AN ABSTRACT OF THE DISSERTATION OF

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Title: Theoretical Predictors of Successfully Transitioning from Supervised to Home-Based (Unsupervised) Exercise Programs Among Elderly Women with Breast Cancer

Abstract approved:

Bradley J. Cardinal

Supervised exercise interventions can elicit numerous positive health outcomes in breast cancer survivors. However, to maintain these benefits, exercise needs to continue long after the supervised program. This may be difficult, as in this transitional period (i.e., time period immediately following a supervised exercise program), breast cancer survivors are in the absence of on-site direct supervision from a trained exercise specialist. The purpose of the present study is to identify key determinants of regular participation in exercise during a 6-month follow-up period after a 12-month supervised exercise program among women aged 65+ years who have been previously diagnosed with breast cancer. At the conclusion of a supervised exercise program, and 6-months later, 69 breast cancer survivors completed surveys examining their exercise behavior and key constructs from the Transtheoretical Model. After adjusting for weight status and physical activity prior to transitioning, breast cancer survivors with higher self-efficacy at the point of transition were 10% more likely to be sufficiently active compared to insufficiently active 6-months after leaving the supervised exercise program ($p < 0.01$). Similarly, breast cancer survivors with higher behavioral processes of change use at the point of transition were 13% more

likely to be sufficiently active ($p < 0.05$). These findings suggest that self-efficacy and the behavioral processes of change, in particular, play an important role in exercise participation during the transition from a supervised to a home-based program among older adult women who have been diagnosed with breast cancer.

Theoretical Predictors of Successfully Transitioning from Supervised to Home-Based (Unsupervised) Exercise Programs Among Elderly Women with Breast Cancer

by
Paul D. Loprinzi

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Dean of the Graduate School

I understand that my dissertation will become part of the permanent collection of Oregon State University libraries. My signature below authorizes release of my dissertation to any reader upon request.

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Paul D. Loprinzi, Author

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CHAPTER 1: INTRODUCTION

Except for skin-related cancer, breast cancer is the most common form of cancer among women.[1] In 2006, 191,410 women were diagnosed with breast cancer.[1] In addition to being highly prevalent, it is the second leading cause of cancer death among women behind lung cancer.[1]

Previous research shows that regular participation in physical activity may play an important role in the prevention of breast cancer among women. For example, during a 14-year longitudinal study examining the association between breast cancer and physical activity, Thune and colleagues[2] found that among 25,624 women between 20-54 years of age, greater leisure-time physical activity was associated with a reduced risk of breast cancer. These findings have been corroborated by others.[3-5] Although empirical evidence shows that physical activity plays a key role in the prevention of breast cancer among women, some women are inherently at risk for developing breast cancer due to hereditary factors, such as mutations in tumor suppressor genes (e.g., breast cancer 1 [BRCA1] and breast cancer 2 [BRCA2]).[6] According to recent estimates, about 12% of women in the general population will develop breast cancer in their lifetime, whereas 60% of women who have inherited a mutation in the BRCA1 or BRCA2 gene will develop breast cancer.[7, 8]

Importantly, research has examined the association between physical activity and survival rates among women diagnosed with breast cancer.[9] In their cohort study of

2,987 women diagnosed with breast cancer between 1984 and 1998, Holmes and colleagues[10] observed that women who engaged in more than three MET-hours per week of physical activity were at a significantly lower relative risk of dying from breast cancer than those who engaged in less than three MET-hours per week of physical activity. These results suggest that regular participation in physical activity after breast cancer diagnosis may reduce the risk of death from this disease. Additionally, even among women with BRCA1 and BRCA2 mutation carriers, regular participation in physical activity may reduce the risk of breast cancer.[11]

The positive effect of physical activity on surviving breast cancer is likely a result of physical activity-reducing estrogen and progesterone levels, thereby inhibiting further carcinogenesis in the mammary gland.[12, 13] Physical activity influences energy balance, which may also reduce the risk of recurring breast cancer given that weight gain after diagnosis results in higher rates of breast cancer recurrence and mortality.[14, 15] For this reason, regular engagement in physical activity after a breast cancer diagnosis is very important, as up to 60% of women with breast cancer gain weight during treatment.[16]

Given the beneficial role in reducing breast cancer recurrence and breast cancer-related morbidity and mortality, engaging women in regular physical activity participation after being diagnosed with breast cancer is a public health priority. However, motivating women with breast cancer to engage in regular physical activity may be an enormous challenge given the post-treatment fatigue resulting from chemotherapy and other treatments, as well as other barriers such as persistent pain, fear of injury with physical activity, and lack of knowledge about the appropriate type/dose of physical activity after breast cancer diagnosis.[17] Before interventions that promote physical activity in breast cancer survivors can be developed and implemented, a better understanding of the factors that influence physical activity behavior in this population is needed.

One of the most promising theories used to successfully explain health behavior, including physical activity, is the Transtheoretical Model (TTM).[18, 19] Based on an individual's readiness to change behavior, usually defined by five discrete stages including pre-contemplation, contemplation, preparation, action, and maintenance, the TTM uses cognitive and behavioral processes to provide stage-specific strategies for increasing physical activity.[1] Other key theoretical constructs of the TTM include self-efficacy, an individual's perceived confidence in overcoming physical activity-related barriers, and decisional balance, an individual's reflection of the pros and cons in engaging in regular physical activity.

Research in the general population supports the application of the TTM as a framework for explaining exercise behavior.[18, 20-25] Although fewer in number,

[1] Other stage configurations have been proposed, including a termination or transformation stage, which is the ultimate endpoint of a behavior.

research also shows that the TTM may be a useful theoretical framework for understanding exercise behavior in sub-populations, such as those with disabilities.[26-28] However, with regard to individuals diagnosed with breast cancer, factors that influence their exercise behavior are not well understood, and the utility of the full TTM for understanding factors that influence exercise behavior has not been extensively tested in this population. To prevent recurrence of breast cancer, reduce the risk of dying from breast cancer, and improve quality of life among breast cancer survivors, research examining factors that influence exercise adherence in this population is urgently needed.

The goal of the proposed dissertation is fivefold: 1) overview the observational and intervention studies examining the link between physical activity and breast cancer risk and survival; 2) review the extant literature examining the biological plausibility for the relationship between physical activity and breast cancer risk, recurrence and mortality; 3) summarize the effects of physical activity on common side effects of breast cancer treatment (e.g., fatigue, quality of life); 4) identify the factors associated with physical activity levels among breast cancer survivors; and 5) empirically examine the utility of the TTM at explaining follow-up exercise behavior among women diagnosed with breast cancer who have transitioned from a supervised exercise program to a home-based program.

The specific aim and hypothesis is as follows:

Specific Aim

Among elderly women (65+ yrs) diagnosed with breast cancer, utilize the TTM to identify key determinants of regular participation in exercise during a 6-month follow-up period after a 12-month supervised exercise program.

Hypothesis

Breast cancer survivors who have higher perceptions of exercise-related efficacy, utilize more behavioral and cognitive processes of change, and have more pros and fewer cons of exercise at the end of the supervised program will be more physically active 6-months following the supervised exercise program compared to breast cancer survivors that don't make use of behavioral and cognitive processes of change, have lower self-efficacy, and fewer pros and more cons of exercise.

The results of the proposed dissertation are novel and unique in that 1) it will provide researchers and practitioners with the overall evidence regarding the relationship between physical activity and breast cancer, 2) identify the mechanisms through which physical activity influences breast cancer risk, 3) inform the development of interventions aimed at motivating women with breast cancer to increase their physical activity and exercise behaviors, and 4) identify possible strategies to employ that would aim to increase behavioral change skills prior to transitioning from a supervised to a home-unsupervised program.

CHAPTER 2: LITERATURE REVIEW

The aim of this review is to systematically evaluate the research literature pertaining to the effects of physical activity on breast cancer risk, breast cancer recurrence, and breast cancer-related mortality. Additionally, we will briefly summarize the mechanisms through which physical activity may influence risk, recurrence, and mortality from breast cancer. Furthermore, we will examine the effects of regular physical activity on common side effects of cancer treatment, such as fatigue, decreased muscular strength, and health-related quality of life. Lastly, to inform the development and implementation of effective physical activity interventions for women with breast cancer, we will overview factors related to physical activity behavior in women with breast cancer.

Computerized Searches

An extensive review of the epidemiological literature on the effect of physical activity on breast cancer risk, recurrence, and mortality was conducted using PubMed to December, 2010 using the following key words: physical activity, exercise, breast cancer, breast cancer recurrence, and breast cancer mortality. Manual searches of the reference lists of the retrieved articles were also performed. Existing reviews relevant to the subject area were examined to identify additional studies linking physical activity to breast cancer risk, recurrence, and mortality.

To identify the main biological mechanisms underlying the association between physical activity and breast cancer risk, recurrence, and mortality, a PubMed search was conducted using the following key words: physical activity, exercise, breast cancer, and mechanisms. Articles that had these keywords in the title or abstract were obtained and reviewed. The discussion section of related studies were reviewed and manual searches of the reference lists of the retrieved articles were also performed. To identify studies that examined the effect of physical activity on various health outcomes (e.g., depression, quality of life) following breast cancer diagnosis, PubMed was searched by delimiting the search to review studies and using the following key words: exercise, fatigue, depression, bone loss, muscle strength, aerobic capacity, weight gain, anxiety, body-image, and quality of life. To identify studies that examined factors that influence physical activity behavior in women diagnosed with breast cancer, a PubMed search was conducted using the following key words: physical activity, exercise, breast cancer, psychosocial, and environment. Limitations to the retrieval of all articles was that the article had to be published in the English language.

For the identification of studies examining the association between physical activity and breast cancer risk, recurrence, and mortality, a study was included if: 1) breast cancer risk, recurrence, or mortality served as the dependent variable; 2) physical activity served as the independent variable, 3) and a measure of association between physical activity, breast cancer risk, breast cancer recurrence, or breast cancer mortality was reported. For the identification of studies examining factors that influence physical activity behavior in women diagnosed with breast cancer, a study was included if 1) physical activity served as the dependent variable, 2) a hypothesized factor served as the independent variable, and 3) a measure of association between physical activity and the hypothesized factor was reported.

Level of Evidence

The effect of physical activity on breast cancer risk, recurrence, and mortality was categorized using the following coding scheme: 1) **protective effect,** if a significant inverse association was reported; 2) **non-significant inverse association,** if a reduction in risk was reported with a non-significant trend or non-significant confidence interval; and 3) **no effect,** if there was a non-significant positive association.

Association Between Physical Activity and Breast Cancer Risk

A total of 76 studies that investigated the association between physical activity and breast cancer risk were identified. Among these studies, there was considerable variation with regard to the study design, populations, contrast in the exposure variable (i.e., physical activity), and adjustment for confounding variables. The study designs included prospective cohort (n = 28),[2, 4, 29-54] retrospective cohort (n = 5),[3, 11, 55-57] and case-control (n = 43).[5, 13, 58-98] Physical activity was assessed during leisure-time,[2-5, 11, 13, 29-49, 51, 53-55, 58-62, 64-77, 79, 80, 82-87, 89-95, 98] transportation,[43, 57] household,[33, 57, [60-62] and in occupational settings.[2, 13, 29-31, 39, 42, 51, 52, 56, 57, 59-62, 65, 67-69, 71, 77, 79, 81, 83, 84, 88, 96, 97] All studies measured physical activity either using self-report,[2-4, 11, 13, 29-50, 52-55, 57, 60, 62, 69-73, 76, 78, 84, 89, 90, 92, 97, 98] interview-administered,[5, 51, 56, 58, 59, 61, 64-68, 74, 75, 77, 79, 82, 83, 85-87, 91, 94, 95] or telephone-administered methods,[80, 81, 88, 93] with no studies using an objective-measure of physical activity and few studies using reliable and/or valid subjective measures of physical activity.[30, 36, 37, 40, 49, 54, 60, 62, 65, 74, 76] The main characteristics and results of the cohort and case-control studies are summarized in Appendix A (see Tables 1 and 2).

Despite the great variability in study characteristics, results generally supported a positive link between physical activity and breast cancer risk. Of the 76 studies reviewed, 40 (53%) reported a statistically significant protective effect for physical activity on breast cancer risk;[2, 5, 13, 30-33, 37, 41, 42, 45, 46, 49, 54-58, 60-64, 67, 68, 70-72, 74, 75, 77-80, 83, 84, 92, 93, 97, 98] 28 (37%) studies found a non-significant risk reduction of physical activity on reducing breast cancer risk;[3, 4, 11, 29, 34, 38-40, 43, 44, 48, 50, 52, 53, 59, 65, 66, 69, 73, 81, 82, 85, 86, 88-91, 95] and only eight (10%) studies had no evidence for an association between physical activity and breast cancer risk.[35, 36, 47, 51, 76, 87, 94, 96] Notably, none of the reviewed studies observed a significant positive (i.e., harmful) association between physical activity and breast cancer risk. Of the 40 studies demonstrating a reduction in breast cancer risk, the magnitude of the decrease was, on average, 36%, with case-control studies (40%) more frequently observing a reduction in breast cancer risk compared to cohort studies (31%). When all the studies were included, the magnitude of decrease was 29%, with again, case control studies (35%) reporting a greater reduction in breast cancer risk than cohort studies (21%) (Figures 1 and 2).

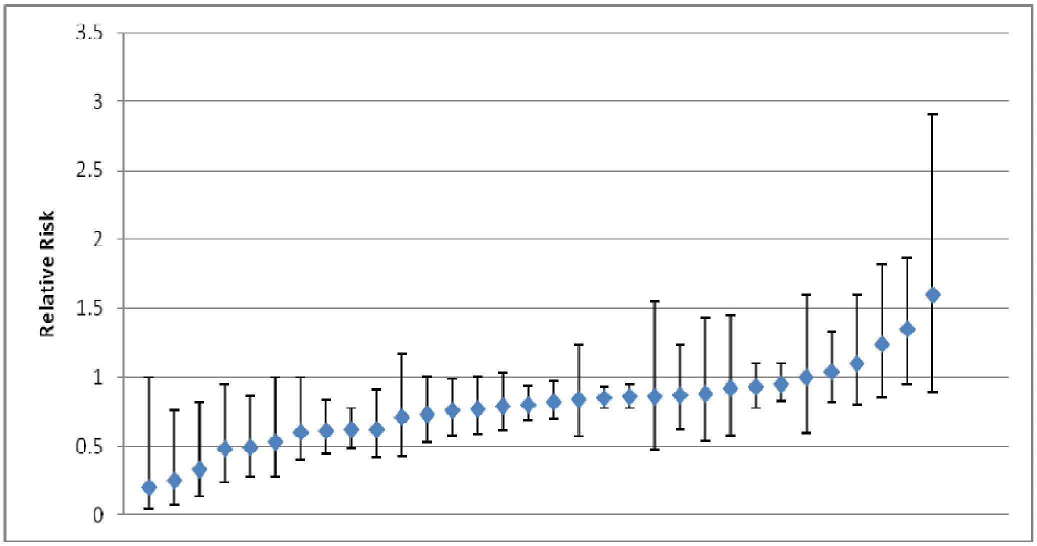

Figure 1. Strength of association between cohort studies and breast cancer risk.

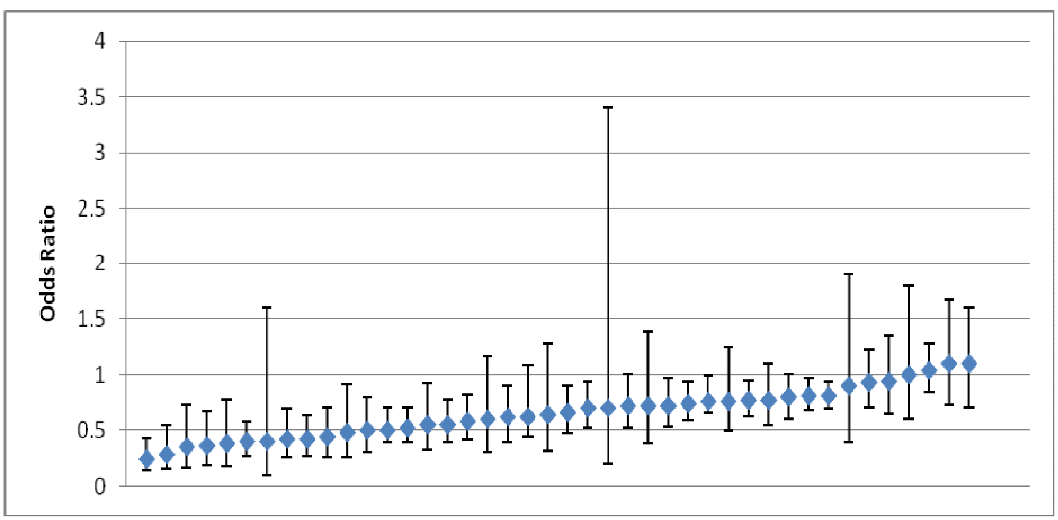

Figure 2. Strength of association between case-control studies and breast cancer risk.

To evaluate whether specific aspects of physical activity participation influence breast cancer risk, studies have examined the effect of timing (i.e., current or historic/past activity behavior) and intensity, including, moderate-intensity[30, 32, 33, 35, 37, 44, 60, 67, 74, 79, 95] and vigorous intensity exercise,[29, 30, 32-35, 37, 40, 44, 46, 47, 60, 61, 65, 67, 72, 74, 75, 79, 90, 91, 95] on reductions in breast cancer risk. To investigate the influence of the timing of physical activity on breast cancer risk, studies have assessed activity behavior in different periods of the lifespan, such as adolescences,[13, 30, 35, 37, 40, 62, 65, 69, 72, 74, 76-80, 82, 83, 87, 89-91, 93, 94, 98] young adulthood,[30, 40, 42, 47, 61, 62, 69, 72, 74, 76, 78, 87, 98] middle-age,[13, 30, 35, 37, 38, 40, 61, 62, 72, 74, 76, 79, 83] and late-adulthood,[13, 37, 40, 57, 61, 62, 72, 74, 76, 83] as well as different time-intervals prior to breast cancer diagnosis, such as one to two years prior,[32, 47, 65, 70, 78, 79, 82, 87, 90] 10-years prior,[41, 65, 66, 73, 77] 20-years prior,[65] and an average of these time-periods (i.e., lifetime activity behavior).[32, 46, 54, 58, 60-62, 64-68, 74, 76, 77, 79] When compared, the effect of physical activity on reducing breast cancer was stronger for vigorous-intensity physical activity (26%) than moderate-intensity physical activity (13%), and assessment of lifetime physical activity (30%) was more consistently associated with reduced breast cancer risk, compared to regular participation in physical activity during adolescence (26%), young-adulthood (11%), middle-age years (12%), and late-adulthood (23%).

Studies have also examined potential effect modifiers on the association between physical activity and breast cancer risk. The most common effect modifiers included menopausal status,[2, 4, 13, 29, 31, 34, 41, 43, 49, 58, 60, 62, 65, 67, 68, 70, 72, 74, 75, 77, 84, 85, 87-89, 92, 95, 98] body mass index,[2, 4, 13, 30-34, 36-39, 41-44, 49, 61, 68, 70, 78, 79, 87, 88] family history of breast cancer,[32, 44, 61, 64, 66, 70, 79] and parity.[5, 13, 30, 32, 33, 44, 70, 78, 79, 88, 93] When compared, the effect of physical activity on reducing breast cancer was stronger for postmenopausal women (30%) than premenopausal women (26%); participants not overweight (37%) compared to overweight participants (19%); women without a history of breast cancer (21%) compared to women with a family history of breast cancer (12%), and little difference was found between parous women (23%) and nulliparous women (25%).

Collectively, the epidemiologic literature provides substantial evidence that regular participation in physical activity can reduce the risk of breast cancer. To aid in the prevention of breast cancer, regular participation in physical activity should begin in early childhood, persist throughout adulthood, and be of at least moderate-intensity. While some might conclude that the data are conclusive, the lesson learned regarding the use of hormone replacement therapy gives us pause. Hormone replacement therapy was considered, by many, to be convincingly shown to decrease the risk of heart disease and cognitive function loss based on epidemiologic data, only to be shown to be associated with increased risks of heart disease and cognitive dysfunction from the results of placebo-controlled, double-blind, randomized clinical trials.[99, 100] Understanding the causal pathway between physical activity and breast cancer risk may be helpful in informing the development of physical activity interventions by providing further information on the dose, intensity, and frequency of physical activity across various exercise domains needed to protect against cancer.

Mechanisms Explaining the Relationship Between Physical Activity and Breast Cancer Risk

Establishing the biological mechanisms that underlie an association between physical activity and breast cancer risk is an important next step in developing a body of evidence linking health behavior to disease outcomes. The proposed mechanisms by which physical activity exerts a protective effect against cancer can be broadly divided into the following categories: 1) decreases in sex hormones, 2) decreases in adiposity, 3) increases in immune function, and 4) changes in markers of insulin resistance. Some studies support that physical activity reduces breast cancer risk through favorable changes in the following biological mechanisms/biomarkers: decreased adiposity, decreased available sex hormones (i.e., lower estrogens and androgens, higher sex hormone binding globulin (SHBG) levels, decreased metabolic hormones (leptin and adiponectin), reductions in markers of insulin resistance (i.e., insulin, glucose, C-peptide, and glycosylated hemoglobin), and reduced inflammatory markers (i.e., tumor necrosis factor alpha, interleukin-6 (IL-6), and C-reactive protein).[101-104]

<u>Sex Hormones and Adiposity</u>

It is well-established that women with increased exposure to sex hormones, namely estrogen and progesterone, are at an increased risk for breast cancer.[12, 105] Elevated levels of sex hormones and cumulative exposure to sex hormones stimulates tumor development and growth through mammary cell proliferation.[106] Consequently, women with an early onset of menarche, regular lifetime ovulatory cycles, and late menopause are at an elevated risk for breast cancer,[107] with an increased risk ranging from 20% to over 400%.[108-112]

Regular physical activity participation may reduce circulating levels of sex hormones, and thus reduce breast cancer risk, by delaying the onset of menarche in childhood, and in adulthood, inducing menstrual cycle irregularities, such as anovulation, oligomenorrhoea and amenorrhea. This assertion is supported by both observational studies[113-115] and exercise intervention studies.[116, 117] Importantly, in addition to the direct influence of physical activity, it is likely that delaying the onset of menarche and inducing anovulation is influenced by levels of adiposity. Adipose cells act as a secondary hormonal gland by secreting estrone and estradiol; thus, reduced circulating levels of sex hormones may require both prolonged exercise and caloric restriction to minimize adipose cell hypertrophy and proliferation. Future research is needed to determine if physical activity can affect sex hormones independent of changes in adiposity.

<u>Immune Function</u>

Chronic inflammation has been recognized as a risk factor for cancer,[118] particularly through cellular changes and oxidative stress associated with inflammation.[119] At moderate levels and intensities, regular participation in physical activity may help reduce inflammation by decreasing proliferation of immunological products, such as C-reactive protein, interleukin-6, macrophages, natural killer cells, lymphokineactivated killer cells, and lymphocytes.[101, 120] A randomized controlled trial in obese non-cancer postmenopausal women showed that a 6-month weight loss program, comprised of regular exercise and a hypocaloric diet, significantly decreased levels of interleukin-6, C-reactive protein, and tumor necrosis factor-alpha.[121] In contrast, there were no changes in these immunological biomarkers in the diet-only control group. Additional research warrants whether physical activity can reduce inflammation in women with breast cancer.

Insulin-Related Factors

Long-term exposure to elevated levels of insulin has also been associated with breast cancer risk,[122] as well as a two and three times higher risk for breast cancer recurrence and breast cancer death, respectively.[123] Specifically, high insulin levels stimulate the production of insulin-like growth factors (IGFs), which are associated with increased breast cancer risk through their stimulatory effect on cell turnover.[124] In addition to specific biomarkers (e.g., IGFs), insulin-resistance is thought to play an important role in breast cancer development. For example, in a meta-analysis conducted by Larsson,[125] a 20% increased breast cancer risk among individuals with type-2 diabetes was found, though not all studies have shown such an association.[126] Regular participation in physical activity is positively associated with insulin sensitivity[127] and inversely associated with fasting insulin levels[128] and IGFs.[129] The physical activity-lowering effect on IGFs may not only inhibit mammary cell turnover, but decreased

IGFs may also reduce the availability of sex hormones through hepatic synthesis of sex hormone binding globulin.[130]

Other Potential Factors

In addition to the previously discussed potential mechanisms, there are other possible mechanisms that might mediate the relationship between physical activity and breast cancer risk. It is conceivable that physical activity could influence breast cancer risk indirectly through behavioral practices such as cancer screening; therefore, future studies investigating the biological mechanisms responsible for the protective effect of exercise on breast cancer should control for such behavioral practices, as it is possible that physically active, health conscious individuals are likely to employ other practices, such as cancer screening (e.g., mammography), to help prevent cancer development.

Association Between Physical Activity and Breast Cancer Recurrence and Mortality

Although numerous studies have examined the influence of physical activity on breast cancer risk, the literature on the relationship between physical activity and breast cancer recurrence and mortality is less developed. Only six studies,[10, 131-135] to date, have examined the influence of physical activity on mortality from breast cancer, with two of these studies also investigating the influence of physical activity on breast cancer recurrence (Table 3, Appendix A). Of these six studies, four studies (67%) found a protective effect of physical activity on breast cancer mortality,[10, 131-133] with two studies (33%) reporting physical activity to have a non-significant risk reduction on breast cancer mortality.[134, 135] Among these six studies demonstrating a reduction in breast cancer mortality, the hazards ratio ranged from 0.51 to 0.78 (Figure 3).

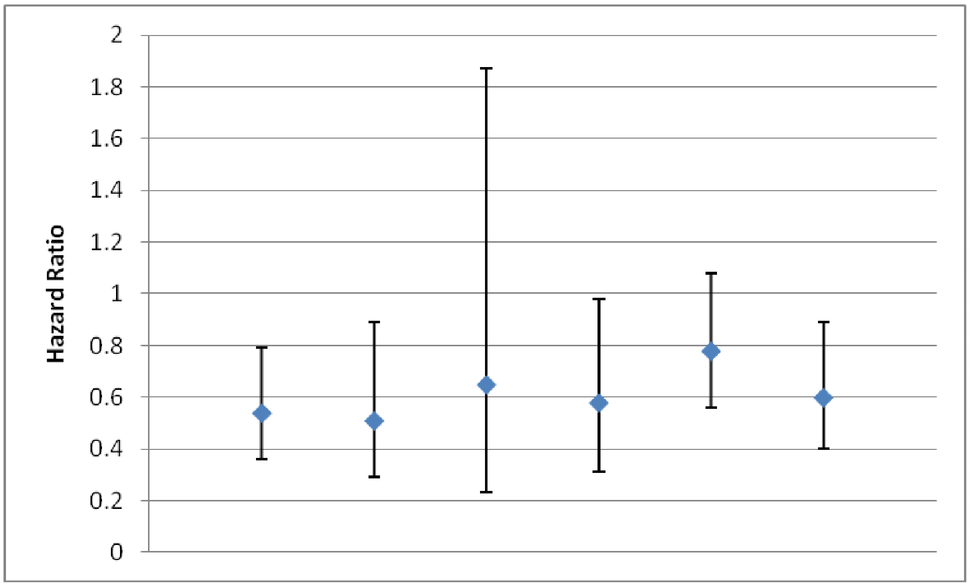

Figure 3. Strength of association between physical activity and breast cancer mortality.

Of the two studies examining the influence of physical activity on breast cancer recurrence, both reported a non-significant trend with relative risks ranging from 0.74-0.76 (Figure 4).[10, 132] Details regarding these trials will be provided below.

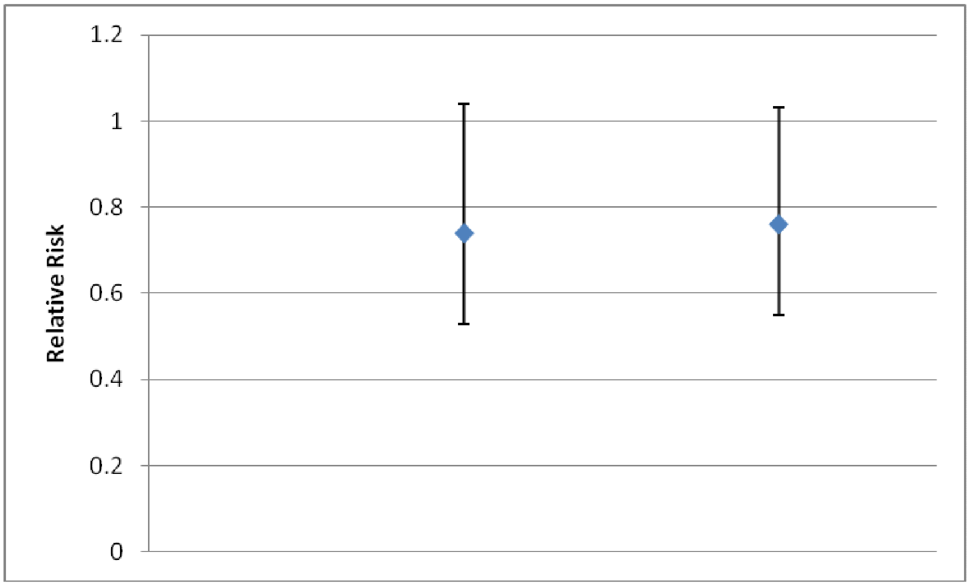

Figure 4. Strength of association between physical activity and breast cancer recurrence.

In a prospective observational study of 2,987 registered nurses with a history of breast cancer, Holmes and colleagues[10] showed that, compared to women who engaged in less than 1-hr of physical activity per week, those who walked 3 to 5 hours per week were 43% less likely to develop recurrent breast cancer and 50% less likely to die from breast cancer. Similarly, in a cohort of 1,231 women diagnosed with breast cancer, Friedenreich et al.[132] showed that, after adjustments for confounders, women in the highest (>19 MET-hrs/wk) versus lowest (≤ 5 MET-hrs/wk) quartiles of recreational physical activity were 46% less likely to die from breast cancer. Both moderate (HR =0.56, 95% CI = 0.38-0.82) and vigorous intensity recreational activity (HR = 0.74, 95% CI = 0.48-0.98) also decreased the risk of breast cancer death. Additionally, those in the highest quartile of physical activity were 34% (HR = 0.76, CI = 0.55-1.03) less likely to develop recurrent breast cancer. In support of these studies, Pierce et al. showed that among 1,490 women diagnosed with breast cancer, those exercising between 1,320 and 6,420 MET-min/wk, compared to less than 226 MET-min/wk, were 42% (Cox Hazard = 0.58; *p*-trend = 0.02) less likely to die from breast cancer.

Also examining the association between physical activity and breast cancer survival, Holick and colleagues[133] showed a dose response relationship between physical activity and breast cancer-related mortality among 4,482 women with breast cancer. Women who engaged in > 21 MET-h/wk in physical activity had the lowest risk of dying from breast cancer (HR = 0.51, 95% CI = 0.29-0.89), compared to women exercising less than 2.8 MET-h/wk.

Irwin and colleagues[134] reported a non-significant inverse association between physical activity and breast cancer mortality among 983 women in the Health, Eating, Activity, and Lifestyle Study. When physical activity was assessed one-year before diagnosis, women who exercised greater than or equal 9 MET-hrs/wk, compared to 0 MET-hrs/wk, were 17% (HR = 0.83, CI = 0.49-1.38) less likely to die from breast cancer. When physical activity was assessed two years after diagnosis, the more active women were 35% (HR = 0.65, CI = 0.23-1.87) less likely to die from breast cancer. Also reporting a non-significant inverse association, Abrahamson et al.[135] showed that women exercising 75.6-98 MET-hrs/wk, compared to 1.6-21.5 MET-hrs/wk, were 22% (HR = 0.78, CI = 0.56-1.08) less likely to die from breast cancer.

Although too few studies have been conducted to draw strong conclusions, these studies suggest that to minimize breast cancer recurrence and mortality, breast cancer survivors should engage in at least 180-240 minutes of moderate-intensity physical activity per week, which is higher than the current 150-minutes of at least moderate-intensity physical activity recommendation for U.S. adults. Given that all of these studies provided observational evidence only, randomized controlled trials are needed to confirm the protective effect of exercise on breast cancer recurrence and mortality.

Effect of Exercise Interventions on Health Outcomes Affected by Breast Cancer Treatment

Some of the common side effects of breast cancer treatment include fatigue,[136] depression,[137] bone loss,[138] decreased levels of muscular strength,[139] decreased aerobic capacity,[140] increased weight gain,[141, 142] and ultimately, impaired quality of life.[143] Consequently, researchers have investigated the effects of regular exercise as a therapeutic intervention for targeting these commonly-occurring side effects of breast cancer adjuvant therapies. The following narrative will briefly summarize the research evidence examining the effect of exercise on fatigue, muscular strength, aerobic capacity, bone health, weight loss, and overall quality of life.

<u>Psychosocial Factors</u>

In 2010, Velthuis and colleagues[144] performed a meta-analysis of randomized controlled trials that investigated the effectiveness of exercise during cancer treatment on reducing cancer-related fatigue. In total, the authors identified 16 randomized controlled trials that examined the effect of exercise on patient-reported fatigue. Of these 16 studies, 12 were among women with breast cancer, whereas two were among men with prostate cancer, with the last two in other cancer patients. Among the 12 breast cancer studies, seven employed a home-based, self-monitored exercise intervention, whereas, in the other five studies, exercise was performed under supervised conditions. In six of the seven home-based exercise interventions, the exercise regimen consisted predominately of walking, with the other study incorporating both resistance training and walking. Among all seven home-based exercise interventions, patients walked between three and six times per week for 10-45 minutes each time. The intensity of walking ranged from a self-selected pace to 70% of maximum heart rate. Importantly, the adherence to the exercise intervention was reported in all but one study, with 70-100% of participants reporting full completion of the home-based exercises. In the five supervised exercise interventions, participants completed aerobic and resistance training exercises. Aerobic exercises consisted of 10-30 min in duration at an intensity of 40-80% of maximum heart rate. Resistance training was carried out for 15-30 minutes or at an intensity of 60-70% of one repetition maximum ([1RM] 2 sets x 12 repetitions). When all 12 studies were pooled together, the results showed a significant reduction in cancer-related fatigue in the exercise group (standardized mean difference [SMD] = 0.29, 95% CI: 0.06-0.52). Overall, these results support that patient-reported fatigue can be reduced with exercise among women undergoing adjuvant therapy for breast cancer.

In 2010, Duijts and colleagues[145] conducted a meta-analysis examining the effects of randomized controlled trials on psychosocial factors that influence quality of life, including fatigue, depression, and body-image, among breast cancer patients and survivors. In total, 14 randomized controlled trials were identified. Overall, the results were supportive of a positive effect of exercise on these psychosocial factors. For the effect of the randomized controlled trials, statistically significant results were found for fatigue (effect size [ES] = -0.315, $p = 0.004$), depression (ES = -0.262, $p = 0.016$), and body-image (ES = 0.28, $p = 0.007$).

Quality of Life

In addition to examining various psychosocial influences that may influence overall quality of life, Duijts and colleagues[145] also examined the direct effect of exercise on health-related quality of life of breast cancer survivors. Results showed strong evidence for a positive effect of exercise on quality of life (ES = 0.298, $p = 0.001$) within this group.

Complementing these results, Bicego and colleagues[146] summarized the research literature pertaining to the effects of exercise on quality of life in women living with breast cancer. The authors' literature search identified nine intervention studies. Of these exercise intervention trials, two employed an aerobic exercise intervention, one studied the effects of a resistance training program, and three examined the effect of combined aerobic and resistance training, with the remaining three studies not specifying the intervention as aerobic or resistance (i.e., these studies used Tai Chi Chuan, dance and movement therapy, and a seated gentle active range of motion program). The length of each training session ranged from 10-20 minutes to 90 minutes, with the frequency ranging from two to five times per week. The duration of the exercise interventions ranged from eight weeks to six months. In nearly all of the studies, some aspect of quality of life improved in the exercise group, suggesting that exercise positively influences quality of life in women living with breast cancer.

Resistance Training

In 2009, De Backer and colleagues[147] conducted a systematic review to summarize the research of previous studies that used resistance training in the post-treatment phase of patients with cancer. Among the 26 studies reviewed, 15 were conducted in curatively treated patients during the post-treatment phase of breast cancer. The duration of the resistance training programs ranged from three to 24 weeks, with a median of 12 weeks. Most of the training programs prescribed two or three sessions per week. Notably, in 20 of the studies, a combination of resistance and aerobic training was applied. With respect to the prescription of resistance training, only nine studies described the number of sets and repetitions, and among the 10 studies reporting exercise intensities, intensities ranged anywhere from 30-60% of 1RM to 60-85% of 1RM, which is not consistent with the resistance training guidelines recommended by the American College of Sports Medicine (i.e., one set of 8-12 repetitions to the point of volitional fatigue). With regard to the aerobic exercises, treadmill walking and stationary cycling were the most frequently prescribed sessions. Intensities of aerobic exercises varied from 40-90% of heart rate maximum. Most of the studies (71%) assessed muscle strength (1RM), endurance tests (maximal number of repetitions at 60-75% of 1RM), hand grip tests, and flexibility tests as outcomes measures. Overall, of the 15 breast cancer studies, eight examined muscle strength as an outcome variable and, among these, seven reported increases in muscle strength, as assessed with various exercises, such as bench press, biceps curl, and leg press. With regard to muscle endurance, two of the breast cancer studies examined this variable, with one showing an increase in muscle endurance and the other reporting a decrease. These results demonstrate that increases in muscular strength occur in women with breast cancer who receive resistance training. Further research is needed to clarify the extent to whether muscular endurance improves with resistance training among women with breast cancer.

Bone Health

In 2010, Winters-Stone et al.[148] reviewed the extant literature to examine the effectiveness of exercise intervention trials on bone health in individuals with cancer. In total, eight exercise intervention studies were identified, with seven studies conducted in women with breast cancer and one study in men with prostate cancer. Of the eight trials, three were uncontrolled trials and five were controlled trials. In the five controlled trials, three compared an exercise group to a typical non-exercise group, and two used pharmacological comparison groups. With regard to setting, three trials were home-based, two were center-based, and in the remaining three trials, participants were allowed to exercise in the setting of their choice. With respect to the type of exercise, half of the trials employed resistance training and the other half aerobic training. The intensity of the programs ranged from moderate to vigorous, with few studies providing relative levels of intensity. Duration of the aerobic trials varied, with some reporting steps per day (i.e., 10,000), minutes per session (i.e., 15-30 minutes/day), and minutes per week (i.e., 120 min/wk). Three of the trials lasted five-months in duration and the remaining five trials lasted between six and 24 months. Adherence to the training programs was assessed with different criteria, with estimates ranging from 60-96%. Retention rates ranged from 81-93%.

Among the two uncontrolled breast cancer trials, one showed a decrease in total bone mineral density (one group; pre/post test), and in the other trial (one group; pre-post test; resistance training + drug therapy), bone mineral density increased at the total hip and spine, but decreased at the wrist. Of the three controlled trials among breast cancer survivors that compared aerobic exercise (n = 2) or resistance training (n = 1) to a usual care control group, two reported bone mineral maintenance at the spine or total body in the aerobic exercise groups. In the resistance training group, both the resistance training and control groups lost bone mass. In the 2 trials with a pharmacological comparison group, bone mineral density did not improve with either aerobic or resistance exercise. With regard to changes in bone markers, one uncontrolled trial reported a slight decrease in bone markers with aerobic exercise, and one controlled trial reported an increase with aerobic exercise. Although these data are limited and inconclusive, they suggest that moderate-intensity exercise among breast cancer survivors may play a beneficial role in preserving bone health, particularly bone mineral density of the spine. However, before firm conclusions can be made regarding the effect of exercise on bone health in breast cancer survivors, additional randomized controlled trials are needed.

Weight Loss

In addition to reviewing studies that examined the effects of resistance training on muscle strength and endurance among breast cancer survivors, De Backer and colleagues[147] also examined body composition, specifically, body weight, body mass index, fat mass, lean body mass, and waist or hip circumference, as outcomes variables. Of the 12 breast cancer studies, with some employing resistance-only training and others implementing both resistance and aerobic training, six studies examined body weight as an outcome variable. All six of these interventions showed no changes in body weight. Similarly, all four of the intervention studies measuring body mass index reported no changes in this variable. Three intervention studies assessed fat mass, and again, the intervention did not elicit any changes in this variable. Lastly, two exercise interventions evaluated waist or hip circumference, and of these studies, one reported a decrease and the other reported no change.

In 2009, Kim and colleagues[149] performed a meta-analysis to examine the effectiveness of aerobic exercise interventions on body composition in women with breast cancer. In total, 10 randomized controlled trials were identified. Of these, eight exercise intervention studies implemented the protocol during the participants' cancer adjuvant therapy, whereas, in two studies, the exercise intervention was implemented after the completion of the cancer adjuvant therapy. In eight of the trials, only aerobic exercise was implemented, with the other two trials combining both aerobic and muscle strength training. In most of the studies, the control group was instructed to maintain their habitual levels of exercise. The median frequency of exercise was three sessions per week with a range of two to five sessions weekly. The median duration was 30-40 minutes per session, and the intensity of exercise was moderate, at 40% to 75% of oxygen uptake or at a rating of perceived exertion between 11 and 13 on a 20-point scale. With regard to setting, in five studies, exercise was done in a supervised environment. In two studies, exercise was completed at home, and in the remaining three studies, exercise was performed in both the home and in a supervised setting. The adherence rate was reported in six of the studies, with the mean being 87.4%. Overall, results showed that among the 10 randomized controlled trials, aerobic exercise significantly improved body composition as assessed by percentage of body fat (SMD = -0.89, $p < 0.001$).

The contrasting results from the studies conducted by De Backer et al.[147] and Kim et al.[149] likely result from the intervention design. The exercise intervention studies, that found no effect on body composition, primarily used resistance training or a combination of resistance and aerobic training, whereas the exercise interventions that demonstrated a decrease in body composition employed aerobic-based interventions. These results suggest that, for the purpose of decreasing body fat percentage, women with breast cancer should undertake aerobic exercise rather than resistance training.

Aerobic Capacity

In addition to examining the effects of aerobic exercise on body composition, the meta-analysis by Kim and colleagues[149] also assessed the effectiveness of the 10 randomized controlled trials on aerobic capacity, as assessed by absolute VO_2 peak, relative VO_2 peak, and a 12-minute walk test. Among these 10 exercise interventions, absolute VO_2 peak was evaluated in three studies; relative VO_2 peak was evaluated in two studies; and the 12-minute walk test was reported in three studies. The findings showed that aerobic exercise significantly improved cardiopulmonary function as assessed by absolute VO_2 peak (SMD = 0.916, p <0.001), relative VO_2 peak (SMD = 0.424, $p < 0.05$), and the 12-minute walk test (SMD = 0.502, $p < 0.001$). These results suggest that aerobic exercise during or after cancer adjuvant therapy is an effective method of exercise for improving aerobic capacity in women with breast cancer.

Factors that Influence Physical Activity Behavior in Women with Breast Cancer

Despite the benefits of physical activity on reducing breast cancer recurrence and mortality, a significant percentage of women with breast cancer do not engage in regular physical activity. Data from a prospective study of leisure-time exercise in 231 women with early-stage breast cancer showed that prior to breast cancer diagnosis, 70% of women met current physical activity guidelines.[150] However, after the first course of adjuvant therapy, the percent meeting guidelines dropped to 39%. After the second course of cancer treatment, the percent dropped further, to 15%. Two- and 6-months after completing treatment, respectively, 41% and 37% of individuals continued to be insufficiently active, not meeting physical activity guidelines. Similarly, Harrison and colleagues[151] showed that among 287 breast cancer patients, only 33%, 35%, and 33% met current physical activity guidelines at 6, 12, and 18-months, respectively, following diagnosis of breast cancer.

Given that increasing evidence for physical activity benefits women diagnosed with breast cancer, the demand for physical activity programs for breast cancer survivors should increase. To maximize the success of these programs in making breast cancer survivors more active, it is important to understand the factors that influence physical activity participation among these women. Surprisingly, researchers have not extensively examined physical activity determinants among women with breast cancer. Among the studies that have, however, researchers have examined 1) predictors of exercise behavior prior to a randomized controlled exercise intervention,[152] 2) factors that predict exercise adherence during an exercise intervention,[153, 154] 3) predictors of follow-up exercise behavior after a randomized controlled exercise intervention,[155] and 4) determinants of exercise behavior in breast cancer survivors.[156, 157]

Predictors of Exercise Behavior before Exercise Intervention

Prior to randomization of the Women's Healthy Eating and Living exercise intervention study, Hong and colleagues[152] examined demographic, clinical, physical health, psychosocial and lifestyle behaviors that influenced self-reported physical activity among 2,819 women with breast cancer (post-treatment). Results showed that among evaluated demographic variables, which included age, education, race, marital status, and body mass index, only education ($p \leq 0.001$), ethnicity ($p \leq 0.001$), and BMI ($r = -0.27$, $p \leq 0.001$) were significantly related to physical activity levels. Among the clinical variables (cancer stage, time since diagnosis, and treatment), only current stage at diagnosis (r = -0.05, $p < 0.01$) and treatment type ($F = 3.92$, $p \leq 0.001$) were significantly associated with activity behavior. The physical health factors that were examined included physical functioning, role limits due to physical health problems, pain, and general health. Of these, only physical functioning ($r = 0.29$, $p \leq 0.001$) and general health ($r = 0.23$, $p \leq 0.001$) were significant. An assessment of mental health included measuring role limitations due to emotional problems, vitality, emotional well being, social functioning, and depression. Among these mental health factors, vitality ($r = 0.33$, $p \leq 0.001$) and depression ($r = -0.11$, $p \leq 0.001$) were significantly related to physical activity behavior. Health behaviors included alcohol intake, current smoking, and dietary composition. All of these health behaviors (alcohol intake, $r = 0.1$, $p \leq 0.001$; dietary composition, $r = 0.26$, $p \leq 0.001$; smoking, $p \leq 0.001$) were related to physical activity participation. However, after controlling for all of these variables in a multiple regression analysis, education (beta = -0.055), body mass index (beta = -0.175), a composite of the physical and mental health factors (beta = 0.162), alcohol intake (beta = 0.048) and dietary intake (beta = 0.195) emerged as significant independent predictors of physical activity.

Factors that Predict Exercise Adherence during Exercise Intervention

Using the theory of planned behavior (TPB),[158] Courneya and colleagues[153] examined the influence of this theory's constructs in predicting six-month adherence to a supervised aerobic vs. resistance training program for women with breast cancer during chemotherapy ($N = 242$). Adherence to the exercise training was 70%. Surprisingly, none of the key constructs from TPB, including intention, perceived control, instrumental attitude, affective attitude, or subjective norm, significantly predicted aerobic or resistance exercise adherence. Rather, location (beta = 0.28, p = 0.001), VO_{2peak} (beta = 0.19, $p = 0.016$), disease stage (beta = 0.18, $p = 0.015$), and depression (beta = -0.16) remained significant and explained 21% of the variance in exercise adherence.

Also examining predictors of exercise adherence in a randomized controlled trial of home-based exercise in recently treated breast cancer survivors ($N = 43$), Pinto and colleagues[154] assessed the influence of demographic and medical variables as well as constructs from the Transtheoretical Model (TTM). In this home-based program, women received weekly exercise counseling from research staff via telephone, with the counseling sessions based on TTM and social cognitive theory. The variables assessed included, age, education, marital status, stage of cancer, time since diagnosis, history of exercise, baseline activity levels, and some of the constructs from the TTM (e.g., stage of change, self-efficacy, and decisional balance), but not all (e.g., processes of change). Exercise adherence was assessed by evaluating minutes of exercise participation per week, number of steps taken during planned exercise per week, and whether the participant met her weekly exercise goal. With respect to predicting mean minutes of weekly exercise, only self-efficacy emerged as a significant predictor (beta = 19.46, $p = 0.004$), with cons for exercise approaching significance (beta = -16.93, $p = 0.07$). Similar results were found when predicting mean steps per week and percent of meeting weekly exercise goals.

The divergent results from these two studies are likely attributable to the time period in which the exercise intervention occurred. Although speculative, it is possible that psychosocial and motivational factors are more instrumental in influencing exercise adherence once a certain amount of time has elapsed since adjuvant chemotherapy. During adjuvant chemotherapy, it is plausible that patients' psychosocial perceptions toward physical activity are acutely elevated; consequently, this ceiling effect may attenuate the associations toward the null. This assertion is supported by the baseline data in the study by Courneya and colleagues.[153]

Predictors of Follow-up Exercise Behavior after Exercise Intervention

Courneya and colleagues[155] reported the predictors of follow-up self-reported exercise behavior 6-months after a randomized exercise trial (aerobic vs. resistance training) in breast cancer patients (*N* = 242). Predictor variables that were assessed included various demographic variables (i.e., location, age, marital status, education, income, and employment status), psychosocial constructs (i.e., quality of life, self-esteem, fatigue, anxiety, depression, motivation, perceived control, instrumental attitude, affective attitude, and subjective norms), medical information (i.e., disease stage, lumpectomy vs. mastectomy, non-taxane chemotherapy vs. taxane chemotherapy, RDI < 85% vs. RDI ≥ 85%), 4 cycles of chemotherapy vs. 6+ cycles), behavioral variables (i.e., smoking status, pre-trial exercise status, trial adherence, intervention arm), and physical fitness/body composition variables (i.e., VO_{2peak}, strength, body mass index, % body fat, and lean body mass).

Among the demographic variables, only age (< 50 yrs and ≥ 50 yrs) was significantly related to follow-up exercise behavior ($p = 0.03$). Of the psychosocial constructs, post-intervention fatigue ($p = 0.03$), change in fatigue ($p = 0.03$), aerobic exercise motivation ($p = 0.03$), resistance exercise motivation ($p = 0.004$), resistance exercise perceived control ($p = 0.008$), aerobic exercise instrumental attitude ($p = 0.002$), resistance exercise instrumental attitude ($p = 0.006$), and aerobic exercise subjective norms (p = 0.04) were significantly associated with follow-up exercise behavior. Regarding medical information, lumpectomy vs. mastectomy ($p = 0.02$) and non-taxane chemotherapy vs. taxane chemotherapy ($p = 0.01$) were significantly related to follow-up exercise behavior. For the behavioral variables, only pre-trial exercise ($p < 0.001$) was related to follow-up exercise behavior. Lastly, for the physical fitness and body composition variables, post-intervention VO_{2peak} ($p < 0.01$), post-intervention strength ($p = 0.01$), change in strength ($p = 0.04$), post-intervention BMI ($p = 0.03$), and post-intervention percent body fat ($p = 0.03$) were significantly related to follow-up exercise behavior.

These results suggest that demographic, medical, behavioral, fitness, psychosocial, and motivational variables play important roles in exercise participation 6-months after an exercise intervention among women with breast cancer.

Determinants of Exercise Behavior in Breast Cancer Survivors

In a sample of 558 breast cancer survivors who were not undergoing cancer therapy, Milne and colleagues[156] utilized the self-determination theory (SDT) to explain their exercise behavior. In addition to measuring key constructs from SDT, including amotivation, extrinsic motivation, introjected regulation, identified regulation, intrinsic motivation, perceived competence, and autonomy support, demographic variables (i.e., age, marital status, education, income, employment status, menopausal status, treatments received, and date of treatments) and medical variables (i.e., diagnosis, cancer stage, and location of residence) were assessed. Results showed that not having lymphedema ($p < 0.01$) and income ($p < 0.01$) were associated with meeting physical activity guidelines. Moreover, compared to breast cancer survivors not meeting physical activity guidelines, those that met guidelines reported more identified regulations and intrinsic motivation ($p < 0.01$), autonomy support ($p < 0.01$), and competence ($p < 0.01$). Hierarchical regression showed that the SDT constructs explained 20% ($p < 0.01$) of the variance in physical activity.

Pinto and colleagues[157] conducted a cross-sectional study to examine motivators of health behaviors (i.e., physical activity and dietary fat intake) among 86 women diagnosed with breast cancer within the last 10-years who were not currently undergoing any cancer-related treatments. In addition to assessing physical activity and dietary fat intake, participants completed a questionnaire assessing overweight or obesity status, motivational readiness for exercise and weight loss, and some (i.e., stage of change, decisional balance, and self-efficacy), but not all (i.e., processes of change) of the constructs from the TTM. Results showed that those in the higher stages of motivational readiness (e.g., maintenance) engaged in more moderate-to-vigorous physical activity than those in lower stages (e.g., pre-contemplation and contemplation). Moreover, compared to women who were considered unhealthy (dietary fat ≥ 30% fat and not in the action/maintenance stage of change for exercise), women who were considered healthy (i.e., low-fat diet and exercising at recommended levels) reported significantly higher self-efficacy for exercise (mean: 3.27 vs. 2.26, $p \leq 0.001$). Additionally, compared to non-overweight women, overweight and obese women were more likely to be in early stages of motivational readiness for weight loss

($p = 0.01$), and reported significantly lower exercise self-efficacy (mean: 2.71 vs. 3.18, $p = 0.01$).

Although additional studies are needed, these results support that, among breast cancer survivors, psychosocial factors can predict physical activity behavior. Future studies should continue to use a theoretical framework for studying exercise motivation among women with breast cancer.[159] Theoretical predictors of physical activity will allow for a better understanding of the key determinants of physical activity behavior that can be targeted in physical activity interventions. Such information may be helpful for increasing the activity levels of women with breast cancer. Studies, although limited, suggest that the TTM is a useful framework for explaining exercise behavior among women with breast cancer,[157] as well as individuals with other diseases and disabilities.[26, 160] When applying the TTM, future studies, particularly longitudinal designs, should use all the key constructs of the TTM as, in a meta-analysis by Marshall and Biddle,[161] only 3 of the 71 studies included all of the TTM constructs, and most studies were cross-sectional. Specifically, future longitudinal studies utilizing the TTM to explain exercise behavior among women with breast cancer should include an assessment of processes of change, as this TTM construct remains relatively unexamined in this population. Processes of change are not only important in describing strategies individuals use to change exercise behavior, but they are highly important for informing intervention programs.

CHAPTER 3: MATERIALS AND METHODS

Setting and Participants

Participants for the present study were part of a three-armed, 12-month randomized controlled trial. In the present study, we examined the influence of TTM variables on changes in exercise behavior after the 12-month trial. Participants were recruited from the Oregon State Cancer Registry and through direct community recruitment. All testing procedures were conducted at Oregon Health & Science University (OHSU) in Portland, OR. Ethical approval was obtained by the institutional review board at OHSU and written informed consent was obtained from each participant prior to participation. Eligibility criteria included women aged 65+ years who have completed breast cancer treatment. Inclusion criteria were that eligible participants completed chemotherapy or radiation therapy more than two years prior to the supervised randomized controlled trial and were currently inactive (i.e., less than 30 minutes of planned moderate-intensity exercise three days a week) prior to the supervised program. Participants were excluded if they had 1) cognitive difficulties that precluded them from answering survey questions, participating in the performance tests during the supervised exercise period, or giving informed consent, 2) a medical condition, movement or neurological disorder, or medication that contraindicates participation in moderate-intensity aerobic or resistance exercise, and 3) plans to move out of the immediate Portland area within 18-months.

Design and Procedures

Participants were part of a prospective, three-armed, randomized controlled trial. The supervised intervention period was 12-months, with outcomes measured at baseline, 3, 6, and 12 months. Following the supervised program, additional assessments were made at 18-months (6-month follow-up). At baseline, participants were randomized into one of three groups: aerobic exercise training, resistance exercise training, and a control group that consisted of stretching and relaxation exercises. Briefly, participants in each group attended supervised classes 3 days a week for 12-months with each class lasting approximately 60 minutes. Both the aerobic and resistance training groups were matched as closely as possible in progression from the low to high end of the range for moderate-intensity over the first 9-months, with the intensity maintained for the final 3-months. After the 12-month supervised exercise program, participants were instructed to continue their intervention exercises as a part of a home-based program for an additional 6-months. At the end of the supervised program, participants were provided with their own equipment, an instructional DVD, and a 6-month training program to follow.

Assessment of Predictors

<u>Stage of Change</u>

To be consistent with stages of change in the TTM, regular participation in exercise was defined as "equal to five or more days per week of at least 30-minutes at a moderate-intensity." As used in previous studies,[28, 162] participants chose one of five statements describing their readiness to change their exercise behavior. The five different stages of change include: precontemplation, contemplation, preparation, action, and maintenance. For example, participants who reported "No, I don't plan to start in the next six months" were classified in the pre-contemplation stage. The stage of change algorithm has demonstrated evidence of reliability and validity in adults of the general population and those with chronic diseases.[28, 162] Using the participants' stage of change score at the 12- and 18-month assessment periods, five transitional shift groups were created: 1) stable sedentary (pre-contemplation and/or contemplation at both assessment periods); 2) activity relapsers (action or maintenance at baseline moving to contemplation or pre-contemplation at 6-months); 3) perpetual preparers (preparation at both assessment; preparation at baseline moving to pre-contemplation or contemplation at 6-months; action or maintenance at baseline moving to preparation at 6-months); 4) activity adopters (pre-contemplation, contemplation, or preparation at baseline moving to action or maintenance at 6-months); and 5) stable active (action and/or maintenance at both assessment periods). *Activity status* at the 6-month follow-up period (i.e., 18-month assessment period) was assessed, with participants in the activity adopters and stable active transitional shift groups classified as "sufficiently active" and those in the remaining transitional shift groups classified as "insufficiently active." These transitional shift groups have been validated in the general population and among adults with chronic diseases.[22, 23, 28]

Processes of Change

To examine the strategies individual's use to change their exercise behavior, a 30-item measure was used to assess both behavioral and cognitive processes of change. Fifteen items assessed behavioral processes of change (i.e., contingency management, counterconditioning, helping relationships, self-liberation, and stimulus control), whereas the other 15-items assessed cognitive processes of change (i.e., consciousness raising, dramatic relief, environmental reevaluation, self-reevaluation, and social liberation). Participants responded to each question using a Likert scale, with endpoints ranging from 1 (never) to 5 (repeatedly). A sample behavioral processes of change item is "Instead of relaxing by watching TV or eating, I take a walk or do physical activity." A sample cognitive processes of change item is "I believe that regular physical activity will make me a healthier, happier person." Reliability and validity of both the behavioral and cognitive processes of change have been previously established.[163] In this sample, internal consistency, as measured by Cronbach's alpha, was 0.80 and 0.82 for cognitive processes of change at the 12- and 18-month assessment periods, respectively. For behavioral processes of change, internal consistency was 0.79 and 0.86 at the 12- and 18-month assessment periods, respectively.

Self-Efficacy

To assess self-efficacy, or an individual’s confidence in their ability to overcome physical activity-related barriers, a 18-item measure, which has demonstrated evidence of reliability and validity, was used.[164, 165] For each question, participants responded using a Likert scale, with endpoints ranging from 1 (not at all confident) to 5 (very confident). A sample item is "I feel confident that I can participate in physical activity when I don't feel like it." In this sample, internal consistency, as measured by Cronbach's alpha, was 0.93 and 0.95 for self-efficacy at the 12- and 18-month assessment periods, respectively.

Decisional Balance

An individual's reflection of the pros and cons in engaging in regular physical activity, referred to as decisional balance, was evaluated using a 10-item measure. Five items assessed pros of regular exercise, whereas the other five items evaluated the cons of engaging in regular exercise. Using a Likert scale anchored by 1 (not at all) and 5 (very much), participants rated their degree of agreement with each perceived positive and negative consequence of exercise involvement. A sample item of pros for exercise is "physical activity would help me reduce tension or manage stress." A sample item of cons for exercise is "physical activity would take too much of my time." This measure has previously demonstrated evidence of reliability and validity.[166] In this sample, internal consistency, as measured by Cronbach's alpha, was 0.77 and 0.84 for the pros of exercise at the 12- and 18-month assessment periods, respectively. For the cons of exercise, internal consistency, as measured by Cronbach's alpha, was 0.77 and 0.86 at the 12- and 18-month assessment periods, respectively.

Self-Reported Physical Activity

To validate the transitional shift groups and to control for physical activity at the 12-month assessment period, participants self-reported their physical activity levels using the Community Healthy Activities Model Program for Seniors (CHAMPS) questionnaire. CHAMPS is a 41-item questionnaire estimating caloric expenditure per week in moderate-to-vigorous intensity exercise-related activities and all exercise-related activities. Additionally, it estimates frequency per week in moderate-to-vigorous intensity exercise-related activities and all exercise-related activities. The CHAMPS questionnaire has demonstrated evidence of reliability and validity.[167-169]

Other Variables

Prior to the supervised exercise program, demographic data were collected by self-report and consisted of age, race-ethnicity, education, marital status, and employment. Medical data immediately prior to the transition (i.e., at the end of the 12-month supervised exercise program) were collected by self-report and assessed whether the participants were diagnosed or experienced any of the following within the last 6-months: bone fracture, fall, hypertension, diabetes, high cholesterol, osteoporosis, arthritis, vision changes, heart disease, myocardial infarction, transient ischemic attack, stroke, seizure, fainting, and pulmonary embolism. Other medical variables self-reported included questions on the participants' stage of breast cancer, months since breast cancer diagnosis, and whether they were currently taking hormone replacement therapy. Body mass index (BMI) was calculated from measured weight and height (weight in kilograms divided by the square of height in meters). Overweight was defined as a BMI between 25.0 and 29.9 and obese was defined as a BMI greater than or equal 30.0.

Statistical Analyses

All analyses were performed in STATA. Means were calculated for continuous variables and proportions were calculated for categorical variables. Statistical differences between continuous variables were tested using a student's *t*-test and statistical differences between categorical variables were tested with Pearson chi-square (χ^2) tests (Table 1). Due to positively skewed data, the distributions of self-reported CHAMPS physical activity data were normalized through a square-root transformation. For composite score variables (e.g., self-efficacy), there were 54 missing values. Of the possible 4,002 values for the TTM variables, this resulted in a 99% completion of all TTM items. For these 54 missing values, row mean substitution was used. There were 6 missing values for the stage of change variable at either the 12- or 18-month assessment period. Values were not imputed or substituted for the stage of change variable..[170]

Pairwise correlation coefficients were calculated to examine the inter-relationships between caloric expenditure in moderate-to-vigorous intensity exercise-related activities, as measured by CHAMPS, and the TTM variables (i.e., processes of change, self-efficacy, and decisional balance) (Table 6). The significance of the pairwise correlations coefficients was tested using the pairwise significance option. A one-way analysis of variance was used to examine the association between the TTM variables at the 12-month period and stage of change, as well as activity status, at the 6-month follow-up period (Tables 7 and 8). TTM variables at the 12-month assessment period that were significantly associated ($p < 0.05$) with either caloric expenditure in moderate-to-vigorous intensity exercise-related activities, stage of change, or activity status (i.e., "sufficiently active" and "insufficiently active") at the 18-month period were examined in a logistic regression analysis (Table 9). For the logistic regression analysis, activity status served as the dependent variable, with "insufficiently active" coded as 0, and "sufficiently active" coded as 1. To validate activity status at the 18-month period, a student *t*-test was used to determine whether there was a statistically significant difference in caloric expenditure in moderate-to-vigorous intensity exercise-related activities at the 18-month period between those classified as "sufficiently active" (i.e., activity adopters and stable active) and "insufficiently active" (i.e., all those in the remaining three transitional shift groups). To obtain odds ratios for the association of the TTM variables at the 12-month period and activity status at the 18-month period, an adjusted logistic regression analysis was used that controlled for weight status and physical activity levels at the 12-month assessment period. Weight status was controlled for in this model because this variable was significantly associated with activity status (see Table 1). Physical activity levels at the 12-month assessment period was also included in the logistic regression because this was the only variable that was significantly associated with activity status in an additional model that also controlled for the following covariates: age, weight status, education, marital status, stage of breast cancer, months since breast cancer diagnosis, exercise attendance during the 12-month supervised program, and the group assignment during the supervised program. Note, the results of this overly adjusted model are not presented as they were similar to the model controlling for only weight status and physical activity at the 12-month period. ,[152, 153, 155, 156, 171-173] Statistical significance was established as $p < 0.05$.

CHAPTER 4: RESULTS

Of the 115 participants enrolled and randomized to one of the three intervention groups (n = 39 strength training; n = 37 aerobic training; and n = 39 control group) at the start of the randomized controlled trial, 84 participants were still enrolled in the study at the point of transition (i.e., 12-month assessment period). Of those, 69 participants completed the health history, TTM, and CHAMPS surveys at both the 12- and 18-month assessment periods. Therefore, the retention rate was 60% of the original sample (i.e., 69/115) and 82.1% of the available sample from point of transition at 12-months to 18-months follow-up (i.e., 69/84). With the exception of age (63.0 ± 3.3 vs. 70.6 ± 1.2 yrs, $p < 0.05$; mean ± S.E.) and months since breast cancer diagnosis (164.4 ±45.3 vs. 80.6 ± 5.4, $p < 0.05$; mean ± S.E.), there were no differences between the 115 participants enrolled and randomized to the supervised program and the 69 participants who completed questionnaires at the 12- and 18-month assessment periods with respect to race, education, employment, and stage of breast cancer. Descriptive characteristics stratified by activity status among these 69 participants are displayed in Table 1. Among all the demographic variables, only weight status differed by activity status ($\chi^2 = 9.7$, $p = 0.02$). Descriptive statistics for the TTM variables assessed at the 12-month period are shown in Table 2.

Table 1. Descriptive characteristics (mean or proportion [standard error]) of the analyzed sample at baseline (12-months).

Variable	**Sufficiently Active**[c]	**Insufficiently Active**[d]	**Test Statistic**
N	36	27	
Age	71.5 (0.94)	72.0 (1.0)	$t = 0.33$, $p = 0.75$
Race/Ethnicity			$\chi^2 = 0.74$, $p = 0.39$
% Non Hispanic White	97.2 (0.3)	100	
% Non Hispanic Black	2.8 (2.8)	0	
Education			$\chi^2 = 4.2$, $p = 0.38$
% High School	22.2 (7.0)	19.2 (7.9)	
% Associate/Technical Degree	13.9 (5.8)	23.1 (8.4)	
% Bachelor's Degree	33.3 (7.9)	19.2 (7.8)	
% Advanced Degree	19.4 (6.6)	34.6 (9.5)	
% Other	11.1 (5.3)	3.8 (3.8)	
Marital Status			$\chi^2 = 1.6$, $p = 0.44$
% Married	69.4 (7.8)	57.7 (9.8)	
% Divorced	19.4 (6.6)	19.2 (7.8)	
% Widowed	11.1 (5.3)	23.1 (8.4)	
Employment			$\chi^2 = 3.6$, $p = 0.46$
% Retired	80.6 (6.6)	76.9 (8.4)	
% Full-time	0	3.8 (3.8)	
% Part-Time	11.1 (5.3)	11.5 (6.3)	
% Homemaker	2.7 (2.7)	7.6 (5.3)	
% Unemployed	5.5 (3.8)	0	
BMI	27.8 (0.9)	28.6 (0.9)	t = 0.56, $p = 0.57$
Weight Status[a]			$\chi^2 = 9.7$, $p = 0.02$
% Underweight	0	3.7 (3.7)	
% Normal Weight	36.1 (8.1)	7.4 (5.1)	
% Overweight	30.6 (7.8)	59.3 (9.6)	
% Obese	33.3 (7.9)	29.6 (8.9)	
% Taking Hormones for Breast Cancer	22.8 (7.2)	18.5 (7.6)	$\chi^2 = 0.17$, $p = 0.68$
% Bone Fracture[b]	2.8 (2.8)	0	$\chi^2 = 0.78$,

			$p = 0.38$
% Fallen [b]	25.7 (7.4)	18.5 (7.6)	$\chi^2 = 0.45$, $p = 0.50$
% Hypertension [b]	11.4 (5.4)	14.8 (6.9)	$\chi^2 = 0.15$, $p = 0.69$
% Diabetes [b]	5.8 (4.0)	0	$\chi^2 = 1.6$, $p = 0.20$
% High Cholesterol [b]	5.7 (3.9)	11.1 (6.1)	$\chi^2 = 0.59$, $p = 0.44$
% Osteoporosis [b]	8.8 (4.9)	0	$\chi^2 = 2.5$, $p = 0.11$
% Arthritis [b]	14.7 (6.1)	14.8 (6.9)	$\chi^2 = < 0.01$, $p = 0.99$
% Hearing Loss [b]	8.8 (4.9)	14.8 (6.9)	$\chi^2 = 0.53$, $p = 0.46$
% Vision Changes [b]	15.1 (6.3)	22.2 (8.1)	$\chi^2 = 0.49$, $p = 0.48$
% Heart Disease [b]	0	3.7 (3.7)	$\chi^2 = 1.2$, $p = 0.25$
% Myocardial Infarction [b]	0	0	N/A
% Transient Ischemic Attack [b]	0	0	N/A
% Stroke [b]	0	0	N/A
% Seizure [b]	0	0	N/A
% Fainting Episode [b]	2.9 (2.9)	0	$\chi^2 = 0.7$, $p = 0.37$
% Pulmonary Embolism [b]	0	0	N/A
Stage of Breast Cancer			$\chi^2 = 2.0$, $p = 0.72$
0	11.1 (5.3)	19.2 (7.8)	
I	50.0 (8.4)	57.7 (9.8)	
IIa	25.0 (7.3)	15.3 (7.2)	
IIb	8.3 (4.6)	3.8 (3.8)	
IIIa	5.5 (3.8)	3.8 (3.8)	
Months Since Breast Cancer Diagnosis	84.4 (7.8)	71.7 (8.7)	$t = -1.1$, $p = 0.27$
% Who had a Health Problem that Prevented Exercise [b]	33.3 (8.3)	29.6 (8.9)	$\chi^2 = 0.09$, $p = 0.75$

[a] Underweight defined as a BMI < 18.5; normal weight defined as a BMI between 18.5 and 24.9; overweight defined as a BMI between 25.0 and 29.9; and obese defined as a BMI greater than or equal 30.0.
[b] Diagnosed or experienced this outcome within the last 6-months (i.e., between the point of transition at 12-months and the 18-months follow-up)
[c] Participants in the activity adopters or stable active transitional shift groups

[d] Participants in the stable sedentary, perpetual preparers, and activity relapsers transitional shift groups

Table 2. Descriptive statistics of the TTM variables assessed at the 12-month period.

Variable	**Mean (SD)**	**Range**
Self-Efficacy	67.7 (11.4)	37-90
Pros	19.2 (3.3)	11-25
Cons	8.9 (3.6)	5-20
Decisional Balance (Pros – Cons)	10.3 (5.2)	-4 - 20
Cognitive Processes of Change	51.9 (7.1)	34-69
Behavioral Processes of Change	48.8 (7.5)	34-69
Processes of Change (All)	100.7 (12.9)	74-129

Table 3 displays the correlation matrix between caloric expenditure in moderate-to-vigorous intensity exercise-related activities, as measured by CHAMPS, and the TTM variables (i.e., processes of change, self-efficacy, and decisional balance) at both the 12- and 18-month assessment periods. For the TTM variables, self-efficacy at 12-months was significantly associated with physical activity at 18-months ($r = 0.35$, $p < 0.05$). Similarly, cons for exercise ($r = -0.35$, $p < 0.05$) and behavioral processes of change ($r = 0.30$, $p < 0.05$) at 12-months were significantly associated with physical activity at 18-months. Pros for exercise ($r = 0.09$) and cognitive processes of change ($r = 0.07$) at 12-months, however, were not significantly associated with physical activity at 18-months ($p > 0.05$). Overall decisional balance (i.e., pros minus cons for exercise) at 12-months was significantly associated with physical activity at 18-months ($r = 0.30$, $p < 0.05$). However, overall processes of change (cognitive plus behavioral processes of change) at 12-months was not associated with physical activity at 18-months ($r = 0.21$, $p > 0.05$). physical activity at 12-months was significantly associated with physical activity at 18-months ($r = 0.68$, $p < 0.01$). Similarly, with the exception of the cognitive processes of change, all of the TTM variables were significantly associated with each other at both assessment periods.

Table 3. Correlation matrix between moderate-intensity physical activity and each of the Transtheoretical Model variables at the 12- and 18-month assessment periods.

	PA_12	PA_18	SE_12	SE_18	Pro_12	Pro_18	Con_12
PA_12	1						
PA_18	0.68*	1					
SE_12	0.21	0.35*	1				
SE_18	0.13	0.35*	0.60*	1			
Pro_12	0.13	0.09	0.32*	0.32*	1		
Pro_18	0.13	0.27*	0.42*	0.56*	0.62*	1	
Con_12	-0.26*	-0.35*	-0.35*	-0.43*	-0.14	-0.21	1
Con_18	-0.34*	-0.28*	-0.25*	-0.31*	-0.03	-0.04	0.50*
DB_12	0.27*	0.30*	0.44*	0.50*	0.73*	0.53*	-0.78*
DB_18	0.33*	0.39*	0.46*	0.59*	0.43*	0.70*	-0.50*
Cog_12	0.01	0.07	0.13	0.06	0.44*	0.41*	-0.02
Cog_18	0.11	0.16	0.28*	0.29*	0.45*	0.60*	-0.15
Beh_12	0.25*	0.30*	0.42*	0.45*	0.38*	0.55*	-0.31*
Beh_18	0.26*	0.37*	0.31*	0.49*	0.40*	0.57*	-0.36*
PC_12	0.15	0.21	0.31*	0.29*	0.46*	0.55*	-0.19
PC_18	0.22	0.30*	0.32*	0.44*	0.47*	0.65*	-0.30*

	Con_18	DB_12	DB_18	Cog_12	Cog_18	Beh_12	Beh_18	PC_12	PC_18
Con_18	1								
DB_12	-0.37*	1							
DB_18	-0.74*	0.62*	1						
Cog_12	-0.03	0.29*	0.30*	1					
Cog_18	-0.13	0.39*	0.49*	0.74*	1				
Beh_12	-0.12	0.45*	0.46*	0.55*	0.54*	1			
Beh_18	-0.18	0.50*	0.51*	0.41*	0.63*	0.72*	1		
PC_12	-0.09	0.42*	0.43*	0.87*	0.72*	0.89*	0.65*	1	
PC_18	-0.17	0.50*	0.55*	0.61*	0.87*	0.71*	0.93*	0.75*	1

PA_12 = square-root transformation of caloric expenditure for moderate-intensity physical activity at 12-month period (CHAMPS)
PA_12 = square-root transformation of caloric expenditure for moderate-intensity physical activity at 18-month period (CHAMPS)
SE_12 = self-efficacy at 12-months
SE_18 = self-efficacy at 18-months
Pro_12 = pro score at 12-months
Pro_18 = pro score at 18-months
Con_12 = con score at 12-months
Con_18 = con score at 18-months
DB_12 = decisional balance score (pro minus con) at 12-months
DB_18 = decisional balance score (pro minus con) at 18-months
Cog_12 = cognitive processes of change score at 12-months
Cog_18 = cognitive processes of change score at 18-months
Beh_12 = behavioral processes of change score at 12-months
Beh_18 = behavioral processes of change score at 18-months
PC_12 = processes of change score (cognitive plus behavioral) at 12-months
PC_18 = processes of change score (cognitive plus behavioral) at 18-months
* $p < 0.05$

Activity status at the 18-month period was validated by comparing caloric expenditure in moderate-to-vigorous intensity exercise-related activities between those classified as "sufficiently active" (i.e., activity adopters and stable active) and "insufficiently active" (i.e., all those in the remaining three transitional shift groups). Using the transformed physical activity data, those classified as sufficiently active had significantly higher caloric expenditure than those classified as insufficiently active (M = 43.7 [95% CI: 37.7-49.7] vs. M = 21.1 [95% CI: 14.4-27.8], $p < 0.001$).

Results from the one-way analysis of variance are displayed in Table 4 for the TTM variables at 12-months stratified by stage of change at the 6-month follow-up. Table 5 shows the results for the TTM variables at 12-months stratified by activity status at the 6-month follow up period. For the TTM variables at the 12-month period, breast cancer survivors with higher perceptions of self-efficacy ($p = 0.01$) and greater use of the behavioral processes of change ($p < 0.01$) were more likely to be in a higher stage of change at the 6-month follow-up. Similarly, breast cancer survivors with higher perceptions of self-efficacy ($p < 0.001$) and greater use of the behavioral processes of change ($p < 0.001$) were more likely to be classified as sufficiently active, compared to insufficiently active, at the 6-month follow-up.

Table 4. Associations between TTM variables at 12-months and stage of change at the 6-month follow-up period

	Mean (*SD*)						
Variable	Precontemplation (n = 3)	Contemplation (n = 9)	Preparation (n = 17)	Action (n = 5)	Maintenance (n = 31)	F	p-value
Self-Efficacy	58.5 (7.7)	60.4 (18.4)	64.0 (12.3)	72.8 (5.1)	71.6 (10.9)	3.46	0.01
Pros	17 (1.7)	18.4 (2.2)	19.2 (3.2)	20.2 (4.3)	19.4 (3.5)	0.61	0.66
Cons	8.7 (1.2)	11.2 (3.9)	8.7 (3.9)	11.8 (4.8)	8.1 (3.0)	2.21	0.07
Decisional Balance (Pros-Cons)	8.3 (2.9)	7.2 (3.6)	10.5 (5.5)	8.4 (7.4)	11.3 (4.9)	1.41	0.24
Cognitive Processes of Change	52.7 (4.5)	49.7 (5.4)	51.6 (7.7)	56 (7.6)	52.2 (7.5)	0.64	0.64
Behavioral Processes of Change	47.0 (8.2)	42.5 (6.1)	47.0 (5.4)	51.4 (10.2)	52.0 (7.1)	4.11	< 0.01
Processes of Change (All)	99.8 (10.2)	92.1 (10.8)	98.6 (11.7)	107.4 (17.3)	104.2 (12.7)	2.14	0.08

Table 5. Associations between TTM variables at 12-months and activity status at the 6-month follow-up period.

	Mean (*SD*)			
Variable	Insufficiently Active ($n = 27$)	Sufficiently Active ($n = 36$)	*F*	*p*-value
Self-Efficacy	61.7 (11.0)	71.8 (10.2)	13.8	< 0.001
Pros	18.6 (2.8)	19.5 (3.5)	1.20	0.27
Cons	9.8 (3.8)	8.6 (3.4)	1.64	0.20
Decisional Balance (Pros – Cons)	8.8 (4.6)	10.9 (5.2)	2.63	0.11
Cognitive Processes of Change	51.5 (6.5)	52.7 (7.5)	0.39	0.54
Behavioral Processes of Change	45.4 (6.2)	52.0 (7.4)	13.45	< 0.001
Processes of Change (All)	97.0 (11.5)	104.7 (13.1)	5.74	0.02

Results from the logistic regression analysis are shown in Table 6. The adjusted logistic regression model including self-efficacy, cons for exercise, behavioral processes of change, physical activity at the 12-month assessment period and weight status significantly predicted activity status, $\chi^2(5) = 26.37$, $p < 0.001$. Thirty-one percent of the total variability of activity status was accounted for in this model. Breast cancer patients that had higher self-efficacy at the point of transition had 10% greater odds of being sufficiently active, compared to insufficiently active, 6-months after leaving the supervised exercise program ($p < 0.01$). Similarly, breast cancer survivors utilizing more of the behavioral processes of change at the point of transition had 13% greater odds of being sufficiently active, compared to insufficiently active, 6-months after the supervised exercise program ($p < 0.05$). Women with higher physical activity levels at the point of transition had 5% greater odds of being sufficiently active, compared to those insufficiently active, at 6-months post-supervised program ($p < 0.05$).

Table 6. Results of the logistic regression analysis.

Transtheoretical Model Variable[a]	**Adjusted Odds Ratio (95% CI) of Being Sufficiently Active at 6-Month Follow-Up (*N* = 63)**[b,c]
Self-efficacy	1.10 (1.01-1.18)*
Cons for exercise	1.14 (0.92-1.40)
Behavioral processes of change	1.13 (1.02-1.26)*
	Psuedo-R^2 = 0.31

[a] Variable assessed prior to the transition from supervised to home-based exercise (i.e., 12-month assessment period).
[b] Participants in the activity adopters and stable active transitional shift groups.
[c] Model adjusted for moderate-to-vigorous physical activity at the 12-month assessment period (continuous) and weight status (underweight, normal weight, overweight, and obese) at the 12-month assessment period.
Participants in the stable sedentary, perpetual preparers, and activity relapsers transitional shift groups served as the reference group.
* $p < 0.05$

CHAPTER 5: DISCUSSION

To date, few studies have examined theoretical factors that influence changes in exercise behavior among breast cancer survivors. Moreover, our knowledge in this area is even more limited for the elderly (i.e., 65+ years), as the few studies that have examined determinants of exercise behavior have been conducted in younger breast cancer survivors. Therefore, the aim of the present study was to utilize the TTM to identify theoretical determinants of regular participation in exercise during a 6-month follow-up period after a 12-month supervised exercise program among breast cancer survivors aged 65+ years. Six-months after the supervised exercise program, 57% of breast cancer survivors were considered to be sufficiently active. These exercise participation rates are very similar to those reported by Courneya et al.,[155] who reported that 58% of breast cancer survivors were meeting exercise guidelines 6-months after a supervised exercise program. Given the empirical evidence that regular participation in exercise among breast cancer survivors may reduce the risk of breast cancer recurrence and breast cancer-related mortality,[9] these exercise participation rates 6-months following a supervised exercise program are less than optimal. To increase the likelihood of breast cancer survivors maintaining their exercise program following a supervised exercise program, it is important to understand factors that influence follow-up exercise participation rates. In partial support of our hypothesis, the major finding of the present study was that breast cancer survivors who had higher self-efficacy and utilized more behavioral processes of change at the end of a 12-month supervised exercise program had greater odds of being sufficiently active 6-

months after the supervised program compared to women that were insufficiently active during the follow-up assessment.

Given the benefits of regular participation in exercise among breast cancer survivors, it is surprising that our knowledge of correlates of increased exercise participation among breast cancer survivors is limited. Although a few studies have examined cross-sectional correlates of exercise behavior in breast cancer survivors,[152, 156, 157] or examined correlates of exercise adherence during a supervised exercise program[153] or an unsupervised home-based program,[154] we were only able to identify one study examining predictors of follow-up exercise behavior after an exercise-based intervention in breast cancer survivors.[155] Courneya and colleagues[155] examined predictors of follow-up exercise behavior 6-months after a randomized trial of exercise training among 201 women with breast cancer. In addition to examining the influence of demographic, behavioral, medical, and physical fitness variables, these authors investigated the influence of psychosocial variables on changes in exercise behavior, specifically examining key constructs from the Theory of Planned Behavior (TPB). The TPB asserts that the most important determinant of behavior is behavioral intention, with key antecedents to intention including an individual's attitude (i.e., overall evaluation of the behavior) toward the behavior, their subjective norm (i.e., belief about whether most people approve or disapprove of the behavior) associated with the behavior, and their perceptions of control over the behavior (e.g., whether they feel the behavior is under their control or not under their control).[174] Their results showed that breast cancer survivors with more favorable attitudes toward exercise, stronger perceptions of control over exercise, and a stronger subjective norm for exercise were more likely to meet exercise guidelines 6-months after the supervised exercise program. Although the present study did not examine the utility of the TPB in explaining changes in exercise behavior, our findings are similar to those of Courneya et al.[155] in that psychological constructs play an important role in exercise participation. In fact, constructs from the TPB and TTM share many conceptual similarities in terms of explaining changes in exercise behavior. For example, attitude from the TPB includes all of the individual beliefs of decisional balance (pros and cons for exercise); perceived behavioral control from the TPB has similar qualities as self-efficacy from TTM; and the stage of change construct from TTM reflects both intention and behavior in the TPB.[175]

Allowing for some comparison to our study, Pinto and colleagues[157] conducted a cross-sectional study to examine the inter-relationships between TTM variables, physical activity, dietary behavior, and weight status among 86 women diagnosed with breast cancer within the last 10-years who were not currently undergoing any cancer-related treatments. Importantly, as with the majority of other studies,[161] this study assessed some (i.e., stage of change, decisional balance, and self-efficacy), but not all (i.e., processes of change) of the constructs from the TTM. Results showed that those in the higher stages of motivational readiness (e.g., maintenance) engaged in more moderate-to-vigorous physical activity than those in lower stages (e.g., precontemplation and contemplation). Moreover, compared to women who were considered unhealthy (dietary fat ≥ 30% fat and not in the action/maintenance stage of change for exercise), women who were considered healthy (low-fat diet and exercising at recommended levels) reported significantly higher self-efficacy for exercise (M = 3.27 vs. M = 2.26, F = 20.82, $p \leq 0.001$). Additionally, compared to non-overweight women, overweight and obese women were more likely to be in the early stages of motivational readiness for weight loss ($\chi^2 = 6.22$, $df = 1$, $p = 0.01$), and reported significantly lower exercise self-efficacy (M = 2.71 vs. M = 3.18, F = 6.89, p = 0.01). Collectively, these findings, along with the findings of the present study, suggest that the TTM is a useful theoretical framework for explaining exercise behavior among breast cancer survivors.

In addition to self-efficacy and the behavioral processes of change, and as expected, women with higher exercise levels at the point of transition had greater odds of being sufficiently active, compared to those insufficiently active, at 6-months post-supervised program. This finding is consistent with that of Courneya and colleagues[155] who demonstrated that past exercise behavior was a significant predictor of 6-month follow-up exercise behavior among breast cancer survivors. It is important to note, though, that all of the other covariates did not predict activity status at the 6-month follow-up. With respect to null findings for the demographic variables, this is similar to the longitudinal findings of Courneya and colleagues,[155] but in contrast to cross-sectional studies showing that age[171] and education[152] were significant predictors of exercise behavior in breast cancer survivors. These findings, along with, for example, the non-significant association of group assignment (i.e., strength training, aerobic training, and control group) on follow-up activity status, suggest that all breast cancer survivors in a supervised exercise program can benefit from being taught behavioral skills and strategies to enhances perceptions of exercise-related efficacy.

On the basis of our findings, we recommend that, prior to transitioning into a home-based exercise program, supervised exercise interventions teach behavioral skills and strategies to increase self-efficacy among breast cancer survivors. The five behavioral processes of change that should be addressed include: counterconditioning, helping relationships, reinforcement management, self-liberation, and stimulus control. Within the context of exercise, counterconditioning, or alternatively referred to as making substitutions, refers to the substitution of a less desirable behavior with a more desirable behavior, such as substituting a sedentary behavior with exercise.[176] Among all populations, but particularly older breast cancer survivors that may experience chronic fatigued as a side effect of their breast cancer treatment, substituting a sedentary behavior with exercise may seem difficult. To overcome such difficulty, breast cancer survivors could be reminded that regular exercise may actually increase their level of energy.[177] Helping relationships refers to enlisting social support to help facilitate exercise behavior.[176] When enlisting the support of others, breast cancer survivors should be taught to: 1) identify a reliable individual who would likely be willing to provide support for their exercise behavior, 2) identify different ways someone could provide support for their exercise behavior (e.g., be a walking buddy during lunch), 3) be courageous enough to actually ask the supportive individual for exercise-related support, and 4) reward the individual for their support (e.g., purchase an exercise-related shirt for them or walk with them on their favorite trail). Reinforcement management refers to rewarding oneself for engaging or maintaining exercise behavior, or being rewarded by others for such engagement.[176] Rather than always rewarding exercise behavior with sedentary behavior (e.g., going to the theater), breast cancer survivors should be encouraged to reward their exercise-related accomplishments with items that may encourage and facilitate future exercise behavior (e.g., new pair of walking shoes). Self-liberation refers to committing oneself to becoming or staying a regular exerciser.[176] For those in an early stage of behavior change, making a public statement or informing a supportive person of their exercise goals may be one way for an individual to progress into the action stage of behavior change.[177] Additionally, individuals in later stages of change (e.g., action stage) may benefit from contingency contracts or exercise contracts that indicate a reward will be obtained from accomplishing the stated exercise-related goal(s). Lastly, stimulus control involves using cues to remember to engage in exercise.[176] Examples include displaying a calendar that has exercise scheduled for particular times each day, as well as displaying an exercise-related magazine in a conspicuous location.[177]

It is important to note that processes of change, as well as self-efficacy, increase in a linear sequence across the stages of change (i.e., from precontemplation to maintenance).[20, 178] More specifically, behavioral processes of change demonstrate a greater strength of association with the later stages of change (i.e., action and maintenance stages), whereas the cognitive processes of change may be more influential in progressing through the earlier stages of change (i.e., precontemplation to preparation stages). In the present study, 62% of the breast cancer survivors were in either the action or maintenance stage at the 12-month assessment period (data not shown); thus, possibly explaining why the cognitive processes of change at 12-months did not predict activity status at the 6-month follow-up period. This suggests that, with more variability in the stages of change, cognitive processes of change may have played an important role in shaping exercise behavior. If future research corroborates this speculation, then teaching cognitive skills during the early part of a supervised intervention may be a sensible strategy too.

In addition to behavioral processes of change, breast cancer survivors with higher perceptions of self-efficacy at the conclusion of the supervised program had greater odds of being sufficiently active 6-months later. This finding is consistent with other cross-sectional studies among women with breast cancer,[154, 157] as well as other non-cancer populations.[20, 22, 26] In accordance with the tenets of TTM,[179-181] self-efficacy perceptions can be influenced from past performances, vicarious experiences (modeling), verbal encouragement, and physiological state. Therefore, to increase exercise-specific self-efficacy among breast cancer survivors, supervised exercise programs should: 1) provide enjoyable and appropriate positive exercise experiences (e.g., moderate intensity activities such as brisk walking); 2) create opportunities to observe other influential individuals (e.g., other breast cancer survivors) perform exercise; 3) provide reinforcement to participate in exercise; and 4) reduce any potential stress or anxiety associated with exercise (e.g., encourage exercising in a safe and enjoyable location). Another possible strategy for gaining self-efficacy is to have breast cancer survivors make a list of exercise-related activities at the following three difficulty levels: easy, moderate, and hard.[177] For example, and as suggested by Jordan and Nigg,[177] an older individual may rate the act of purchasing walking shoes as easy, walking around the block as moderate in difficulty, and walking a mile as hard. The individual should then be encouraged to see how many of the easy items they can accomplish, with the idea that successful completion of the easy items will enhance their perceptions of confidence, which in turn, may provide them with the confidence to attempt some of the moderate or hard items they have identified.

Limitations of the present study include the relatively small sample size and the use of self-reported physical activity data. To increase statistical power and reduce any biases associated with self-reported activity behavior, future studies should employ a larger sample size and use an objective measure of physical activity. In summary, our findings suggest that the behavioral processes of change and exercise-specific self-efficacy play an important role in follow-up exercise behavior after a supervised exercise program for breast cancer survivors. These key constructs should be considered when designing exercise-based interventions for breast cancer survivors.

CHAPTER 6: CONCLUSION

There is convincing evidence that regular participation in physical activity can reduce the risk of breast cancer. Evidence, although limited, also suggests that regular engagement in physical activity after breast cancer diagnosis can help protect against breast cancer recurrence and breast cancer-related mortality. The mechanisms responsible for the protective effect of physical activity on breast cancer are likely through changes in sex hormone levels, immune function, adiposity, and insulin-related factors. Sufficient research evidence also indicates that regular participation in physical activity after breast cancer diagnosis can mitigate common side effects of breast cancer adjuvant therapy, including fatigue, depression, quality of life, decreased muscular strength, decreased aerobic capacity, and weight gain. Studies indicate that psychosocial factors play an important role in influencing the activity patterns of breast cancer survivors. Specifically, our data suggests that self-efficacy and behavioral processes of change play an important role in follow-up exercise behavior after a supervised exercise program.

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APPENDICES

Appendix A: Tables

Table 1. Chronological overview of cohort studies examining the influence of physical activity on breast cancer risk

Study	Participants	Study Design	PA Measure	Reliability/ Validity of PA Measure	Setting of PA	Adjusted Variables	Results
Eliassen et al. 2010[54]	95,369 Postmenopausal Women in the Nurses' Health Study	Prospective	Self-reported leisure-time physical activity	Evidence of validity	Leisure-time	Age at menarche, BMI, height, parity and age at first birth, alcohol intake, postmenopausal hormone use, age at menopause, family history of breast cancer, and history of benign breast disease	***Protective Effect*** Leisure-Time Physical Activity: <1 h/wk walking (3 MET/hr/wk) to ≥ 27 MET/hr/wk: HR = 0.85 (0.78-0.93); p-trend = <0.001
George et al. 2010[57]	97,039 Postmenopausal Women	Prospective	Self-reported occupational, household,	Not provided	Occupational, household, and	Age, energy intake, recreational	***Protective Effect*** Work or at

	from the NIH-AARP Diet and Health Study		and transportation physical activity		transportation	moderate-vigorous physical activity, parity or age at first live birth, menopausal hormone therapy use, number of breast biopsies, smoking, alcohol intake, race, and BMI	Home Mostly sitting to heavy work: RR = 0.62 (0.42-0.91); p-trend = 0.024
Pijpe et al. 2010[11]	155 Premenopausal and 63 Postmenopausal women with BRCA 1/2 mutation Age: 18+ yrs (mean age: 45.5 ± 12.7 yrs)	Retrospective	Self-reported sports participation	Not provided	Leisure-time	Menopause status, use of oral contraceptives, use of hormone replacement therapy, BMI, parity, alcohol consumption.	***Non-Significant Inverse Association*** Leisure-Time Physical Activity: Never vs. Ever lifetime sports: RR= 0.84 (0.57-

							1.24) Mean MET hrs/wk: RR = Low = 1.06 (0.70-1.59), Medium = 0.64 (0.38-1.06), High=0.83 (0.5-1.37); p-trend = 0.29
Howard et al. 2009[29]	440 Premenopausal, 424 Postmenopausal Mean age: 47.2 yrs	Prospective	Self-reported physical activity in strenuous activities, walking or hiking for exercise, and walking at home or at work.	Not provided	Leisure-time and occupation	Age at menarche, parity, age at first live birth, age at menopause, family history, personal history, use of oral contraceptives, race, menopausal hormone therapy use,	***Non-Significant Inverse Association*** Total Physical Activity: Postmenopausal Women: HR for total METscore for Q2 = 0.66 (0.40-1.08), Q5 = 0.71 (0.43-

						smoking, alcohol consumption, BMI.	1.17); p-trend = 0.23
Maruti et al. 2008[30]	64,777 Premenopausal Women from the Nurses' Health Study II Age Range: 33-51 yrs	Prospective	Self-reported leisure-time PA in strenuous, moderate, and walking to and from school. Self-reported work activity	Evidence of reliability and validity.	Leisure-time and occupational	Age, childhood body shape, oral contraceptive use, family history, parity and age at first birth, alcohol consumption, smoking, height, animal fat intake, birth weight, SES, television watching, multivitamin use.	***Protective Effect*** Total Physical Activity: RR for Total activity, MET hrs/wk: 21.0-29.9 (RR=0.98, CI=0.77-1.25), >53.9 (RR=0.77, CI=0.59-1.01); p-trend = 0.04.
Suzuki et al. 2008[31]	30,157 Japanese women Age Range: 40-69 yrs	Prospective	Self-reported time spent walking per day and time spent	Not provided	Leisure-time	Age, BMI, alcohol drinking, age at menarche, education	***Protective Effect*** Leisure-Time Physical

			exercising per week			level, parity, age at birth of first child, use of exogenous female hormone, family history, menopausal status, and menopausal age for post-menopausal women.	Activity: Time spent walking per day, <30 min (reference), 30-59 min (HR=1.13, CI=0.80-1.61), >1 hr (HR=0.73, CI=0.53-1.01); p-trend = 0.04.
Dallal et al. 2007[32]	110,599 Californian Women Age Range: 20-79 yrs	Prospective	Self-reported moderate and vigorous leisure time physical activity	Not provided	Leisure-time physical activity	Race, family history, age at first full-term pregnancy, parity, hormone therapy and menopausal status combined, BMI, smoking,	***Protective Effect*** Lifetime Physical Activity: Strenuous Activity: 0-0.5 hr/wk (reference), >5 hrs/wk (RR=0.80, CI=0.69-0.94; p-

						alcohol consumption, history.	trend=0.02).
Tehard et al. 2006[33]	90,509 French Women from the E3N Cohort Age Range: 40-65 yrs	Prospective	Self-reported leisure time physical activity (moderate and vigorous), and household activity	Not provided	Leisure-time and household	BMI, menopausal status, hormone replacement therapy use, age at menarche, age at first full-term pregnancy, parity, marital status, use of oral contraceptive use, family history, employment.	***Protective Effect*** Vigorous Leisure-Time Physical Activity: None (reference), >5 hr/wk (RR=0.62, CI=0.49-0.78), p-trend <0.0001.
Silvera et al. 2006[34]	40,318 Canadian Women Age Range: 40-59 yrs	Prospective	Self-reported leisure time physical activity, sports, and household work	Not provided	Leisure-time	Age, alcohol, smoking, use of oral contraceptives, use of hormone replacement therapy,	***Non-Significant Inverse Association*** Leisure-Time Physical Activity:

						parity, age at menarche, age at first live birth, family history, menopausal status, study center, randomization group.	Vigorous physical activity: 0-30 min/day (HR=1.06, CI=0.88-1.27), 30-60 min (HR=0.98, CI=0.83-1.16), >60 min (HR=0.93, CI=0.78-1.10); p-trend =0.38
Margolis et al. 2005[35]	51,429 Norwegian and 48,075 Swedish Women from the Norwegian-Swedish Women's Lifestyle and Health Cohort Study Age Range: 30-49 yrs	Prospective	Self-reported physical activity	Not provided	Leisure-time	Age at enrollment, education, BMI, height, smoking, alcohol intake, age at menarche, parity, age at first birth, months of breast feeding, oral contraceptive	***No Effect*** Leisure-Time Physical Activity: Physical activity at enrollment: None (reference), Vigorous (RR=1.24, CI=0.85-1.82); p-

						use, family history, menopausal status, country of origin.	trend = 0.85
Colditz et al. 2003[36]	110,468 premenopausal US nurses from the Nurses' Health Study II Age Range: 25-42 yrs	Prospective	Self-reported leisure-time activities including	Evidence of reliability and validity	Leisure-time	Age, height, alcohol intake, age at menarche, age at first birth, oral contraceptive use, history, BMI.	***No Effect*** Leisure-Time Physical Activity: Total Activity (MET-hrs/wk): <3 (reference), ≥27 (RR=1.04, CI=0.82-1.33); p-trend = 0.86.
McTiernan et al. 2003[37]	74,171 postmenopausal US Women from the Women's Health	Prospective	Self-reported strenuous and moderate-intensity physical	Evidence of reliability	Leisure-time	5-year age groups, BMI, hormone therapy status, race, geographic	***Protective Effect*** Leisure-Time Physical Activity:

	Initiative Cohort Study Age Range: 50-79 yrs		activity			region, income, education, breastfeeding history, hysterectomy status, history, smoking status, parity, age at first birth, number of mammograms, alcohol use, age at menarche and menopause.	Strenuous Physical Activity by Age: At age 35: Not participating in strenuous activity (reference), participating in strenuous activity (RR=0.86, CI=0.78-0.95); p-value = 0.003.
Patel et al. 2003[38]	72,608 postmenopausal Women from the American Cancer Society Cancer Prevention Study II Age Range:	Prospective	Self-reported leisure time physical activity	Not provided	Leisure-time	Age, race, BMI, weight change, history, duration of oral contraceptive use, hormone therapy use, parity, age at menarche,	***Non-Significant Inverse Association*** Leisure-Time Physical Activity: At age 40: >0-7 MET-hrs/wk

	50-74 yrs					smoking, alcohol intake, caloric intake, education, mammography history	(reference) to >42 MET-hrs/wk (RR=0.79, CI=0.61-1.03; p-trend = 0.36).
Moradi et al. 2002[39]	9,539 Pre- and Postmenopausal Swedish Women Age Range: 42-70 yrs	Prospective	Self-reported leisure and occupational physical activity	Not provided	Leisure-time and occupational	Place of residence, parity, alcohol intake, smoking, BMI, height	***Non-Significant Inverse Association*** Postmenopausal Women (Leisure): Sedentary (reference) to Regular (RR=0.6, CI=0.4-1.0; p-trend=0.07)
Lee et al. 2001[40]	39,322 US Women (primarily nurses) Age: 45+ yrs	Prospective	Self-reported leisure-time physical activity	Evidence of reliability and validity	Leisure-time	BMI, alcohol consumption, age at menarche, age at first	***Non-Significant Inverse Association*** Leisure-

	(mean=54 yrs)					pregnancy lasting greater than 6 months, parity, menopausal status, use of contraceptives, history, use of postmenopausal hormones (if applicable)	Time Physical Activity: For both Pre- and Postmenopausal women combined: <840 kJ/wk (reference) to ≥6300 kJ/wk (RR=0.92, CI=0.58-1.45; p-trend = 0.11.
Berslow et al. 2001[41]	6,160 Pre- and Postmenopausal US Women from NHANES I Age Range: 24-75 yrs	Prospective	Self-reported leisure time physical activity	Not provided	Leisure-time	Height, BMI at age 25, adult weight change, sample design variables	***Protective Effect*** Postmenopausal Women: Consistently low (reference) to consistently high active (RR=0.33,

							CI=0.14-0.82; p-trend = 0.03).
Dirx et al. 2001[42]	62,573 postmenopausal Women from the Netherlands Cohort Study Age Range: 55-69 yrs	Prospective	Self-reported leisure-time, sports, and occupational physical activity	Not provided	Leisure-time and occupational	Age, age at menarche, age at menopause, history, parity, age at first birth, education, height, and baseline alcohol and energy intake	***Protective Effect*** Leisure-Time Physical Activity: Total Leisure Activity: < 30 min/day (reference) to >90 min/day (RR=0.76, CI=0.58-0.99), p-trend = 0.003.
Luoto et al. 2000[43]	30,548 Pre- and Post Menopausal Finnish Women from the Finnish Adult Health Behavior	Prospective	Self-reported leisure-time physical activity including time spent actively commuting	Not provided	Leisure-time and transportation	Length of follow-up, education, BMI, parity and age at first birth as a joint categorical	***Non-Significant Inverse Association*** Active Commuting to Work: Unemploye

	Survey Age Range: 15-64 yrs		to work			variable and the two variables on physical activity	d/work at home (reference) to ≥30 min/day (RR=0.87,CI=0.62-1.24); p-trend = 0.83
Moore et al. 2000[44]	37,105 postmenopausal women in the Iowa Women's Health Study Age Range: 55-69 yrs	Prospective	Self-reported leisure-time physical activity	Not provided	Leisure-time	Age, age at menopause, age at first live birth, BMI at age 18, family history, education, estrogen use	***Non-Significant Inverse Association*** Leisure-Time Physical Activity: Total Physical Activity: Low (reference) to High (RR=0.95, CI=0.83-1.10).
Wyrwich and Wolinsky	3,131 postmenopausal women	Prospective	Self-reported leisure-time physical	Not provided	Leisure-time	Age, education, height,	***Protective Effect*** Regional or

2000[45]	from the Longitudinal Study on Aging Age Range: 70-98 yrs		activity			weight, BMI, physician visits in the year prior to baseline	Distant Breast Cancer: Inactive (reference), Moderate-to-Vigorous Intensity (HR=0.25, CI=0.08-0.76).
Wyshak and Frisch 2000[55]	3,940 Women (1945 athletes and 1995 non-athletes) Age Range: 21-80 yrs	Retrospective	Self-reported leisure-time participation in athletics	Not provided	Leisure-time	Age, ever pregnant, family history, smoking, current exercise, contraceptive use for women under 45 yrs, hormonal replacement therapy use for women older than 45 yrs, menopausal status,	***Protective Effect*** Leisure-Time Physical Activity: Athletes vs. Non-Athletes: Premenopausal (under 45 yrs): Women Never Pregnant: OR=0.16 (CI=0.04-0.63; p-value=0.009

						percent body fat	). All Ages: OR=0.61 (CI=0.44-0.84; p-value=0.002).
Rockhill et al. 1999[46]	121,701 Women from the Nurses' Health Study Age Range: 30-55 yrs	Prospective	Self-reported leisure-time physical activity	Not provided	Leisure-time	Age at baseline, age at menarche, history, height, parity and age at first birth, BMI at age 18, menopausal status, and postmenopausal hormone use	***Protective Effect*** Leisure-Time Physical Activity: Cumulative Average Hrs per Week of Moderate or Vigorous Activity (updated every 2 yrs): <1 hr/wk (reference) to ≥7 hrs/wk (RR=0.82, CI=0.70-0.97).
Rockhill et al. 1998[47]	116,671 Women from the Nurses'	Prospective	Self-reported leisure-time physical	Not provided	Leisure-time	Age at baseline, age at menarche,	***No Effect*** Leisure-Time

	Health Study Age Range: 25-42 yrs		activity			history, recent alcohol consumption, height, oral contractive history, parity and age at first birth (combined)	Physical Activity: Vigorous-Intensity Physical Activity: Never (reference) to 10-12 months/yr (RR=1.1, CI=0.8-1.6).
Cerhan et al. 1998[48]	1,806 Postmenopausal Women from the Iowa 65+ Rural Health Study Age Range: 62-102 yrs	Prospective	Self-reported leisure-time physical activity and physical function	Not provided	Leisure-time	Age, education, BMI, age at menstruation, age at menopause, use of hormone replacement therapy, systolic blood pressure	***Non-Significant Inverse Association*** Leisure-Time Physical Activity: All Types of Breast Cancer Combined: Inactive (reference) to Highly Active (RR=0.2,

							CI=0.05-1.0; p-trend=0.006).
Sesso et al. 1998[49]	2,608 Women from the College Alumni Health Study Age Range: 37-69 yrs	Prospective	Self-reported leisure-time physical activity	Evidence of reliability and validity	Leisure-time	Age, age at menarche, age at menopause, history, parity, postmenopausal hormone use	***Protective Effect*** Postmenopausal Women (after age 55): <500 kcal/wk (reference) to 1,000+ kcals/wk (RR=0.49, CI=0.28-0.86; p-trend=0.02).
Thune et al. 1997[2]	25,624 Norwegian Women Age Range: 20-54 yrs	Prospective	Self-reported leisure-time and occupational physical activity	Not provided	Leisure-time and Occupational	Age at entry, BMI, height, county of residence, number of children	***Protective Effect*** Occupational (Premenopausal): Sedentary (reference) to Heavy Manual Labor (RR=0.48,

							CI=0.24-0.95; p-trend=0.03).
Steenland et al. 1995[50]	593 Women from NHANES 1 Mean Age for Cases and Controls: 60 and 48 yrs, respectively	Prospective	Self-reported non-leisure-time physical activity	Not provided	Non-Leisure-Time	Age, BMI, smoking, alcohol, income, recreational physical activity, menopausal status	***Non-Significant Inverse Association*** Non-Leisure-Time Physical Activity: Little (reference), Lot (OR=0.86, CI=0.48-1.55).
Dorgan et al. 1994[51]	2,321 Women from The Framingham Heart Study Age Range: 35-68 yrs	Prospective	Physician-administered leisure-time and occupational physical activity	Not provided	Leisure-time and occupational	Age, number of pregnancies, menopausal status, age at first pregnancy, education, occupation, alcohol ingestion	***No Effect*** Leisure-Time Physical Activity: Low (reference) to High (RR=1.6, CI=0.9-2.9; p-trend=0.13).

Zheng et al. 1993[56]	2,736 Women Cases from Shanghai, China Age: 30+yrs	Record Linkage	Interview-administered occupational physical activity	Not provided	Occupational	Age	***Protective Effect*** Occupational Physical Activity: SIR for Professionals vs. Base Population: Long Sitting Time, 127, p≤0.01 Low Energy Expenditure, 131, p≤0.01
Pukkala et al. 1993[52]	1,499 Women PE teachers and 8,619 Women Language teachers from Finland Age Range: 20-74 yrs	Prospective	Self-reported occupational physical activity	Not provided	Occupational	Age, age at menarche, age at first full-term pregnancy, menopause, parity, hysterectomy and oophorectomy considered but not	***Non-Significant Inverse Association*** Occupational Physical Activity: SIR for PE Teachers vs. Total Finnish Female

						adjusted for	Population: 1.35 (CI=0.95-1.87).
Paffenbarger et al. 1992[53]	2,370 Women who were alumni from the University of Pennsylvania Age Range = 40-50 yrs	Prospective	Self-reported leisure-time	Not provided	Leisure-time	Unknown	***Non-Significant Inverse Association*** Leisure-Time Physical Activity: Less Active (reference) to Expended 1000 kcals/wk (RR=0.88, CI=0.54-1.43).
Albanes et al. 1989[4]	7,407 Women from NHANES I Age Range: 25-74 yrs	Prospective	Self-reported leisure-time and non-leisure-time physical activity	Not provided	Leisure and non-leisure-time	Age, smoking, economic status history, BMI, energy intake	***Non-Significant Inverse Association*** Leisure-Time Physical Activity:

							Much Exercise (reference) to Little or No Exercise (RR=1.0, CI=0.6-1.6; p-trend=0.98).
Frisch et al. 1985[3]	5,398 Women (2,622 athletes and 2,776 non-athletes) Age Range: 21-80 yrs	Retrospective	Self-reported leisure-time participation in athletics	Not provided	Leisure-Time	Age, parity, history, athletic status, leanness, age of menarche, smoking, use of oral contraceptives, use of hormones for menopausal symptoms	***Non-Significant Inverse Association*** Leisure-Time Physical Activity: Athlete vs. Non-Athlete: RR=1.86 (CI=1.0-3.47).

Table 2. Chronological overview of case-control studies examining the influence of physical activity on breast cancer risk

Study	Participants	PA Measure	Reliability/ Validity of PA Measure	Setting of PA	Adjusted Variables	Results
Suzuki et al. 2010[98]	405 Women Cases and 405 Women Controls from Nagano, Japan	Self-reported leisure-time physical activity	Evidence of validity	Leisure-Time	Age, residential area, BMI, alcohol intake, smoking, education, age	***Protective Effect*** Leisure-Time Physical Activity Strenuous Physical Activity

					at menarche, age at first birth and number of live birth, menopausal status, energy-adjusted isoflavone intake, and total energy-adjusted vegetable consumption	at Age 12: None vs. 5 days/wk: OR = 0.24 (0.14-0.43) Moderate-Intensity Physical Activity in Previous 5 years: None vs. 1 day/wk: OR = 0.35 (0.18-0.67)
Awatef et al. 2010[58]	400 Women Cases and 400 Women Controls from Sousse, Tunisia Age Range: 25-75 yrs	Interview-administered leisure-time physical activity	Not provided	Leisure-Time	BMI, breastfeeding, parity	***Protective Effect*** Lifetime Leisure-Time Physical Activity: Postmenopausal Women: <110 MET-hrs/wk/yr (reference) to >150 MET-hrs/wk/yr (OR=0.44, 0.26-0.70; p-trend=0.001).
Gao et al. 2009[59]	669 Women Cases and 682 Women	Interview-administered leisure-	Not provided	Occupational and Leisure-time	Age, menopausal status,	***Non-Significant Inverse Association***

	Controls from China Age: Majority between 40-59 yrs	time physical activity			recreational physical activity, BMI, income, smoking, drinking, history, menarche age, parity	Leisure-Time Physical Activity: 0 times per week (reference) to ≥6 times/wk (OR=0.72, CI=0.52-1.00; p-trend=0.03).
Kruk 2009[60]	858 Women Cases and 1085 Women Controls from Poland Age Range: 28-79 yrs	Self-reported leisure-time, household, and occupational physical activity	Evidence of reliability	Occupational , Household, and Leisure-time	Age, breast-feeding, smoking, age at menarche, BMI.	***Protective Effect*** Lifetime Leisure-time Physical Activity: Postmenopausal Women: Vigorous Activity: 0-<2.6 hrs/wk/yr (reference) to ≥10.7 hrs/wk/yr (OR=0.40, CI=0.27-0.58; p-trend=<0.0001).
Peplonska et al. 2008[61]	2,176 Cases and 2,326 Controls from Women in Poland Age Range: 20-74 yrs	Interview-administered leisure-time, occupational and household	Not provided	Leisure-time, Occupational and Household	Age, study site, education, BMI, age at menarche, menopausal status, age at menopause (in	***Protective Effect*** Lifetime Leisure-Time Physical Activity: <39.1 MET-hrs/wk (reference) to ≥70

		physical activity			postmenopausal women) parity, age at first full-term birth, breastfeeding, history, previous screening mammography	MET-hrs/wk (OR=0.81, CI=0.68-0.97; p-trend=0.029).
Kruk 2007[62]	250 Cases and 301 Controls among Women Living in the Region of Western Pomerania Age Range: 35-75 yrs	Self-reported leisure-time, occupational and household physical activity	Evidence of reliability	Leisure-time, occupational, and household	Age, BMI, smoking, breastfeeding, income, parity	***Protective Effect*** Lifetime Leisure-Time Physical Activity: Postmenopausal Women: <4.6 MET-hrs/wk/yr (reference) to >23 MET-hrs/wk/yr (OR=0.36, CI=0.19-0.67; p-trend=0.0001)
Kamarudin et al. 2006[63]	204 Women Cases and 203 Women Controls from Malaysia Mean Age for Cases: 48.7±9.5 yrs;	Unknown	Not provided	Unknown	Age at first pregnancy, age at last pregnancy, parity, history, lactation, breastfeeding	***Protective Effect*** Regular Exercise: Women who did not exercise regularly had a greater odds of developing breast cancer (OR=3.49,

	Mean Age for Controls: 47.8±12.8 yrs					CI=1.8-6.6).
Bernstein et al. 2005[64]	4538 Women Cases and 4649 Women Controls from the Women's Contraceptive and Reproductive Experiences Study Age Range: 35-64 yrs	Interview-administered leisure-time physical activity	Not provided	Leisure-time	Age, race, study site, exercise activity questionnaire type, history, age at menarche, menopausal status, age at menopause, age at first pregnancy, total number of pregnancies, BMI at 5 yrs before reference date, number of months of breastfeeding	***Protective Effect*** Leisure-Time Physical Activity: Annual MET-Hrs/Wk: ≤2.2 MET-h/wk (reference) to ≥15.2 MET-h/wk (RR=0.77, CI=0.62-0.95; p-trend=0.003).
Dorn et al. 2003[65]	740 Women Cases and 810 Women Controls from the U.S. Age Range: 40-85 yrs	Interview-administered leisure-time and occupational physical activity	Evidence or reliability	Occupational and Leisure-time	Age, education, age of menarche, history, BMI, age at first pregnancy	***Non-Significant Inverse Association*** At age 16 yrs: Postmenopausal Women: 0 hrs/yr (reference) to

						182+ hrs/yr (OR=0.77, CI=0.54-1.1; p-trend=0.93)
Carpenter et al. 2003[66]	1,883 Postmenopausal Women Cases and 1,628 Postmenopausal from the Cancer Surveillance Program Age Range: 55-72 yrs	Interview-administered leisure-time physical activity	Not provided	Leisure-time	Age at first full-term pregnancy, age at menarche and menopause, history, and interviewer	***Non-Significant Trend*** Leisure-Time Physical Activity: Lifetime Exercise: 0 MET-hrs/wk (reference) to ≥17.6 MET-hrs/wk (OR=0.66, CI=0.48-0.90, p-trend=0.07). Effect modification by family history (homogeneity of trends p-value = 0.03).
John et al. 2003[67]	1250 Women Cases and 1548 Women Controls from the Surveillance, Epidemiology, and End	Interview-administered leisure-time and occupational physical activity	Not provided	Leisure-time and occupational	Age, race, country of birth, education, history, age at menarche, parity, age at first full-term pregnancy,	***Protective Effect*** Leisure-Time Physical Activity: Total Moderate-Intensity Activity: Postmenopausal Women: <7.6 hrs/wk

	Results program and the California Cancer Registry Age Range: 35-79 yrs				breast-feeding, BMI, age at menopause for menopausal women	(reference) to ≥17.8 hrs/wk (OR=0.74, CI=0.59-0.94).
Yang et al. 2003[68]	501 Women Cases and 594 Women Controls among Asian-Americans in L.A. Age Range: 25-74 yrs	Interview-administered leisure-time and occupational physical activity	Not provided	Leisure-time and occupational	Parity, history, menopausal status, years with active jobs, job activity category, soy intake.	***Protective Effect*** Leisure-Time Activity: Postmenopausal Women: 0-3 MET-hrs/wk (reference) to >12 MET-hrs/wk (OR=0.55, CI=0.33-0.92; p-trend=0.003).
Steindorf et al. 2003[69]	706 Cases and 1,381 Controls among Premenopausal German Women Age Range: <51 yrs	Self-reported leisure-time and occupational physical activity	Not provided	Leisure-time and occupational	History, number of full term pregnancies, height, change in BMI between age 20 and 30 yrs, breastfeeding, alcohol consumption	***Non-Significant Inverse Association*** Leisure-Time Physical Activity: 17.2-70.4 MET-hrs/wk (reference) to 145-564.4 MET-hrs/wk (OR=0.94, CI=0.65-1.35; p-

						trend=0.29).
Hirose et al. 2003[70]	2,376 Japanese Women Cases and 18,977 Japanese Women Controls from data from the Hospital-Based Epidemiologic Research Program at Aichi Cancer Center Ages: 30+ yrs	Self-reported leisure-time physical activity	Not provided	Leisure-time	Age, visit year, menopausal status, age at menarche, history, parity, age a first full-term pregnancy, drinking, intake of fruit, dietary restriction, stomach cancer screening, BMI, occupation	***Protective Effect*** Leisure-Time Physical Activity: All Women: No Exercise (reference) to ≥2 times/wk (OR=0.81, CI=0.69-0.94; p-trend=0.015).
Johnson et al. 2002[71]	81 ***Male*** Cases and 1,905 ***Male*** Controls from the National Enhanced Cancer Surveillance System in Canada Age Range: 42-74 yrs	Self-reported leisure-time and occupational physical activity	Not provided	Leisure-time and Occupational	5-year age group, marriage status, coffee consumption, BMI, providence	***Protective Effect*** Moderate and Strenuous Physical Activity Plus Occupational Physical Activity: 0-<7 sessions/month (reference) to ≥37 sessions/month (OR=0.48, CI=0.26-0.91; p-trend=0.025).
Adams-	716 Women	Self-	Not	Leisure-time	Education, age	***Protective Effect***

Campbell et al. 2001[72]	Cases and 1408 Women Controls from the Black Women's Health Study Age Range: 21-69 yrs	reported leisure-time physical activity	provided		at menarche, BMI at age 18, age at first birth, history	Leisure-Time Physical Activity: Premenopausal Women (exercise at age 21): <1 hr/wk of strenuous exercise (reference) to 7+ hrs/wk (OR=0.5, CI=0.3-0.8; p-trend=0.01).
Ewertz et al. 2001[73]	156 ***Male*** Cases and 468 ***Male*** Controls from Scandinavia Mean Age: ~65 yrs	Self-reported leisure-time physical activity	Not provided	Leisure-time	Not provided	***Non-Significant Inverse Association*** Leisure-Time Physical Activity: Sedentary (reference) to Heavy (OR=0.4, CI=0.1-1.6; p-trend>0.5).
Friedenreich et al. 2001[74]	1,237 Women Cases and 1,241 Women Controls from Alberta Age Range: <80 yrs	Interview-administered leisure-time physical activity	Evidence of reliability	Leisure-time	Age, waist-to-hip ratio, education, history, hormone replacement therapy use,	***Protective Effect*** Leisure-Time Physical Activity: Postmenopausal Women (total lifetime physical activity):

	(mean=56 yrs)				alcohol, smoking	0-<86.6 MET-hrs/wk/yr (reference) to ≥134.9 MET-hr/wk/yr (OR=0.7, CI=0.52-0.94).
Gilliland et al. 2001[75]	712 Women Cases and 844 Women Controls from the New Mexico Women's Health Study Age Range: 35-74 yrs	Interview-administered leisure-time physical activity	Not provided	Leisure-time	Age, age at first full-term birth, months of lactation, parity, years of oral contraceptive use,	***Protective Effect*** Leisure-Time Physical Activity: Hispanic Postmenopausal Women (total physical activity): 0-<25 MET-hrs/wk (reference) to ≥90 MET-hrs/wk (OR=0.38, CI=0.18-0.77; p-trend=0.002).
Lee et al. 2001[76]	394 Women Cases and 788 Women Controls from the Women's Health Study Mean age: 56 yrs	Self-reported leisure-time physical activity	Evidence of reliability	Leisure-time	Randomized treatment, age, BMI, alcohol, age at menarche, age at first pregnancy, parity,	***No Effect*** Leisure-Time Physical Activity: Lifetime Physical Activity: 0-3 MET-hrs/wk (reference) to ≥52.9 MET-

					menopausal status, use of oral contraceptive use, use of postmenopausal hormone replacement therapy, history	hrs/wk (OR=1.1, CI=0.73-1.67; p-trend=0.47).
Matthews et al. 2001[77]	1,459 Women Cases and 1,556 Women Controls from the Shanghai Breast Cancer Study Age Range: 25-64 yrs	Interview-administered leisure-time and occupational physical activity	Not provided	Leisure-time and Occupational	Age, education, income, history, age at menarche, age at first live birth, age at menopause	***Protective Effect*** Leisure-Time Physical Activity (during adolescents): No Exercise (reference) to 4.30+ MET-hrs/day/yr (OR=0.52, CI=0.39-0.70; p-trend<0.01).
Moradi et al. 2000[78]	3,347 Cases and 3,455 Controls from Postmenopausal Women in Sweden Mean Age for Cases and	Self-reported leisure-time and occupational physical activity	Not provided	Leisure-time and Occupational	Age, age at menarche, parity and age at first birth (combined), BMI at 1-year before data collection,	***Protective Effect*** Leisure-Time Physical Activity (recent years): >2 hrs/wk (reference) to < 1 hr/wk (OR=1.3, CI=1.1-1.5; p-

	Controls: 63.4±6.6 yrs, 64.3±6.5 yrs, respectively				height, use of hormone replacement therapy, age at menopause, use of oral contraceptives	trend=0.005).
Verloop et al. 2000[79]	918 Cases and 918 Controls among Dutch Women Age Range: 20-54 yrs	Interview-administered leisure-time and occupational physical activity	Not provided	Leisure-time and Occupational	Education, BMI, age at menarche, history, parity, duration of breast feeding, smoking, alcohol	***Protective Effect*** Leisure-Time and Occupational Physical Activity combined: No leisure-time/light occupational (reference) to Yes Leisure-time/moderate occupational (OR=0.58, CI=0.42-0.82).
Shoff et al. 2000[80]	4,614 Cases and 5,817 Controls among Postmenopausal U.S. Women Age Range: 20-74 yrs	Telephone interview assessing strenuous physical activity or team sports participation	Not provided	Leisure-time	BMI at age 18, age of first full-term pregnancy, parity, age at menarche, history, education, age at menopause	***Protective Effect*** Leisure-Time Physical Activity: Frequency of Activity (times/yr): 0.0 (reference) to ≥364 (OR=0.55, CI=0.39-0.78; p-

						trend=0.002).
Coogan and Aschengrau 1999[81]	233 Cases and 670 Controls among U.S. Women in the Massachusetts Cancer Registry Age: Majority >60 yrs	Telephone interview assessing occupational physical activity	Not provided	Occupational	Vital status, education, total duration of work	***Non-Significant Inverse Association*** Occupational Physical Activity: Exclusively Sedentary Job (reference) to Medium or Heavy Job (OR=0.9, CI=0.4-1.9; p-trend=0.63).
Marcus et al. 1999[82]	864 Cases and 790 Controls from the Carolina Breast Cancer Study Age Range: 20-74 yrs	Interview-administered leisure-time physical activity	Not provided	Leisure-time	Race, age at diagnosis, sampling design	***Non-Significant Inverse Association*** Leisure-Time Physical Activity at Age 12 years: No reported Activity (reference), Any Reported Activity (OR=0.8, CI=0.6-1.0).
Levi et al. 1999[83]	246 Cases and 374 Controls among Women in the Swiss Canton of	Interview-administered leisure-time and occupationa	Not provided	Leisure-time and Occupational	Age, education, age at menarche, age at first birth, number of	***Protective Effect*** Leisure-Time Physical Activity (age 15-19 yrs): Low (reference)

	Vaud Age Range: 27-74 yrs	l physical activity			births, menopausal status, age at menopause, calorie intake, history	to High (OR=0.42, CI=0.26-0.69; p-trend=0.001).
Ueji et al. 1998[84]	148 Cases and 236 Controls among Japanese Women Age Range: 26-69 yrs	Self-reported leisure-time and occupationa l physical activity	Not provided	Leisure-time and Occupational	History, education, age at menarche, age at first birth, parity, menopausal status, height, BMI	***Protective Effect*** Leisure-Time Physical Activity: None (reference) to ≥15.3 METs/wk (OR=0.35, CI=0.17-0.73; p-trend=0.005).
Mezzetti et al. 1998[85]	2,569 Cases and 2,588 Controls among Women in Italy Age Range: 23-74 yrs	Interview-administere d leisure-time physical activity	Not provided	Leisure-time	Age, center, B-carotene, Vitamin E, alcohol, BMI, calorie intake, education, menopausal status	***Non-Significant Inverse Association*** Total Physical Activity: Postmenopausal Women: High (reference) to Low (OR=1.61, CI=0.91-2.23).
Hsing et al. 1998[86]	178 ***Male*** Cases and 512	Next-of-kin Interviewed	Not provided	Leisure-Time	Age at death and SES	***Non-Significant Inverse***

	Male Control Cases from the National Mortality Followback Survey Age: 25+ yrs	administered leisure-time physical activity				***Association*** Leisure-Time Physical Activity: Regular Exerciser (reference) to Hardly Any (OR=1.3, CI=0.8-2.0).
Gammon et al. 1998[87]	1,668 Case and 1,505 Controls among U.S. Women Age Range: <45 yrs	Interview-administered leisure-time physical activity	Not provided	Leisure-time	Age, center, age at first birth, age at menarche, parity, lactation, number of abortions, number of miscarriages, menopausal status, marital status, education, family income, race, BMI at age 20 yrs, BMI in adulthood, months or oral contraceptive use, use of menopausal estrogens,	***No Effect*** Leisure-Time Physical Activity: Premenopausal Women: 1.62-18.07 MET-hrs/wk (reference) to 42.96-98.00 MET-hrs/wk (OR=1.04, CI=0.84-1.28).

					alcohol use, smoking, calorie intake in the past year, history	
Coogan et al. 1997[88]	4,863 Cases and 6,783 Controls among U.S. Women Age: <74 yrs	Telephone interview assessing occupational physical activity	Not provided	Occupational	Age, state, BMI, history, age at menarche, parity, age at first birth, education, physical activity during ages 14-22, alcohol consumption	***Non-Significant Inverse Association*** Occupational Physical Activity Premenopausal Women: Sedentary (reference) to Heavy (OR=0.64, CI=0.32-1.28; p-trend=0.16).
Hu et al. 1997[89]	157 Women Cases and 369 Women Controls from Japan Age Range: 26-75 yrs	Self-reported leisure-time physical activity	Not provided	Leisure-Time	Unadjusted	***Non-Significant Inverse Association*** Leisure-Time Physical Activity: Premenopausal Women: Total Energy Expenditure (kcal/wk): 0 (reference) to 1100+ (RR=0.72,

						CI=0.38-1.38), p-trend=0.29.
Chen et al. 1997[90]	747 Women Cases and 961 Women Controls from the Seattle-Puget Sound Surveillance, Epidemiology, and End Results registry Age Range: 21-45 yrs	Self-reported leisure-time physical activity	Not provided	Leisure-time	County of residence, age at menarche, age at first term pregnancy, parity, history, BMI, education, family income, smoking status, alcohol	***Non-Significant Inverse Association*** Leisure-Time Physical Activity (two-years prior to reference date): 0 episodes/wk (reference) to 4+ episodes/wk (OR=0.93, CI=0.71-1.22; p-trend=0.91).
McTiernan et al. 1996[91]	537 Women Cases and 492 Women Controls from the National Cancer Institute's Surveillance, Epidemiology, and End Results program Age Range: 50-64 yrs	Interview-administered leisure-time physical activity	Not provided	Leisure-time	Age, age at first full-term pregnancy, BMI, history, use of oral contraceptives, use of hormone replacement therapy, alcohol use, dietary fat intake, education, number of previous screening	***Non-Significant Inverse Association*** Leisure-Time Physical Activity: Pre- and Postmenopausal Women (hours exercised per week): 0 (reference) ... 3.6 (OR=0.6, CI=0.4-0.9), >5 (OR=1.1, CI=0.7-1.6); p-trend =

					mammograms	0.29.
D'Avanzo et al. 1996[13]	2,569 Cases and 2588 Controls among Women in Italy Age Range: 20-74 yrs	Self-reported leisure-time and occupational physical activity	Not provided	Leisure-time and Occupational	Age, center, age at menarche, age at first birth, parity, menopausal status, age at menopause, calorie intake, history	***Protective Effect*** Occupational Physical Activity: Postmenopausal Women: Very Low (reference) to Very High (OR=0.62, CI=0.4-0.9; p-trend<0.05).
Hirose et al. 1995[92]	1,186 Cases and 23,163 Controls Among Japanese Women Age Ranges: 20-80+ yrs	Self-reported leisure-time physical activity	Not provided	Leisure-time	Age, age at menarche, parity, education, BMI	***Protective Effect*** Leisure-Time Physical Activity: Postmenopausal Women: No Exercise (reference) to ≥2 times/wk (OR=0.72, CI=0.53-0.97; p<0.05).
Mittendorf et al. 1995[93]	6,888 Cases and 9,539 Controls among U.S. Women Age Range:	Telephone interview to assess participation in strenuous physical	Not provided	Leisure-time	Age, state, age at menarche, age at first birth, parity, history, BMI, menopausal	***Protective Effect*** Leisure-Time Physical Activity: No Strenuous Physical Activity at ages 14-22

	17-74 yrs	activity			status, age at menopause, type of menopause, recent alcohol consumption, interaction of menopausal status and BMI	(reference), Daily Strenuous Physical Activity at ages 14-22 (OR=0.5, CI=0.4-0.7; p-trend=0.02).
Taioli et al. 1995[94]	617 Cases and 531 Controls among U.S. Women Age: 25+ yrs	Interview-administered leisure-time physical activity	Not provided	Leisure-time	Age, education, BMI, age at menarche, pregnancies	***No Effect*** Leisure-Time Physical Activity (hrs of exercise per week): No Exercise (reference) to ≥3 (OR=1.0, CI=0.6-1.8).
Friedenreich and Rohan 1995[95]	451 Cases and 451 Controls among South Australian Women Age Range: 20-74 yrs	Interview-administered leisure-time physical activity	Not provided	Leisure-time	BMI and energy intake	***Non-Significant Inverse Association*** Leisure-Time Physical Activity: Premenopausal Women: 0 kcals/wk (reference) to >4,000 kcals/wk (OR=0.6, CI=0.3-1.17; p-

						trend=0.09)
Bernstein et al. 1994[5]	545 Cases and 545 Controls among U.S. Women in the University of Southern California Cancer Surveillance Program Age: <40 yrs	Interview-administered leisure-time physical activity	Not provided	Leisure-time	Age at menarche, age at first full-term pregnancy, parity, months of lactation, history, reference date, oral contraceptive use,	***Protective Effect*** Leisure-Time Physical Activity: Inactive (reference), Active (at least 3.8 hrs of exercise per week; OR=0.42, CI=0.27-0.64).
Dosemeci et al. 1993[96]	3,486 ***Males*** Cases, 379 Female Cases, 2,217 ***Male*** Controls, and 244 Female Controls from Istanbul, Turkey Age: Majority <55 yrs	Occupational physical activity	Not provided	Occupational	Age, smoking, SES	***No Effect*** Occupational Physical Activity (kJ/min): Males: > 12 kJ/min (reference) to <8 kJ/min (OR=0.3, CI=0.0-2.4; p-trend=0.34). Females: > 12 kJ/min (reference) to <8 kJ/min (OR=0.7, CI=0.2-3.4; p-

						trend=0.23).
Vena et al. 1987[97]	25,000 Working Women in Wash. State; 791 Cases Age Range: 30-79 yrs	Self-reported occupational physical activity	Not provided	Occupational	Age	***Protective Effect*** Occupational Physical Activity: Active vs. Inactive: Proportionate Mortality Ratio = 85, p<0.05.

Table 3. Chronological overview of epidemiological studies on physical activity for breast cancer survivors

Study	Participants	Study Design	PA Measure	Psychometrics of PA Measure	Adjusted Variables	Influence on Breast Cancer Recurrence	Influence on Mortality from Breast Cancer
Friedenreich et al. 2009[132]	1,231 Canadian women diagnosed with breast cancer Mean age at diagnosis: 56±12.1 yrs	Prospective Cohort	Interview-administered lifetime leisure-time, occupational, and household physical activity	Not provided	Age, tumor stage, treatment, SBR grade, BMI, other types of physical activity	***Moderate Effect*** Lifetime Leisure-Time Physical Activity: ≤5 MET-hrs/wk/yr (reference) to >19 MET-hrs/wk/yr (HR=0.76, CI=0.55-1.03; p-trend=0.07)	***Protective Effect*** Lifetime Leisure-Time Physical Activity: ≤5 MET-hrs/wk/yr (reference) to >19 MET-hrs/wk/yr (HR=0.54, CI=0.36-0.79; p-trend=0.001)

Holick et al. 2008[133]	18,273 women from the Collaborative Women's Longevity Study who were diagnosed with breast cancer Mean age at diagnosis: ~59 yrs	Case-Control	Questionnaire assessing leisure-time physical activity after breast cancer diagnosis	Evidence of validity	Age at diagnosis, stage of disease at diagnosis, state of residence, interval between diagnosis and physical activity assessment, postdiagnosis BMI, postdiagnosis menopausal status, postidagnosis hormone therapy use, total energy intake year	N/A	***Protective Effect*** Total Leisure-Time Physical activity: <2.8 MET-hrs/wk (reference) to ≥21 MET-hrs/wk (HR=0.51, CI=0.29-0.89; p-trend=0.05) Moderate-Intensity Physical Activity: <2.0 MET-hrs/wk (reference) to ≥10.3 MET-hrs/wk (HR=0.47, CI=0.26-0.83; p-trend=0.03)

					before enrollment, education level, family history, initial treatment modality		Vigorous-Intensity Physical Activity: 0.0 MET-hrs/wk (reference) to ≥15.1 MET-hrs/wk (HR=1.02, CI=0.53-1.97; p-trend=0.92)
Irwin et al. 2008[134]	983 women diagnosed with breast cancer from the Health, Eating, Activity, and Lifestyle Study	Prospective Cohort	Interview-administered leisure-time, occupational, and household physical activity assessed the year before diagnosis and 2-yrs after diagnosis	Not provided	Age, race, disease stage, initial treatment, tamoxifen use (BMI and fruit/vegetable controlled for 2-yrs after diagnosis)	N/A	***Non-Significant Inverse Association*** Physical Activity Assessed 1-YR Before Diagnosis: 0-MET-hrs/wk (reference) to >9MET-hrs/wk (HR=0.83, CI=0.49-

							1.38; p-trend=0.27). Physical Activity Assessed 2-YRS After Diagnosis: 0-MET-hrs/wk (reference) to ≥9MET-hrs/wk (HR=0.65, CI=0.23-1.87; p-trend=0.46). Note, significant trends (p<0.05) occurred for both assessment periods when the outcome was total deaths (not just death

							from breast cancer).
Pierce et al. 2007[131]	1,490 U.S. women diagnosed with breast cancer Age: ≤70 yrs at diagnosis	Prospective Cohort	Questionnaire assessing leisure-time physical activity at baseline	Evidence of reliability and validity	Unadjusted	N/A	***Protective Effect*** 0-225 MET-min/wk (reference) to 1,320-6,420 MET-min/wk (Cox Hazard=0.58; p-trend=0.02)
Abrahamson et al. 2006[135]	1,264 women diagnosed with breast cancer Age Range: 20-54 yrs (mean age at diagnosis: 42 yrs)	Prospective Cohort	Questionnaire assessing leisure-time physical activity	Not provided	Following variables were considered and removed using backward elimination: Menopausal status, age at diagnosis, race, stage, ER and PR	N/A	***Non-Significant Inverse Association*** Year Before Diagnosis: 1.6-21.5 MET-hrs/wk (reference) to 75.6-98.0 MET-hrs/wk (HR=0.78, CI=0.56-1.08; p-trend=0.10)

					status, study site, prior breast history, family history, age at menarche, use of oral contraceptives, parity, age at first live birth, number of miscarriages, number of induced abortions, lactation history, income, education, marital status, alcohol, smoking, energy		

					intake, BMI at age 20 yrs, BMI 1-yr before diagnosis, presence of co-morbidities at the time of interview, initiation of chemotherapy or radiation therapy prior to interview		
Holmes et al. 2005[10]	2,987 women diagnosed with breast cancer from the Nurses' Health Study	Prospective Cohort	Questionnaire assessing leisure-time physical activity 2-yrs after diagnosis	Not provided	Age, interval between diagnosis and physical activity assessment,	***Moderate Effect*** <3 MET-hrs/wk (reference) to ≥24 MET-hrs/wk (RR=0.74, CI=0.53-	***Protective Effect*** <3 MET-hrs/wk (reference) to ≥24 MET-hrs/wk (RR=0.60, CI=0.40-

					smoking, BMI, menopausal status, hormone therapy use, age at first birth, parity, oral contraceptive use, energy intake, disease stage, radiation treatment, chemotherapy, tamoxifen treatment	1.04; p-trend=0.05).	0.89; p-trend=0.004).

Appendix B: Transtheoretical Model Questionnaire

Directions: Have you been *regularly* participating in physical activities of *moderate intensity* (such as walking, recreational swimming, cycling, dancing and other similar activities)? Activities that are primarily sedentary, such as bowling, playing golf with a cart, and passive stretching, would not be considered physical activity. REGULAR PHYSICAL ACTIVITY = 5 DAYS OR MORE PER WEEK FOR 30 MINUTES OR MORE DAILY.

Note: the accumulation of 30 minutes of daily activity can be obtained *consecutively* or in an *additive manner* of two separate 15-minute activity sessions.

Please indicate the statement that most closely applies to your activity level.

❐ Yes, I have been for more than 6 months.

❐ Yes, I have been, but for less than 6 months.

❐ Not regularly, but I engage in such activities occasionally and plan to start on a regular basis within the next month.

❐ No, but I'm thinking of starting in the next 6 months.

❐ No, and I am not thinking of starting in the next 6 months.

Section 2: Self-efficacy

<u>Directions</u>: Listed below are 18 statements designed to assess your beliefs in your ability to engage in physical activity under various circumstances or conditions. Please rate each statement as it applies to you and your situation by circling the appropriate number.

<u>**The following stem precedes each question:** *I am confident I can participate in regular physical activity when…*</u>

1. I am under a lot of stress.

Not at all Confident	Not Confident	Uncertain	Confident	Very Confident
1	2	3	4	5

2. I am depressed.

Not at all Confident	Not Confident	Uncertain	Confident	Very Confident
1	2	3	4	5

3. I am anxious.

Not at all Confident	Not Confident	Uncertain	Confident	Very Confident

1	2	3	4	5

4. I feel I don’t have the time.

Not at all Confident	Not Confident	Uncertain	Confident	Very Confident
1	2	3	4	5

5. I don’t feel like it.

Not at all Confident	Not Confident	Uncertain	Confident	Very Confident
1	2	3	4	5

6. I am busy.

Not at all Confident	Not Confident	Uncertain	Confident	Very Confident
1	2	3	4	5

7. I am alone.

Not at all Confident	Not Confident	Uncertain	Confident	Very Confident
1	2	3	4	5

8. I have to exercise alone.

Not at all Confident	Not Confident	Uncertain	Confident	Very Confident
1	2	3	4	5

9. My exercise partner decides not to exercise that day.

Not at all Confident	Not Confident	Uncertain	Confident	Very Confident
1	2	3	4	5

10. I don’t have access to exercise equipment.

Not at all Confident	Not Confident	Uncertain	Confident	Very Confident
1	2	3	4	5

11. I am traveling.

Not at all Confident	Not Confident	Uncertain	Confident	Very Confident
1	2	3	4	5

12. My gym is closed.

Not at all Very

Confident	Not Confident	Uncertain	Confident	Confident
1	2	3	4	5

13. My friends don't want me to exercise.

Not at all				Very
Confident	Not Confident	Uncertain	Confident	Confident
1	2	3	4	5

14. My significant other does not want me to exercise.

Not at all				Very
Confident	Not Confident	Uncertain	Confident	Confident
1	2	3	4	5

15. I am spending time with friends or family who do not exercise.

Not at all				Very
Confident	Not Confident	Uncertain	Confident	Confident
1	2	3	4	5

16. It's raining or snowing.

Not at all				Very
Confident	Not Confident	Uncertain	Confident	Confident
1	2	3	4	5

17. It’s cold outside.

Not at all Confident	Not Confident	Uncertain	Confident	Very Confident
1	2	3	4	5

18. The roads or sidewalks are snowy.

Not at all Confident	Not Confident	Uncertain	Confident	Very Confident
1	2	3	4	5

Section 3: Decisional Balance

Directions: This section looks at positive and negative aspects of physical activity. Please read the following items and indicate how important each statement is with respect to your decision to be physically active or not to be physically active in your leisure time. Please rate each item by circling the appropriate number.

1. Physical activity would help me reduce tension or manage stress.

Not at All	Somewhat	Moderately	Very	Extremely
1	2	3	4	5

2. I would feel more confident about my health by getting physical activity.

Not at All	Somewhat	Moderately	Very	Extremely
1	2	3	4	5

3. I would sleep better.

Not at All	Somewhat	Moderately	Very	Extremely
1	2	3	4	5

4. Physical activity would help me have a more positive outlook.

Not at All	Somewhat	Moderately	Very	Extremely
1	2	3	4	5

5. Physical activity would help me control my weight.

Not at All	Somewhat	Moderately	Very	Extremely
1	2	3	4	5

6. I am too tired to get physical activity because of my other daily responsibilities.

Not at All	Somewhat	Moderately	Very	Extremely
1	2	3	4	5

7. Physical activity would take too much of my time.

Not at All	Somewhat	Moderately	Very	Extremely
1	2	3	4	5

8. I would have less time for my family and friends if I participated in physical activity.

Not at All	Somewhat	Moderately	Very	Extremely
1	2	3	4	5

9. I'd worry about looking awkward if others saw me being physically active.

Not at All	Somewhat	Moderately	Very	Extremely
1	2	3	4	5

10. Getting physical activity would cost too much money.

Not at All	Somewhat	Moderately	Very	Extremely

1 2 3 4 5

Section 4: Processes of Change

Directions: The following experiences can affect the physical activity habits of some people. Think of similar experiences you may be currently having or have had during the past month. Please rate how frequently the event occurs by circling the appropriate number.

1. I read articles to learn more about physical activity.

Never	Seldom	Occasionally	Often	Repeatedly
1	2	3	4	5

2. I get upset when I see people who would benefit from physical activity but choose not to be active.

Never	Seldom	Occasionally	Often	Repeatedly
1	2	3	4	5

3. I realize that if I don't do physical activity regularly, I may get ill and be a burden to others.

Never	Seldom	Occasionally	Often	Repeatedly
1	2	3	4	5

4. I feel more confident when I do physical activity regularly.

Never	Seldom	Occasionally	Often	Repeatedly
1	2	3	4	5

5. I have noticed that many people know physical activity is good for them.

Never	Seldom	Occasionally	Often	Repeatedly
1	2	3	4	5

6. When I feel tired, I make myself do physical activity anyway because I know I will feel better afterwards.

Never	Seldom	Occasionally	Often	Repeatedly
1	2	3	4	5

7. I have a friend who encourages me to do physical activity when I don't feel up to it.

Never	Seldom	Occasionally	Often	Repeatedly
1	2	3	4	5

8. One of the rewards of regular physical activity is that it improves my mood.

Never	Seldom	Occasionally	Often	Repeatedly
1	2	3	4	5

9. I tell myself that I can keep doing physical activity if I try hard enough.

Never	Seldom	Occasionally	Often	Repeatedly
1	2	3	4	5

10. I keep a set of physical activity clothes with me so I can do physical activity whenever I get the time.

Never	Seldom	Occasionally	Often	Repeatedly
1	2	3	4	5

11. I look for information related to physical activity.

Never	Seldom	Occasionally	Often	Repeatedly

1	2	3	4	5

12. I am afraid of the results to my health if I do not do physical activity.

Never	Seldom	Occasionally	Often	Repeatedly
1	2	3	4	5

13. I think that by doing physical activity regularly I will not be a burden to the health care system.

Never	Seldom	Occasionally	Often	Repeatedly
1	2	3	4	5

14. I believe that regular physical activity will make me a healthier, happier person.

Never	Seldom	Occasionally	Often	Repeatedly
1	2	3	4	5

15. I am aware of more and more people who are making physical activity a part of their lives.

Never	Seldom	Occasionally	Often	Repeatedly
1	2	3	4	5

16. Instead of taking a nap after work, I do physical activity.

Never	Seldom	Occasionally	Often	Repeatedly
1	2	3	4	5

17. I have someone who encourages me to do physical activity.

Never	Seldom	Occasionally	Often	Repeatedly
1	2	3	4	5

18. I try to think of physical activity as a time to clear my mind as well as a workout for my body.

Never	Seldom	Occasionally	Often	Repeatedly
1	2	3	4	5

19. I make commitments to do physical activity.

Never	Seldom	Occasionally	Often	Repeatedly

1	2	3	4	5

20. I use my calendar to schedule my physical activity time.

Never	Seldom	Occasionally	Often	Repeatedly
1	2	3	4	5

21. I find out about new methods of being physically active.

Never	Seldom	Occasionally	Often	Repeatedly
1	2	3	4	5

22. I get upset when I realize that people I love would have better health if they did physical activity.

Never	Seldom	Occasionally	Often	Repeatedly
1	2	3	4	5

23. I think that regular physical activity plays a role in reducing health care costs.

Never	Seldom	Occasionally	Often	Repeatedly
1	2	3	4	5

24. I feel better about myself when I do physical activity.

Never	Seldom	Occasionally	Often	Repeatedly
1	2	3	4	5

25. I notice that famous people often say they do physical activity regularly.

Never	Seldom	Occasionally	Often	Repeatedly
1	2	3	4	5

26. Instead of relaxing by watching TV or eating, I take a walk or do physical activity.

Never	Seldom	Occasionally	Often	Repeatedly
1	2	3	4	5

27. My friends encourage me to do physical activity.

Never	Seldom	Occasionally	Often	Repeatedly
1	2	3	4	5

28. If I engage in regular physical activity, I find that I get the benefit of having more energy.

Never	Seldom	Occasionally	Often	Repeatedly
1	2	3	4	5

29. I believe that I can do physical activity regularly.

Never	Seldom	Occasionally	Often	Repeatedly
1	2	3	4	5

30. I make sure I always have a clean set of physical activity clothes.

Never	Seldom	Occasionally	Often	Repeatedly
1	2	3	4	5