. *Social Science in Health*. 1995;1:206-219.

27. Basch C.Focus group interview: An under-utilised research technique for improving theory and practice in health education. *Health Education Quarterly*. 1987;14:411-418.
28. Ontario Women's Health Network. Guide to Focus Groups. 2009. Toronto, ON:OWNH.
29. Krueger RA, Casey MA. Focus groups: A practice guide for applied research. 2000. Sage Publications, Thousand Oaks.
30. Richardson CA, Rabiee F. "A Question of Access"—an exploration of the factors influencing the health of young males aged 15-19 living in Corby and their use of health care services. *Health Education Journal*. 2001;60:3-6.
31. Kreuger RA. Is it a focus group? Tips on how to tell. *Journal of Wound, Ostomy and Continence Nursing*. 2006;33:363-366.
32. Richards L. Handling qualitative data: A practical guide. 2009. London, England: SAGE Publications Inc.
33. Blazely P. Qualitative data analysis: Practical strategies. 2013. London, England: SAGE Publications Inc.
34. Lahart IM, Metsios GS, Nevill AM, Carmichael AR. Physical activity, risk of death and recurrence in breast cancer survivors: A systematic review and meta-analysis of epidemiological studies. *Acta Oncol*. 2015;54(5):635-654.

35. Stout N, Binkley JM, Schmitz KH, Andrews K, Hayes SC, Campbell KL, et al. A prospective surveillance model for rehabilitation for women with breast cancer. *Cancer*. 2012;118(8 Suppl):2191-2200.
36. Hayes SC, Johansson K, Stout NL, Prosnitz R, Armer JM, Gabram S, Schmitz KH. Upper-body morbidity after breast cancer: Incidence and evidence for evaluation, prevention, and management within a prospective surveillance model of care. *Cancer.* 2012;118(8 Suppl):2237-2249.
37. Stout N, Pfalzer LA, Springer B, Levy E, McGarvey C, Danoff J, Gerber L, Soballe P. Breast cancer related lymphedema: Comparing direct costs of a prospective surveillance model and traditional model of care. *Phys Ther*. 2012;92(1):152-163.
38. Silver JK. Cancer prehabilitation and its role in improving health outcomes and reducing health care costs. *Semin Oncol Nurs*. 2015;31(1):13-30.
39. Silver JK, Baima J, Newman R, Galantino ML, Shockney LD. Cancer rehabilitation may improve function in survivors and decrease the economic burden of cancer to individuals and society. *Work.* 2013;46(4):455-472.
40. Santa Mina D, Alibhai SM, Matthew AG, Guglietti CL, Steele J, Trachtenberg J, Ritvo PG. Exercise in clinical cancer care: A call to action and program development description. *Curr Oncol.* 2012;19(3):136-144.
41. Ahmed S, Ware P, Visca R, Barell C, Chouinard MC, Desforges J, et al.

The prevention and management of chronic disease in primary care: Recommendations from a knowledge translation meeting. *BMC Res Notes*. 2015;15(8):571.

42. Canadian Physiotherapy Association. Scope of Practice Briefing Note. https://www.physiotherapy.ca/getmedia/e2541bbc-f95d-4d8b-b689-98365bc4abbd/Scope-of-Practice_EN.pdf.aspx. Accessed 15 Jan 2016
43. College of Physiotherapists of Ontario. Scope of Practice Resources. http://www.collegept.org/Resources#ScopePractice. Accessed 15 Jan 2016.
44. Smith-Turchyn J, Richardson J. A critical review of the Theory of Planned Behaviour to predict and explain exercise behaviour in women with breast cancer. *Critical Reviews in Physical and Rehabilitation Medicine.* 2015;27(1):53-66.
45. Courneya KS, Friedenreich CM. Utility of the Theory of Planned Behavior for understanding exercise during breast cancer treatment. *Psycho-oncol*. 1999;8(2):112-122.

TABLES

Table 1: Participant Characteristics

Characteristic	**Number**
Health Profession:	
- Medical Oncologist	2
- Radiation Oncologist	1
- General Practitioner in Oncology	1
- Nurse Practitioner	1
- Primary Care Nurse	1
- Physiotherapist	2
- Dietician	1
Gender:	
- Male	2
- Female	7

Table 2: Quotations Representing Suggested Exercise Interventions for Main Challenges Described

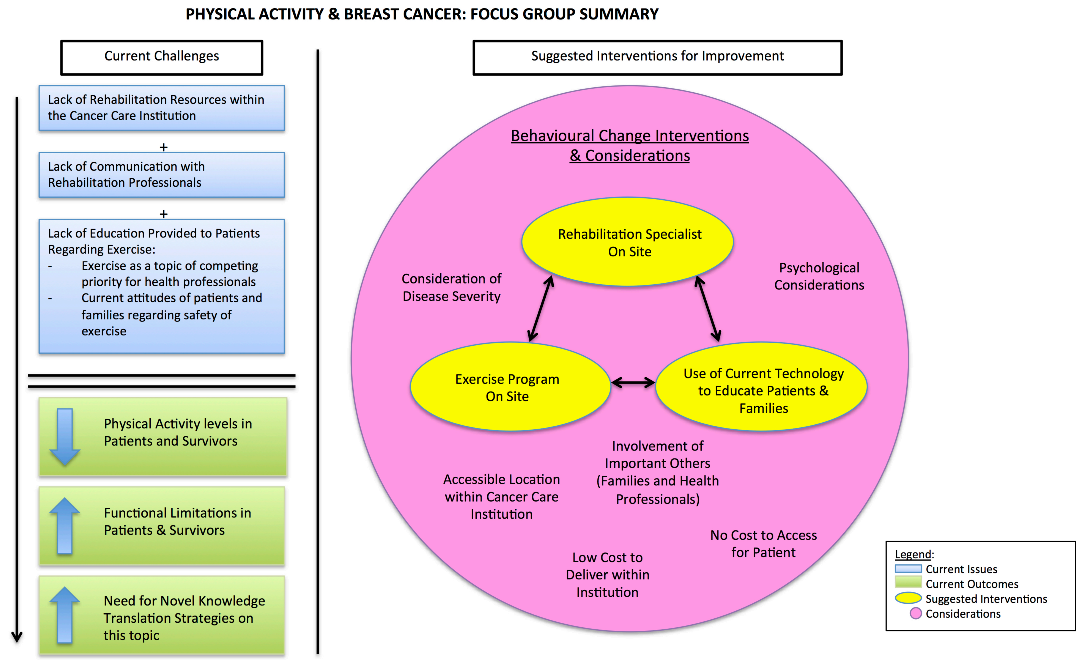
Category (Challenge)	**Quotation**
Lack of exercise programming and equipment available within the cancer care institution in Ontario	*"I want a meditation room and…an exercise room in the chemo suite so when they (patients) are waiting for their chemo appointment they can either go into the meditation room and have either reflexology or meditate or whatever and then the other room if they wanted to have, you know, go on the treadmill or whatever or do some weights, and have someone there supervising them. So that's my utopia."*
	"I'm thinking something a lot simpler…it's just a walking track that is metered out in the cancer…centre over to the hospital. You could have a little book that says OK…how many steps are you going to do…and we'll put a little guidance out there (for the patients)."
Lack of communication with rehabilitation resources	*"You know, just to have somebody…just to even have a go to (rehabilitation person), we don't even have a "go to" person. Its very, very dispersed."*
	"…a really good example is yesterday…a patient of mine

	was being seen and was having their file reviewed. They had bone mets and basically the recommendation is that she probably needs immediate surgery and should have, what's it, feather touch. So, I'm looking at this…and we don't even know what this means…what are we suppose to be telling the patient. And there's no resource, who do you go to?"
	"So, ideally I think every patient should have the right to be screened by a physiotherapist or kinesiologist to determine whether they are safe to exercise. A pre-determined level of exercise should be made…are you a never exerciser, an exerciser, you know, how much, etc. Then patients should have the opportunity to be triaged according to their needs…whether they are OK to exercise or might need some guidance from an exercise program."
Lack of effective exercise education strategies available for patients with breast cancer and their families	*"I was wondering about the computer screen that you are suppose to go through in the waiting room and fill in…perhaps there could be something related to exercise that is actually an exercise algorithm where you are getting what the person is all about and what they would prefer in terms of there pathway to exercise, whether it is*

	during active treatment or afterwards.”
	“One more thing about the waiting rooms…just as a patient…maybe instead of ‘life of the Kardashian’s’ showing up on the TV…it perhaps could be something correlated to exercise or maybe something personalized like everyone gets a little ipad when they come in and you know, they could select the channel that they want, but the channels are related to health promotion as oppose to reality TV.”
	“I would love for our breast cancer patients to have a little hand held device and look at some video on how to increase the mobilization of their shoulder while they are sitting around, maybe at their radiation planning point…”

FIGURES

Figure 1: Interventions to Overcome Exercise Challenges



CHAPTER 4: BRIDGING THE GAP: INCORPORATING EXERCISE EVIDENCE INTO CLINICAL PRACTICE IN BREAST CANCER CARE IN ONTARIO-A PILOT RANDOMIZED CONTROL TRIAL PROTOCOL

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TITLE

Bridging the Gap: Incorporating Exercise Evidence into Clinical Practice in Breast Cancer Care in Ontario-A Pilot Randomized Control Trial Protocol

AUTHORS

Jenna Smith-Turchyn* PT, PhD(c) (smithjf@mcmaster.ca), Julie Richardson* PT, PhD (jrichard@mcmaster.ca), Richard Tozer MD, PhD[+] (tozer@hhsc.ca), Lehana Thabane PhD** (thabanl@mcmaster.ca), Margaret McNeely[++] PT, PhD (mmcneely@ualberta.ca)

INSTITUTION

*McMaster University
School of Rehabilitation Science,
IAHS Rm. 403
1400 Main Street West
Hamilton, ON, Canada
L8S 1C7

[+]Juravinski Cancer Centre,
Department of Oncology
699 Concession St.
Hamilton, ON, Canada
L8V 5C2

**McMaster University
Department of Clinical
Epidemiology & Biostatistics
50 Charlton Ave. E
Hamilton, ON, Canada
L8N 4A6

[++]University of Alberta
School of Rehabilitation Medicine
8205 114 St., 3-48 Corbett Hall
Edmonton, AB, Canada
T6G 2G4

CORRESPONDING AUTHOR:
Jenna Smith-Turchyn*
Business telephone: 905-869-0599
Business fax: 905-524-0069
Email: smithjf@mcmaster.ca

ABSTRACT

Background: Breast cancer (BC) and its treatments lead to numerous side effects that affect a person's life for years after treatment has ended. Research shows that regular exercise limits many of these side effects. However, less than 30% of BC survivors regularly exercise due to many barriers at both the patient and health care professional level. The purpose of this pilot trial is to assess the feasibility and effectiveness of conducting a novel KT intervention using exercise and self-management versus usual care among BC survivors.

Methods: *Study Design:* Pilot randomized controlled trial. *Eligibility:* Women older than 18 years who are currently undergoing chemotherapy treatment for BC. *Intervention:* The intervention group includes an 8-session multi-component intervention with a structured aerobic exercise program plus SM supervised by a physiotherapist. *Randomization*: Participants will be randomly allocated using a 1:1 allocation ratio to receive the intervention of structured exercise plus SM program or usual care. *Outcomes:* The primary feasibility outcomes include recruitment rate, retention rate, and adherence rate. The secondary outcomes include exercise knowledge and behavior, HRQoL and resource utilization. *Analysis:* A blinded assessor will assess outcomes at baseline, post intervention, at 2- and 4-month follow up. Intervention feasibility and effectiveness will be assessed using descriptive statistics and analysis of covariance for continuous outcomes.

Discussion: This study aims to assess the feasibility of a novel KT intervention to close the current KT gap and increase exercise awareness for women with BC. This project will assess process and resource variables before implementation of a larger scale intervention. The overall project goal is to promote sustainable exercise behaviour to help manage the burden of BC.

Trial Registration: This trial was registered on ClinicalTrials.gov on March 21, 2017 (Identifier: NCT03087461).

KEYWORDS

Breast neoplasms, exercise, translational medical research, pilot study, rehabilitation

INTRODUCTION

Breast cancer (BC) and its treatments lead to numerous side effects that affect a person's quality of life (QOL) for years after treatment has ended [1-5]. Research has shown that regular exercise limits many of these side effects and can prevent disease recurrence [5-10]. However, less than 30% of survivors participate in regular exercise [11-13]. Previous research conducted by our team has shown that over 80% of BC survivors in southwestern Ontario are unaware of the benefits of exercise and are not educated on the need to stay physically active [11], health professionals face many institutional, personal, and patient-related barriers to promoting exercise [14], and there is a need for novel knowledge translation (KT) strategies within cancer institutions that focus on easy-to-access exercise interventions and education by physiotherapists (PTs) [15].

Moreover, the societal burden of this disease is projected to increase substantially over the next two decades. The Canadian Cancer Society's 2015 Statistics report [16] suggests that the number of new cancer cases in women will increase by 74% by the year 2032 due to the aging Canadian population. The number of new cases of BC is projected to increase by more than 10,000 in this same time period [16]. Fortunately, due to improved screening and treatment techniques, survival rates for BC are increasing [3]. However, physical and functional sequelae prevent survivors from returning to their activities associated with work, leisure, and domestic roles [3]. Exercise is an effective, safe, and cost-efficient way to manage this burden and return women to their pre-cancer activity levels. Therefore KT research is needed to determine how to best translate and integrate this research knowledge into clinical practice in order to elicit sustainable behaviour change for this population. Pilot work completed for this project has shown that in order to change clinical practice, implementation strategies using accessible exercise options and education are needed within the institution to maximize women's engagement with exercise information provided and to partake in this behaviour [15]. Along with this, self-management (SM) programs have been shown to improve QOL and physical side effects in BC survivors, however, the implementation of these programs in clinical practice is scarce [17]. The current knowledge to practice gap in the field of BC rehabilitation shows that novel KT strategies are needed.

A pilot study is an, "investigation designed to test the feasibility of methods and procedures for later use on a large scale or to search for possible effects and associations that may be worth following up in a subsequent larger study" [18]. For this project, a pilot study is needed as the first step in order to assess process and resource variables before implementation of a large-scale intervention [19]. Process variables include measuring recruitment rate, retention rate, and adherence rates to the intervention provided [19]. Resource variables include determining the centers willingness and capacity to house a specific intervention, equipment availability, intervention location, and budget concerns

[19]. There is currently a lack of pilot trials for a novel KT intervention of this sort and therefore this pilot study will aid in shaping and guiding a larger, phase III trial.

METHODS & MATERIALS

Study Purpose:

The purpose of this study is to determine whether KT strategies, focusing on accessible exercise locations and SM education by PTs using technology, are feasible and impact exercise knowledge and behaviour, QOL, and need for additional health care services among women with BC. Specifically, the objectives of this project are to: (1) Determine the feasibility (through recruitment, retention and adherence rates) of providing a complex KT intervention designed specifically for women with BC using technology, and (2) Determine preliminary estimates of effects of the KT intervention on levels of exercise knowledge and behaviour, health related quality of life and, resource utilization, among BC survivors over a four month period.

Study Design & Participants:

This study is a pilot randomized controlled trial. Eligible participants will include community-dwelling, English-speaking women, over 18 years, who are currently undergoing chemotherapy for Stage 1-3 BC and have been cleared by their oncologist to participate in moderate intensity aerobic exercise. Participants will be excluded from the study if they have another chronic disease, cognitive impairment or injury that prevents them from participating independently in moderate intensity exercise.

Recruitment:

Medical oncologists and Primary Care Nurses at the Juravinski Cancer Centre (JCC) will recognize possible participants for this study within their patient caseload. For those they think are eligible, the health care professional will briefly discuss the study with their patient and get consent for the patient to be contacted by a member of the research team. Possible participants will be contacted by phone to discuss eligibility and potential study enrollment. The Hamilton Integrated Research Board approved this study (reference #: 3124) in April 2017. All participants will provide written informed consent on the approved consent forms prior to enrollment in this study.

Intervention:

This pilot project will implement a multi-dimensional KT intervention including an exercise and SM program. Refer to **Figure 1** for study flow chart.

The exercise intervention will involve an evidence-based moderate intensity aerobic exercise program, using recumbent bikes, delivered within the cancer institution. Results from participants in our focus group run during the pilot work for this project suggest that exercise programs should be delivered in the institution where women are waiting for their chemotherapy. Delivering the program in this environment will increase the accessibility of the services and we anticipate this approach will increase exercise awareness. Participants will take part in the 30-minute, moderate intensity (50-70% HRmax or 4-6/10 on Rate of Perceived Exertion scale) aerobic exercise program for 8 sessions. The intervention will be supervised by a PT educated in cancer rehabilitation and who has been trained in the specific protocol used and in working with women with BC.

The SM component will include educational modules created by a PT. Participants will view these 30 minute modules prior to each exercise intervention, over the same 8 sessions. Content provided within the program will include information on the benefits of exercise during and after BC treatment, safe exercise prescription, how to self-monitor exercise levels, action planning for specific exercise strategies, and precautions related to exercise and BC. Refer to **Table 1** for details of SM content for each week of the program. A variety of tools will be used in the SM program, including a mobile app and e-health resources for BC. Having numerous sessions will allow the PT to provide consultation in respect to exercise adaptation, parameters, and programming in order to facilitate long-term exercise engagement and participation. Adherence and fidelity to the specified exercise and self-management protocol will be monitored through random observation by study investigators.

Outcomes:

Primary Outcomes: The feasibility and effectiveness of the KT intervention will be assessed using quantitative outcomes. The primary outcomes of feasibility variables will be assessed at baseline and post intervention, where applicable. Feasibility will be assessed by measuring recruitment (percentage (%) of eligible patients recruited), retention (% of consented patients who complete the intervention), and adherence rates (% of sessions attended) to the intervention).

Secondary Outcomes: Secondary effectiveness outcomes will be assessed at four time points: baseline, post intervention, and at 2 and 4 month follow up. At baseline, participants will be instructed on how to complete each self-report measure by an assessor blinded to participant group allocation. All post-intervention, 2 and 4 month follow up, assessments will be mailed to participants to complete and return to study investigators using pre-paid postage envelops. No identifiers will be used on these assessments and therefore assessors performing the analysis of data will be blinded to participant group allocation. Hard copies of the completed outcome measures will be stored in a locked filing cabinet only accessible by the study investigators at McMaster University and data entered into statistical analysis software will be stored on a password protected computer.

Level of exercise knowledge and behaviour will be assessed using a Theory of Planned Behaviour (TPB) [20] based questionnaire. The TPB has been used extensively to determine levels of intention and behaviour for various health behaviours, including exercise [21,22].

Quality of life will be measured using the FACT-B [23], a self-report measure designed to assess multi-dimensional QOL specifically for women with BC.

Need for additional health care services will be measured using the EQ-5D [24] and a piloted self-report questionnaire assessing health care facility visits, doctor visits, procedures received, support services used, loss of work, and prescription medications used.

Sample Size:

Debate exists as to whether sample size calculations for pilot studies are necessary. Some authors suggest that no calculation is needed as long as the pilot study is large enough to provide useful information about the aspects that are being examined for feasibility [19]. However other authors suggest using a percentage of the sample required for a full study [25,26], or to use a confidence interval (CI) to establish feasibility [19,26]. For this project we have decided to calculate sample size based on the proportion of success of the primary outcome of feasibility (using estimates for adherence rates) [19,25,26].

Therefore, using a Z value from the standard normal distribution to reflect a 95% confidence interval (1.96), E as the desired margin of error (0.2), and p as the proportion of successes in the population (0.75-estimated adherence rates), the sample size for this pilot study will be at least 18 participants (9/group). With an expected drop out rate of 25%, based on previous exercise based literature with this population, the final sample size for this project should be 23 participants. In order to ensure an even number of individuals can be randomized to each group, this will be rounded up to a total of 24 participants (12/group).

Randomization-Sequence Generation:

Prior to participant randomizations, all eligible participants will complete the following forms: (a) patient information form, (b) Godin Leisure-Time exercise questionnaire, (c) consent form, and (d) baseline measures. All participants will be informed verbally in person and in writing that they have equal chance of being randomized into the intervention or control group. They will not be made aware of the study hypotheses. Randomization to intervention or control group will be completed by a member of the research team who is independent of the intervention on a record by record basis using a computer software program (STATA/MP v14). This researcher will remain blind to the identity of each treatment group (by randomizing only to group A or B) during the randomization process. Participants may withdraw from the study at any time. Investigators may withdraw a participant from the research study if circumstances arise which warrant doing so (for example, safety).

Allocation Concealment & Implementation:

Allocation of participant randomization will be concealed in sequentially numbered, opaque, sealed envelops. The envelops will be opened sequentially by the researchers only after participant details have been written on the envelop by the researcher who completed randomization. If the participant is allocated to the intervention group, they will receive a phone call to organize details of the first intervention session (such as time and location).

Blinding:

Due to the nature of this knowledge translation study, participants and persons administering the intervention will not be blinded to group assignment. However, the assessor receiving the self-reported outcome measures will be blind to group allocation and will not be involved in running of the intervention. A researcher blinded to the group allocation of the participants will conduct all statistical analysis.

Statistical Methods:

Participant characteristics will be analyzed at baseline to ensure no significant differences exist between groups. Means and standard deviations (SD) will be used to report continuous variables and t-tests will be used to assess differences between the two groups for these variables. Frequencies will be used to report categorical variables and Pearsons X^2 test will be used to assess differences between groups for these variables. All statistical analysis will be completed using STATA/MP 14. Refer to **Table 2** for a summary table of study objective and methodology.

Research Questions 1: Descriptive statistics will be used to measure feasibility (recruitment rate, retention rate, and adherence rates). Recruitment rates will be calculated by determining the percentage of eligible patients that were actually enrolled in the study. A recruitment log will be kept, detailing reasons for non-participation of eligible patients. Retention rate will be defined by calculating the percentage of enrolled patients who complete the intervention. Adherence rates will be calculated as a percentage of total sessions attended. Attendance will be tracked on the feasibility data collection sheet and reasons for non-participation on scheduled intervention days will be documented using an adherence log.

Research Question 2: Effectiveness outcomes will be assessed at four time points: baseline, 16 weeks (post intervention), and at 2 and 4 month follow up. An analysis of covariance will be used to determine within and between group differences. An intention to treat analysis will be used for these analyses.

DISCUSSION

There is a small risk of participant injury during the exercise intervention. While it has been well documented that exercise is safe for this population if proper screening and precautions are followed, minor injuries have the potential to occur in any active intervention. In order to ensure safety, all participants will need medical clearance to participate in moderate intensity exercise from their medical oncologists and will be supervised by a physiotherapist during each session. Heart rate, blood pressure, rate of perceived exertion and oxygen saturation measurement tools will be present and used during each exercise session. While uncommon, all side effects secondary to exercise will be tracked using Exercise logs. Type, intensity, duration, and management of any side effect will be documented using these logs.

The findings of this KT pilot study will help to determine the feasibility and preliminary effectiveness of a novel implementation strategy. This project will inform a larger intervention trial which has the potential to change the way rehabilitation services are provided in clinical practice and impact all levels of BC prevention; secondary and tertiary prevention of treatment-related side effects, *and* primary prevention of disease recurrence through sustained behaviour change. The results from this pilot project should be interpreted with an understanding of the potential threats to the generalizability of the results. Specifically, the results of this pilot study will only be relevant to the implementation of a larger intervention at sites comparable to the JCC and will be specific to the unique characteristics of women with BC. As the intervention process and management is more extensive with larger numbers of participants, the researcher team will have to take into consideration additional time and resource needs when implement the larger scale project.

TRIAL STATUS

Protocol Version Number: 3. Date: April 11, 2017. Approximate recruitment start date: June, 2017. Approximate recruitment end date: August, 2017. Any trial modifications will be updated in a timely manner on ClinicalTrials.gov and sent via email to appropriate parties.

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REFERENCES

1. Shapiro SL, Lopez AM, Schwartz GE et al. Quality of life and breast cancer: relationship to psychosocial variables. *J Clin Psychol* 2001;57(4):501-19.
2. Wengstrom Y, Haggmark C, Strander H et al. Perceived symptoms and quality of life in women with breast cancer receiving radiation therapy. *Eur J Oncol Nurs* 2000;4(2):78-88.
3. Ewertz M, Jensen AB. Late effects of breast cancer treatments and potentials for rehabilitation. *Acta Oncol* 2011;50:187-93.
4. Knobf MF, Sun Y. A longitudinal study of symptoms and self-care activities in women treated with primary radiotherapy for breast cancer. *Cancer Nurs* 2005;28(3):210-18.
5. Cella D, Fallowfield LJ. Recognition and management of treatment-related side effects for breast cancer patients receiving adjuvant endocrine therapy. *Breast Cancer Res Treat* 2008;107:167–180.
6. Cormie P, Pumpa K, Galvao D, et al. Is it safe and efficacious for women with lymphedema secondary to breast cancer to lift heavy weights during exercise: a randomized controlled trial. *J Cancer Surviv* 2013;7(3):413-424.
7. Pastakia K, Kumar S. Exercise parameters in the management of breast cancer: a systematic review of randomized controlled trials. *Physiother Res Int* 2011;16(4):237-244.
8. Chan D, Lui L, So W. Effectiveness of exercise programmes on shoulder

mobility and lymphedema after axillary lymph node dissection for breast cancer: systematic review. *J Adv Nurs* 2010;66(9):1902-1914.

9. Bicego D, Brown K, Ruddick M, et al. Effects of exercise on quality of life in women living with breast cancer: a systematic review. *Breast J* 2009;15(1):45-51.
10. McNeely M, Campbell K, Rowe B, et al. Effects of exercise on breast cancer patients and survivors: a systematic review and meta-analysis. *CMAJ* 2006;175(1):34.41.
11. Fernandez S, Franklin J, Amlani N, et al. Physical activity and cancer: A cross-sectional study on the barriers and facilitators to exercise during cancer treatment. *Can Oncol Nurs J* 2015;42(1):37-72.
12. Courneya KS, Katzmarzyk PT, Bacon E. Physical activity and obesity in Canadian cancer survivors. *Cancer* 2008;112(11):2475-82
13. Cheifetz O. Clinicians commentary on Sing et al. *Physiother Can* 2013;65(2):192-3.
14. Smith-Turchyn J, Richardson J, McNeely M, et al. Physical activity and breast cancer: A study on the barriers and facilitators to exercise promotion from the perspective of health care professionals. *Physiother Can* doi:10.3138/PTC.2015-84.

15. Smith-Turchyn J, Richardson J, Tozer R, et al. Physical activity and breast cancer: Results of a focus group to devise novel exercise interventions for women with breast cancer. Submitted to *Rehabilitation Oncology* 2016.
16. Canadian Cancer Society's Advisory Committee on Cancer Statistics. *Canadian Cancer Statistics 2015.* Toronto, ON: Canadian Cancer Society; 2015.
17. Boogaard L., Gater L., Mori M., et al. Efficacy of self-management programs in managing side effects of breast cancer: A systematic review and meta-analysis of randomized control trials. *Rehabil Oncol* 2016;34(1):14-26.
18. Everitt B. Medical Statistics from A to Z: A Guide for Clinicians and Medical Students. Cambridge University Press: Cambridge, 2 2006.
19. Thabane L, Ma J, Chu R, Cheng J, Ismalia A, Rios L, et al. A tutorial on pilot studies: The what, why and how. *BMC Medical Research Methodology* 2010;10(1).
20. Ajzen I. The theory of planned behavior. *Organ Behav Hum Dec* 1991;50:179-211.
21. McEachan RR, Conner M, Taylor NT, Lawton RJ. Prospective prediction of health- related behaviours with the Theory of Planned Behaviour: a meta-analysis. *Health Psych Rev* 2011;5(2):97-144.

22. Smith-Turchyn J, Richardson J. Critical Review of the Theory of Planned Behavior to Predict and Explain Exercise Behavior in Women with Breast Cancer. *Crit Rev Phys Rehabil Med* 2015; 27(1).
23. Brady MJ, Cella DF, Mo F, et al. Reliability and validity of the functional assessment of cancer therapy-breast quality of life instrument. *J Clin Oncol* 1997;15(3):974-986.
24. Simon Pickard A, Wilke C, Lin H, Lloyd A. Health utilities using the EQ-5D in studies of cancer. *PharmacoEconomics* 2007;25(5):365-384.
25. Hertzog MA. Considerations in determining sample size for pilot studies. *Res Nurs Health* 2008;31:180-191.
26. Cocks K, Torgerson D. Sample size calculations for pilot randomized trials: a confidence interval approach. *J Clin Epidemiol* 2013;66:197-201.

TABLES

Table 1: Self-Management Content

Session	Content
1	Introductions. What are the side effects of treatment? Why do they happen? Benefits of exercise for women with breast cancer. Types of exercise and safety precautions during exercise (how to monitor BP, HR, RPE) What is self-management? How to participate in effective self-management. Self-management and breast cancer. Introduction to goal setting/action planning.
2	Review of previous week goal/action plan. The importance of posture for women with breast cancer (common postural issues, how to assess posture, how to ensure optimal posture). Relaxation and breathing techniques to manage anxiety and stress. Set goal/action plan for week.
3	Review of previous week goal/action plan. Appropriate exercise techniques to maintain/increase endurance: - Description of aerobic exercise - Types of aerobic exercise - Parameters for aerobic exercise Set goal/action plan for week.
4	Review of previous week goal/action plan Appropriate exercise techniques to maintain/increase strength - Description of strengthening exercise - Types of strengthening exercise - Parameters for strengthening exercise Set goal/action plan for week.
5	Review of previous week goal/action plan Other forms of Exercise (flexibility, yoga, Tia Chi, etc.) Appropriate exercise techniques to maintain/increase flexibility: - Description of flexibility exercises - Types of flexibility exercises - Parameters for flexibility exercise Description of other forms of exercise: - Types of other forms of exercise - Parameters of other forms exercise Set goal/action plan for week.

6	Review of previous week goal/action plan. Self-monitoring physical activity levels: - Introduction to Breast Cancer Physio Guide (App) - Introduction to Stanford Action Planning App - Other techniques to monitor physical activity levels Set goal/action plan for week.
7	Review of goal/action plan. Communicating with others (family, health professionals) about exercise and physical activity. Available exercise programs in the community. How to move forward: how to evaluate progress. Set goal/action plan for week.
8	Review of goal/action plan. Summary of self-management program. How did you use self-management information? Questions/comments.

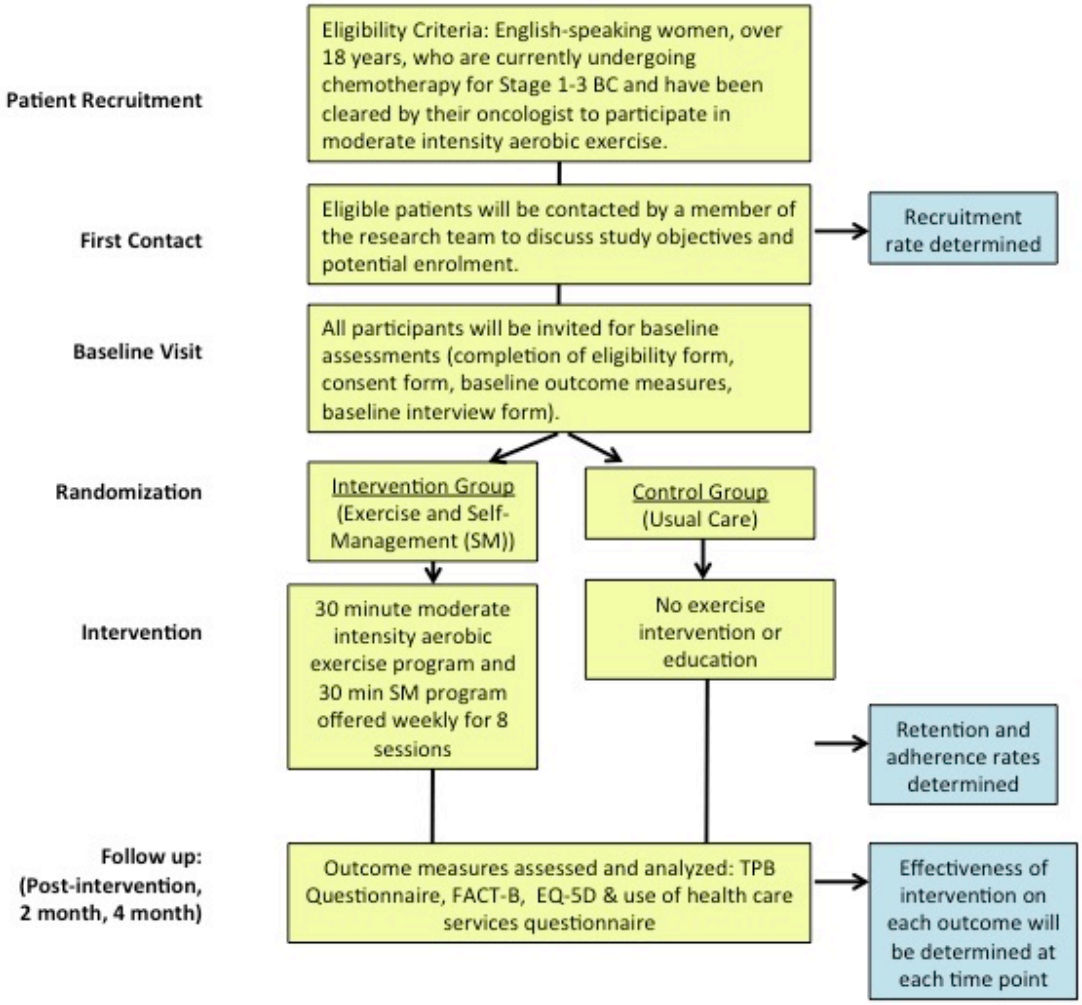
Table 2: Summary Table

Objective	Hypothesis	Outcome	Analysis Method
Determine the feasibility (through recruitment, retention and adherence rates) of providing a complex KT intervention including accessible exercise programs delivered within the cancer institution and a SM program designed specifically for women with BC using technology	Implementing and providing a complex KT intervention for women with BC is feasible (recruitment, retention, and adherence rates are 50%, 75%, and 75% respectively).	Recruitment Rate	Descriptive statistics (percentage (%) of eligible patients recruited). Recruitment logs will be kept, detailing reasons for non-participation of eligible patients.
		Retention Rate	Descriptive statistics (% of consented patients who complete the intervention).
		Adherence Rate	Descriptive statistics (% of sessions attended). Adherence rates will be tracked using the data collection sheet. Reasons for non-participation on scheduled intervention days will be documented using adherence logs.
Determine preliminary estimates of effects of the KT intervention of exercise plus SM versus usual care among BC survivors over a	Compared to the control group, BC survivors participating in the KT intervention will have higher levels of	Levels of exercise knowledge and behaviour (using a Theory of Planned Behaviour based questionnaire)	An analysis of covariance will be used to determine within and between group differences. An intention to treat analysis will be used for these analyses.
		Health related quality of life (using the FACT-B)	

four-month period.	exercise knowledge and behaviours and QOL, and less need for additional health care services.	Resource utilization (using the EQ-5D and a piloted self-report questionnaire assessing health care facility visits, doctor visits, procedures received, support services used, loss of work, and prescription medications used)	

FIGURES

Figure 1: Study Flow Chart



CHAPTER 5: BRIDGING THE GAP: INCORPORATING EXERCISE EVIDENCE INTO CLINICAL PRACTICE IN BREAST CANCER CARE-A PILOT RANDOMIZED CONTROL TRIAL

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TITLE

BRIDGING THE GAP: INCORPORATING EXERCISE EVIDENCE INTO CLINICAL PRACTICE IN BREAST CANCER CARE-A PILOT RANDOMIZED CONTROL TRIAL

AUTHORS

Jenna Smith-Turchyn* PT, PhD(c) (smithjf@mcmaster.ca), Julie Richardson* PT, PhD (jrichard@mcmaster.ca), Richard Tozer MD, PhD+ (tozer@hhsc.ca), Margaret McNeely++ PT, PhD (mmcneely@ualberta.ca), Lehana Thabane PhD** (thabanl@mcmaster.ca),

INSTITUTION

*McMaster University
School of Rehabilitation Science,
IAHS Rm. 403
1400 Main Street West
Hamilton, ON, Canada
L8S 1C7

+Juravinski Cancer Centre,
Department of Oncology
699 Concession St.
Hamilton, ON, Canada
L8V 5C2

**McMaster University
Department of Health
Research Methods, Evidence,
and Impact
50 Charlton Ave. E
Hamilton, ON, Canada
L8N 4A6

++University of Alberta
Department of Physical Therapy
Faculty of Rehabilitation Medicine
2-50 Corbett Hall
Edmonton, AB, Canada
T6G 2G4

CORRESPONDING AUTHOR

Jenna Smith-Turchyn*
Business telephone: 905-869-0599
Business fax: 905-524-0069
Email: smithjf@mcmaster.ca

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PREVIOUS PRESENTATIONS & DISCLAIMERS

None.

RUNNING HEAD

Bridging the Gap: Exercise and Breast Cancer

ABSTRACT

Objective: To determine the feasibility (through recruitment, retention and adherence rates) of providing a complex knowledge translation (KT) intervention designed specifically for women with breast cancer using technology, and to explore preliminary estimates of effects of the KT intervention on physical activity level, exercise knowledge and behaviour, health related quality of life, overall health status, and resource utilization among breast cancer survivors.

Methods: *Design:* Single-centre pilot randomized controlled trial. *Participants:* Community-dwelling, women, over 18 years of age, currently undergoing chemotherapy for Stage 1-3 BC at the Juravinski Cancer Centre. *Randomization & Blinding:* A blinded researcher randomized participants on a record-by-record basis to the intervention or control group. Participants and persons administering the intervention were not blinded to group assignment, however, a researcher blinded to the group allocation of the participants conducted the statistical analysis.

Intervention Group: Eight sessions of moderate intensity aerobic exercise along with eight self-management modules were delivered. *Control Group:* Usual care. *Primary Outcome:* Feasibility measured through recruitment, retention, and adherence rates. *Secondary Outcomes:* Physical activity level, exercise knowledge and behaviour, health related quality of life, and overall health status

were assessed at baseline and post intervention. Use of additional health care services was assessed post intervention.

Results: Twenty-nine women were screened for this study. Twenty-seven met inclusion criteria and twenty-six participants were enrolled in the study (13 in each group). The intervention was determined to be feasible and had a recruitment rate of 96%, retention rate of 100%, and adherence rate of 89%. The intervention group had significantly higher physical activity levels (mean difference= 25.38, 95%CI=(9.35, 41.42) post intervention compared to the control group. No adverse events were reported.

Conclusions: This innovative KT intervention is feasible and demonstrates preliminary effects for secondary outcomes for women with breast cancer during chemotherapy. Findings support the examination of the intervention in a larger scale randomized trial.

Trial Registration: This trial is registered at ClinicalTrials.gov (NCT03087461).

Funding: The Hamilton Division of the Ontario Physiotherapy Association funded this project.

INTRODUCTION

The burden of cancer in Canadian women is growing; one in eight Canadian women are expected to develop breast cancer in their lifetime.[1] Breast cancer is the most common form of cancer in Canadian women (25.5% of female cancers).[1] With improved screening methods and new treatment approaches more women are surviving cancer; the five-year survival rate for breast cancer is 87%.[1] However, survivors are living with treatment related side effects for years after their cancer treatments have ended.[1-3] These include physical and emotional side effects such as fatigue, pain, loss of strength, loss of functioning, anxiety and depression.[1-3]

The benefits of exercise for women with breast cancer are well established in the literature.[4-7] Beneficial effects occur both during[8-10] and after treatment[11-13] and include improvements in treatment related physical[14,15] and psychological[16,17] side effects. In addition, preliminary evidence supports participation in regular exercise as a potential means to decrease breast cancer recurrence[18,19] as well as all-cause and cancer-specific mortality rates.[18-20] However, less than 30% of survivors self-report regular participation in exercise.[21-23] Barriers to exercise participation for this population show that a large proportion (>80%) are not educated on the benefits of exercise and physical activity during or after treatment.[21] Physical side effects, time and travel also pose barriers to participation.[21] Furthermore, health care professionals working in oncology describe institutional, personal, and patient level barriers to exercise promotion such as a lack of time with patients and a lack of funding for rehabilitation interventions, a lack of knowledge on proper exercise prescription, and patient side effects.[24] This highlights the need for novel knowledge translation (KT) strategies within cancer institutions that focus on easy-to-access exercise interventions and education delivered by rehabilitation professionals.[25]

Providing accessible and effective exercise strategies is important as the societal burden of cancer is projected to increase substantially over the next two decades; the number of new cases of breast cancer is projected to increase by more than 10,000 in Canada by the year 2032.[26] Exercise is a safe and low-cost way to manage this increasing burden.[6] Pilot work completed for this project suggested that in order to change clinical practice, implementation strategies should use accessible exercise options and education within the cancer institution to maximize women's engagement in exercise.[25] The inclusion of self-management education is vital to provide women with strategies so that they have knowledge and confidence to independently maintain healthy lifestyle behaviours, such as diet and exercise, on a daily basis over the long-term. Furthermore, self-management strategies result in beneficial effects on quality of life for women with breast cancer.[27,28]

A pilot study assessing the feasibility of methods and procedures is beneficial in informing a future larger scale trial.[29] This pilot study was undertaken to assess process and resource variables before implementation of a large-scale intervention.[30] Process variables include measuring recruitment rate, retention rate, and adherence rates to the intervention provided.[30] Resource variables include a center's willingness and capacity to house a specific intervention, referral sources, equipment availability, intervention location, and budget concerns.[30] There are currently no pilot trials for a KT intervention using exercise and self-management for women with breast cancer during chemotherapy within the cancer institution in Ontario, and therefore this study will aid in shaping and guiding a larger trial.

The purpose of this study is to determine whether KT strategies, focusing on an accessible exercise location and self-management education, are feasible and impact physical activity level, exercise knowledge and behaviour, quality of life (QOL), overall health status, and use of additional health care services among women with breast cancer. Specifically, the objectives of this project are to: (1) Determine the feasibility (through recruitment, retention and adherence rates) of providing a complex KT intervention designed specifically for women with breast cancer using technology, and (2) explore preliminary estimates of effects of the KT intervention on physical activity level, exercise knowledge and behaviour, health related quality of life, overall health status, and resource utilization among breast cancer survivors.

MATERIALS AND METHODS

Study Design & Participants:

This study is a single-centre pilot randomized controlled trial. Reporting of this trial is in accordance with the CONSORT guidelines for pilot and feasibility trials (http://www.equator-network.org/reporting-guidelines/consort-2010-statement-extension-to-randomised-pilot-and-feasibility-trials/). Eligible participants included: (1) community-dwelling, (2) English-speaking women, (3) over 18 years of age, (4) who were currently undergoing chemotherapy for Stage 1-3 BC and (5) had been cleared by their oncologist to participate in moderate intensity aerobic exercise. Participants were excluded from the study if they self-reported on the patient intake form any chronic condition, cognitive impairment, or injury that prevented them from participating independently in moderate intensity exercise. The Hamilton Integrated Research Ethics Board approved this study in April 2017 (#3124). This trial is registered at ClinicalTrials.gov (NCT03087461). A study protocol has been previously published.[31]

Procedure:

Recruitment:

Medical oncologists and Primary Care Nurses at the Juravinski Cancer Center (JCC) in Hamilton, Ontario identified possible participants for this study within their patient caseload. The oncologist or nurse obtained consent from the patient for the study investigator (JST) to contact them directly. The study investigator

(JST) also recruited patients at the JCC 'chemotherapy education class'. All patients receiving chemotherapy attend this class prior to starting their chemotherapy treatment. Potential participants were contacted by phone to discuss eligibility and potential study enrollment. All participants provided written informed consent prior to enrollment in this study.

Randomization & Allocation Concealment:

Prior to participant randomization, eligible participants completed baseline information and measures including: (a) patient information intake form, (b) consent form, and (c) baseline measures. A statistician not involved with the study created a computer generated randomization schedule. A research team member (JR), who was independent of the intervention, randomized participants on a record-by-record basis to the intervention or control group. Allocation of participant randomization was concealed in sequentially numbered, opaque, sealed envelopes by the same member of the research team. A research coordinator held the envelops and was responsible for releasing group allocating once the baseline assessment was completed. The study investigator (JST) informed the participant by phone or email of the assigned group allocation.

It was not possible to blind participants and the person administering the intervention was not blinded to group assignment. However, a researcher (JR) blinded to the group allocation of the participants conducted the statistical analysis.

Intervention:

This pilot study implemented a multi-dimensional KT intervention including an exercise and a self-management program.

The exercise intervention involved a moderate intensity aerobic exercise, using recumbent bikes, delivered within the cancer institution. Participants took part in up to 30-minutes of moderate intensity (50-70% HRmax or 4-6/10 on Rate of Perceived Exertion scale) aerobic exercise for 8 sessions during the course of their chemotherapy treatment. A physiotherapist with seven years of experience in cancer rehabilitation (JST), and trained in the specific protocol used for this study, supervised the intervention.

The self-management component included eight educational modules. Participants viewed these 15-minute modules on an iPad at the same 8 sessions. The goal of the self-management modules was to aid participants in developing physical activity goals and action plans to continue with between sessions, with an overarching goal of helping them reach exercise guidelines for cancer survivors[6] and the Canadian Physical Activity Guidelines.[32] Refer to **Table 1** for details of the self-management content for each session of the program.

Outcomes:

The feasibility and effectiveness of the intervention was assessed using quantitative outcomes.

Primary Outcomes:

The primary outcome of this pilot RCT was feasibility. This was assessed at baseline and post intervention, where applicable. Feasibility was assessed by measuring recruitment (percentage (%) of identified eligible patients who were recruited), retention (% of consented patients who completed the intervention), and adherence rates (% of sessions attended) to the intervention. A priori, feasibility of the intervention would be demonstrated if the following were achieved: a recruitment rate >50%, an adherence rate >75%, and a retention rate >75%. These values were chosen to determine feasibility based on previous research looking at exercise for women with breast cancer during chemotherapy. Adverse outcomes that resulted due to this intervention were also reported. Adverse outcomes considered included any form of orthopedic injury or pain, cardiac event, or trip or fall that occurring during or after the intervention that the participant related specifically to the exercise intervention provided.

Secondary Outcome Assessment:

Secondary outcomes were assessed pre and post intervention. At baseline, participants were instructed on how to complete each self-report measure by a study investigator (JST). The post-intervention assessments were completed in person or mailed to participants to complete and return to study investigators using pre-paid postage envelops. Assessors performing the analysis of data were blinded to participant group allocation.

Secondary Outcome Measures:

Physical activity level was assessed using the Godin Leisure-Time Exercise Questionnaire.[33] This is a self-report measure that gives weekly frequencies of strenuous, moderate, and mild activities and a total weekly leisure activity score, which classifies respondents into ‘active’ and ‘insufficiently active’ categories.[33] Use of a self-report measure to obtain this outcome, rather than an objective measure, is suitable because the aim of this project is to increase purposeful rather than random bouts of physical activity or lifestyle movement. Research has found this questionnaire to be reliable and valid to classify healthy populations[34] and individuals with cancer into ‘active’ and ‘insufficiently active’ groups.[35,36] Respondents are classified as ‘active’ by obtaining a leisure score index of 24 or more on this scale.[34-36] This outcome was added as an assessment after the study protocol was developed, but prior to recruitment in order to quantify activity levels of participants.

Level of exercise knowledge and behaviour was assessed using a Theory of Planned Behaviour (TPB) based questionnaire. The TPB has been used extensively to determine levels of intention and behaviour for various health behaviours, including exercise.[37,38] Although this specific measure has not been used for breast cancer populations, measures using the theory of planned behaviour components are supported in the literature for individuals with cancer.[38,39]

Quality of life was measured using the FACT-B,[40] a self-report measure designed to assess multi-dimensional QOL specifically for women with breast cancer. This measure is valid and reliable when used to assess quality of life in women with breast cancer.[40]

Health status was measured using the EQ-5D-3L.[41] This scale has two components: a descriptive scale assessing problems with five dimensions of health (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression), and a visual analogue scale recording respondents self-rated health on a scale of 0-10 (0 worst imaginable health state, 10 best imaginable health state).[41] The EQ-5D is a valid and reliable tool in assessing health status in individuals with cancer.[42]

Need for additional health care services was measured using a piloted self-report questionnaire assessing health care facility visits, overnight hospital stays, procedures received, and support services used.

Statistical Analysis:

For this project we calculated sample size based on the proportion of success of the primary outcome of feasibility (using estimates for adherence rates).[30,43,44] Using a Z value from the standard normal distribution to reflect a 95% confidence interval (1.96), E as the desired margin of error (0.2), and p as the proportion of successes in the population (0.75-estimated adherence rates), the sample size for this pilot study was to be at least 18 participants (9/group). With an expected drop out rate of 25%, based on previous exercise based literature with this population, the final sample size for this project was set at 23 participants. In order to ensure an even number of individuals be randomized to each group, this was rounded up to a total of 24 participants (12/group). Participant characteristics were analyzed at baseline to ensure no significant differences existed between groups. Means and standard deviations (SD) were used and independent t-tests or Wilcoxon-Mann-Whitney tests were used to assess differences between the two groups to report continuous variables. Frequencies were used to report categorical variables and Fisher's exact test was used to assess differences between groups for these variables.

Descriptive statistics were used to measure feasibility (recruitment rate, retention rate, and adherence rates). Recruitment rates were calculated by determining the percentage of identified eligible patients that were actually enrolled in the study. A recruitment log was kept, detailing reasons for non-participation of eligible patients. Retention rate was defined by calculating the percentage of enrolled patients who completed the intervention. Adherence rates were calculated as a percentage of total sessions attended. Attendance was tracked on the feasibility data collection sheet and reasons for non-participation on scheduled intervention days were documented using an adherence log.

Effectiveness outcomes were assessed pre and post intervention. As the main objective of this trial was to determine feasibility, these analyses are exploratory and will be used to guide a larger trial. Independent t-tests, Wilcoxon-Mann-Whitney tests, or Fischer's exact tests were used to explore between group differences where appropriate. An intention to treat analysis was used by imputing last observation carried forward. Refer to **Table 2** for a description of how each outcome was assessed. All statistical analysis was completed using STATA/MP 14.

RESULTS

Participants:

Twenty-six participants were included in this study. Recruitment took place between June-December 2017. See **Figure 1** for patient flow from referral to intervention completion. Baseline characteristics are included in **Table 3**. The scores for the control group on the Theory of Planned Behaviour Exercise Knowledge and Behaviour Questionnaire were significantly higher than participants in the intervention group at baseline. No significant differences existed in any other outcome between the two groups at baseline. The majority of participants had stage 2 (46%) or 3 (46%) breast cancer. The mean age for participants was 46.64 years (SD: 12.49), with the majority being in their 50's (31%). Only two of the participants reported a previous cancer diagnosis (8%). One participant, in the control group, failed to return post-chemotherapy outcome measures.

Feasibility Outcomes:

Recruitment Rate:

In total, 29 women were screened for eligibility in this study. Twenty-seven of these individuals were eligible for the study. One patient was ineligible due to stage of cancer (pathology report stage 4) and one because she had been diagnosed with dementia and was not able to understand the consent form. A total of 26 participants enrolled in the study (recruitment rate of 96%). No specific reason was given for the one eligible patient who did not enroll in the study; at last contact she wanted to discuss her suitability for the intervention with her oncologist and did not return follow up correspondence.

Retention Rate:

Retention rate to the intervention was 100%. All consented participants in the treatment group completed the intervention.

Adherence Rate:

Overall adherence to the intervention was 89%. A large portion of missed sessions were due to physical side effects of treatment (8 sessions, 35% of all missed sessions). Also numerous sessions were missed due to late referral to the study (12 sessions, 52%).

Adverse Events:

No adverse events occurred during the intervention.

Secondary Efficacy Outcomes:

Physical Activity Level:

Post intervention physical activity levels were significantly higher in the intervention group compared to the control group (mean difference= 25.38, 95%CI=(9.35, 41.42), p=0.003) as measured by the Godin Leisure-Time Exercise Questionnaire. Post chemotherapy 9 of 13 participants in the intervention group and 3 of 13 participants in the control group were classified as 'active' by obtaining a Godin Leisure-Time Exercise Questionnaire leisure score index of 24 or greater. See **Table 4** for details of the results.

Exercise Knowledge:

Post intervention exercise knowledge scores did not differ significantly between intervention and control groups (mean difference= 3, 95%CI= (-3.60, 9.60), p=0.36) as measured by the Theory of Planned Behaviour Questionnaire. See **Table 4** for details of the results.

Quality of Life:

There was no significant difference on the scores of the FACT-B between groups at follow-up (mean difference= -4.72, 95%CI= (-20.95, 11.51,), p=0.55). A minimal clinically important difference for the FACT-B is defined as a total score change of 7-8 points.[45] Neither group demonstrated clinically important changes between the two assessment points (intervention mean change score: -0.63 points, control mean change score: -6.1 points). See **Table 4** for details of the results.

Overall Health Status:

Overall health status was measured using the EQ-5D-3L. EQ-VAS scores were not significantly different between groups post intervention (mean difference: 0.27; (-1.44, 1.98). The number of problems identified on the EQ-5D-3L scale did not differ significantly between groups post intervention (p=0.74). See **Table 4** for details of the results.

Use of Health Care Services:

Figure 2 provides a description of the number of health care services utilized outside of regular cancer treatment for the intervention and control groups. One individual in the intervention group was excluded from all calculations, and one individual in the control group was excluded from support services usage calculations because they were identified as significant outliers (health care facility visit-total group mean=1, intervention outlier=5; overnight hospital stay-total group mean=0.64, intervention outlier=20; procedures-total group mean=0.72, intervention outlier=11; use of support services-total group mean=0.76, intervention outlier=16, control group outlier=17). Total number of health care facility visits was 25 (intervention group mean: 1.17, control group mean: 0.85), total number of overnight hospital stays was 16 (intervention group mean: 1.08, control group mean: 0.23), total number of procedures was 18 (intervention group mean: 1.08, control group mean: 0.38), and total number of support service visits was 19 (intervention group mean: 0.58, control group mean: 0.92).

DISCUSSION

The present study assessed the feasibility of an innovative knowledge translation intervention and explored the preliminary effectiveness of this intervention. The program was designed within the cancer institution for women with breast cancer during chemotherapy and used an aerobic exercise intervention alongside self-management education using technology. Feasible was to be demonstrated by a recruitment rate >50%, adherence rate >75%, and retention rate >75%. Results support the feasibility of the intervention with high values demonstrated for all measurements (Recruitment= 96%, adherence= 89%, and retention=100% respectively). Furthermore, positive outcomes related to the secondary measures of physical activity level supports the implementation of this study on a larger scale.

Compared to other physical activity intervention trials for women with breast cancer during chemotherapy, this study demonstrates high feasibility of outcomes. The recruitment rate for this study was 96%. Other studies on exercise interventions for women with breast cancer during adjuvant therapy have reported recruitment rates ranging from 33% to 55%.[46-49] One postulated reason for the high rate of recruitment to this study is the recommendation and support of the intervention program by the participants' oncologists. This support is important in promoting exercise behaviour in individuals with cancer.[39,50] However, this recruitment strategy may have led to an overestimation of recruitment rate as only those participants who gave consent to their oncologist for referral to the study were subsequently contacted and screened for eligibility by study investigators. Other studies commonly report recruitment rate based on total number of all eligible participants enrolled in the study, therefore this result should be interpreted with caution. Retention rate for the study intervention was 100%; all individuals who began the intervention program completed it. Retention rates demonstrated within the literature for exercise interventions for this population range from 75% to 98%.[46-49] Retention of study participants is important to ensure adequate power and internal validity of longitudinal research.[51,52] Retention strategies most commonly used in research include participant reminders, emphasis of study benefits, contacting/scheduling strategies, and study visit characteristics.[52] All of these strategies were considered within this intervention and the retention rate of 100% demonstrates that retention strategies were appropriate and successful and should be considered in the design of a future larger scale study. The adherence rate to the intervention presented in this study was 89%. Previous studies have reported adherence rates during chemotherapy for this population ranging from 67% to 79%.[46,48,49,53,54] However, this number may be an underestimation because many participants did not start the intervention until after they had received their first chemotherapy session (a total of 12 sessions missed, which had the potential to make the adherence rate 92.79% if all were attended). This highlights a process variable to consider before implementation of a larger study; how do we enroll participants earlier or prior to the start of their chemotherapy so that they can be offered all intervention sessions? Two suggestions to consider include (1) having a standardized referral form within all new patient charts available at treatment planning appointments or (2) having a rehabilitation professional screen individuals with breast cancer at the treatment planning appointment to determine program eligibility. Other common reasons for missed sessions include physical illness and hospitalization, which is consistent with previous literature.

The high feasibility outcomes demonstrated within this study are likely due to the unique parameters of the intervention provided. These include the smaller number of sessions provided within this intervention and that sessions were scheduled when participants were already coming to the cancer centre for another appointment promoted adherence and accessibility of the intervention. Additionally, a large focus of the intervention provided participants with the knowledge, skills, and tools to continue physical activity safely at home between sessions. Both of these components address barriers to exercise participation presented previously in the literature, including knowledge, cost, time, and travel.[21,22,55] More than 42% of participants in this study lived further than 20 km away from the cancer centre where they were being treated (26.92% lived greater than 50 km away). Some participants resided in rural areas of southwestern Ontario where access to physiotherapy and physical activity programs for cancer survivors does not exist locally. Providing exercise programming and self-management education within the cancer institution where they are treated addresses many of barriers to exercise participation for this group of Ontarians. Housing the intervention within the cancer institution for women undergoing chemotherapy also fosters communication between rehabilitation professionals and other health care professionals treating these patients.

Research exploring the use of the theory of planned behaviour to explain exercise behaviour in cancer survivors has shown that an individual's attitude and subjective norms contribute equally as strong predictors in determining a person's intention to exercise during and after treatment.[39] Disease specific characteristics are thought to highlight the importance of the subjective norm component of explaining behaviour (the perceived social pressure to perform a behavior), which is different from the general population who focus less on subjective norm influences and more on components related to perceived behavioural control.[39] For example, cancer is often an unpredictable disease where the individual has no past experience as a point of reference.[39] Therefore patients feel as though they have little control over their illness and rely more heavily on the experience of others including the opinions of trusted health care professionals.[39] Housing the intervention within the cancer centre allowed the medical team (oncologists, primary care nurses) to be more aware and supportive of the intervention and facilitated communication with the rehabilitation team. Thus, the intervention was successfully integrated into the care of women undergoing treatment.

The promising findings of the exploratory secondary outcomes are consistent with previous literature using exercise and physical activity for women with breast cancer during chemotherapy. Specifically, this intervention showed promising effects in regards to improving physical activity levels for women with breast cancer during chemotherapy. This is important as previous research has shown that exercise levels decrease significantly during adjuvant treatment[56,57] and knowing the benefits of regular exercise for this population in relation to symptom management and cancer recurrence.[4-20] It is also important to highlight that quality of life scores remained constant across the two assessment time points in the intervention group, while overall perceptions of health status significantly improved in the intervention group during the individual's chemotherapy. This is important, as previous studies on women undergoing chemotherapy treatment report a decrease in these two outcomes for women with breast cancer.[58,59] These findings provide evidence for the adoption of this novel intervention strategy to put the current research evidence into clinical practice. It supports the use of further exploration and analysis of these measures in a larger scale trial.

Limitations:

While this study describes the feasibility and effectiveness of a novel knowledge translation intervention, the results should be viewed with an understanding of its limitations. Firstly, the principle investigator was the physiotherapist who developed and delivered the intervention with participants. This may introduce “therapist effects” where this individual demonstrates a level of excitement or eagerness in the intervention that are relayed to participants that are peculiar to a study environment. Funding limitations for this pilot trial did not allow other health professionals to lead this intervention, however, in future studies therapists should ideally be independent. Secondly, due to the nature of the intervention, participants were not blinded to group allocation. This is common in rehabilitation research and may introduce bias. Knowledge of group assignment may affect participant’s behaviour and their responses to subjective outcome. Finally this study was not powered to demonstrate significant findings in the secondary outcomes listed. Sample size calculations were based on the primary outcome of feasibility. Furthermore, the outcome measures used for secondary outcome measures were all self-report measures. This may have elicited social desirability bias where individuals try to answer questions to portray themselves in the best way possible. Therefore, these results should be interpreted with caution.

Future Direction:

This study demonstrates the feasibility of implementing this intervention within a cancer centre for breast cancer survivors during chemotherapy. It strongly supports further investigation of this intervention within a larger scale trial. As this trial was a single centre pilot RCT the generalizability of results are limited to this geographical area in southwestern Ontario. We recommend using this data to implement a larger multi-centered trial within numerous settings in this geographical location. This will help to increase generalizability to other settings within Ontario and Canada and increase power for the outcome measures used. Additionally, we suggest creating a second, self-management only, treatment group (three groups total: (1) exercise plus self-management, (2) self-management only, and (3) usual care groups). This will allow researchers to explore which component of the intervention is most effective and what additional effect the exercise component has over self-management alone. Recruiting participants prior to the start of their chemotherapy session will be vital in ensuring they get the most benefit out of the intervention provided. Finally, future research should continue to explore strategies to make rehabilitation interventions accessible and available for all individuals with breast cancer. Education, socioeconomic status, and where you live should not affect accessibility to rehabilitation during and after cancer treatment. Having options available, free of charge, within the cancer centre for all individuals during adjuvant treatment is more likely to facilitate behavioural change. This has the potential to minimize the side effects of breast cancer treatment and prevent recurrence.

CONCLUSION

In summary, this study provides one strategy to bridge the gap and incorporate exercise evidence into clinical practice in breast cancer care in Ontario. Results of this study demonstrate the feasibility and promising effects for secondary outcomes, primarily physical activity levels during chemotherapy treatment. Together this supports further investigation of this intervention in a large-scale trial. Physiotherapists and exercise specialists should continue to advocate and support exercise and physical activity interventions for all women with breast cancer.

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REFERENCES

1. Canadian Cancer Society's Advisory Committee on Cancer Statistics. Canadian Cancer Statistics 2017. 6/17. http://www.cancer.ca/~/media/cancer.ca/CW/cancer%20information/cancer%20101/Canadian%20cancer%20statistics/Canadian-Cancer-Statistics-2017-EN.pdf?la=en.
2. Cella D, Fallowfield LJ: Recognition and management of treatment-related side effects for breast cancer patients receiving adjuvant endocrine therapy. Breast Cancer Res Treat 107(2):167-180, 2008
3. Ewertz M, Jensen AB: Late effects of breast cancer treatment and potentials for rehabilitation. Acta Oncol 50(2):187-193, 2011
4. Dennett AM, Peiris CL, Shields N, et al: Moderate-intensity exercise reduces fatigue and improves mobility in cancer survivors: a systematic review and meta-regression. J Physiother 62(2):68-82, 2016
5. Lynch BM: Sedentary Behavior and Cancer: A Systematic Review of the Literature and Proposed Biological Mechanisms. Cancer Epidemiol Biomarkers Prev 19(11):2691-2709, 2010

6. Schmitz KH, Courneya KS, Matthews C, et al: American College of Sports Medicine Roundtable on Exercise Guidelines for Cancer Survivors. Med Sci Sports Exerc 42(7):1409-1426, 2010
7. Cramp F, Byron-Daniel J: Exercise for the management of cancer-related fatigue in adults. Cochrane Database of Syst Rev (11):CD006145, 2012
8. van Vulpen JK, Peeters PHM, Velthuis MJ, et al: Effects of physical exercise during adjuvant breast cancer treatment on physical and psychosocial dimensions of cancer-related fatigue: A meta-analysis. Maturitas 85:104-111, 2016
9. Travier N, Velthuis MJ, Steins Bisschop CN, et al: Effects of an 18-week exercise programme started early during breast cancer treatment: a randomised controlled trial. BMC Med 8;13:121, 2015
10. Stene GB, Helbostad JL, Balstad TR, et al: Effect of physical exercise on muscle mass and strength in cancer patients during treatment-A systematic review. Crit Rev Oncol Hematol 88(3):573-593, 2013
11. Juvet LK, Thune I, Elvsaas IKO, et al: The effect of exercise on fatigue and physical functioning in breast cancer patients during and after treatment and at 6 months follow-up: A meta-analysis. Breast 33:166-177, 2017
12. Chou F, Dodd MJ, Paul SM: Timing and Sustainability of an Exercise Intervention in Women With Breast Cancer During and After Cancer Treatment. Oncol Nurs Forum 39(1):91-97, 2012

13. Schmitz KH, Ahmed RL, Troxel AB, et al: Weight Lifting for Women at Risk for Breast Cancer-Related Lymphedema A Randomized Trial. JAMA 304(24):2699-2705, 2010
14. Courneya KS, Segal RJ, Mackey JR, et al: Effects of aerobic and resistance exercise in breast cancer patients receiving adjuvant chemotherapy: A multicenter randomized controlled trial. J Clin Oncol 25(28):4396-4404, 2007
15. McNeely ML, Campbell K, Ospina M, et al. Exercise interventions for upper-limb dysfunction due to breast cancer treatment. Cochrane Database Syst Rev 6:CD005211, 2010.
16. Brown JC, Huedo-Medina TB, Pescatello LS, et al: The Efficacy of Exercise in Reducing Depressive Symptoms among Cancer Survivors: A Meta-Analysis. PLoS One 27;7(1):e30955, 2012.
17. Hagstrom AD, Marshall PWM, Lonsdale C, et al: Resistance training improves fatigue and quality of life in previously sedentary breast cancer survivors: a randomised controlled trial. Eur J Cancer Care 25(5):784-794, 2016
18. Ibrahim EM, Al-Homaidh A: Physical activity and survival after breast cancer diagnosis: meta-analysis of published studies. Med Oncol 28(3):753-765, 2011

19. Lahart IM, Metsios GS, Nevill AM, et al: Physical activity, risk of death and recurrence in breast cancer survivors: A systematic review and meta-analysis of epidemiological studies. Acta Oncol 54(5):635-654, 2015
20. Cormie P, Zopf EM, Zhang X, et al: The Impact of Exercise on Cancer Mortality, Recurrence, and Treatment-Related Adverse Effects. Epidemiol Rev 39(1):71-92, 2017
21. Fernandez S, Franklin J, Amlani N, et al: Physical activity and cancer: A cross-sectional study on the barriers and facilitators to exercise during cancer treatment. Can Oncol Nurs J 42(1):37-72, 2015
22. Courneya KS, Katzmarzyk PT, Bacon E: Physical activity and obesity in Canadian cancer survivors. Cancer 112(11):2475-82, 2008
23. Cheifetz O. Clinicians commentary on Sing et al. Physiother Can 65(2):192-3, 2013
24. Smith-Turchyn J, Richardson J, McNeely M, et al. Physical activity and breast cancer: A study on the barriers and facilitators to exercise promotion from the perspective of health care professionals. Physiother Can 68(4):383-390, 2016
25. Smith-Turchyn J, Richardson J, Tozer R, et al. Physical activity and breast cancer: Results of a focus group to devise novel exercise interventions for women with breast cancer. Clinical Nursing Studies 6(2):39-46, 2018

26. Canadian Cancer Society's Advisory Committee on Cancer Statistics. Canadian Cancer Statistics 2015. Canadian Cancer Society, 2015. http://www.cancer.ca/~/media/cancer.ca/CW/cancer%20information/cancer%20101/Canadian%20cancer%20statistics/Canadian-Cancer-Statistics-2015-EN.pdf?la=en
27. Van Dijck S, Neilssen P, Verbelen H, et al: The effects of physical self-management on quality of life in breast cancer patients: A systematic review. Breast 28:20-28, 2016
28. Boogaard L., Gater L., Mori M., et al. Efficacy of self-management programs in managing side effects of breast cancer: A systematic review and meta-analysis of randomized control trials. Rehabil Oncol 34(1):14-26, 2016
29. Everitt B: Medical Statistics from A to Z: A Guide for Clinicians and Medical Students. Cambridge University Press: Cambridge, 2006
30. Thabane L, Ma J, Chu R, et al: A tutorial on pilot studies: The what, why and how. BMC Med Res Methodol 10(1), 2010
31. Smith-Turchyn J, Richardson J, Tozer R, et al: Bridging the Gap: Incorporating Exercise Evidence into Clinical Practice in Breast Cancer Care in Ontario-A Pilot Randomized Control Trial Protocol. Cancer Stud Ther J 2(2):1-5, 2017.

32. Canadian Society of Exercise Physiologists. Canadian Physical Activity Guidelines. 7/18. http://csep.ca/CMFiles/Guidelines/CSEP_PAGuidelines_0-65plus_en.pdf.
33. Godin G, Shephard R: A simple method to assess exercise behavior in the community. Can J Appl Sport Sci 10(3):141-146, 1985
34. Amireault S, Godin G. The Godin-Shephard Leisure-Time Physical Activity Questionnaire: Validity Evidence Supporting its use for Classifying Healthy Adults into Active and Insufficiently Active Categories. Percept Mot Skills 120(2):604-622, 2015
35. Amireault S, Godin G, Lacombe J, et al: Validation of the Godin-Shephard Leisure-Time Physical Activity Questionnaire classification coding system using accelerometer assessment among breast cancer survivors. J Cancer Surviv 9(3):532-540, 2015
36. Amireault S, Godin G, Lacombe J, et al: The use of the Godin-Shephard Leisure-Time Physical Activity Questionnaire in oncology research: a systematic review. BMC Med Res Methodol 15:60, 2015
37. McEachan RR, Conner M, Taylor NT, et al: Prospective prediction of health- related behaviours with the Theory of Planned Behaviour: a meta-analysis. Health Psych Rev 5(2):97-144, 2011

38. Smith-Turchyn J, Richardson J: Critical Review of the Theory of Planned Behavior to Predict and Explain Exercise Behavior in Women with Breast Cancer. Crit Rev Phys Rehabil Med 27(1), 2015
39. Courneya KS, Friedenreich CM: Utility of the theory of planned behavior for understanding exercise during breast cancer treatment. Psycho-oncol 8(2):112-122, 1999
40. Brady MJ, Cella DF, Mo F, et al. Reliability and validity of the functional assessment of cancer therapy-breast quality of life instrument. J Clin Oncol 15(3):974-986, 1997
41. EuroQOL Group. EQ-5D-3L User Guide: Basic information on how to use the EQ-5D-3L instrument. Version 5.1. 2015. https://euroqol.org/wp-content/uploads/2016/09/EQ-5D-3L_UserGuide_2015.pdf.
42. Simon Pickard A, Wilke C, Lin H, et al: Health utilities using the EQ-5D in studies of cancer. Pharmacoeconomics 25(5):365-384, 2007
43. Hertzog MA: Considerations in determining sample size for pilot studies. Res Nurs Health 31:180-191, 2008
44. Cocks K, Torgerson D: Sample size calculations for pilot randomized trials: a confidence interval approach. J Clin Epidemiol 66:197-201, 2013
45. Eton DR, Cella D, Yost KJ, et al. A combination of distribution- and anchor-based approaches determined minimally important differences (MIDs) for four endpoints in a breast cancer scale. J Clin Oncol 57(9):898-910, 2004

46. Courneya KS, Segal RJ, Mackey JR, et al: Effects of aerobic and resistance exercise in breast cancer patients receiving adjuvant chemotherapy: A multicenter randomized controlled trial. J Clin Oncol 25(28):4396-4340, 2007
47. Djuric Z, Ellsworth JS, Weldon AL, et al. A diet and exercise intervention during chemotherapy for breast cancer. Open Obes J 3:87-97, 2011
48. Adamsen L, Quist M, Andersen C, et al: Effect of a multimodal high intensity exercise intervention in cancer patients undergoing chemotherapy: Randomised controlled trial. BMJ 339:b3210, 2009
49. Courneya KS, McKenzie DC, Mackey JR, et al: Subgroup effects in a randomized trial of different types and doses of exercise during breast cancer chemotherapy. Br J Cancer. 111:1718-1725, 2014
50. Jones L, Courneya KS, Fairey AS, et al: Effects of an oncologist's recommendation to exercise on self-reported exercise behavior in newly diagnosed breast cancer survivors: A single-blind, randomized controlled trial. Ann Behav Med 28(2):105-113, 2004
51. Fewtrell MS, Kennedy K, Singhal A, et al: How much loss to follow-up is acceptable in long-term randomized trials and prospective studies? Arch Dis Child 93(6):458-461, 2008

52. Abshire M, Dinglas VD, Cajita MI, et al: Participant retention practices in longitudinal clinical research studies with high retention rates. BMC Med Res Methodol 17(1):30, 2017
53. Pickett M, Mock V, Ropka ME, et al: Adherence to moderate-intensity exercise during breast cancer therapy. Cancer Pract 10(6):284-292, 2002
54. Courneya KS, Segal RJ, Gelmon K, et al: Predictors of adherence to different types and doses of supervised exercise during breast cancer chemotherapy. Int J Behav Nutr Phys 11:85, 2014
55. Blaney JM, Lowe-Strong A, Rankin-Watt J, et al: Cancer survivors' exercise barriers, facilitators and preferences in the context of fatigue, quality of life and physical activity participation: A questionnaire-survey. Psycho-Oncol 22:186-194, 2013
56. Andrykowski MA, Beachman AO, Jacobsen PB. Prospective, longitudinal study of leisure-time exercise in women with early-stage breast cancer. Cancer Epidemiol Biomarkers Prev 16(3):430-438, 2007
57. Kwan ML, Sternfeld B, Ergas IJ, et al: Change in physical activity during active treatment in a prospective study of breast cancer survivors. Breast Cancer Res Treat. 131(2), 2012
58. Kayl AE, Meyers CA: Side-effects of chemotherapy and quality of life in ovarian and breast cancer patients. Curr Opin Obstet Gynecol 18(1):24-28, 2006.

59. Tiezzi MF, de Andrade JM, Romao AP, et al: Quality of life in women with breast cancer treated with or without chemotherapy. Cancer Nurs 40(2):108-116, 2017

TABLES

Table 1: Self-Management Content

Session	Content
1	Side effects of treatment. Benefits of exercise for women with breast cancer. Types of exercise and safety precautions during exercise. What is self-management? How to participate in effective self-management. Introduction to goal setting/action planning.
2	Review of previous week goal/action plan. The importance of posture for women with breast cancer (common postural issues, how to assess posture, how to ensure optimal posture). Relaxation and breathing techniques to manage anxiety and stress. Goal setting & action planning.
3	Review of previous week goal/action plan. Appropriate exercise techniques to maintain/increase endurance: - Description of aerobic exercise - Types of aerobic exercise - Parameters for aerobic exercise Goal setting & action planning.
4	Review of previous week goal/action plan Appropriate exercise techniques to maintain/increase strength - Description of strengthening exercise - Types of strengthening exercise - Parameters for strengthening exercise Goal setting & action planning.
5	Review of previous week goal/action plan Other forms of Exercise (flexibility, yoga, Tia Chi, etc.) Appropriate exercise techniques to maintain/increase flexibility: - Description of flexibility exercises - Types of flexibility exercises - Parameters for flexibility exercise Other forms of exercise: - Other types of exercise: what are they? - Parameters for other forms of exercise Goal setting & action planning.
6	Review of previous week goal/action plan. Self-monitoring physical activity levels: - Introduction to Breast Cancer Physio Guide (App)

	- Introduction to Stanford Action Planning App - Other techniques to monitor physical activity levels Goal setting & action planning.
7	Review of goal/action plan. Communicating with others (family, health professionals) about exercise and physical activity. Available exercise programs in the community. How to move forward: how to evaluate progress. Goal setting & action planning.
8	Review of goal/action plan. Summary of self-management program. Moving forward. Questions/comments.

Table 2: Description of Outcome Assessment

Objective	Hypothesis	Outcome	Analysis Method
Determine the feasibility (through recruitment, retention and adherence rates) of providing a complex KT intervention including accessible exercise programs delivered within the cancer institution and a SM program designed specifically for women with BC using technology	Implementing and providing a complex KT intervention for women with BC is feasible (recruitment, retention, and adherence rates are 50%, 75%, and 75% respectively).	Recruitment Rate	Descriptive statistics (percentage (%) of eligible patients recruited). Recruitment logs were kept, detailing reasons for non-participation of eligible patients.
		Retention Rate	Descriptive statistics (% of consented patients who complete the intervention).
		Adherence Rate	Descriptive statistics (% of sessions attended). Adherence rates were tracked using the data collection sheet. Reasons for non-participation on scheduled intervention days were documented using adherence logs.
Determine preliminary estimates of effects of the KT intervention of exercise plus SM versus usual care among BC survivors over a four-month period.	Compared to the control group, BC survivors participating in the KT intervention will have higher levels of physical activity,	Physical activity level (using the Godin Leisure-Time Exercise Questionnaire)	Independent t-tests were used to assess between group difference post intervention (when the assumption for normality was met). Wilcoxon-Mann-Whitney test was used for analysis
		Levels of exercise knowledge and behaviour (using a Theory of Planned Behaviour based questionnaire)	

	exercise knowledge and behaviours and QOL, and less need for additional health care services.	Health related quality of life (using the FACT-B)	when data did not meet the assumption for normality.
		Health status (using the EQ-5D-3L VAS sub-scale)	
		Health status (using the EQ-5D-3L “Problems” sub-scale)	Fisher’s exact tests were used to assess difference between intervention and control groups post intervention for these categorical variables.
		Use of health care services (using a piloted self-report questionnaire assessing health care facility visits, overnight hospital stays, procedures received, and support services used)	

Table 3: Participant Characteristics

Characteristic	Intervention Group (n=13)	Control Group (n=13)
Mean age (SD), y	46.62 (12.75)	51.38 (11.88)
Breast Cancer Stage	Stage 1: 1 (3.85%) Stage 2: 5 (19.23%) Stage 3: 7 (26.92%)	Stage 1: 1 (3.85%) Stage 2: 7 (26.92%) Stage 3: 5 (19.23%)
Chemotherapy received	AC*: 2 (15.38%) AC&T*: 11 (84.62%)	AC*: 1 (7.69%) AC&T*: 12 (92.31%)
Home distance from JCC	> 50 km: 3 (23.08%) 20-49.9 km: 3 (23.08%) < 20 km: 7 (53.85%)	> 50 km: 4 (30.77%) 20-49.9 km: 1 (7.69%) < 20 km: 8 (61.54%)
Godin Leisure-Time Exercise Questionnaire (mean, (SD))	21.23 (21.87)	22.07 (17.17)
Exercise Knowledge Theory of Planned Behaviour Questionnaire (mean, (SD))	43.31 (4.07)	49.31 (4.75)
FACT-B (mean, (SD))	97.94 (14.31)	108.13 (22.56)
EQ-5D-3L Health Questionnaire-VAS	6.46 (2.59)	7.88 (1.39)
EQ-5D-3L Health Questionnaire-Health Profile	No problems: 0 1 problem: 4 2 problems: 7 3 problems: 1 4 problems: 1 5 problems: 0	No problems: 3 1 problem: 5 2 problems: 3 3 problems: 0 4 problems: 2 5 problems: 0

**AC: Anthracyclines/Cyclophophamide combination, T: Taxane*

*** Wilcoxon-Mann-Whitney test used for analysis*

Table 4: Results

Outcome	**Intervention Group (n=13)**	**Control Group (n=13)**	**Between Group Difference (mean difference= intervention group score - control group score); (95%CI); p-value)***
Godin Leisure-Time Exercise Questionnaire (mean (SD))	43.46 (23.02)	18.08 (15.97)	25.38; (9.35, 41.42); p=0.003
Exercise Knowledge & Behaviour Theory of Planned Behaviour Questionnaire (mean, (SD))	45.62 (8.15)	42.62 (8.16)	3; (-3.60, 9.60); p=0.358
FACT-B (mean, (SD))	97.31 (20.91)	102.03 (19.16)	-4.72; (-20.95, 11.51,); p=0.5542
EQ-5D-3L Health Questionnaire-VAS	7.35 (2.54)	7.08 (1.57)	0.27; (-1.44, 1.98); p=0.392**
EQ-5D-3L Health Questionnaire-Health Profile	No problems: 1 1 problem: 5 2 problems: 4 3 problems: 0 4 problems: 2 5 problems: 1	No problems: 3 1 problem: 5 2 problems: 2 3 problems: 1 4 problems: 2 5 problems:0	p=0.742

**p-values should be interpreted with caution, as these are exploratory*

*** Wilcoxon-Mann-Whitney test used for analysis*

FIGURES

Figure 1: CONSORT diagram. Patient Flow.

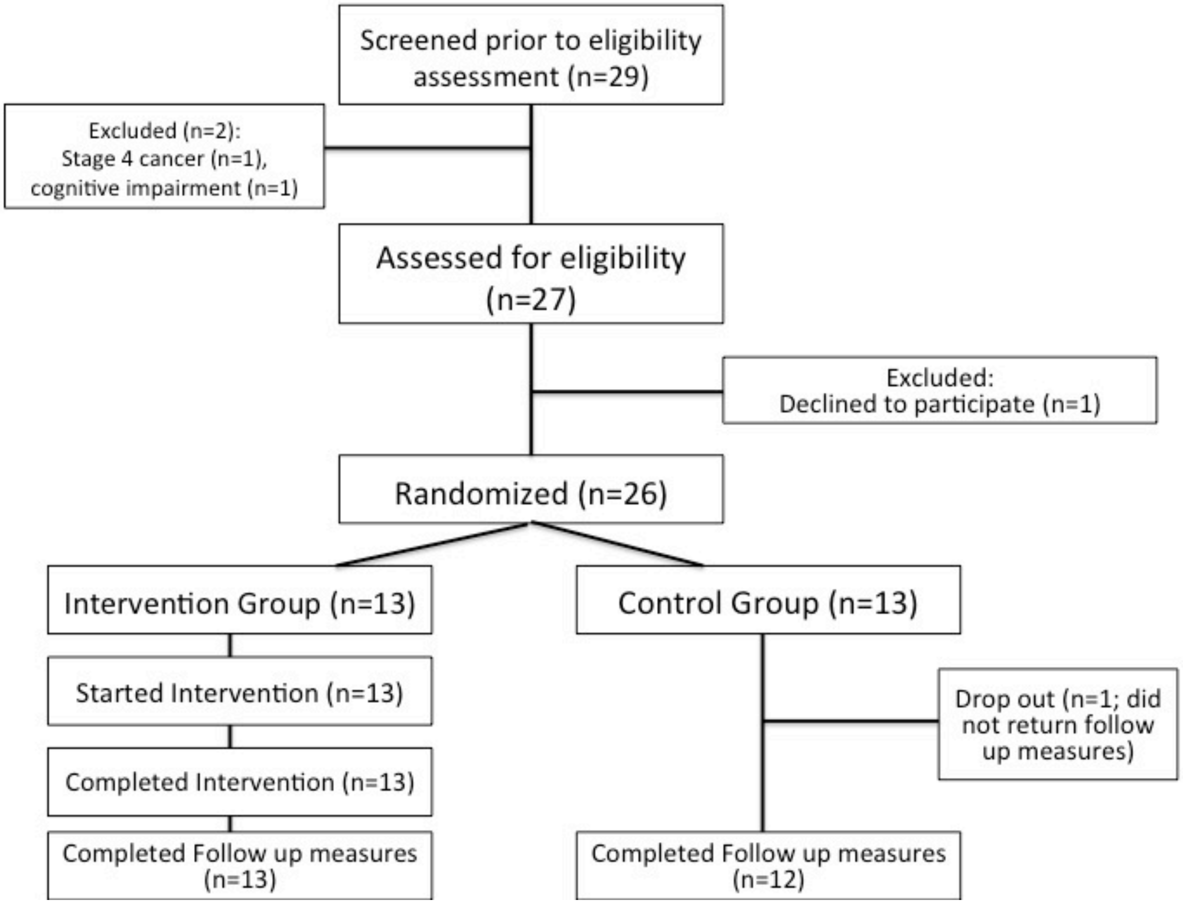
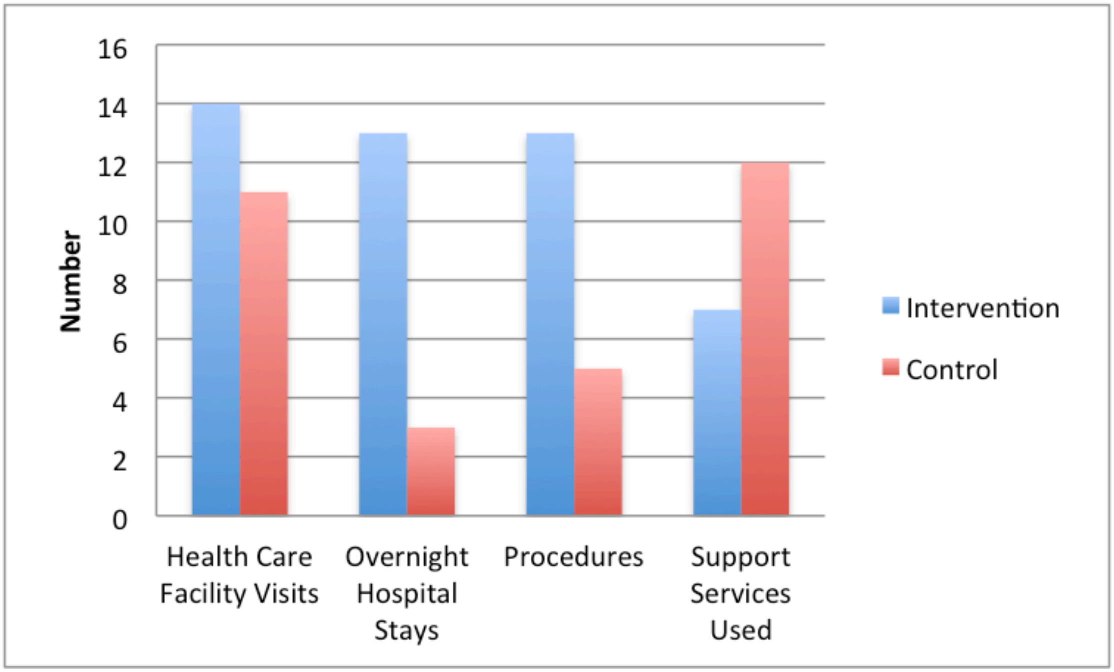


Figure 2: Use of Health Care Services



APPENDIX 1: CONSORT CHECKLIST FOR REPORTING A PILOT TRIAL

Section/Topic	Item No	Checklist item	Reported on page No
Title and abstract			
	1a	Identification as a pilot or feasibility randomised trial in the title	PG 1
	1b	Structured summary of pilot trial design, methods, results, and conclusions (for specific guidance see CONSORT abstract extension for pilot trials)	PG 2-3
Introduction			
Background and objectives	2a	Scientific background and explanation of rationale for future definitive trial, and reasons for randomised pilot trial	PG 3-4
	2b	Specific objectives or research questions for pilot trial	PG 5
Methods			
Trial design	3a	Description of pilot trial design (such as parallel, factorial) including allocation ratio	PG 5
	3b	Important changes to methods after pilot trial commencement (such as eligibility criteria), with reasons	NA
Participants	4a	Eligibility criteria for participants	PG 5
	4b	Settings and locations where the data were collected	PG 5-6
	4c	How participants were identified and consented	PG 6
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	PG 7
Outcomes	6a	Completely defined pre-specified assessments or measurements to address each pilot trial objective specified in 2b, including how and when they were assessed	PG 7-9
	6b	Any changes to pilot trial assessments or measurements after the pilot trial commenced, with reasons	PG 8-9
	6c	If applicable, pre-specified criteria used to judge whether, or how, to proceed with future definitive trial	PG 8
Sample size	7a	Rationale for numbers in the pilot trial	PG 10
	7b	When applicable, explanation of any interim analyses and stopping guidelines	NA
Randomisation:			

Sequence generation	8a	Method used to generate the random allocation sequence	PG 6
	8b	Type of randomisation(s); details of any restriction (such as blocking and block size)	PG 6
Allocation concealment mechanism	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	PG 6
Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions	PG 6
Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those assessing outcomes) and how	PG 6-7
	11b	If relevant, description of the similarity of interventions	NA
Statistical methods	12	Methods used to address each pilot trial objective whether qualitative or quantitative	PG 10-11
Results			
Participant flow (a diagram is strongly recommended)	13a	For each group, the numbers of participants who were approached and/or assessed for eligibility, randomly assigned, received intended treatment, and were assessed for each objective	PG 11-12, Figure 1
	13b	For each group, losses and exclusions after randomisation, together with reasons	PG 11-12, Figure 1
Recruitment	14a	Dates defining the periods of recruitment and follow-up	Figure 1
	14b	Why the pilot trial ended or was stopped	NA
Baseline data	15	A table showing baseline demographic and clinical characteristics for each group	Table 3
Numbers analysed	16	For each objective, number of participants (denominator) included in each analysis. If relevant, these numbers should be by randomised group	Table 4
Outcomes and estimation	17	For each objective, results including expressions of uncertainty (such as 95% confidence interval) for any estimates. If relevant, these results should be by randomised group	PG 12-14, Table 4
Ancillary analyses	18	Results of any other analyses performed that could be used to inform the future definitive trial	Table 3, Table 4
Harms	19	All important harms or unintended effects in each group (for specific guidance see CONSORT for harms)	PG 12
	19a	If relevant, other important unintended consequences	NA

Discussion			
Limitations	20	Pilot trial limitations, addressing sources of potential bias and remaining uncertainty about feasibility	PG 18
Generalisability	21	Generalisability (applicability) of pilot trial methods and findings to future definitive trial and other studies	PG 19
Interpretation	22	Interpretation consistent with pilot trial objectives and findings, balancing potential benefits and harms, and considering other relevant evidence	PG 14-19
	22a	Implications for progression from pilot to future definitive trial, including any proposed amendments	PG 19
Other information			
Registration	23	Registration number for pilot trial and name of trial registry	PG 5
Protocol	24	Where the pilot trial protocol can be accessed, if available	PG 5
Funding	25	Sources of funding and other support (such as supply of drugs), role of funders	PG 20
	26	Ethical approval or approval by research review committee, confirmed with reference number	PG 5

**Citation: Eldridge SM, Chan CL, Campbell MJ, Bond CM, Hopewell S, Thabane L, et al. CONSORT 2010 statement: extension to randomised pilot and feasibility trials. BMJ. 2016;355.*

CHAPTER 6: DISCUSSION

Breast cancer is the most prevalent form of Cancer in Canadian women (Canadian Cancer Society's Advisory Committee on Cancer Statistics (CCSACCS), 2017). Breast cancer mortality rates are the lowest they have been since the 1950's; since the late 1980's over 32,000 breast cancer deaths have been avoided due to improved screening techniques and advances in breast cancer treatments (CCSACCS, 2017). It is well documented that survivors live with physical, psychological and social sequela of the condition and its treatments for years after treatments have ended (Cella & Fallowfield, 2008; Ewertz & Jensen, 2011). The Public Health Agency of Canada estimated that cancer accounts for $4.4 billion in economic costs including direct health care costs and indirect costs (CCSACCS, 2017). With Canada's aging population and the rise in breast cancer survival rates, these costs are expected to grow exponentially in the next decade (CCSACCS, 2017). Exercise can be used to manage the treatment related side effects associated with cancer (Schmitz et al., 2010; Cramp & Byron-Daniel, 2012; Shobeiri, Masoumi, Nikravesh, Moghadam & Karami, 2016; Murtezani et al., 2014; Blacklock, Rhodes, Blanchard & Gaul, 2010; Schmitz et al., 2010-2; Winters-Stone et al., 2013; McNeely et al., 2010; Cramer et al., 2017; Cramer, Lange, Klose, Paul & Dobos, 2012; Mustian, Palesh & Flecksteiner, 2008), however, exercise is not a regular component of cancer care for all women with breast cancer in Canada (Courneya, Katzmarzyk &

Bacon, 2008; Fernandez et al., 2015; Schmidt, Wiskemann, Ulrich, Schneeweiss & Steindorf, 2017). Knowledge translation research is needed to determine novel ways to bridge the gap and effectively incorporate the research evidence into clinical practice (Santa Mina et al., 2012).

This thesis included four manuscripts. Together the aim of these projects was to develop, implement, and evaluate meaningful strategies to move the research evidence into practice and increase exercise knowledge and behaviour in women with breast cancer. Below, a brief summary of each study is presented along with implications for practice and research. This is followed by a description of overall thesis contributions to the field of cancer rehabilitation, a discussion of the limitations of this work, and suggestions for future research.

Summary of Findings from Individual Manuscripts

Chapter 2: Physical Activity and Breast Cancer: A Qualitative Study on the Barriers to and Facilitators of Exercise Promotion from the Perspective of Health Care Professionals

The purpose of this study was to determine the barriers to and facilitators of exercise promotion by health care professionals for women with breast cancer. Results of this study added new information to the field of cancer rehabilitation and found that barriers to exercise promotion exist at the institutional, health care professional, and patient level. The most commonly described institutional barriers included a lack of time with each patient, a lack of identification of which health professional's role it was to discuss exercise, and a lack of funding for both exercise interventions and for the role of rehabilitation professionals within the cancer institution. Health care professionals stated their own personal barriers included a lack of knowledge related to specific exercise prescription, viewing exercise as a low priority in relation to their other responsibilities, and simply omitting to discuss exercise in the busy institutional environment. Health care professionals also reported perceived patient barriers, including patients having a negative attitude towards exercise, poor accessibility to exercise programs, insufficient time, and experiencing side effects, as reasons why they did not promote exercise with their patients. They also described the complexity of the patient and the availability of services and resources as important factors in whether or not they discussed exercise. One of the clinical implications derived from this project is that successful exercise promotion by health care professionals is dependent on multiple factors, including the ability to overcome the institutional, health care professional, and perceived patient barriers as described above. Exercise promotion was also variable depending on an individual patients characteristic, such as medical comorbidities, psychosocial issues, pre-cancer fitness level, and treatments received (refer to Table 4 and Figure 1, Chapter 2). Therefore, to increase the likelihood of exercise promotion by health care professionals for women with breast cancer, rehabilitation professionals and researchers need to create interventions that both minimize the described health promotion barriers and consider the complexity of this population while providing easy access to sustainable resources and services.

Chapter 3: Physical Activity and Breast Cancer: Results of a Focus Group to Devise Novel Exercise Interventions for Women with Breast Cancer

The purpose of this study was to bring together a multidisciplinary group of health care professionals to determine innovative exercise intervention strategies to implement within the cancer care institution to overcome exercise related barriers. The goal of this project was to reach a consensus on specific exercise interventions to implement in the final phase of this project (related to type of exercise, specific location within the institution, delivery of the services, and timing in relation to patient treatment plans). Results suggested three approaches to overcome current barriers to exercise participation and promotion. Firstly, it was strongly suggested that an on-site exercise program was needed for this patient population. Having an exercise program available on site was thought to have the potential to decrease patient accessibility problems (with regard to cost and transportation). It would also increase exercise awareness, by having patients and their families view others in similar situations participating safely in exercise. Secondly, all participants agreed that having a rehabilitation professional on site would allow them to give their patients better information to support their rehabilitation needs. The strategies proposed for including a rehabilitation professional within the institution varied from having a physiotherapist perform pre-treatment functional assessments and triaging patients based on their needs, to providing general education on physical activity and exercise, or providing exercise interventions on site. Finally, all participants agreed that more effective self-management educational strategies describing the benefits of exercise during and after breast cancer treatment were needed for patients and their families. All focus group participants thought this should be done through the use of technology. This study highlighted the perceived importance that rehabilitation has within the cancer trajectory. The overwhelming consensus was that rehabilitation should be included as part of the health care services provided to women with breast cancer within the cancer institution. It provides rehabilitation clinicians and researchers specific strategies to overcome the barriers to exercise and to increase exercise knowledge and participation for this patient population.

Chapter 4: Bridging the Gap: Incorporating Exercise Evidence into Clinical Practice in Breast Cancer Care in Ontario-A Pilot Randomized Control Trial Protocol

This manuscript was a study protocol for the pilot randomized controlled trial to be conducted in Chapter 5. The intervention described within this protocol was created based on the results obtained from Chapter 3 and current research evidence. The purpose of this protocol was to describe a pilot study that would assess the feasibility and effectiveness of conducting an innovative knowledge translation intervention for breast cancer survivors using exercise and self-management versus usual care. The publication of trial protocols is important to enhance the transparency of research being conducted (Skogvoll & Kramer-Johansen, 2013; Eysenbach, 2004). It also reduces publication bias, prevents selective reporting of outcomes, and helps fellow researchers, patients, and the public knows what trials are occurring (Skogvoll & Kramer-Johansen, 2013; Eysenbach, 2004). The publication of study protocols allows researchers to gain feedback through peer review prior to implementation of the trial (Eysenbach, 2004). The primary outcome of feasibility was to be assessed through recruitment, retention and adherence rates. These were to be measured at baseline and post treatment where applicable. The intervention was to be considered feasible if the recruitment rate reached >50%, adherence rate >75%, and retention rate >75%. The outcomes of these analyses are described in Chapter 5. Effectiveness of secondary outcomes related to exercise knowledge and behaviour, health related quality of life, and overall health status were to be measured at four time points: baseline, post chemotherapy, and at 2- and 4-month follow up. Level of exercise knowledge and behaviour was to be assessed using a Theory of Planned Behaviour (Ajzen, 1991) based questionnaire. Health related quality of life was to be measured using the FACT-B (Brady et al., 1997), while the EQ-5D-3L (Simon Pickard, Wilke, Lin & Lloyd, 2007) was to be used to give an overall impression of health status. Health care resource utilization was to be measured using a piloted questionnaire at three time points: post chemotherapy, and at 2- and 4- month follow up. The outcomes of the baseline and post intervention analyses are described in Chapter 5. The outcomes related to the 2- and 4- month follow up periods are currently being collected and analyzed and will be reported in a manuscript later this year. Together, the outcomes of these analyses will have important implications for both clinicians and researchers. Firstly, the feasibility outcomes help to determine the need for and willingness of patients and the institution to house an innovative exercise and self-management intervention program. These outcomes will help to guide future implementation of interventions within the institution and provide insight into which variables need to be considered to increase the likelihood of success with this program. Secondly, the analyses of secondary outcomes explore preliminary estimates of effect for important outcomes for patients with breast cancer. This will provide clinicians and researchers' realistic outcome expectations in the short and long term for their patients related to these results.

Chapter 5: Bridging the Gap: Incorporating Exercise Evidence into Clinical Practice in Breast Cancer-A Pilot Randomized Control Trial

The overall purpose of this study was to determine the feasibility (through recruitment, retention and adherence rates) of providing a complex KT intervention designed specifically for women with breast cancer using technology. This study also set out to explore preliminary estimates of effects of the KT intervention on physical activity level, exercise knowledge and behaviour, health related quality of life, overall health status, and resource utilization among breast cancer survivors. The results show that the intervention was feasible. This was demonstrated by a study recruitment rate of 96%, intervention retention rate of 100%, and intervention adherence rate of 89%. This study highlighted an important process variable to be addressed prior to larger implementation of this study. How do we recruit, screen, and enroll participants into the intervention prior to their first chemotherapy treatment? The feasibility outcomes strongly support the implementation of this intervention within a larger scale study. The exploratory findings of secondary outcomes found a significant between group difference in physical activity levels post intervention (mean difference= 25.38, 95%CI=(9.35, 41.42), p=0.003) as measure by the Godin Leisure-Time Exercise Questionnaire. No significant between group differences were found for exercise knowledge scores, health related quality of life, or overall health status. While the secondary analysis was exploratory, the results support the implementation of this intervention within a larger trial. These results suggest that this innovative knowledge translation intervention housed within the cancer centre is feasible, safe, and may be effective in overcoming some of the barriers to exercise for women with breast cancer. This intervention is likely also to increase accessibility to rehabilitation services for women with breast cancer who otherwise would not have had access to these services, either due to financial constraints or geographical location. In addition, housing the intervention within the cancer centre fostered communication and support of this rehabilitation program by the participant’s health care team. Oncologists referred patients to the study, and therefore supported the inclusion of exercise into the participant’s daily lives, and often requested feedback on the participant’s progress in regards to exercise and physical activity. This continued communication about the exercise intervention may have aided in the high feasibility outcomes demonstrated within this study.

Contribution of Thesis Work to the Field of Cancer Rehabilitation

Knowledge Translation Framework:

Together, the studies conducted within this thesis project have made an important contribution to cancer rehabilitation knowledge translation research in Canada. The knowledge to action model was used to build on current research evidence and determine strategies to bridge the current knowledge to practice gap in breast cancer rehabilitation. This model includes two main parts; the knowledge funnel and action cycle (Graham et al., 2006). The knowledge funnel represents the process of how knowledge is refined, distilled, and tailored to the needs of the knowledge end users and includes three steps: knowledge inquiry, knowledge synthesis, and knowledge tools/products (KT Clearinghouse, 2014). Previous research has provided knowledge related to the identified benefits of moderate intensity exercise for women with breast cancer. (Cramp & Byron-Daniel, 2012; Shobeiri et al., 2016; Murtezani et al., 2014; Blacklock, Rhodes, Blanchard & Gaul, 2010; Schmitz et al., 2010-2; Winters-Stone et al., 2013; McNeely et al., 2010; Mishra, et al., 2012; Cramer et al., 2017; Cramer, Lange, Klose, Paul & Dobos, 2012; Mustian et al., 2008). Benefits include improvements in outcomes of cancer related fatigue (Level 1A, SMD: -0.27, 95% confidence interval (CI): -0.37 to -0.17) (Cramp & Byron-Daniel, 2012), post-operative shoulder range of motion (Level 1A, weighted mean difference: 12.92 degrees, 95% CI: 0.69 to 25.16) (McNeely et al., 2010), lymphedema occurrence in at risk individuals (Level 1B, cumulative incidence difference= -15.0%, 95% CI= -18.6% to -11.4%) (Schmitz et al., 2010-2), bone mineral density at the hip (Level 1B, $p<0.01$) (Winters-Stone et al., 2013), anxiety (Level 1A, SMD= -0.26, 95% CI= -0.07 to -0.44) (Mishra et al., 2012), and quality of life (Level 1A, SMD 0.48, 95% CI= 0.16 to 0.81 (Mishra et al., 2012), and Level 1B, $p<0.001$ (Shobeiri et al., 2016). This knowledge has been analyzed and synthesized into exercise guidelines for this population (Schmitz et al., 2010; Segal et al., 2015). The action cycle is used to describe the phases of activities that are needed for knowledge applications to lead to actual behavioural change (KT Clearinghouse, 2014). The seven phases of the action cycle include: (1) identify the knowledge-to-action gaps, (2) adapt knowledge to local context, (3) assess the barriers to knowledge use, (4) select/tailor/implement interventions, (5) monitor knowledge use, (6) evaluate outcomes, and (7) sustain knowledge use (KT Clearinghouse, 2014). Prior to the work of this thesis, a knowledge to practice gap in the field of cancer rehabilitation had been identified (action cycle stage 1); the benefits of regular exercise were clear, however, few survivors took part in regular physical activity and exercise (Courneya et al., 2008; Fernandez et al., 2015; Schmidt, Wiskemann, Ulrich, Schneeweiss & Steindorf, 2017). The knowledge had been adapted to the local context of southwestern Ontario; a gap had been identified and the needs of this population related to cancer rehabilitation had been stated (Fernandez et al., 2015; Santa Mina et al., 2012). Also, community based programs had been developed for individuals with cancer, but uptake was low (Cheifetz, 2014) (action cycle stage 2). Also, a substantial body of research had described the barriers and facilitators to exercise participation from the patient's perspective (action cycle stage 3) (Blaney et al., 2010; Sander, Wilson, Izzo, Mountford & Hayes, 2012; Brunet, Taran, Burke & Sabiston, 2013; Fernandez et al., 2015). This thesis provided information to move this field of work forward starting at the third action cycle stage (assess the barriers to knowledge use) and ending at the sixth (evaluate outcomes) stage of the action cycle. Chapter 2 built on the literature describing barriers to exercise participation for women with cancer by providing new information on health care professional barriers to exercise promotion (action cycle stage 3). Chapter 3 addressed the fourth stage of the action cycle by using a multi-disciplinary focus group to select and tailor interventions to the needs of end users. Chapter 4 and Chapter 5 built on these findings by implementing the interventions developed in Chapter 3 (stage 4 of the action cycle), while Chapter 5 monitored the knowledge use and evaluated outcomes of the knowledge translation strategy (stages 5 and 6 of the action cycle). Future work must address the seventh and final stage of the action cycle by examining the sustainability of this knowledge use. Conducting follow up assessments of secondary outcomes at long term follow up is one way to do this. See **Table 1** for a summary of the knowledge to action stages covered in this thesis project.

Theoretical Considerations:

The Theory of Planned Behaviour (TPB) (Ajzen, 1991) was used as the theoretical foundation in the development of interventions within this thesis. The TPB is one of most influential theoretical models of behavioural change to accurately explain health related behaviours, including exercise (Manstead, 2011; Godin & Kok, 1996). The concepts in the TPB that explain behavioural intention include an individual's attitude (the degree that a person has a favourable or unfavourable evaluation of the behaviour in question), subjective norms (social pressure to perform a behaviour), and perceived behavioural control (a person's perception of their ability to perform the behaviour of interest) (Ajzen, 1991). The interventions in Chapters 4 and 5 of this thesis addressed these components during development. Specifically, the recruitment strategy was based on the subjective norm component of this theory; members of the health care teams suggested enrollment and supported the intervention. The content within the self-management modules was created in part to improve the attitude of participants in relation to exercise during and after cancer treatment and to increase their perceived behavioural control to exercise throughout the cancer trajectory. Finally, the outcome measures chosen reflect the importance of assessing these components. Specifically, a TPB Questionnaire was used to assess all components of this theory and the Godin Leisure-Time Exercise Questionnaire was used to assess exercise behaviour. Future work should continue to explore the use of the TPB to predict and explain exercise behaviour in women with breast cancer. However, affective processes (such as physical and emotional distress) are not well accounted for in this theory. These are important considerations for women with breast cancer during treatment and may affect exercise behaviour, even when intentions are high. Therefore, further exploration for the most appropriate theory to use to explain exercise behaviour for this population may be needed. Bandura's Social Cognitive Theory may be more suitable to take affective processes into considerations (Bandura, 1989). Also, adherence rates may be further increased if intervention strategies are tailored specifically to an individual's stage of change, as described in the Trans-theoretical model (Prochaska & Velicer, 1997). Theory-based exercise interventions specifically designed for women with breast cancer should be further explored in future research.

Overall Contributions:

The stages of this thesis project involved various stakeholders, built on one another and informed subsequent actions in order to provide a meaningful intervention for this population. The early and continuous involvement of various stakeholders was necessary to ensure support and advocacy from members of the interdisciplinary team and institutional support, when driving this program forward.

The most substantial contribution of this thesis to cancer rehabilitation was the success of the unique parameters of the intervention provided. Current literature finds exercise to be effective in managing side effects both during treatment (van Vulpen, Peeters, Velthuis, van der Wall & May, 2016; Travier, et al., 2015; Stene, et al., 2013) and after cancer treatments have ended (Juvet, et al., 2017; Chou, Dodd & Paul, 2012). In Canada, oncology rehabilitation services are not a usual part of treatment provided for individuals with cancer (Santa Mina et al. 2012; Canestraro et al., 2013). A recent study found only 20 sites offering cancer rehabilitation programs across Canada (Canestraro et al., 2013). These sites included a mix of hospital based (n=10) (Segal et al., 1999; Santa Mina et al, 2012; Chasen, Feldstain, Gravelle, MacDonald & Pereira, 2013) and community based programs (n=5) (Nobel, Russell, Kraemer & Sharratt, 2012; Cheifetz et al., 2014) and the majority focused on survivors post treatment (Canestraro et al, 2013). A large portion of interventions delivered in recent research studies are delivered in community centers not directly linked with the health care facility where individuals with cancer are treated (Cheifetz et al, 2014; Demark-Wahnefried et al., 2015; Nock et al., 2015, Schmitz et al., 2010-2). The intervention sessions provided within these programs occurred multiple times each week (Canestrara et al., 2013). Findings in this thesis show that an eight session exercise intervention housed within the cancer institution coupled with disease specific self-management focusing on goal setting and action planning was feasible and has the potential to benefit women with breast cancer while undergoing chemotherapy. A novel parameter of this intervention was the number of sessions provided; only eight "in-person sessions" were delivered to participants. These were performed over the course of the individual's chemotherapy treatment, usually once every two weeks immediately prior to chemotherapy treatments. It is likely that having less frequent face-to-face sessions and having them occur when the individual was already coming into the cancer centre for another appointment led to the high adherence and retention rates seen within this study. Having the intervention occur during chemotherapy is important to introduce patients to the benefits of exercise early in their cancer trajectory. This allows women to develop strategies to maximize the timing and frequency of physical activity into their daily lives. Research has suggested early integration of rehabilitation strategies to manage functional sequela for breast cancer survivors (Campbell et al., 2012).

There is also great variability in the literature in regards to who should provide cancer rehabilitation interventions. Canadian literature in this field shows this is most often done by a physiotherapist (Segal et al., 1999; Chasen et al., 2013; Canestraro et al, 2013), or kinesiologist/exercise specialist (Santa Mina et al., 2012; Nobel et al., 2012; Canestraro et al, 2013). Nurse led cancer rehabilitation programs are also found in the literature (de Leeuw & Larsson, 2013). Findings in this thesis highlight that there is a lack of defined role around which health care professional is to discuss exercise with women with breast cancer in Ontario (Chapter 2). This confusion is especially apparent in this area of Canada, where neither physiotherapists nor other exercise specialists are included as part of the health care team treating patients with breast cancer within the institution. A solution to this problem would be to include physiotherapists on the oncology health care team in Ontario to fill this role and conduct functional screenings. Physiotherapists are appropriate to fill this role, as they are exercise specialists trained in exercise prescription for individuals with chronic conditions. An alternative solution would be to have physiotherapists act as consultants for other health professionals related to exercise, physical activity, and functioning within the cancer institution. This would allow other health care professionals to deliver more specific exercise promotion information and to make the delivery of this information more effective. Continued advocacy across Canada for the role of physiotherapy within the cancer institution is needed.

This thesis also contributes to the literature supporting the use of self-management strategies for women with breast cancer. A recent systematic review and meta-analysis found self-management programs for breast cancer survivors effective in improving quality of life, psychological distress, coping, and levels of fatigue (Boogaard, Gater, Mori, Trincado & Smith-Turchyn, 2015). However, only nine studies were found for inclusion in this review. These interventions had large variability in the parameters of the self-management interventions used (Boogaard et al., 2015), with only three trials including specific education on exercise. Goal setting and action planning were not described as a specific component of these programs (Boogaard et al., 2015). The self-management program used in this thesis project contributes to the literature in cancer rehabilitation by providing disease specific self-management information related to exercise during and after breast cancer treatment. For this thesis project, eight modules were developed using Microsoft PowerPoint and were delivered on a laptop computer or iPad to intervention group participants during or after each individual exercise session. A critical focus of the intervention was to provide participants with the information for them to become active self-managers of their condition early on in the course of their disease trajectory. Through education, discussion, goal setting, and action planning women in the intervention group became more knowledgeable about the physical aspects of their condition and how to deal with these conditions if they arose. Women also were able to set realistic, achievable, personalized exercise and physical activity goals and action plans for themselves in between sessions. The physiotherapist who led the program was present during these sessions and available to answer any questions that arose as participants viewed the modules. The physiotherapist also assisted participants in the goal setting and action-planning processes as needed. This was especially important during initial sessions where women were learning these skills. Including self-management as a component of this intervention likely led to the high levels of physical activity that were demonstrated within the intervention group during chemotherapy treatment. Having patients develop effective self-management skills early on in their treatment has the potential to allow this process to carry forward into survivorship phases of care in order to prevent an unnecessary decline in physical activity and function in survivors.

Limitations and Future Research

The limitations of each Chapter of this thesis project are described within each manuscript. However, there are some general limitations of this project. Firstly, all parts of this thesis project were conducted at the Juravinski Cancer Centre in Hamilton, Ontario. This is a regional health team and therefore professionals involved within this team practice and communicate with other health professionals working with this population in southwestern Ontario. However, this limits the generalizability of the results to this specific area of southwestern

Ontario. Secondly, the principal investigator was the physiotherapist who led all parts of this study. In Chapter 2 and Chapter 3, the health care professionals were aware of this and were aware of the beliefs of the investigators, which may introduce bias in the results. In Chapter 5 the principle investigator also led the intervention. This makes it difficult to discriminate intervention effects from therapist effects. Lastly, Chapter 5 was not powered to determine intervention effectiveness for the secondary outcome measures. The goal of this trial was to determine feasibility; therefore sample size calculations were based on the feasibility outcomes and the secondary analyses should be viewed with caution and regarded solely as rationale for implementation of a larger scaled trial. Therefore, future research should include a larger scale, multi-centered trial where the intervention is powered to determine effectiveness of secondary measures and run by a variety of health care professionals. In order to determine the active ingredients of the intervention provided in Chapter 5 it is also suggested that future research include a third intervention group which receives the self-management education modules only (groups to include (1) self-management plus exercise, (2) self-management only, (3) usual care). This will help to determine the effectiveness of exercise in addition to self-management education alone. In addition, conducting a detailed cost analysis of the intervention components will be important to rationalize inclusion of this program within the current system and to ensure sustainability. Future research should also look at additional outcomes of this intervention, such as chemotherapy completion rate. It is also suggested that a qualitative component be incorporated into future analysis in order to determine the key components of the intervention that support adherence. This is necessary as we strive to facilitate sustainable behavioural change in this population.

Conclusions

In summary, this dissertation contributes to the literature by identifying barriers to exercise promotion for health care professionals working with women with breast cancer. These include institutional, health professional, and perceived patient barriers. Secondly, this thesis project identified strategies to overcome these barriers. This included the need for an on site exercise program for this population, the need for a rehabilitation professional on site for patients and fellow health care professionals to access, and finally more effective educational strategies on the benefits and parameters of exercise for this population, which use technology. Lastly, this project took these suggestions and determined the feasibility of an innovative exercise and self-management intervention housed within the cancer institution for women with breast cancer during chemotherapy. Collectively, this project used the knowledge to action cycle to determine one strategy to bridge the gap and incorporate exercise evidence into clinical practice in breast cancer care in Ontario.

Table 1: Knowledge-to-Action Framework, Action Cycle Stages

Action Cycle Stage	Previous Research	Thesis Contribution
1 (Identify Problem)	Identified a knowledge to practice gap between the research evidence, supporting the use of exercise to minimize the side effects of breast cancer treatment, and clinical practice.	
2 (Adapt knowledge to local context)	Identified the research gaps and practices related to exercise for women with breast cancer in southwestern Ontario. Explored the needs of breast cancer survivors related to cancer rehabilitation.	
3 (Assess barriers to knowledge use)	Identified barriers and facilitators to exercise participation from the patient's perspective.	**Chapter 2:** Identified barriers to and facilitators of exercise promotion from the perspective of health care professionals for women with breast cancer.
4 (Select, tailor, implement interventions)		**Chapter 3:** Selected and tailored the most appropriate interventions to close the knowledge to practice gap for women with breast cancer. **Chapter 4:** Developed a protocol describing the implementation process of an innovative KT exercise and self-management program for women with breast cancer. **Chapter 5:** Implemented the intervention in a group of women with breast cancer.
5 (Monitor		**Chapter 5:** Assessed the feasibility and preliminary

knowledge use)		effectiveness of the innovative KT intervention for this population.
6 (Evaluate outcomes)		**Chapter 5:** Assessed the feasibility and preliminary effectiveness of the innovative KT intervention for this population.
7 (Sustain knowledge use)		Made suggestions for future research to monitor the sustainability of this program and the outcomes achieved from this intervention.

BIBLIOGRAPHY

Ajzen, I. (1991). The theory of planned behavior. *Organizational Behavior and Human Decision Processes, 50(2)*, 179-211.

American College of Sport Medicine. (2013). Resistance Training for Health and Fitness. Retrieved from: https://www.acsm.org/docs/brochures/resistance-training.pdf.

Asegaonkar, SB., Asegaonkar, BN., Takalkar, UV., Advani, S. & Thorat, AP. (2015). C-Reactive protein and breast cancer: New insights from old molecule. *International Journal of Breast Cancer,* 145647.

Ballard-Barbash, R., Friedenreich, CM., Courneya, KS., Siddiqi, SM., McTierrnan, A. & Alfano, CM. (2012). Physical activity, biomarkers, and disease outcomes in cancer survivors: A systematic review. *Journal of the National Cancer Institute, 104(11),* 815-840.

Bandura, A. (1989). Human agency in social cognitive theory. *American Psychologist,* 44(9), 1175-1184.

Blacklock, R., Rhodes, R., Blanchard, C. & Gaul, C. (2010). Effects of exercise intensity and self-efficacy on state anxiety with breast cancer survivors. *Oncology Nursing Forum, 37(2)*, 206-212.

Blaney, JM., Lowe-Strong, A., Rankin, J., Campbell, A., Allen, J. & Gracey, J. (2010). The cancer rehabilitation journey: barriers to and facilitators of exercise among patients with cancer-related fatigue. *Physical Therapy, 90,* 1135-47.

Boogaard, L., Gater, L., Mori, M., Trincao, A., Smith-Turchyn, J. (2016). Efficacy of self-management programs in managing side effects of breast cancer: A systematic review and meta-analysis of randomized control trials. *Rehabilitation Oncology,* 34(1), 14-26.

Brady, M.J., Cella, D.F., Mo, F., Bonomi, A.E., Tulsky, D.S., Lloyd, S.R., Deasy, S., Cobleigh, M., Shiomoto, G. (1997). Reliability and validity of the functional assessment of cancer therapy-breast quality of life instrument. *Journal of Clinical Oncology,* 15(3), 974-986.

Brown, JC., Huedo-Medina, TB., Pescatello, LS., Ryan, SM., Pescatello, SM., Moker, E., LaCroix, JM., Ferrer, RA., Johnson, BT. (2012). The efficacy of exercise in reducing depressive symptoms among cancer survivors: a meta-analysis. *PLoS One, 7(1),* e30955.

Brunet, J., Taran, S., Burke, S. & Sabiston, CM. (2013). A qualitative exploration of barriers and motivators to physical activity participation in women treated for breast cancer. *Disability & Rehabilitation*, *35(24)*, 2038-2045.

Campbell, K.L., Pusic, A.L., Zucker, D.S., McNeely, M.L., Binkley, J.M., Cheville, A.L., Harwood, K.J. (2012). A prospective model of care for breast cancer rehabilitation: Function. *Cancer, 118(8 Suppl),* 2300-2311.

Canadian Breast Cancer Foundation. (2017-1). Hormone Therapy. Retrieved from: http://www.cbcf.org/atlantic/AboutBreastCancerMain/TreatmentOptions/Pages/Hormone-Therapy.aspx.

Canadian Breast Cancer Foundation. (2017). How Breast Cancer Treatment can affect your Body. Retrieved from: http://www.cbcf.org/central/AboutBreastCancerMain/TreatmentOptions/Pages/Side-Effects.aspx.

Canadian Cancer Society. (2017-1). What is Breast Cancer. Retrieved from: http://www.cancer.ca/en/cancer-information/cancer-type/breast/breast-cancer/?region=on.

Canadian Cancer Society. (2017-2). Grading Breast Cancer. Retrieved from: http://www.cancer.ca/en/cancer-information/cancer-type/breast/grading/?region=on.

Canadian Cancer Society. (2017-3). Staging Breast Cancer. Retrieved from: http://www.cancer.ca/en/cancer-information/cancer-type/breast/staging/?region=on.

Canadian Cancer Society. (2017-4). Treatments for Breast Cancer. Retrieved from: http://www.cancer.ca/en/cancer-information/cancer-type/breast/treatment/?region=on.

Canadian Cancer Society. (2017-5). Side Effects of Chemotherapy. Retrieved from: http://www.cancer.ca/en/cancer-information/diagnosis-and-treatment/chemotherapy-and-other-drug-therapies/chemotherapy/side-effects-of-chemotherapy/?region=on.

Canadian Cancer Society. (2017-6). Side Effects of Radiation Therapy. Retrieved from: http://www.cancer.ca/en/cancer-information/diagnosis-and-treatment/radiation-therapy/side-effects-of-radiation-therapy/?region=on.

Canadian Cancer Society. (2017-7). Hormonal Therapy for Breast Cancer. Retrieved from: http://www.cancer.ca/en/cancer-information/cancer-type/breast/treatment/hormonal-therapy/?region=on.

Canadian Cancer Society's Advisory Committee on Cancer Statistics. (2017). *Canadian Cancer Statistics 2017*. Toronto, ON: Canadian Cancer Society.

Canadian Cancer Society's Advisory Committee on Cancer Statistics. (2016). *Canadian Cancer Statistics 2016*. Toronto, ON: Canadian Cancer Society.

Canadian Cancer Society's Advisory Committee on Cancer Statistics. (2015). *Canadian Cancer Statistics 2015*. Toronto, ON: Canadian Cancer Society.

Canadian Cancer Society's Advisory Committee on Cancer Statistics. (2011). *Canadian Cancer Statistics 2011*. Toronto, ON: Canadian Cancer Society.

Canadian Society of Exercise Professionals (CSEP). (2016). Guidelines Glossary. Retrieved from: http://www.csep.ca/en/guidelines/glossary-2016.

Canestraro, A., Nakhle, A., Stack, M., Strong, K., Wright, A., Beauchamp, M., Berg, K., Brooks, D. (2013). Oncology rehabilitation provision and practice patterns across Canada. *Physiotherapy Canada, 65(1),* 94-102.

Cella, D. & Fallowfield, LJ. (2008). Recognition and management of treatment-related side effects for breast cancer patients receiving adjuvant endocrine therapy. *Breast Cancer Research and Treatment*, *107,* 167–180.

Chasen, M., Feldstain, A., Gravelle, D., MacDonald, N., Pereira, J. (2013). An interprofessional palliative care oncology rehabilitation program: Effects on function and predictors of program completion. *Current Oncology, 20*, 301-309.

Cheifetz, O., Park Dorsay, J., Hladysh, G., Macdermid, J., Serediuk, F., Woodhouse, L.J. (2014). CanWell: meeting the psychosocial and exercise needs of cancer survivors by translating evidence into practice. *Psychooncology,* 23(2):204-215.

Cheville, A., Nyman, J., Pruthi, S. & Basford, JR. (2012). Cost considerations regarding the prospective surveillance model for breast cancer survivors. *Cancer*, *188(S8),* 2325-2330.

Chou, F., Dodd, M.J., Paul, S.M. (2012). Timing and Sustainability of an Exercise Intervention in Women With Breast Cancer During and After Cancer Treatment. *Oncology Nursing Forum*, 39(1), 91-97.

Cormie, P., Zopf, E., Zhang, X. & Schmitz, K. (2017). The Impact of Exercise on Cancer Mortality, Recurrence, and Treatment-Related Adverse Effects. *Epidemiologic Reviews, 39(1),* doi:10.1093/epirev/mxx007.

Courneya, KS., Katzmarzyk, PT. & Bacon, E. (2008). Physical activity and obesity in Canadian cancer survivors. *Cancer, 112(11)*, 2475-82.

Courneya, KS., Segal, RJ., Mackey, JR., Glemon, K., Reid, RD., Fridenreich, CM., Ladha, AB., Proulx, C., Vallance, JK., Lane, K., Yasui, Y., McKenzie, DC. (2007). Effects of aerobic and resistance exercise in breast cancer patients receiving adjuvant chemotherapy: A multicenter randomized controlled trial. *Journal of Clinical Oncology, 25(28)*, 4396-4404.

Cramer, H., Lange, S., Klose, P., Paul, A. & Dobos, G. (2012). Yoga for breast cancer patients and survivors: A systematic review and meta-analysis. *BMC Cancer, 18(12)*, 412.

Cramer, H., Lauch, R., Klose, P., Lange, S., Langhorst, J. & Dobos, G. (2017). Yoga for improving health-related quality of life, mental health and cancer-related symptoms in women diagnosed with breast cancer. *Cochrane Database of Systematic Reviews, 3(1*), CD010802.

Cramp, F. & Byron-Daniel, J. (2012). The effect of exercise on fatigue associated with cancer. *Cochrane Database of Systematic Reviews, 14(11),* doi10.1002/14651858.CD006145.pub3

Cummins, C., Kayes, NM., Reeve, J., Smith, G., MacLeod, R. & McPherson, KM. (2016). Navigating physical activity engagement following a diagnosis of cancer: A qualitative exploration. *European Journal of Cancer Care,* doi:10.1111/ecc.12608.

De Leeuw, J. & Larsson, M. (2013). Nurse-led follow-up care for cancer patients: what is known and what is needed. *Supportive Care in Cancer,* 21, 2643-2649.

Demark-Wahnefried, W., Colditz, G.A., Rock, C.L., Sedjo, R.L., Liu, J., Wolin, K.Y., Krontiras, H., Byers, T., Pakiz, B., Parker, B.A., Naughton, M., Elias, A., Ganz, P.A., ENERGY Trial Group. (2015). Quality of life outcomes from the Exercise and Nutrition Enhance Recovery and Good Health for You (ENERGY)-randomized weight loss trial among breast cancer survivors. *Breast Cancer Research and Treatment,* 154(2), 329-337.

Devoogdt, N., Van Kampen, M., Christiaens, MR., Troosters, T., Piot, W., Beets, N., Nys, S., Gosselink, R. (2011). Short- and long-term recovery of upper limb function after axillary lymph node dissection. *European Journal of Cancer Care*, 20, 77–86.

Duggan, C., Wang, C-Y., Neuhouser, ML., Xiao, L., Smith, AW., Reding, KW., Baumgartner, RN., Bernstein, L., Ballard-Barbash, R., McTiernan, A. (2013). Associations of insulin-like growth factor and insulin-like growth factor binding protein-3 with mortality in women with breast cancer. *International Journal of Cancer, 32,* 1191–1200.

Edwards, BK., Brown, ML., Wingo, PA., Howe, HL., Ward, E., Ries, LA., Schrag, D., Jamison, PM., Jemal, A., Wu, XC., Friedman, C., Harlan, L., Warren, J., Anderson, RN., Pickle, LW. (2005). Annual report to the nation on the status of cancer, 1975–2002, featuring population-based trends in cancer treatment. *Journal of the National Cancer Institute*, *97(19),* 1407–27.

Eisen, A., Fletcher, GG., Gandhi, S., Mates, M., Freedman, OC., Dent, SF., Trudeau, ME., and members of the Early Breast Cancer Systemic Therapy Consensus Panel. (2015). Optimal systemic therapy for early breast cancer in women: a clinical practice guideline. *Current Oncology, 22(S1),* S67-S81.

Endogenous Hormones and Breast Cancer Collaborative Group, Key, TJ., Appleby, PN., Reeves, GK. & Roddam, AW. (2010). Insulin-like growth factor 1 (IGF1), IGF binding protein 3 (IGFBP3), and breast cancer risk: pooled individual data analysis of 17 prospective studies. *The Lancet Oncology, 11,* 530–42.

Ewertz, M. & Jensen, AB. (2011). Late effects of breast cancer treatments and potentials for rehabilitation. *Acta Oncologica, 50,* 187-193.

Eysenbach, G. (2004), Peer Review and Publication of Research Protocols and Proposals: A Role for Open Access Journals. *Journal of Medical Intervention Research,* 6(3), e37.

Fernandez, S., Franklin, J., Amlani, N., DeMilleVille, C., Lawson, D. & Smith, J. (2015). Physical activity and cancer: A cross-sectional study on the barriers and facilitators to exercise during cancer treatment. *Canadian Oncology Nursing Journal, 25(1),* 37-42.

Godin, G. & Kok, G. (1996). The theory of planned behavior: a review of its applications to health-related behaviors. *American Journal of Health Promotion, 11(2),* 87-98.

Graham, I., Logan, J., Harrison, MB., Straus, SE., Tetroe, J., Caswell, W. & Robinson, N. (2006). Lost in knowledge translation? Time for a map. *Journal of Continuing Education in the Health Professions, 26,* 13-24.

Hagstrom, AD., Marshall, PW., Lonsdale, C., Cheema, BS., Fiatarone Singh, MA. & Green, S. (2016-1). Resistance training improves fatigue and quality of life in previously sedentary breast cancer survivors: A randomized controlled trial. *European Journal of Cancer Care, 25(5),* 784-794.

Hagstrom, AD., Marshall, PW., Lonsdale, C., Papalia, S., Cheema, BS., Toben, C., Baune, BT., Fiatarone Singh, MA., Green, S. (2016-2). The effect of resistance training on markers of immune function and inflammation in previously sedentary women recovering from breast cancer: a randomized controlled trial. *Breast Cancer Research and Treatment, 155(3),* 471-82.

Hayes, SC., Rye, S., Battistutta, D. & Newman B. (2010). Prevalence of upper-body symptoms following breast cancer and its relationship with upper-body function and lymphedema. *Lymphology*, *43,* 178–187.

Juvet, L.K., Thune, I., Elvsaas, I.K.O., Fors, E.A., Lundgren, S., Bertheussen, G., Leivseth, G., Oldervoll, L.M. (2017). The effect of exercise on fatigue and physical functioning in breast cancer patients during and after treatment and at 6 months follow-up: A meta-analysis. *Breast*, 33, 166-177.

Kraft, P., Rise, J., Sutton, S. & Roysamb, E. (2005). Perceived difficulty in the theory of planned behavior: Perceived behavioural control or affective attitude? *British Journal of Social Psychology, 2005, 44*, 479-496.

KT Clearinghouse. (2014). The Knowledge to Action Cycle. Retrieved from: http://ktclearinghouse.ca/knowledgebase/knowledgetoaction.

Lim, C., Devi, M. & Ang, E. (2011). Anxiety in women with breast cancer undergoing treatment: a systematic review. *International Journal of Evidence-Based Healthcare, 9(3),* 215-235.

Manstead, A. (2011). The benefits of a critical stance: A reflection on past papers on the theories of reasoned action and planned behavior. *British Journal of Social Psychology, 50,* 366-373.

McAnaw, MB. & Harris, KW. (2002). The role of physical therapy in the rehabilitation of patients with mastectomy and breast reconstruction. *Breast Disease, 16*, 163-174.

McNeely, ML., Campbell, K., Ospina, M., Rowe, BH., Dabbs, K., Klassen, TP., Mackey, J., Courneya, K. (2010). Exercise interventions for upper-limb dysfunction due to breast cancer treatment. *Cochrane Database of Systematic Reviews, 6:*CD005211.

Mishra, S.I., Scherer, R.W., Geigle, P.M., Berlanstein, D.R., Topaloglu, O., Gotay, C.C., Snyder, C. (2012). Exercise interventions on health-related quality of life for cancer survivors. *Cochrane Database of Systematic Reviews, 8;* CD007566.

Mohamaday, HM., Elsis, HF. & Aneism YM. (2017). Impact of moderate intensity aerobic exercise on chemotherapy-induced anemia in elderly women with breast cancer: A randomized controlled clinical trial. *Journal of Advanced Research, 8(1)*, 7-12.

Monteiro, M. (1997). Physical therapy implications following the TRAM procedure. *Physical Therapy, 77(7)*, 765-770.

Murtezani, A., Ibraimi, Z., Bakalli, A., Krasniqi, S., Disha, E. & Kurtishi, I. (2014). The effect of aerobic exercise on quality of life among breast cancer survivors: A randomized controlled trial. *Journal of Cancer Research and Therapeutics, 10(3)*, 658-664.

Mustian, KM., Palesh, OG. & Flecksteiner, SA. (2008). Tai Chi Chuan for breast cancer survivors. *Medicine and Sport Science, 52,* 209-217.

National Cancer Institute. (2017). Breast Reconstruction After Mastectomy. Retrieved from: https://www.cancer.gov/types/breast/reconstruction-fact-sheet.

National Cancer Institute. (2017-1). NCI Dictionary of Cancer Terms: "neoadjuvant therapy". Retrieved from: https://www.cancer.gov/publications/dictionaries/cancer-terms?cdrid=45800.

National Comprehensive Cancer Network-Guidelines for Patients. (2016). Breast Cancer Surgery. Retrieved from: https://www.nccn.org/patients/guidelines/stage_i_ii_breast/files/assets/basic-html/page-32.html.

Nobel, M., Russell, C., Kraemer, L., Sharratt, M. (2012). UW WELL-FIT: The impact of supervised exercise programs on physical capacity and quality of life in individuals receiving treatment for cancer. *Supportive Care in Cancer*, 20, 865-873.

Nock, N.L., Owusu, C., Flocke, S., Krejci, S.A., Kullman, E.L., Austin, K., Bennett, B., Cerne, S., Harmon, C., Moore, H., Vargo, M., Hergenroeder, P., Malone, H., Rocco, M., Tracy, R., Lazarus, H.M., Kirwan, J.P., Heyman, E., Berger, N.A. (2015). A community based exercise and support group program improves quality of life in African-American breast cancer survivors: A qualitative and quantitative analysis. *International Journal of Sports and Exercise Medicine,* 1(3): pii:020.

Ottenbacher, AJ., Day, RS., Taylor, WC., Sharma, SV., Sloane, R., Snyder, DC., Kraus, WE., Denmark-Wahnefried, W. (2011). Exercise among breast and prostate cancer survivors – what are their barriers? *Journal of Cancer Survivorship, 5(4)*, 413-19.

Patnaik, JL., Byers, T., DiGuiseppi, C., Dabelea, D. & Denberg, TD. (2011). Cardiovascular disease competes with breast cancer as leading cause of death for older females diagnosed with breast cancer: A retrospective cohort study. *Breast Cancer Research, 13(3)*, R64.

Prochaska, J.O., Velicer, W.F. (1997). The transtheoretical model of health behavior change. *American Journal of Health Promotion,* 12(1), 38-48.

Provinciali, N., Puntoni, M., Nanni, O., Bruzzi, P., DeCensi, A., Paleari, L., Freschi, A., Amaducci, L., Bologna, A., Gianni, L., Rocca, A., Amadori, D., Gennari, A. (2015). Insulin resistance (IR) and prognosis of metastatic breast cancer (MBC) patients. *The Breast*, *24(S3),* S66.

Sander, AP., Wilson, J., Izzo, N., Mountford, SA. & Hayes, KW. (2012). Factors that affect decisions about physical activity and exercise in survivors of breast cancer: a qualitative study. *Physical Therapy, 92*, 525-36.

Santa Mina, D., Alibhai, S.M.H., Matthew, A.G., Gugliette, C.L., Steele, J., Trachtenberg, J., Ritvo, P.G. (2012). Exercise in clinical cancer care: A call to action and program development description. *Current Oncology*, 19(3), e136-e144.

Santa Mina, D., Scheeded-Bergdal, C., Gillis, C. & Carli, F. (2015). Optimization of surgical outcomes with prehabilitation. *Applied Physiology, Nutrition, and Metabolism, 40(9),* 966-969.

Santen, RJ. (2011). Effect of endocrine therapies on bone in breast cancer patients. *Journal of Clinical Endocrinology & Metabolism, 96(2)*, 308–319.

Schmidt, ME., Wiskemann, J., Ulrich, CM., Schneeweiss, A. & Steindorf, K. (2017). Self-reported physical activity behavior of breast cancer survivors during and after adjuvant therapy: 12 months follow-up of two randomized exercise intervention trials. *Acta Oncologica, 56(4)*, 618-627.

Schmitz, KH., Ahmed, RL., Troxel, AB., Cheville, A., Lewis-Grant, L., Smith, R., Bryan, CJ., Williams-Smith, CT., Chittams, J. (2010). Weight lifting for women at risk for breast cancer-related lymphedema: A randomized trial. *Journal of the American Medical Association, 304(24),* 2699-2705.

Schmitz, KH., Courneya, KS., Matthews, C., Denmark-Wahnefried, W., Galvao, DA., Pinto, BM., Irwin, ML., Wolin, KY., Segal, RJ., Lucia, A., Schneider, CM., von Gruenigen, VE., Schwartz, AL., American College of Sports Medicine. (2010). American College of Sports Medicine roundtable on exercise guidelines for cancer survivors. *Medicine & Science in Sports & Exercise, 42(7), 1*409-1426.

Schmitz, KH., DiSipio, T., Gordon, LG. & Hayes, SC. (2015). Adverse breast cancer treatment effects: The economic case for making rehabilitative programs standard of care. *Supportive Care Cancer, 23(6)*, 1807-1817.

Segal, R., Evans, W., Johnson, D., Smith, J., Colletta, S.P., Corsini, L., Reid, R. (1999). Oncology rehabilitation program at the Ottawa Regional Cancer Centre: program description. *Canadian Medical Association Journal,* 161(3), 282-285.

Segal, R., Zwaal, C., Green, E., Tomasone, J., Loblaw, A., Petrella, T., and the Exercise for People with Cancer Guideline Development Group. (2015). A Quality initiative of the program in evidence-based care (PEBC), Cancer Care Ontario. Retrieved from: https://www.cancercare.on.ca/common/pages/UserFile.aspx?fileId=342807.

Shapiro, CL., Manola, J. & Leboff, M. (2001). Ovarian failure after adjuvant chemotherapy is associated with rapid bone loss in women with early-stage breast cancer. *Journal of Clinical Oncology, 19(14),* 3306– 3311.

Shields, M. & Wilkins, K. (2009). An update on mammography use in Canada. *Health Reports, 20(3)*, 7–19. Retrieved from: http://www.statcan.gc.ca/access_acces/archive.action?loc=/pub/82-003-x/2009003/%20article/10873-eng.pdf&archive=1.

Shobeiri, F., Masoumi, SZ., Nikravesh, A., Heidari Moghadam, R. & Karami, M. (2016). The Impact of Aerobic Exercise on Quality of Life in Women with Breast Cancer: A Randomized Controlled Trial. *Journal of Research in Health Sciences, 16(3)*, 127-132.

Simon Pickard A, Wilke C, Lin H, Lloyd A. (2007). Health utilities using the EQ-5D in studies of cancer, *PharmacoEconomics,* 25(5), 365-384.

Skogvoll, E., Kramer-Johansen, J. (2013). Publication of clinical trial protocols—what can we learn? *Scandinavian Journal of Trauma, Resuscitation and Emergency Medicine*, 21, 12, doi: 10.1186/1757-7241-21-12.

Smith, L., Croker, H., Fisher, A., Williams, K., Wardle, J., Beeken, RJ. (2017). Cancer survivors' attitudes towards and knowledge of physical activity, sources of information, and barriers and facilitators of engagement: A qualitative study. *European Journal of Cancer Care,* doi:10.1111/ecc.12641.

Steindorf, K., Schmidt, ME., Klassen, O., Ulrich, CM., Oelmann, J., Habermann, N., Beckhove, P., Owen, R., Debus, J., Wiskemann, J., Potthoff, K. (2014). Randomized, controlled trial of resistance training in breast cancer patients receiving adjuvant radiotherapy: results on cancer-related fatigue and quality of life. *Annals of Oncology, 25(11)*, 2237-2243.

Stene, G.B., Helbostad, J.L., Balstad, T.R., Riphagen, I.I., Kaasa, S., Oldervoll, L.M. (2013). Effect of physical exercise on muscle mass and strength in cancer patients during treatment-A systematic review. *Critical Reviews in Oncology/ Hematology,* 88(3), 573-593.

Stout, N. (2009). Cancer prevention in physical therapist practice. *Phys Ther, 89(11)*, 1119-1122.

Stout, N., Binkley, J., Schmitz, K., Andrews, K., Hayes, SC., Campbell, KL., McNeely, ML., Soballe, PW., Berger, AM., Cheville, AL., Fabian, C., Gerber, LH., Harris, SR., Johansson, K., Pusic, AL., Prosnitz, RG., Smith, RA. (2012). A prospective surveillance model for rehabilitation for women with breast cancer. *Cancer, 188(S8)*, 2191-2200.

Thabane, L., Ma, J., Chu, R., Cheng, J., Ismalia, A., Rios, L., Robson, R., Thabane, M., Giangregorio, L., Goldsmith, C.H. (2010). A tutorial on pilot studies: The what, why and how. *BMC Medical Research Methodology*, 10(1).

Travier, N., Velthuis, M.J., Steins Bisschop, C.N., van den Buijs, B., Monninkhof, E.M., Backx, F., Los, M., Erdkamp, F., Bloemendal, H.J., Rodenhuis, C., de Roos, M.A., Verhaar, M., ten Bokkel Huinink, D., van der Wall, E., Peeters, P.H., May, A.M. (2015). Effects of an 18-week exercise programme started early during breast cancer treatment: a randomised controlled trial. *BMC Medicine*, 8(13), 121.

van Vulpen, J.K., Peeters, P.H.M., Velthuis, M.J,, van der Wall, E., May, A.M. (2016). Effects of physical exercise during adjuvant breast cancer treatment on physical and psychosocial dimensions of cancer-related fatigue: A meta-analysis. *Maturitas,* 85, 104-111.

Van Waart H, Stuiver MM, van Harten WH, Geleijn E, Kieffer JM, Buffart LM, de Maaker-Berkhof, M., Boven, E., Schrama, J., Geenen, MM., Meerum Terwogt, JM., van Bochove, A., Lustig, V., van den Heilgenberg, SM., Smorenburg, CH., Hellendoorn-van Vreeskijk, JA., Sonke, GS., Aaronson, NK. (2015). Effect of low-intensity physical activity and moderate- to high-intensity physical exercise during adjuvant chemotherapy on physical fitness, fatigue, and chemotherapy completion rates: results of the PACES randomized clinical trial. *Journal of Clinical Oncology, 33(17),* 1918-1927.

Vehmanen, L., Saarto, T., Elomaa, I., Makela, P., Valimaki, M. & Blomqvist, C. (2001), Long-term impact of chemotherapy-induced ovarian failure on bone mineral density (BMD) in premenopausal breast cancer patients. The effect of adjuvant clodronate treatment. *European Journal of Cancer, 37(18)*, 2373–2378.

Winters-Stone, KM., Dobek, J., Nail, LM., Bennett, JA., Leo, MC., Torgrimson-Ojerio, B., Luoh, SW., Schwartz, A. (2013). Impact + resistance training improves bone health and body composition in prematurely menopausal breast cancer survivors: A randomized controlled trial. *Osteoporosis International, 24,* 1637-1646.

Yang, EJ., Park, WB., Seo, KS., Kim, SW., Heo, CY. & Lim, JY. (2010). Longitudinal change of treatment-related upper limb dysfunction and its impact on late dysfunction in breast cancer survivors: a prospective cohort study. *Journal of Surgical Oncology, 101,* 84–91.

Yu, AF. & Jones, LW. (2016). Breast cancer treatment-associated cardiovascular toxicity and effects of exercise countermeasures. *Cardio-Oncology, 2,* 1-12.