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Role of physical exercise in reducing depression and improving mental health in cancer survivors

Gregory Levin
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depression and improving mental health
in cancer survivors

Gregory Levin
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**ROLE OF PHYSICAL EXERCISE IN REDUCING
DEPRESSION AND IMPROVING MENTAL HEALTH IN
CANCER SURVIVORS**

Gregory Tony Levin

This thesis is presented in fulfilment of the requirements for the degree of

Doctor of Philosophy

Date of Submission: 01 July 2014

School of Exercise and Health Sciences
Faculty of Health, Engineering and Science
Edith Cowan University
Joondalup, Western Australia

USE OF THESIS

The Use of Thesis statement is not included in this version of the thesis.

ABSTRACT

Cancer survivors are more than twice as likely as the general population to suffer the debilitating effects of depression. This comorbid condition is associated with several negative consequences, such as reduction in compliance with cancer treatments, and hastened mortality. Recent research has examined the therapeutic effect of exercise on depression and reported excellent results of similar magnitude to those achieved with pharmacotherapy or psychological intervention. However, no research, to date, has examined the effectiveness of exercise on reducing depression in depressed cancer survivors. In order to address this important question this thesis reviewed previous literature in the area of cancer and depression, explored the exercise preferences of depressed cancer survivors living in Australia, and completed the first exercise intervention with a cohort of depressed cancer survivors.

Two descriptive reviews provided background information about the types of exercise programs that have been prescribed for cancer survivors as well as the exercise preferences of many cancer survivors. These reviews identified that there was a lack of available information relating to the optimal exercise program to improve depression and, further, that no information was available to determine the preferred exercise options of depressed cancer survivors and whether this group would be interested in engaging in exercise.

The first research study was a cross-sectional comparison of the physical activity habits and exercise preferences of depressed ($n = 158$) and non-depressed ($n = 650$) Australian cancer survivors. It was found that depressed survivors were less active (-48 mins/wk; $p < .05$), yet a greater number of depressed cancer survivors (78.5% vs 71.6%) expressed a desire to participate in an exercise program ($p = .044$). Contrary to expectations, depressed survivors were more interested in supervised sessions ($p < .001$), and were also more willing to attend their local fitness centre ($p = .049$). These findings suggest that being depressed does influence the preferred exercise program and that these differences should be considered before prescribing exercise to cancer survivors.

Secondary analysis of the dataset was conducted to examine the differences between metropolitan and regional cancer survivors, living in New South Wales, Australia. The role of exercise may be even more important for isolated regional survivors who lack access to

traditional form of psychological support and service providers. Results obtained from 366 participants revealed that the incidence of depression (~21%) was not related to location of residence. There was no difference in physical activity participation between metropolitan ($n = 236$) and regional ($n = 130$) survivors, with only 40% of all participants being sufficiently active. No differences were found for the primary perceived benefits of improving aerobic fitness, controlling weight, and improving overall health. However, metropolitan residents were more interested in the performing exercise that elicited strength and functional improvements ($p = .041$). Furthermore, there were no differences in barriers to exercise. These findings indicate that many cancer survivors, including those living in regional locations, are familiar with health benefits of exercise, yet remain insufficiently active to obtain these positive outcomes.

The final study was a longitudinal controlled trial that aimed to examine whether exercise was indeed able to produce an antidepressant effect in depressed cancer survivors. Eligible participants were allocated to a clinic-based, supervised exercise group ($n = 10$), an unsupervised, home-based exercise group ($n = 8$), or a usual care control group ($n = 14$). The supervised exercise group completed two sessions of combined resistance and aerobic training per week for the duration of the 12-week program. The home-based group were provided with printed material about the benefits of exercise and were encouraged to complete 150 minutes of exercise per week, but received no specific prescriptive information about the form of exercise they should undertake. The control group received no exercise or printed material, and were encouraged not to alter their usual activity. Intention-to-treat analysis, with the last response carried forward, found that both exercise groups improved depression, with a greater response seen in the supervised program (-56%; $p = .002$) compared to the home-based group (-48%; $p = .016$). No significant differences were found when comparing the results between the two exercise groups. When per-protocol analysis was used to examine the responses in depression, it was found that the home-based group decrease depression more rapidly, measured at week 6, and to a greater extent, than the supervised group ($d = 0.50$). At the final assessment (week 12) the home-based group and supervised group produced a similar response for a reduction in depression. These findings are the first to indicate the antidepressant effect of exercise in depressed cancer patients and the outcomes match those previously reported for people living with depression. Combined with the fact that no adverse effects were reported, the results should be used to promote exercise as a therapeutic treatment option for cancer survivors experiencing comorbid depression.

In summary, this research has demonstrated that depressed cancer survivors are able to obtain antidepressant benefits from commencing a well-designed, structured, and supervised exercise program. Despite willingness to engage in exercise, and knowledge of the perceived benefits, almost 60% of depressed cancer survivors are not performing enough physical activity. Therefore, there is need for future research to examine how to increase the uptake of exercise. Engagement is likely to increase if recommendations to commence exercise are made by the survivors' referring specialist, and, therefore, it is suggested that referral for specialised exercise should be included within best practice cancer care, to remediate comorbid depression.

DECLARATION

I certify that this thesis does not, to the best of my knowledge and belief:

- (i) incorporate without acknowledgment any material previously submitted for a degree or diploma in any institution of higher education.
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Date: 1 July 2014

Name: Gregory Tony Levin

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“Education is the most powerful weapon which you can use to change the world”

- Nelson Mandela

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CONFERENCE PRESENTATION, COMMUNITY ENGAGEMENT, AND AWARDS FROM THIS RESEARCH

Oral Presentations

1. **Levin, G.T.**, Greenwood, K.M., Newton, R.U. *A Brief clinical screen to assess depressed status in cancer survivors*. Australian Society for Medical Research WA Scientific Symposium, Perth, Australia, 5 Jun, 2013.
2. **Levin, G.T.**, Greenwood, K.M., Chapman, M., Levitt, M., & Newton, R.U. *Physical activity levels and exercise preferences of depressed and non-depressed cancer survivors*. Cancer Council 4th Biennial Research Symposium, Perth, Australia, 29 Nov, 2012.

Poster Presentations

1. **Levin, G.T.**, Greenwood, K.M., Di Benedetto, M., Newton, R.U. Exercise improves depression and satisfaction with life in cancer survivors. Exercise Sports Science Australia Conference, Adelaide, 10-12 Apr, 2014.
2. **Levin, G.T.**, Singh, F., Tsoi, D., Greenwood, K.M., Newton, R.U. Exercise improves satisfaction with life and physical function for brain cancer survivors: two exploratory case studies. Exercise Sports Science Australia Conference, Adelaide, 10-12 Apr, 2014.

Community Engagement

1. **Levin, G.T.** Exercise for physical and mental health in cancer patients. Leukaemia Foundation, Redemptorist Monastery, North Perth, WA. 17 September 2013.
2. **Levin, G.T.** Exercise for physical and mental health in cancer patients. Sir Charles Gairdner Hospital, Nedlands, WA. 3 August 2013.
3. **Levin, G.T.** Physical activity levels and exercise preferences of depressed and non-depressed cancer survivors. Cancer Council News South Wales, Sydney, NSW. 25 Jan 2013.

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CHAPTER ONE

Introduction

1.1 Introduction

1.1.1 Overview

Depression is known to cause severe disability and to negatively affect quality of life (Moller, 2008; Singh et al., 2005). Depression affects more than 300 million people globally (Carek, Laibstain, & Carek, 2011) and cancer survivors are more likely than the general population to develop depression (Satin, Linden, & Phillips, 2009). It has been reported that the rate of clinical depression is approximately 2 to 4 times higher in cancer patients than in the general population (Ramasubbu et al., 2012).

Cancer is a chronic disease that affects the lives of many people worldwide and there is a ~40% likelihood that a person will be diagnosed with cancer during their lifetime (Ferrer, Huedo-Medina, Johnson, Ryan, & Pescatello, 2011). Throughout the cancer journey, it is likely that one in two people diagnosed with cancer will experience depression or associated psychological illness (Spoletini et al., 2008). This estimation of the prevalence of depression being up to 50% of cancer survivors includes not only clinically-diagnosed depression but also takes into account all depressive disorders (Pasquini & Biondi, 2007). Many cancer survivors will suffer with symptoms of depression, but will never be diagnosed and, thus, have little or no access to psychological assistance (Sellick & Crooks, 1999).

Depression is not a single condition, but a term that can be used to cover a broad spectrum of closely related mental health conditions (Rimer et al., 2012). The most severe of these conditions is major depressive disorder (MDD) which requires an accurate diagnosis, by way of a clinical interview, performed by a qualified clinician. In accordance with criteria set by the American Psychological Association and stated in the Diagnostic and Statistics Manual for Mental Disorders (*4th Edition*, 2000), MDD requires that an individual meet at least five specific symptoms including at least one of two primary diagnostic symptoms of feeling depressed or experiencing anhedonia. Further, these symptoms must occur for a period of at least 14 days, and be unrelenting before a clinical diagnosis can be confirmed. Other established mood disorders, which are considered less severe than MDD include, depressive disorder and dysthymia (Spoletini et al., 2008). However, more recently emphasis has also been placed on the need to identify sub-clinical/subsyndromal depression, despite not meeting clinical criteria (NICE, 2009). The National Institute for Health and Clinical Excellence have identified that even subclinical levels of depression are associated with increased mortality and

cause psychological disability (2009). It has therefore been suggested, by some, that depression should be examined as a condition along a continuum, as opposed to imposing a pre-set threshold for each particular diagnosis (Maj, 2011). Measurement along this continuum could be determined by screening instruments which are known to not accurately predict MDD (Pirl, Greer, Temel, Yeap, & Gilman, 2009), but can quantify the extent of depressive symptoms.

It is well known that all forms of depression compromises quality of life and is associated with increased morbidity and mortality (Blumenthal et al., 2007; Mead et al., 2009). The negative effects are compounded in cancer survivors, who often require medical intervention that disrupts functional abilities and interferes with activities of daily living (Mock et al., 2001). Depression negatively influences the life of a cancer survivor and increases mortality (Pinquart & Duberstein, 2010; Satin et al., 2009), decreases adherence to treatment (Jehn et al., 2006; Pasquini & Biondi, 2007), and reduces quality of life (Hopwood et al., 2000). Persistent depression is also associated with an increased risk of cancer recurrence (Miller, Ancoli-Israel, Bower, Capuron, & Irwin, 2008). Therefore, there is a need to examine how to effectively treat and manage both clinical and subsyndromal depression.

However, cancer is a non-specific term that is used to characterise over 100 different types of diseases (Dimeo, 2000), many of which influence the body and immune system differently (Reiche, Nunes, & Morimoto, 2004). Similarly, psychological responses to cancer are not uniform with varying rates of depression reported dependent on the type of cancer as well as the stage of the disease (Humpel & Iverson, 2007). Sellick and Edwardson (2007) found in a sample of 3034 newly diagnosed cancer survivors that the cancer site significantly influenced depressive symptoms, with lung cancer (17.6%) and colorectal cancer (10.5%) far more likely to be probable cases of depression than prostate (4.0%) or breast cancer (5.3%). Furthermore, the type of treatment protocol and side-effects suffered can influence the probability of depression (Satin et al., 2009). Moreover, the timing of depression can vary and may be experienced at the stage of diagnosis or may only manifest many years after diagnosis and post-treatment (Pasquini & Biondi, 2007).

Significant evidence has emerged indicating that physical exercise decreases depression (Rimer et al., 2012) and may provide a therapeutic benefit similar to antidepressant medication (Blumenthal et al., 2007). However, the side-effects and health complications caused by cancer and its treatment often make exercising difficult (Ferrer et al., 2011). Nevertheless, exercise

oncology guidelines stipulate that cancer survivors should avoid physical inactivity and that exercise is safe both during and following treatment (Hayes, Spence, Galvao, & Newton, 2009; Schmitz et al., 2010). Therefore, cancer survivors, especially those that are depressed, are likely to attain improvements in their physical and mental health from exercise.

To date, however, there has been insufficient research that has examined the role of exercise to manage depression in cancer survivors. Within the American College of Sports Medicine landmark guidelines on exercise for cancer, 85 randomised controlled trials were examined, and only eight reported on outcomes related to depression (Schmitz et al., 2010). Further, none of those studies were specifically designed to examine depression as a primary outcome and therefore, in most cases the groups studied had low levels of depressive symptoms which confounds the results attained. Therefore, further research is required to explore the role of exercise for depressed cancer survivors.

1.1.2 Exercise and depression

Much research has confirmed that physical activity provides a protective effect against developing depression and improving overall mental health (Carek et al., 2011; Mossner et al., 2007). Similarly, newer research has emerged to suggest that depression can be managed and even treated using exercise, with reported reductions of between 67% and 75% of depressive symptoms (Daley, 2008). Therefore, exercise should be considered as a therapeutic option for depression, especially for the 30% of patients that reportedly do not respond positively to prescribed pharmacotherapy (Carek et al., 2011). Moreover, antidepressant medication may itself cause several adverse effects including metabolic imbalance, elevated blood pressure, or sleep problems (Li, Fitzgerald, & Rodin, 2012). Exercise therapy can minimize these effects whilst simultaneously alleviating fatigue, a common somatic symptom of depression, which does not appear to be improved with medication or behavioural therapy (Daley, 2008).

The exact exercise prescription that achieves the greatest outcome remains unknown. However, studies have demonstrated that various exercise programs are able to produce a clinically-relevant reduction in depression. For example, aerobic treadmill exercise performed daily for 10 days (30 min/day) in an in-patient setting was effective at doubling the reduction in depressive symptoms compared to a placebo control group (Knubben et al., 2007). Singh and colleagues (2005) examined the effect of high versus low intensity resistance training

compared to usual care control in a sample of depressed older adults. Exercise was performed 3 times/week for eight weeks and the results were that depression reduced by 53% in the high intensity training, 36% in the low intensity training, and 26.9% in the control group (Singh et al., 2005). Reductions in depression were related to change in muscle strength, suggesting that intensity of training and the consequent physiological adaptations are central to improvements in depressive symptoms. However, aerobic exercise performed in a home-based setting was demonstrated to be as effective as supervised aerobic training, despite not producing the same increase in aerobic capacity (Blumenthal et al., 2007). Therefore, psychological responses are likely not entirely dependent on physiological outcomes of the exercise program.

These findings, although positive, do not elucidate the optimal exercise parameters such as intensity, duration, frequency, and modality, required to alleviate depression. Therefore, it has been suggested that further research should examine the role of the specific exercise program modality in achieving beneficial outcomes as well as considering the exercise preferences of the individuals (Perraton, Kumar, & Machotka, 2010).

1.1.3 Exercise preferences for depression and cancer survivors

Despite several randomised controlled trials that have examined the effectiveness of exercise on depression, little is known about the ideal exercise prescription for overcoming depression. Therefore, there is a need to determine both the optimal exercise program and to consider patients' preferences, thus ensuring effectiveness, uptake, and adherence. Preferences are important, as it has previously been suggested that the therapeutic effects of exercise will not be attained if the program is not optimally targeted towards the population and therefore not accepted resulting in no engagement of exercise (Maddocks, Armstrong, & Wilcock, 2011). To date, only one study has examined the exercise preferences of people with mental illness (Ussher, Stanbury, Cheeseman, & Faulkner, 2007). Ussher et al. (2007) interviewed 120 psychiatric patients ($n = 20$ diagnosed with clinical depression) and found that walking in a home-based environment was the preferred mode of activity.

Specific exercise preferences are available for various cancer populations including breast cancer (Emslie et al., 2007; Milne, Guilfoyle, Gordon, Wallman, & Courneya, 2007), ovarian cancer (Stevinson et al., 2009), bladder cancer (Karvinen, Courneya, Venner, & North, 2007), non-Hodgkin's lymphoma (Vallance, Courneya, Jones, & Reiman, 2006), and endometrial

cancer (Karvinen et al., 2006). The findings suggest that approximately 90% of survivors believe they are capable of exercising and are open to participating in an exercise program (Karvinen et al., 2006; Karvinen et al., 2007; Lowe, Watanabe, Baracos, & Courneya, 2010; Vallance et al., 2006). Cancer patients appear to prefer a program design that provides at least two sessions per week (Lowe et al., 2010) at a light to moderate intensity (Karvinen et al., 2006; Karvinen et al., 2007; Vallance et al., 2006).

Differences are evident amongst the cancer populations, based on diagnosis and phase of treatment. Therefore, these findings provide a good foundation for understanding the exercise preferences of cancer survivors. However, it is unknown whether depressed survivors would have similar preferences to the previously examined groups, and therefore, there is a need to explore the preferences of depressed cancer survivors.

1.1.4 Exercise for depression in cancer

Exercise is now an accepted necessity in the delivery of effective cancer management. This is particularly important as cancer and its treatment (surgery, chemotherapy, radiotherapy, etc.) is associated with several physical side-effects (Schmitz et al., 2010), which result in increased likelihood of developing additional comorbidities such as hypertension, diabetes, and osteoporosis (Galvao, Newton, Taaffe, & Spry, 2008). These secondary diseases can all be prevented with adequate physical activity and targeted exercise.

There has been no research to date that has examined the effect of exercise in a cohort of depressed cancer survivors. Nonetheless, some exercise trials have reported depression as an outcome measure (Courneya et al., 2009; Payne, Held, Thorpe, & Shaw, 2008; Thorsen et al., 2005). A recent systematic review by Craft and colleagues (2012) examined the role of exercise in treating depression in cancer survivors and concluded that exercise appears to provide consistent benefits and to reduce depression in cancer survivors. Similar outcomes were noted in a second review and meta-analysis on this topic (Brown et al., 2012).

Due to the low number of trials that have assessed depression as an endpoint in exercise trials these recent reviews included trials regardless of baseline level of depression. For example, one trial (Thorsen et al., 2005) reported baseline scores with an average of approximately '3' determined from the HADS-D, which is representative of normal functioning, with almost no

symptoms of depression (Crawford, Henry, Crombie, & Taylor, 2001). Therefore, the clinical relevance of these findings is questionable at best.

In fact, only one trial which has assessed exercise on depression in cancer survivors has reported that the majority (58%) of the participants met criteria for elevated depression (Courneya, Friedenreich, Sela et al., 2003). However, these authors did not evaluate the effects of an exercise program in isolation. They compared the cumulative effect of home-based exercise and psychotherapy to the outcomes of psychotherapy alone and found that exercise did not influence the outcome for depression (Courneya, Friedenreich, Sela et al., 2003). Since the study did not examine the effect of exercise in isolation, there is a need for further research in this area.

1.2 Significance of the research

This thesis aims to address one of the specific research gaps identified in the landmark American College of Sports Medicine roundtable consensus statement regarding exercise guidelines for cancer (Schmitz et al., 2010). The guidelines noted a need for additional research on psychosocial outcomes. In particular there was a lack of information related to exercise and mental health outcomes. Specifically, only 9% of the articles reviewed reported on measures of depression. Therefore, there is a need for research that is focused on the effectiveness of exercise in cancer survivors with already compromised mental well-being.

The outcomes of this work have the potential to improve clinical practice within oncology. By ascertaining exercise preferences for this population and then illustrating that exercise is indeed able to reduce depression, clinicians would be more likely to encourage survivors to commence or continue exercising, for both physical, but also psychological, benefits.

CHAPTER TWO

A Review of Exercise for Depression in Cancer Survivors

2.1 Introduction

Cancer is a chronic, and potentially fatal, disease accounting for a high proportion of all deaths in Australia each year. Approximately 20% of all deaths in Australia are due to cancer, with the highest rates of mortality attributed to lung, colorectal and pancreatic cancer in both males and females whilst, specific to gender, prostate cancer has the highest rate of mortality in males and breast and ovarian cancer are the leading causes of cancer-related deaths for females (Australian Institute of Health and Welfare, 2010).

Despite the high rate of death due to cancer, improvements in medical treatment and early diagnosis are resulting in a growing number of cancer survivors (Schmitz et al., 2010). Survivorship, according to the definition of the National Coalition for Cancer Survivorship, commences post-diagnosis regardless of disease status (Clark et al., 1996). Therefore, a cancer survivor is a term used to define any individual that has been diagnosed with cancer. It has been reported that depression may increase the likelihood of cancer recurrence (Miller et al., 2008) and increases mortality in cancer survivors (risk ratio 1.20) (Pinquart & Duberstein, 2010; Satin et al., 2009). Therefore, depressed survivors are not only at risk of reduced quality of life, but also reduced years of life.

Treatment and management of depression is, therefore, of the utmost importance for cancer survivors, with continual care required beyond the acute treatment phase of the cancer. Physical activity and exercise is gaining popularity in the field of oncology and cancer survivors are encouraged to become or remain active according to the American College of Sports Medicine (Schmitz et al., 2010). Several research trials have examined the benefits of exercise for cancer survivors and their findings are published in an array of reviews and meta-analyses (Fong et al., 2012; Galvao & Newton, 2005; Spence, Heesch, & Brown, 2010).

Two recent reviews examined the literature to date with a focus on the effectiveness of exercise to reduce depression in cancer survivors (Brown et al., 2012; Craft et al., 2012). These two systematic reviews and meta-analyses reported positive outcomes that exercise appears to provide a small, but worthwhile, reduction in depression. This finding is similar to others that examined the effect of exercise on depression in non-cancer survivors (Mead et al., 2009; Rimer et al., 2012). Specifically, they reported that supervised exercise in an exercise facility improved outcomes, whereas home-based exercise performed for only short durations (e.g., 10 minutes per session) did not provide any therapeutic effect (Brown et al., 2012; Craft et al.,

2012). However, due to the low number of trials that have assessed depression as an endpoint in exercise trials with cancer survivors, these reviews included all randomised controlled trials regardless of baseline level of depression; with no studies being conducted on a cohort of exclusively depressed participants. Inferring outcomes on depression for studies measuring depression in non-depressed individuals creates an issue of whether changes are indeed clinically meaningful, as opposed to statistically significant. Furthermore, the findings reported may not be applicable when translated to clinical practice. These two studies, which reviewed the literature for cancer survivors, differ compared to an up-to-date systematic review and meta-analysis by Rimer et al. (2012) on exercise and depression for non-cancer studies, which included only trials with depressed participants. Therefore, there is a need to examine the effect of exercise on depression in cancer survivors with more consideration given to baseline levels of depression.

Craft and colleagues (Craft et al., 2012) acknowledged that studies to date have not specifically recruited depressed patients and that the exercise protocol was not prescribed to manage or treat depression. Nonetheless, there is a need to further examine the effectiveness of exercise, in particular the program variables, and determine what type or setting of exercise is most effective at reducing depression in cancer survivors. Further, there is a need to examine the effectiveness of the exercise interventions, as this has not previously been addressed. Both reviews (Brown et al., 2012; Craft et al., 2012) focus on the change in depression over time, which is important, without having examined the effectiveness of the exercise program. Objective outcomes can be measured by comparing physical or physiological changes between the exercise and non-exercise group over time. However, neither review considered whether the changes in depression were explained by, or related to, the physiological response to the exercise program.

Therefore, there is a need to address some important questions relating to the original research studies. Case-by-case descriptions are not suited to systematic reviews, and therefore, a critical narrative review on this topic has been performed.

2.2 Rationale for a critical review

Over the past few years there has been a shift in the way of disseminating research reviews, with an increase in the number of systematic reviews and meta-analyses, including in the field

of exercise oncology (Craft et al., 2012; Fong et al., 2012; Spence et al., 2010). The strength of these review articles is the ability to condense vast amounts of information and present meaningful results that can be interpreted with ease. It has been reported that this is an effective method of keeping up-to-date, particularly in the field of medicine and health care (Moher, Liberati, Tetzlaff, & Altman, 2009). However, this method of summarizing information may not be ideal for examining the effectiveness of exercise as a therapeutic treatment.

The prescription of exercise is complex and can be modified in several ways including by altering the type of activity (e.g., walking, cycling), the intensity of the exercise (e.g., easy, moderate, hard), the duration of each session, the number of sessions performed per week, the total number of sessions performed, and the social context in which exercise is performed (e.g., alone, in a group, supervised, outdoors). Appropriate exercise prescription is guided by the principle of specificity, which states that physical and physiological changes will occur in accordance with the exercise stimulus delivered (Smith, 2003). For example, a greater increase in leg strength will result from a lower body resistance training program compared to an aerobic, running-type, program. These program variables are well understood when prescribing exercise for physiological adaptations, but less is known about how to structure exercise programs targeting psychological adaptations. Furthermore, the physical capabilities and baseline levels of muscular strength, cardiorespiratory fitness, and functional abilities all influence the rate of adaptation.

Examining exercise as a generic independent variable is not optimal. Each exercise program is unique and the prescriptive factors along with the participants' baseline abilities will influence the effectiveness of the intervention as much as the delivery/non-delivery of the stimulus. The variety of programming factors are usually unable to be addressed within a systematic review, which favours reporting the differential change over time between the exercise and non-exercise group (referred to as the interaction effect throughout).

Another limitation of systematic reviews is that they provide an overall effect, collated from the results of each trial that was examined. However, this method does not provide sufficient scope to examine whether sub-optimal exercise delivery may have been responsible for the outcomes reported. The inclusion of one, or several, exercise interventions that were poorly designed may obscure the beneficial outcomes of well managed and prescribed trials.

Therefore, this review was conducted to critically examine the exercise prescription of each trial on a case-by-case basis.

2.3 Aims of this review

In order to examine the effectiveness of exercise on depression in cancer and whether exercise is indeed able to improve depressive symptoms, a critical narrative review of the literature was conducted. The first aim of this review was to examine the program variables and account for similarities or differences between exercise studies completed with cancer survivors. Second, this review explored the objective physiological outcomes that have been reported following an exercise program delivered to cancer patients. Lastly, the review examined if there was a relationship between physiological adaptation and changes in depression.

2.4 Search methods

Studies for this review were drawn from three recent systematic reviews and meta-analyses. Two of these reviews were specifically examining the effect of exercise on depression in cancer survivors (Brown et al., 2012; Craft et al., 2012) and the third examined the effect of exercise on several outcomes, including depression, in cancer survivors that had completed primary treatment (Fong et al., 2012). Additionally, to ensure an updated review was presented, the Medline database was searched for new research published from 2013. The database search was performed using the following search strategy. Keywords appearing in the text included ‘cancer’ AND ‘exercise’ or ‘physical activity’ AND ‘depression’ AND ‘randomised’ OR ‘randomized’ with words from the title selected to exclude ‘review’ AND ‘meta’.

2.4.1 Selection criteria

Studies were only included in this review if they met the following inclusion criteria: i) published randomised controlled trial conducted with cancer survivors examining the effect of exercise; ii) outcomes for depression reported using a valid depression scale; iii) at least one objective measure of exercise effectiveness reported (e.g., muscle strength, aerobic capacity); and, iv) a non-exercising control group as part of the trial. Furthermore, studies that appeared to meet the above may have been excluded based on: i) the exercise program being specific to one muscle group only (Lee et al., 2010; McClure, McClure, Day, & Brufsky, 2010); ii) depression reported using non-specific questionnaires (e.g., POMS and visual analogue scales); iii) the control group also having access to exercise as part of the standard care (Jarden,

Baadsgaard, Hovgaard, Boesen, & Adamsen, 2009); iv) when alternative forms of activity were used (e.g., yoga, Pilates, dancing); v) if the intervention group received exercise combined with any other stimulus (e.g., dietary advice) and the additional stimuli were not offered to the control group; and, vi) if exercise programs were assessed using self-report measures of physical activity or anthropometrical or morphological measures (e.g., body mass, hip circumference, body composition).

Self-reported measures of activity were excluded based on previous reports which question the accuracy of these measures stating that participants may be influenced by perceived expectations of the researcher (Courneya, Friedenreich, Quinney, et al., 2003). Anthropometric changes were not considered an objective measure of the exercise as these changes can occur in response to cancer treatment or recovery alone, without any additional exercise being performed.

2.4.2 Study characteristics

After a close examination of the methods and results of the published literature, twelve studies were included for review (Table 2.1). Two new studies published in the last two years were retrieved through the Medline search (Midtgaard et al., 2013; Rogers et al., 2014). The remaining 10 studies were drawn from the three recent systematic reviews. Nine were retrieved from the work of Brown and colleagues (Brown et al., 2012). Eight were cited in the review by Craft et al. (2012), with the ninth (Courneya, Friedenreich, Sela, et al., 2003) excluded in their review because the control group were receiving group psychotherapy. However, since the group therapy was standard for both the exercise and control group, that study was included in the current review, as it was considered any between group differences could be attributable to the exercise program. Three studies were cited in the systematic review by Fong et al. (2012), two of which were also included in the other reviews and one which had not previously been referenced (Mehnert et al., 2011).

Since two studies included multiple exercise groups, the 12 studies examined allowed for the interpretation of 14 interaction effects. Courneya et al. (2007), ran a three-arm trial comparing resistance training alone, and aerobic training alone to usual care. Daley and colleagues (2007), included a placebo exercise group that performed low intensity stretching to account for the

social context of the exercise program. Nonetheless, since results were provided for this group, it was included in this review.

Table 2.1

Characteristics of patient population in studies that have examined exercise preferences for cancer survivors

Study	N	N (male)	Cancer Type	Treatment phase	Groups (n)	Age (SD) (Age Range)
Courneya, Friedenreich, Sela et al., (2003)	108	15	Various	Various phases of treatments (44% current)	Exercise group (60) Control (48)	51.6 (10.2)
Courneya et al., (2007)	242	0	Breast	Stage I - III (Beginning adjuvant chemotherapy)	Aerobic exercise (78) Resistance training (82) Control (82)	49.2 (25 - 78)
Courneya et al., (2009)	122	72	HL or NHL	Various but consistent (chemotherapy or no treatment)	Exercise (60) Control (62)	53.2 (18 - 80)
Courneya, Friedenreich, Quinney et al., (2003)	102	54	Colorectal	Post-surgery	Exercise (69) Control (33)	Ex: 59.9 (10.7) Con: 61.1 (9.9)
Culos-Reed et al., (2010)	100	100	Prostate	Androgen Deprivation Therapy	Exercise (53) Control (47)	67.6 (8.6)
Daley et al., (2007)	108	0	Breast	Localised disease only	Exercise (34) Exercise-placebo (36) Control (38)	Ex: 51.6 (8.8) Ex-Pl: 50.6 (8.7) Con: 51.1 (8.6)
Mehnert et al., (2011)	63	0	Breast	Recently completed chemotherapy or radiation	Exercise (30) Control (28)	51.9 (8.5)
Midtgaard et al., (2013)	214	36	Various	Various	Exercise (108) Control (106)	Ex 48.2 (10.1) Con 46.2 (11.6)
Monga et al., (2007)	21	21	Prostate	Radiation therapy	Exercise (11) Control (10)	Ex 68.0 (4.2) Con 70.6 (5.3)
Mutrie et al., (2007)	203	0	Breast	Chemotherapy, radiation therapy or combination	Exercise (101) Control (102)	51.6 (9.5)
Rogers et al., (2014)	46	0	Breast	Post-treatment (hormone therapy)	Exercise (22) Control (24)	56.2 (7.7)
Thorsen et al., (2005)	139	36	Various	Completed treatment	Exercise (69) Control (70)	39.1 (8.4)

2.5 Exercise prescription

Characteristics of the exercise interventions included in each study are provided in Table 2.2. All 14 exercise programs were quite different, even though some similarities were apparent.

2.5.1 Frequency and duration

The duration of the programs extended from 8 to 52 weeks, and the numbers of prescribed sessions per week varied from as few as one to as many as five. Combined with the inconsistent sessions times, the total amount of time spent exercising ranged from as little as 720 minutes (Monga et al., 2007) to a maximum of 4680 minutes (Midtgaard et al., 2013).

2.5.2 Mode of exercise and exercise intensity

The most consistent variable amongst all the studies was that ‘moderate’ intensity exercise was prescribed in 12 of the 14 cases. Nonetheless, there were differences in the descriptive variables of moderate intensity, which was commonly defined relative to heart rate. The lowest reported value used was 50% of maximum heart rate (HR_{max}) (Mutrie et al., 2007) compared to the highest of 85% HR_{max} (Daley et al., 2007). Other measures of intensity were scaled relative to peak power output (Courneya et al., 2009), which is less influenced by medication effects than heart rate response, or determined relative to the participant’s maximal aerobic capacity (Courneya et al., 2007; Mehnert et al., 2011).

One of the studies prescribed exclusively high intensity exercise and another included some high intensity sessions within the overall, more moderate, program. Midtgaard and colleagues (Midtgaard et al., 2013) employed high intensity interval training (HIIT), requiring the participants to cycle at 90% - 95% HR_{max} for periods ranging from 30 second to 6 minutes, with rest intervals between each workload. HIIT is a well-established aerobic training technique which has the potential to cause rapid improvement in aerobic capacity over a relatively short duration (Laursen & Jenkins, 2002). Similarly, Courneya et al. (2009) included high intensity aerobic training within their 12-week exercise program, but only for one of the three sessions per week, and only after the participants had completed the initial 18 sessions (6 weeks) at the lighter intensity.

All but two of the exercise groups performed aerobic activity. Only two interventions, the placebo-exercise group from Daley and colleagues (2007) study, and the resistance training

group from the study by Courneya and colleagues (2007), did not including any aerobic exercises. Seven programs prescribed aerobic training only, and five included a mix of aerobic training and resistance training. Whereas the intensity of the aerobic programs was well explained, in general, insufficient information was provided regarding the specific intensity of the resistance exercises. Thorsen and colleagues (2005) allowed their participants to choose the preferred exercise activity and made particular mention of resistance training, but failed to provide any further detail regarding how many people chose this option or the particular program that was prescribed (i.e., exercise selected, number of sets and repetitions). Another study included ‘strengthening exercises’ in their description of the program delivered, but failed to mention what the exercises were, and whether they were performed against external resistance or body weight (Mutrie et al., 2007). In both these studies the only measure of intensity provided was percentage HR_{max} , a unit which is not effective or appropriate for monitoring resistance exercise. A third study reported using resistance bands to perform resistance exercise, stating that a moderate intensity was recommended (Culos-Reed et al., 2010). However, similar to the previous studies, there was no mention of the specific muscle groups targeted, the exercises performed, or the number of sets and repetitions prescribed. This important prescriptive information was better explained by Rogers and colleagues (2014), who reported that participants performed two sets of 15 repetitions. However, they too failed to provide further detail of exactly which exercises were selected. Only one of these five studies provided all necessary information pertaining to the resistance component of the program that would allow replication, with sufficient details on both the exercises performed and all variables relating to intensity (Midtgaard et al., 2013).

2.5.3 Exercise environment

Despite reports consistently indicating that most cancer survivors prefer home-based walking exercise (see Chapter 3 for a review on this topic), only three of the studies examined employed this type of exercise training (Courneya, Friedenreich, Quinney, et al., 2003; Courneya, Friedenreich, Sela et al., 2003; Thorsen et al., 2005). The remainder prescribed supervised exercise at a specified location (medical centre, fitness centre, exercise clinic). Three of these supervised programs, however, also included an additional home-based component at least once per week (Culos-Reed et al., 2010; Mutrie et al., 2007; Rogers et al., 2014).

The social context also varied between studies. Some supervised sessions were conducted in a group setting (Culos-Reed et al., 2010; Mehnert et al., 2011; Midtgaard et al., 2013; Mutrie et al., 2007), whereas others restricted socialisation by structuring one-on-one supervision for each participant (Daley et al., 2007). These environmental differences may influence the psychosocial responses to exercise.

Table 2.2
Exercise protocols

Study	Freq (d/wk)	Time (min)	Duration (wk)	Intensity	Type of exercise	Exercise Environment	Supervision
Courneya, Friedenreich, Sela, et al., (2003)	3–5	20–30	10	65–75% HR _{max}	Walking, swimming, cycling	Home-based	No
Courneya et al., (2007)	3	15 – 45	~17	60 -80% VO _{2max} 2 Sets, 8-12 RM	Aerobic machines Resistance training	NR	Yes (NR)
Courneya et al., (2009)	3	20–45	12	60 - 75 PPO and 1 interval session/wk from wk 7	Cycle ergometer	NR	Yes (Exercise physiologist)
Courneya, Friedenreich, Quinney, et al., (2003)	3–5	20–30	16	65–75% HR _{max}	Walking, swimming, cycling	Home-based	No
Culos-Reed et al., (2010)	3–5	60	16	Moderate (recommended)	Walking, stretching, and light resistance	1 group session/wk at fitness centre supplemented home-based activity	Yes (Fitness specialist)
Daley et al., (2007)	3	50	8	65 - 85% HR _{max}	Ex: Aerobic exercise Ex-Pl: Light stretching	University centre Individual session	Yes (Exercise specialist)
Mehnert et al., (2011)	2	90	10	60% VO _{2max} (moderate)	Walking, jogging, games, relaxation	Small groups of ~5, Day 1: indoor court, Day 2: outdoors	Yes (Physio/sports therapist)
Midtgaard et al., (2013)	1	90	52	HIIT (90-95% HR _{max}) Resistance training (3 sets of 8-10 @ 70-90% 1-RM)	Resistance and aerobic exercise	Group sessions	Yes (NR)
Monga et al., (2007)	3	30	8	65% HR _{reserve}	Treadmill walking	Medical centre	Yes (Kinesiotherapist)
Mutrie et al., (2007)	2 + 1	45	12	50 - 75% HR _{max}	Walking, cycling, aerobics, and strength exercises	Group sessions 2/wk plus additional home-based session	Yes (Exercise specialists)
Rogers et al., (2014)	4	40	12	48 - 52% HR _{reserve} (moderate)	Walking and Strength training (2 sets of 15 reps)	Individual supervised sessions 2/wk supplemented with 2 home-based sessions	Yes (Exercise specialist)
Thorsen et al., (2005)	2	30	14	60–70% HR _{max} (recommended)	Participant preference	Home-based	No

HR_{max}, maximum heart rate; HIIT, high intensity interval training; PPO, peak power output; VO_{2max}, maximal aerobic capacity; NR, not reported; Ex, exercise group; Ex-Pl, exercise-placebo group

2.6 Outcomes

In order to examine the effectiveness of exercise to reduce depression, it is essential that the effect on depression can be attributed directly to the exercise program. This expectation has been considered to be fulfilled since the design of a randomised controlled trial should ensure that the independent (exercise vs no exercise) variable is the only difference between otherwise similar groups. However, to fulfil the attribution of causation assumption that exercise is the factor responsible for changes rather than some non-specific factor associated with commencing the exercise program (such as improved feelings of mastery), objective physiological changes between the exercise and non-exercise groups should be examined.

Therefore, physiological outcomes for each of the 14 exercise programs were examined (Table 2.3). It is apparent that 10 produced significant results compared to the non-exercise control group, however, four studies failed to report any objective physical or functional changes that favoured the exercise group. These four studies (Courneya, Friedenreich, Quinney, et al., 2003; Courneya, Friedenreich, Sela, et al., 2003; Culos-Reed et al., 2010; Rogers et al., 2014) should not be taken into account when determining the effect of physiological outcomes of exercise on depression, but may be useful to explain how certain exercise programs are not able to address the intended outcomes upon which they were prescribed. In this instance, one or more programming variables may be considered sub-optimal to elicit physiological improvements.

Similarly, each study was examined to explore the change in depression over the duration of the exercise intervention (Table 2.4). It has been acknowledged previously that these studies were not conducted with depression as a primary outcome (Craft et al., 2012) and, therefore, in most cases the level of depression does not appear elevated. Indeed, elevated depression above the threshold for both the exercise and non-exercise group were only reported in one study (Courneya, Friedenreich, Sela, et al., 2003). In two further trials, only one of the groups examined exceeded depression thresholds at baseline, measured using the Beck Depression Inventory (Daley et al., 2007; Mutrie et al., 2007). In an attempt to account for the low baseline level of depression, this review examined the proportion of participants that were reported within each manuscript to have exceeded depression thresholds. However, only one study reported this information, stating that 58% of the sample experienced elevated depressive symptoms measured using the CES-D, but did not report if there was a change post-intervention (Courneya, Friedenreich, Sela, et al., 2003).

Significant outcomes in depression were reported for only five of the 14 comparisons between exercise and non-exercise groups. Both the aerobic exercise group and the placebo-exercise group in the study by Daley et al. (2007), examining exercise in women with localised breast cancer, exhibited improvements in depression greater than the control group. The exercise group performed 50 minutes of supervised aerobic exercise per week for a period of 8 weeks, whereas the placebo-exercise group performed an equal number of sessions but undertook light stretching and flexibility exercise. Interestingly, aerobic fitness enhancements were found for both exercise programs, which significantly outperformed the control group. No analysis was performed to compare results between the two exercise groups. However, when compared to the non-exercise control group, aerobic capacity, extrapolated from the 8-minute walk test, was similar for both exercise groups, with mean differences of +2.89 ml/kg/min and +2.25 ml/kg/min for the exercise and the exercise-placebo groups respectively. Further, the baseline depression scores from the Beck Depression Inventory II for these three groups ranging from 10.8 to 13.6, using the BDI-II, exceeded or approached the threshold of 13 which has previously been used to screen for depression (Craft, 2005). Unfortunately, the authors failed to provide overall group means at follow-up, choosing again to report only the mean differences between the groups (Ex vs Con = -6.01; Ex-Pl vs Con = -5.66) (Daley et al., 2007). This reporting method restricted the ability to examine whether the mean depressive level of the exercise groups fell below the threshold, or whether the groups indeed increased their level of depression to a lesser extent than the control group.

The three other studies that reported significant outcomes for depression comprised samples with levels of depression that could be considered to be within the normal range (Courneya et al., 2009; Mehnert et al., 2011; Midtgaard et al., 2013). It was demonstrated that depression decreased by more than 40% (7.7 to 4.5) in a sample of haematological cancer survivors that commenced aerobic exercise three times per week for a duration of 12 weeks, whereas the control group showed no change in their level of depression (6.0 to 6.1) (Courneya et al., 2009). However, these measures were reported using the short form of the Centre for Epidemiological Studies Depression Scale which has previously been used to examine depression with a conservative threshold of 8 or above (Schulz et al., 2000). The proximity to this cut-off score at baseline suggests that several participants within the sample may have met criteria for elevated depressive symptomology, but unfortunately results were not presented for secondary measures of depression, such as the change in the number of participants that dropped below threshold after the intervention. The improvement in depression may be associated with an

increase in aerobic capacity. Indeed, the exercise group decreased depressive symptoms and increased their aerobic fitness by almost 20% (+4.7 ml/kg/min), whereas the control group showed no change over time for either of these two measures.

In the remaining two studies that reported significant interaction effects for depression, depression was assessed using the subscale of the Hospital Anxiety and Depression Scale (HADS-D). Two different thresholds have been suggested for determining depression according to this scale, one being 11 (Sellick & Edwardson, 2007) and another a more conservative score of 8 (Bjelland, Dahl, Haug, & Neckelmann, 2002). Regardless, the baseline values of less than five (Mehnert et al., 2011) and less than three (Midtgaard et al., 2013) reported in these studies indicate that the significant changes should be interpreted with caution. These low scores indicate that no mood disorders were present and that depression was not a factor for these participants. Improving a non-problematic condition is unlikely to provide further benefit and, therefore, despite the statistical significance, these outcomes should not be considered clinically meaningful or useful.

It has been reported that breast cancer survivors more commonly suffer with depression (Massie, 2004). The baseline level of depression reported by Mutrie and colleagues (2007), in a cohort of early stage breast cancer survivors, indicated that the control group on average exceeded the threshold value for depression and the exercise group was approaching a threshold score of 13. After a 12-week group exercise program, there was a mean difference between-groups of 1.7, favouring exercise, which approached significance ($p = .08$). Despite both groups decreasing depression (-3.2 and -1.5), the exercise group decreased their baseline score by a greater amount than the control group, and, therefore, were no longer close to the depression threshold. Compared to the two studies above that did report significance, this non-significant outcome appears more clinically relevant.

These studies suggest that for exercise to effectively improve depression, increases in aerobic capacity (Courneya et al., 2009; Daley et al., 2007; Mehnert et al., 2011) or maximal strength (Midtgaard et al., 2013) were required. Studies that failed to report physical or functional improvements did not produce significant outcomes for depression. However, an improvement was not always found when objective measures of exercise were confirmed. These findings suggest that physiological responses arising from the commencement of exercise are necessary to improve depression. However, the limitations of the samples within these studies (i.e., low

baseline depression) suggest that more research is required to confirm the precise mechanisms underpinning the change in depressed status. Many mechanisms have been proposed and are discussed in the next section.

Table 2.3

Measures of exercise effectiveness

Study	Exercise outcomes	Results	Significance reported	
Courneya, Friedenreich, Sela, et al., (2003)	Treadmill test (time to 70% age-predicted HR _{max}) (sec)	Ex: 475 (337) to 528 (362) Con 431 (333) to 486 (346)	ns	
Courneya et al., (2007)	VO _{2peak} test (ml/kg/min) 1-RM leg extension (kg) 1-RM chest press (kg)	VO_{2peak} (ml/kg/min) UC 24.8 (6.2) to 23.5 (5.4) RET 25.5 (6.1) to 24.2 (6.1) AET 25.2 (7.2) to 25.7 (7.4) 1-RM leg extension (kg) UC 25.6 (12.6) to 27.1 (14.1) RET 24.4 (11.2) to 32.8 (12.6) AET 24.8 (12.5) to 28.2 (14.2)	1-RM chest press (kg) UC 22.8 (8.9) to 24.6 (7.8) RET 23.2 (7.2) to 31.9 (10.8) AET 22.1 (7.5) to 24.7 (7.5)	VO_{2peak} AET vs RET ($p = .014$) AET vs Con ($p = .006$) 1-RM leg extension RET vs AET ($p < .001$) RET vs Con ($p < .001$) 1-RM chest press RET vs AET ($p < .001$) RET vs Con ($p < .001$)
Courneya et al., (2009)	Maximal GXT (ml/kg/min)	UC 25.4 (9.2) to 25.2 (9.1) AET 24.7 (7.2) to 29.4 (8.6)	$p < .001$	
Courneya, Friedenreich, Quinney, et al., (2003)	Treadmill test (time to 70% age-predicted HR _{max}) (sec)	EX 396 (291) to 548 (300) Con 314 (270) to 406 (301)	ns	
Culos-Reed et al., (2010)	6-min walk test (m)	Ex 650 (143) to 675 (209) Con 702 (151) to 731 (184)	ns	
Daley et al., (2007)	8-min walk test (ml/kg/min)	Ex: 29.1(4.8) to NR Ex-Pl: 30.3 (5.0) to NR Con: 30.0 (5.4)to NR	Mean differences Ex vs Con 2.89 Pl vs Con 2.25 Ex vs Con ($p = .002$) Ex-Pl vs Con ($p = .021$)	
Mehnert et al., (2011)	Maximal aerobic capacity (ml/kg/min)	Ex: 24.71 (4.25) to 26.88 (4.38) Con 26.46 (4.18) to 25.65 (4.71)	$p < .001$	
Midtgaard et al., (2013)	Maximal GXT (ml/kg/min) 1-RM chest press (kg) 1-RM leg press (kg)	VO_{2max} (ml/kg/min) Ex 28.17 to 33.03 Con 27.74 to 31.08 Leg Press (kg) Ex 81.76 to 109.68 Con 84.54 to 92.84	Chest Press (kg) Ex 33.00 to 38.65 Con 34.49 to 36.43 VO _{2max} (ns) 1-RM Chest Press ($p < .001$) 1-RM Leg Press ($p < .001$)	
Monga et al., (2007)	Treadmill test (METS) Chair rise test (sec)	Treadmill test Ex 7.2(1.2) to 9.8 (0.9) Con 7.4 (2.1) to 7.2 (2.3)	Chair rise test Ex 12.6 (2.3) to 11.3 (1.9) Con 10.8 (1.6) to 11.3 (1.6) Treadmill ($p = .006$) Chair rise ($p < .001$)	
Mutrie et al., (2007)	12 minute walk test (m)	Ex 997 (221) to 1135 (143) Con 975 (235) to 984 (221)	Yes, $p < .001$	
Rogers et al., (2014)	Leg strength (N/m), Treadmill test (ml/kg/min)	Leg Strength Ex 61.8 (19.3) to 65.9 (18.2) Con 67.8 (29.8) to 73.1 (26.3)	VO₂ ml/kg/min Ex:- 27.6 (7.0) to 30.9 (6.3) Con 24.0 (5.7) to 25.1 (5.0) ns	
Thorsen et al., (2005)	Astrand-Rhyning test (ml/kg/min)	Ex 28.2 (6.8) to 34.6 (NR) Con 31.7 (6.8) to 34.8 (NR)	$p = .01$	

GXT, graded exercise test; VO₂, Oxygen consumption; HR_{max}, maximum heart rate; RM, repetition maximum; NR, not reported; ns, not significant; Ex, exercise group; Con, control group; RET, resistance training group; AET, aerobic training group, Ex-Pl, exercise-placebo group

Table 2.4

Depression outcome and exercise effectiveness measures

Study	Depression Scale	Depressed cases	Results	Significance reported
Courneya, Friedenreich, Sela, et al, (2003)	CES-D	58.3%	Ex: 21.51 (11.45) to 19.65 (13.28) Con: 18.57 (11.84) to 18.31 (11.37)	ns
Courneya et al., (2007)	CES-D	NR	RET 13.8 (10.1) to 10.6 (9.5) AET 12.8 (9.8) to 9.7 (9.3) Con: 13.9 (9.7) to 10.8 (9.4)	ns
Courneya et al., (2009)	CES-D-10	NR	Ex: 7.7 (5.7) to 5.4 (4.5) Con: 6.0 (4.5) to 6.1 (5.0)	$p = .005$
Courneya, Friedenreich, Quinney, et al., (2003)	CES-D	NR	Ex: 9.8 (8.1) to 8.6 (8.7) Con: 10.1 (12.0) to 9.6 (10.9)	ns
Culos-Reed et al., (2010)	CES-D	NR	Ex: 8.62 (7.94) to 8.22 (6.66) Con: 6.71 (6.38) to 7.67 (8.56)	ns
Daley et al., (2007)	BDI – II	NR	Ex: 13.56 (9.09) to NR Ex-Pl: 11.86 (8.01) to NR Con: 10.79 (7.65) to NR	Ex vs Con; $p = .001$ Ex-Pl vs Con; $p = .001$
Mehnert et al., (2011)	HADS-D	NR	Ex: 4.17 (3.83) to 2.70 (2.95); Con: 4.79 (4.57) to 4.64 (4.43)	$p = .05$
Midtgaard et al., (2013)	HADS-D	NR	Ex: 2.90 (NR) to 0.88 (NR) Con: 2.94(NR) to 1.58 (NR)	$p = .022$
Monga et al., (2007)	BDI	NR	Ex: 3.5 (5.4) to 2.8 (5.5) Con: 3.6 (5.0) to 4.2 (3.4)	ns
Mutrie et al., (2007)	BDI – II	NR	Ex: 11.8 (6.9) to 8.6 (6.8) Con: 13.0 (7.4) to 11.5 (8.6)	ns
Rogers et al., (2014)	PROMIS	NR	Ex: 45.5 (6.9) to 44.2 (8.6) Con: 48.2 (8.7) to 45.7 (8.0)	ns
Thorsen et al., (2005)	HADS-D	NR	Ex: 2.9 (2.7) to 2.22 (NR) Con: 3.1 (3.6) to 1.92 (NR)	ns

CES-D, Centre for Epidemiological Studies Depression scale; BDI, Beck Depression Inventory; HADS-D, depression subscale of the Hospital Anxiety and Depression Scale; NR, not reported; ns, not significant; Ex, exercise group; Con, control group; RET, resistance training group; AET, aerobic training group, Ex-Pl, exercise-placebo group

2.7 Mechanisms that explain the benefits of exercise for depression

Much empirical evidence supports the effectiveness of exercise to treat or manage depression, yet the precise mechanisms by which improvements in mental health and wellbeing are elicited by exercise are still unclear (Craft, 2005; Crone, Smith, & Gough, 2006; Mead et al., 2009). Mechanistic understandings of the effect of exercise may be limited by the complexity of depression (aan het Rot, Collins, & Fitterling, 2009), which itself does not appear to stem from a single cause, and, therefore, can be treated via several different pharmacological drugs in clinical practice (Kent, 2000). Numerous suggestions have been proposed around both physiological and physical effects of exercise, including the role of β -endorphins that are released during and after exercise (Crone et al., 2006) and the influence of exercise on adiposity and associated inflammatory responses (Pedersen, 2000; Pedersen & Toft, 2000; Trayhurn & Wood, 2004). Similarly, psychological mechanisms including the role of increasing self-efficacy (Craft, 2005), and the effect of social interaction resulting from exercise (Crone et al., 2006) have been described.

The onset of depression and the perpetuation of the condition do not occur in isolation, particularly in cancer survivors. A series of related events, commencing with the diagnosis of cancer and the adverse treatment-related effects can negatively influence mood state, which may result in survivors becoming socially withdrawn (Sharpley, Bitsika, & Christie, 2010). Lack of social engagement results in feelings of isolation, which in turn can lead to depression. Moreover, cancer survivors with low levels of social support are known to engage in less physical activity, which places them at increased risk of developing other chronic diseases (Emery, Yang, Frierson, Peterson, & Suh, 2009). These additional comorbid illnesses can lead to further social withdrawal, becoming more sedentary, and increased levels of distress and depression. Therefore, minimising or removing these potential drivers for depression, through exercise, may provide substantial benefits to those cancer survivors with depression.

Both the physiological and psychological mechanisms that may contribute towards exercise reducing depression are presented below.

2.7.1 Physiological mechanisms

There are a range of inter-related physiological mechanisms associated with depression which may be influenced via exercise training reversing adiposity. The performance of physical

exercise, along with diet, contributes to regulating energy balance, and metabolic processes, and influences both overall body mass and the percentage of body fat (Miller, Koceja, & Hamilton, 1997). White adipose tissue is now also recognised as an endocrine gland, which controls the release of pro-inflammatory cytokines and adipokines (Trayhurn & Wood, 2004). Over-secretion of unnecessary pro-inflammatory cytokines is believed to induce ‘sickness behaviour’, described by Dantzer et al. (2008), which can progress to uncontrolled depression.

2.7.1.1 Circulating cytokines and inflammatory markers

Although no definitive biomarker for depression exists (Licinio & Wong, 2001), commonly cited markers of depression include insulin, TNF α (Dantzer et al., 2008), IL-6 (Jehn et al., 2006; Seruga, Zhang, Bernstein, & Tannock, 2008), and C-reactive protein (CRP) (Mossner et al., 2007; Schmidt, Shelton, & Duman, 2011).

It has been suggested that the reduction in fat attributed to exercise reduces markers of inflammation such as CRP (Hammett et al., 2004). Galvao et al. (2010) found a protective effect of regular exercise against chronic inflammation in a sample of prostate cancer survivors that undertaking structured exercise training. After performing a combined strength and endurance exercise program, twice weekly for a period of 12-weeks, CRP was reduced in the exercise group compared to an elevated response seen in the control group ($p = .008$). Similarly, Pedersen and Toft (2000) concluded from their review that exercise appears to regulate the release of both pro- and anti-inflammatory cytokines, ensuring that the body maintains a state of dynamic equilibrium. To date, no research has examined the effect of exercise on cytokines and inflammatory markers in depressed cancer survivors. However, this should not negate the possibility of the proposed mechanism.

2.7.1.2 HPA axis

Depression is related to overactivity of the hypothalamus, pituitary, and adrenal glands (HPA axis), which becomes ineffective at inhibiting the release of cortisol (Brosse, Sheets, Lett, & Blumenthal, 2002; Jehn et al., 2006). The excess cortisol may be produced in response to the pro-inflammatory cytokines, since cortisol, a catabolic glucocorticoid, is a natural response to inflammation within the body (Seruga et al., 2008).

Despite the release of stress hormones during exercise, it has been suggested that regular exercise can resolve the HPA axis dysfunction (aan het Rot et al., 2009; Brosse et al., 2002). Nabkasorn and colleagues examined the influence of aerobic exercise to reduce depression in young (18 – 20 years) female nurses who exceeded depressive symptom thresholds according to the CES-D (Nabkasorn et al., 2006). An 8-week exercise program, performing jogging, was delivered 5 times per week for 50 minutes per session. The authors reported that urinary cortisol and epinephrine were significantly lower after the exercise intervention, matching a significant decrease in depression (values not reported, depicted only in figure) (Nabkasorn et al., 2006). These results suggest that exercise may cause a homeostatic shift, removing catabolic influences (cortisol) and also increasing parasympathetic activity, associated with resting states. The influence of the exercise program to control the sympathetic nervous system (SNS) should not be understated. An overactive SNS will produce a constant elevated state of arousal, which may be responsible for sleep disturbance, another contributing factor of depression.

2.7.1.3 Enhanced sleep quality

Poor sleep quality may be a cause or consequence of depression and directional nature of the relationship is unknown (Palesh et al., 2013). What is known is that there is a relationship between cytokine regulation and sleep patterns, and that people with disrupted sleep have elevated levels of circulating cortisol (Lopresti, Hood, & Drummond, 2013).

A reduction in sleep quality is common for cancer survivors. Not surprisingly sleep quality is most compromised during chemotherapy, as these drugs cause an increase in inflammation (Palesh et al., 2013). Therefore, it has been suggested that the regulation of endocrine and cytokine responses to exercise may provide improvements in sleep, and associated reductions in depression. Exercise may improve sleep quality by regulating serotonin, a hormone responsible for sleep regulation (Stathopoulou, Powers, Berry, Smits, & Otto, 2006). Serotonin is one of several monoamines, along with others such as dopamine and noradrenaline, influenced by exercise. Not only does serotonin regulate sleep, but it has also been proposed to influence mood. Indeed, antidepressant pharmacotherapy (e.g., selective serotonin reuptake inhibitors, and noradrenaline reuptake inhibitors) works in certain cases by acting specifically on serotonin, and noradrenaline pathways, to regulate the release of these monoamines for symptom relief (aan het Rot et al., 2009).

Exercise has been shown to be effective at improving depression and increasing sleep quality in depressed older adults (Singh, Clements, & Fiatarone, 1997b). A randomised controlled trial compared the effects of a 10-week resistance training program to outcomes attained from a health education program. The authors reported that the exercise program significantly improved sleep quality and depression (Singh et al., 1997b).

2.7.1.4 Fatigue

The most commonly reported side-effect of treatment for cancer is fatigue (McTiernan, 2004) and it is closely associated with mood disorders (Dimeo, 2001). In some cases, fatigue can be long lasting and continue to affect survivors even after the completion of treatment (McTiernan, 2004). Fatigue is often attributed to the side-effects of active cancer treatment including chemotherapy and radiotherapy (Mock et al., 2001) which can increase physical inactivity and therefore result in reduced aerobic and functional capacity (McTiernan, 2004). Another potential cause of fatigue is cancer cachexia, which is believed to affect almost half of all cancer survivors (al-Majid & McCarthy, 2001; Bossola, Pacelli, Tortorelli, & Doglietto, 2007). Cancer cachexia is associated with the gradual and continued loss of muscle mass and general weakness (Bossola et al., 2007; Evans et al., 2008) and there is little evidence to suggest that it is reversible through either dietary changes or medical treatment (Bossola et al., 2007; Evans et al., 2008).

Targeted strength training produces an anabolic effect, which results in muscle hypertrophy and possible hyperplasia (Deschenes & Kraemer, 2002). Therefore, structured exercise to preserve muscle mass and increase vigour appears to be the optimal treatment to ameliorate the effects of cachexia. However, a loss of muscle mass will also influence metabolic processes and reduce aerobic and functional capabilities. It has been reported that depression is also associated with mitochondrial dysfunction and a reduced number of mitochondria, which are responsible for energy production within cells (Lopresti et al., 2013). Therefore, cancer patients experiencing fatigue and depression are likely to have compromised energetic pathways, and should also be encouraged to perform not only strength training, but also aerobic exercise. It is well known that aerobic activity is able to increase both the number and size of mitochondria in skeletal muscle (Holloszy & Coyle, 1984).

2.7.2 Psychological mechanisms

Three psychosocial mechanisms proposed may be able to explain the antidepressant effects of exercise, independent of physiological outcomes.

2.7.2.1 Self-efficacy

Self-efficacy is a subjective appraisal of one's own ability to commence and successfully complete a specific task (Bandura, 1977). Although measures of generalised self-efficacy exist, it has been suggested that more accurate measurement should be domain-specific (Manne et al., 2006). Two measures, exercise task-efficacy (Rogers et al., 2006) and coping self-efficacy (Craft, 2005), are important indicators of the success of exercise to improve depressive outcomes. First, exercise task self-efficacy reveals confidence to engage in exercise. Clearly, without engagement the associated benefits cannot be achieved. Coping self-efficacy measures the level of confidence that a person has to manage under particular unfavourable conditions (e.g., coping with cancer, or coping with depression). Coping self-efficacy is not specific to exercise, but commencing and successfully performing exercise may potentially reduce distress, thereby increase feelings of coping.

Philip and colleagues (Philip, Merluzzi, Zhang, & Heitzmann, 2013) recently examined the relationship between coping self-efficacy and depression in cancer survivors. A heterogeneous sample of 124 post-treatment cancer survivors rated their levels of coping self-efficacy (Cancer Behaviour Inventory), depression (CES-D), and severity of cancer symptoms (Symptom Impact Inventory). The authors found that coping self-efficacy accounted for almost half of the variability in level of depression (43%). Importantly, higher self-efficacy also reduced the likelihood of depression even in those survivors with severe adverse treatment effects (Philip et al., 2013). These results suggest that improving coping self-efficacy may decrease depression in depressed cancer survivors.

Depressed women who completed a 9-week aerobic exercise intervention were able to increase their coping self-efficacy, while decreasing their level of depression (Craft, 2005). Exercise was performed three times per week for 20 to 30 minutes per session. It was found the positive responses to exercise were already apparent after as few as three weeks (Craft, 2005). These two studies indicate that a low coping efficacy relates to elevated depression, and that exercise

can increase self-efficacy. Therefore, it is reasonable to suspect that exercise can increase coping efficacy and decrease depression (aan het Rot et al., 2009).

2.7.2.2 *Distraction*

Exercise provides an attentional shift that can disrupt the focus of a depressed individual outwardly, towards achieving the exercise objectives, reducing the ability to ruminate over depressive symptoms (Daley, 2002). Distraction may be even more effective in depressed cancer survivors because not only are they distracted from their negative mood state, but also from their cancer diagnosis and adverse treatment effects. While many stimuli could be used as a distraction for people with depression, the value of exercise is very powerful, because not only does it remove focus away from depressed thoughts, but, exercise provides an environment which is extremely goal orientated (Craft, 2005). Having regular goals provides constant opportunity to notice improvements and thus also increases self-efficacy by creating a sense of task mastery.

Further, self-concept may be altered when one commences exercise. It was reported that a group of cancer survivors enrolled in an exercise program formed a cohesive bond around the unifying attribute of being an active exerciser, and not on their shared identities as cancer survivors, which was the initial criteria needed for enrolment into the program (Midtgaard, Rorth, Stelter, & Adamsen, 2006). Although the participants in that study were not depressed, the finding indicates effective attentional shift away from the disease towards a more positive identity. Exercise has also been reported to be effective at distracting palliative cancer survivors from their advanced disease state and enhanced feelings of well-being (Paltiel, Solvoll, Loge, Kaasa, & Oldervoll, 2009).

Within the general population, one reason that has been suggested for females experiencing greater rates of depression is that women tend to ruminate and blame themselves following undesirable outcomes, whereas men are more likely to ignore their feelings and engage in activities that distract them from their emotions (Boughton & Street, 2007). Ruminating exacerbates distress because the repetitive thoughts are not acted upon and no remediating actions are initiated (Nolen-Hoeksema, Larson, & Grayson, 1999). In direct contrast to rumination, mental health can be improved in cancer survivors when they are able to feel in control of their life, have a sense of purpose (Bloom, Petersen, & Kang, 2007) and take positive action to deal with the disease (Roesch et al., 2005). Enrolling in an exercise program may

provide an opportunity to become proactive and take action to commence a positive lifestyle modification.

2.7.2.3 Social support

One other area in which exercise may be beneficial is in the increased social contact involved in group exercise programs, or even the interaction with an exercise trainer. This group environment can alleviate social withdrawal, since previous findings have suggested that cancer survivors feel comfortable amongst each other (Adamsen, Rasmussen, & Pedersen, 2001; Stevinson & Fox, 2006) and presumably would commit to a specialised exercise program with other cancer survivors. Even when participants joined an exercise program specifically with the intention of physical benefits, they later expressed that the social component provided many important benefits (Paltiel et al., 2009). However, the value of social support of exercise on depression may vary in cancer survivors based on treatment status and cancer stage. Philip et al. (2013), found that social support was not a strong predictor of depression in cancer survivors that had completed treatment and were in the later stages of survivorship.

2.8 Limitations and conclusion

This critical review aimed to extend results presented previously on the topic of exercise for depression in cancer. However, by using primarily the same original research as previous reviews, the main limitation of these reviews was highlighted. The original research studies were not conducted with depressed cancer survivors, or designed with depression as a primary outcome. Only one study reported that the majority of their sample were experiencing elevated levels of depression, but found no benefit for improving depression when exercise was added to a group psychotherapy program, compared to the group therapy alone (Courneya, Friedenreich, Sela, et al., 2003).

A further limitation to translating the findings of this study into practice is that only 5 of the 14 between group comparisons produced significant results and none could be considered clinically meaningful according to baseline levels of depression. Moreover, the large variability between the exercise programs employed, which were often not well described, makes difficult to generalise the optimal program design that should be utilised with depressed cancer patients in the future.

Finally, not all trials have included objective measures of strength, fitness, or other physiological outcomes. Several trials considered for this review were excluded based on this criterion. These

important outcome measures are necessary to explain whether the exercise program was effective in providing a stimulus great enough for physiological adaptations, and are further required to determine whether changes in depression, due to exercise, are related to physiological responses or whether they can be explained by psychological mechanisms. Therefore, it is suggested that all future trials examining the effects of exercise on depression should include at least one measure of either maximal aerobic capacity or maximal muscle strength, and preferably both.

The emerging interest in the field of exercise oncology and the psychological benefits that exercise provides were highlighted in the two previous systematic reviews. There is a definitive need to remediate depression and its adverse effects on cancer survivors. Exercise has been suggested to be a possible adjunctive, or primary therapeutic, option for comorbid depression in cancer survivors. However, this review highlighted the need to examine exercise, not as a generic concept, but rather to pay more attention to the precise program variables that comprise each different exercise program. Physiological outcomes attributed to exercise are known to follow the principle of specificity, whereby adaptations occur in relation to the frequency, duration, intensity, and mode of exercise performed. The results above suggest that psychological adaptation may follow a similar principle and be related to the particular exercise program that is delivered. The lack of significant findings presented above, in combination with the distinctly different programs exercise employed, suggests that there is insufficient empirical evidence to confirm an antidepressant effect of exercise in cancer survivors.

2.8.1 Summary and future directions

Based on the findings from this literature review, there is a need for further trials to determine whether exercise provides a therapeutic effect for cancer survivors experiencing depression. To determine if this is possible it is also important to consider whether depressed cancer survivors would be interested in participating and to consider their preferences for exercise. Therefore, the following research approach was selected:

- 1) Examine the preferences of exercise and current levels of activity for depressed and non-depressed survivors and determine if any differences exist;
- 2) Examine if exercise is able to relieve symptoms of depression in depressed cancer survivors; and,
- 3) Examine if there was a difference in results based on the type of exercise that was performed.

CHAPTER THREE

Exercise Preferences of Cancer Survivors, People living with Depression, and Depressed Cancer Survivors: A Review

3.1 Introduction

The use of exercise therapy to treat or alleviate the negative effects of both cancer and depression has emerged over the past few decades (Mead et al., 2009; Schmitz et al., 2010). Empirical evidence presents positive outcomes for both cancer survivors (used throughout this review in accordance with the definition of the National Coalition for Cancer Survivorship as someone who has been diagnosed with cancer and is still alive, regardless of the stage of their disease or the treatment that they are receiving (Clark et al., 1996)) and also for depressed patients that have engaged in exercise programs. These two patient group typically perform limited physical activity and, therefore, do not derive the therapeutic benefits of exercise voluntarily (Peeters et al., 2009; Ussher et al., 2007).

There is a need to encourage both cancer survivors and depressed individuals to commence exercising and this may be achieved through community programs targeted at these specific populations. Involvement in research exercise trials has been demonstrated to be an effective method of initiating exercise in otherwise inactive cancer survivors, and it has been reported that participants continue to adhere to regular training after the completion of the intervention (Emslie et al., 2007). However, the initial driver to commence exercise in a well-controlled research environment does not appear to translate into clinical practice, when individuals are encouraged to become active, without being placed into a monitored or supervised program. Sinnott et al. (2014) recently reported that depressed patients, from a local psychiatric clinic, failed to increase their level of physical activity, or improve their sense of well-being, three months after they received education about the benefits of physical activity and were encouraged to commence regular exercise.

Translating research findings to practice may be challenging because relatively little is known about the ideal exercise prescription for either depression or cancer management. Many of the research studies conducted have used different exercise modalities, prescribed varying intensities, and modified the duration of both the entire program and the length of each exercise session. It has been suggested that these differences account for the mixed findings within the randomised controlled trials conducted to examine the antidepressant effect of exercise in clinical patients (Mead et al., 2009). Likewise, research trials for cancer survivors have examined exercise effectiveness employing either aerobic exercise (Courneya, Mackey, et al., 2003), resistance training (Segal et al., 2003), or concurrent aerobic and strength training (Galvao et al., 2010). The multitude of prescriptive parameters may not only influence

objective outcomes, but also impact upon uptake and adherence to exercise programs. Recruitment of participants within exercise trials for cancer survivors can be very difficult and enrolment numbers usually do not exceed 50% of the eligible survivors contacted. Further, once exercise has commenced, retention can be troublesome, as participants withdraw for various reasons.

It has been suggested that examining exercise preferences and designing programs based on these findings may increase the number of cancer survivors choosing to commence exercise developed specifically to target their needs (Maddocks et al., 2011; Stevinson et al., 2009). If successful, this strategy would increase not only initial uptake, but also adherence to programs. Therefore, recent research has begun to examine the preferences of cancer survivors (Lowe et al., 2010) and clinically depressed patients.

The primary aim of this review was, therefore, to collate data on the exercise preferences reported to date for these two distinct clinical populations. This was achieved through a targeted, but not systematic, literature search to identify relevant publications reporting only quantitative results. Preferences provided by qualitative feedback were deemed too specific, as they are representative of the preferences of only a small number of individuals and, therefore, were excluded from the outcomes below. A second aim was to determine whether the exercise preferences of cancer survivors with comorbid depression matched the preferences of these groups in isolation. However, no research was available to address this aspect. Therefore, the final aim was to compare the results of the two clinical groups and examine whether cancer survivors and depressed patients prefer similar exercise programs.

3.2 Exercise preferences and cancer

A total of 18 articles were identified relating to preferences for cancer survivors. These covered a broad range of different cancer types (e.g., breast, non-Hodgkin's lymphoma, head and neck), stages of disease progression (e.g., no active treatment, palliative), and characteristics of participants (Table 2.1). In total, 6002 cancer survivors' preferences have been accounted for within the studies reviewed.

Several studies have included a sample of mixed cancer survivors, while others had a more narrow focus to determine exercise preferences for a particular cancer type. Two of the studies

reviewed were predominantly concerned with preferences during the palliative phase of the disease (Lowe et al., 2010; Maddocks et al., 2011), one sampled only patients that had completed all active treatment (Vallance, Lavalley, Culos-Reed, & Trudeau, 2013), whereas the remainder included survivors at various phases of their cancer journey. One study, examining bladder cancer did not include any information on the current treatment phase of their participants (Karvinen et al., 2007).

There was a consistent trend for an average age of between 60-70 years in the majority of the studies. This was noted by Belanger et al, (Belanger, Plotnikoff, Clark, & Courneya, 2012), who specifically recruited younger cancer survivors with the intent of examining their exercise preference. A further study by Jones and colleagues (Jones, Guill, et al., 2007) also examined younger cancer survivors, due to the particular patient group they examined, since brain cancer is a more commonly diagnosed in younger adults. The mean age of the sample was not presented for three studies, which instead presented age as a categorical variable, only expressing the number of participants below or above the age of 65 (Karvinen et al., 2007; McGowan et al., 2013; Rogers et al., 2009).

Table 3.1
Characteristics of patient population in studies that have examined exercise preferences for cancer survivors

Study	N	Males (n)	Age Mean (SD)	Type of Cancer	Treatment phase
Maddocks et al. (2011)	200	97	64 (9)	Various	Palliative
Vallance et al. (2006)	431	224	61 (13)	NHL	Various
Lowe et al. (2010)	50	20	61 (13)	Various	Palliative
Peeters et al. (2009)	66	NR	63 (11)	Various	91% post treatment
Rogers et al. (2009)	90	70	NR	Head & neck	86% no treatment
Stevinson et al. (2009)	359	0	60 (13)	Ovarian	83% disease free
Karvinen et al. (2006)	386	0	65 (11)	Endometrial	52 ± 32 months
Belanger et al. (2012)	588	176	38 (6)	Various	87% disease free
Blaney et al. (2011)	456	109	61 (NR)	Various	83% post treatment
Karvinen et al. (2007)	397	295	NR	Bladder	NR
Trinh et al. (2012)	703	442	65 (11)	Kidney	87% disease free
Vallance et al. (2013)	524	0	62 (11)	Breast	Completed treatment
Jones & Courneya (2002)	307	132	61 (11)	Various	Various
Lin et al. (2013)	81	43	61 (11)	Lung	Various
Philip et al. (2014)	175	64	69 (10)	Lung	91% Stage 1 (post-surgery)
Rogers et al. (2009)	483	0	63 (12)	Breast	60% current treatment
Jones et al. (2007)	106	52	45 (12)	Brain	47% active treatment
McGowan et al. (2013)	600	350	NR	Colorectal	90% post treatment

NR, not reported

3.2.1 Exercise preferences

Only quantitative results were included in this review. Many of the studies have used similar questions when collecting exercise preferences, but no standardised template exists. Therefore, different preferences have been examined across the studies. Outcomes are summarised in Table 2, and blank spaces are used when that preference question was not addressed.

The preferences of brain cancer patients assessed by Jones and colleagues (Jones, Guill, et al., 2007) are not reported in the table below, as the results represented by the authors appear to not properly represent actual preferences. A sample of 106 participants were surveyed regarding their preferences both during active treatment and during non-treatment periods. The outcomes reported were averaged for the entire sample, despite numerous missing data points. For example it was reported that during treatment only 26% ($n = 27$) of patients would chose to exercise at home. However, since only 58 responses were obtained for the preference of location, the response, in fact represent 47% favouring home-based exercise. After examining the preferences more closely, the only noticeable differences were that people felt less able to exercise during treatment (34 of 84) compared to being off treatment (9 of 93).

3.2.1.1 Ability and interest

Regardless of the cancer type, treatment phase, or age, approximately 85% of all cancer survivors believed that they were definitely or possibly capable of commencing an exercise program. Results presented in Table 3.2 are the summed the responses for “yes” and “maybe” to differentiate those that believed they were unable to exercise in any capacity. The same approach was taken to sum “yes” and “maybe” to represent interest in exercise. In all cases, ability to exercise exceeded the number of survivors interested in commencing an exercise program. The reason for the lower number that expressed interest to participate is attributable to several reasons such as illness and lack of motivation. However, not all reasons provided are negative with some survivors already active enough, and having no need to join a new program. This has also been reported as a reason for declining to participate in exercise intervention studies (Courneya et al., 2009; Thorsen et al., 2005).

3.2.1.2 Preferred exercise activity

Due to the large range of exercise options and preferences available, it was decided that the descriptive characteristics would be limited, examining particularly walking and resistance

training. Walking was selected as it is the most common form of exercise and resistance training was selected because it is recognised as a necessary form of exercise according to international physical activity guidelines for healthy individuals and cancer survivors (Garber et al., 2011; Schmitz et al., 2010). In the case where a range of preferences were provided, a third alternative is also listed.

Walking was listed as the most preferred form of exercise (range: 22% to 89%) in all but one of the 16 studies that assessed preferences for specific activities. Maddocks and colleagues (2011) reported, in their sample of 200 palliative cancer patients, that neuromuscular electric stimulation was the most preferred option (36%). However, it is debatable as to whether this should be included as an exercise, since no active movements are required. Furthermore, the authors reported that some responses may have selected the option based on curiosity, rather than as a direct preference (Maddocks et al., 2011).

Resistance exercise was less preferred (range: 3% to 36%), not only compared to walking, but in many cases it also fell below several other aerobic activities. It can be observed from Table 2.2 that in five studies at least one other modality was rated as having a preference between walking and strength training. These other exercises were most commonly swimming and cycling. Several of the reports collected exercise preferences for both winter and summer, and indicated that preferences are indeed seasonal. In all cases, preferences for resistance training increased, whereas preferences for walking decreased, during the colder months.

3.2.1.3 Environmental setting and location

It was found that, in the majority of studies (10/16), participants indicated that they would prefer not to exercise alone and instead be in the company of others. Those that preferred to exercise alone appear to be the groups with the most severe prognoses or receiving current treatment (Lowe et al., 2010; Maddocks et al., 2011; Rogers, Malone, et al., 2009; Rogers, Markwell, Verhulst, et al., 2009). When examining those that preferred exercising with others, it must be considered that this review does not attempt to account for the variety of different options (e.g., with family, with friends, with spouse/partner) included under the ‘others’ category. One such option listed was with ‘other cancer survivors’, since the preference for this option, when presented, was very low. Similarly, there was little interest to perform an exercise

program in a hospital/specialist cancer care centre, the location where most other exercisers would also be cancer patients.

Evidently, the home was the most preferable location for exercising in 13 of the 17 reports. Not surprisingly, the two trials that examined the preferences of late stage palliative patients provided the highest preferences (83% and 84%) for activity in the home environment (Lowe et al., 2010; Maddocks et al., 2011), whereas those that favoured a gym-based setting comprised survivors with minimal disruptions from cancer, typically post-treatment and disease free (Belanger et al., 2012; Blaney et al., 2011; Philip et al., 2014; Vallance et al., 2013). The desire for specialist supervision, more likely available in a gym or fitness centre as opposed to a home-based setting, produced mixed responses ranging from 12% to 68%. Two of the studies that reported the highest desire for supervision were comprised of only female participants with either breast cancer (Vallance et al., 2013) or endometrial cancer (Karvinen et al., 2006).

3.2.1.4 Exercise intensity

Moderate intensity activity was preferred in all 11 studies that reported this measure. Ten of these reports indicated that at least 50% of all participants chose this mid-range intensity followed by a desire for light exercise (~25%), with very few expressing interest in vigorous activity (range: 1% to 11%). The two reports that indicated the highest preference for low intensity training (43% and 39%) both examined lung cancer patients (Lin et al., 2013; Philip et al., 2014), a patient group that experiences treatment-related decrements in cardiorespiratory fitness, increasing the difficulty associated with exercise and exertion (Jones, Peddle, et al., 2007).

3.2.1.5 Timing

Fatigue has been reported to be the most common symptom experienced by cancer survivors and it is exacerbated during active treatments (al-Majid & McCarthy, 2001). This high level of fatigue during active treatment was most likely responsible for most studies finding that cancer survivors would prefer to commence an exercise program only after treatment has been completed. Most of the reports (9/12) indicated that survivors were keen to commence exercise within 6 months of completing their treatment, with a further study indicating that a longer period of more than a year was preferred by participants (Blaney et al., 2011). Only two studies

reported a preference for exercise to commence before treatment (Philip et al., 2014; Vallance et al., 2013). However, several other reasons may also contribute to the lack of interest in exercising during active treatment phases. These reasons can include time commitments due to treatment schedules, recovery from surgery or other treatment limitations, as well as pain and discomfort.

With regards to the preferred timing of exercise within the day, all reports indicated that the morning was the most selected option (37% to 59%). The lowest preference for morning exercise was reported for bladder cancer survivors (Karvinen et al., 2007). However, it should be noted that despite 37% specifically choosing morning as the preferred time, a further 36% had no particular preference. These results were similar to others, indicating that, on average, less than 30% have a particular preference to exercise only in the afternoon or evening. The preferred frequency and duration of exercise session were reported in two studies and provided conflicting outcomes (Blaney et al., 2011; Lowe et al., 2010). Blaney et al. (2011) found that breast cancer survivors reported a preference for one or two exercise sessions per week lasting 20-30 minutes. This contrasted to the reports for a cohort of palliative survivors who were more interested in more sessions per week (2 – 7 times/week) but for a shorter duration (< 20 min). Similarly, the two groups least likely to prefer scheduled exercise were lung cancer (Lin et al., 2013) and head and neck survivors (Rogers, Malone, et al., 2009). These two groups are more likely to require a flexible approach to exercise as they suffer with severe and unpredictable treatment effects.

Table 3.2

Summary of exercise preferences available from current publications included in the review

		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
Uptake	Able to exercise	41-96 ^a	85%	92%		83%	93%	82%	87%	83%	84%	81%	85%		95%	86%	85%	84%
	Interested in exercise	67%	81%	92%	60% ^b	75%	87%	77%	78%	76%	81%	71%	76%		89%	62%	74%	77%
Exercise Type	Walking	22%	55%	72%		47% ^c	63%	69%	51% ^d	77%	81%	69% ^e	51%	81%	89%	43%	55% ^f	49% ^g
	Resistance Training	16%	11%	12%		7% ^c		27%	10% ^d	36%	21%	15% ^e	27%	4%			3% ^f	
	Other					Sports (17%) ^c	Swim (4%)	Swim (16%)	Cycling (33%) ^d	Swim (32%)	Cycling (16%)	Cycling (24%) ^e	Flexibility (36%)	Swim (4%)	Gymnastics (38%)	Swim (9%)	Swim (12%) ^f	Golf (15%) ^g
Setting	Alone	83%	31%	54%		50%	29%	24%	17%	16%	36%	39%	23%	44%	44%	22%	41%	24%
	Others	17%	35%	16%		30%	46%	44%	49%	80%	28%	96%	77%	38%	53%	29%	38%	66%
	Supervised	15%	42%		68%	12%		53%			29%	41%	59%	43%	16%		22%	
Location	Home	83%	43%	84%	60%	33%	49%	33%	44%	15%	54%	52%	37%	40%	20%	20%	38%	56%
	Gym / fitness centre	13%	17%	0%		8%	21%	24%	54%	29%	11%	33%	58%	13%	9%	29%	19%	28%
	Hospital / cancer centre	4%	13%	0%	32%	0%	7%	10%	11%	17%	8%	7%	6%	19%		17%	3%	10%
Intensity	Low		23%			26%		26%		24%	26%	35%	24%	35%	43%	39%	26%	
	Moderate		62%			50%		61%		60%	62%	58%	66%	56%	54%	44%	65%	
	High		10%			6%		8%		5%	7%	6%	11%	4%	1%	4%	4%	
Timing	Initiation of exercise ^h		3 to 6 (38%)				0 to 6 (51%)	0 to 6 (66%)	0 to 6 (50%)	12 + (34%)	0 to 6 (61%)	0 to 6 (59%)	Before (41%)	0 to 6 (46%)	3 to 6 (24%)	Before (60%)		0 to 6 (50%)
	Morning		41%	40%		47%	49%	51%			37%	58%	59%	48%	53%		53%	
	Scheduled sessions		55%			10%		65%			43%	51%	67%	53%	7%		24%	

1, Maddocks et al., (2011); 2, Vallance et al., (2006); 3, Lowe et al., (2010); 4, Peeters et al., (2009); 5, Rogers, Malone, et al., (2009); 6, Stevinson et al., (2009); 7, Karvinen et al., (2006); 8, Belanger et al., (2012); 9, Blaney et al., (2011); 10, Karvinen et al., (2007); 11, Trinh et al., (2012); 12, Vallance et al., (2013); 13, Jones & Courneya (2002); 14, Lin et al., (2013); 15, Philip et al., (2014); 16, Rogers, Markwell, et al., (2009); 17, McGowan et al., (2013)

^a Answers were provided for six specific exercise programs

^b Value represents whether participants would have been willing to exercise during their active treatment

^c Values presented for summer months, winter: walking (44%), resistance training (12%), sports (8%)

^d Values presented for summer months, winter: walking (40%), resistance training (19%), skiing (32%)

^e Values for walking and cycling presented for summer, resistance training only reported for winter

^f Values presented for summer months, winter: walking (41%), resistance training (7%), aerobics (9%)

^g Values presented for summer months, winter: walking (37%), no other activity exceeded 5%

^h Values represent number of months post treatment unless otherwise stated

3.3 Exercise preferences and depression

There is a growing empirical base confirming that exercise is effective at treating or managing clinical depression (Rimer et al., 2012) and, given this, several organisations including the National Institute for Health and Clinical Excellence and the Mayo Clinic now list exercise as a component of the recommended treatment and management plan (Blake, 2012). Despite this increased awareness of the positive benefits of exercise, it is known that individuals diagnosed with depression accumulate less physical activity than the general population (Ussher et al., 2007). Therefore, it is surprising that little research has been conducted to examine the exercise preferences of depressed individuals, in an attempt to increase uptake and adherence in this group. Moreover, the prescription of pharmacotherapy used to treat depression is associated with its own side-effects, such as nausea and hypertension, yet different classes of drugs cause different adverse effects (Kent, 2000). Therefore, it is possible that exercise preferences for people living with depression may differ based on the medical management of their condition.

The exercise preferences of people with severe mental illness have been examined in only two studies. One hundred and twenty psychiatric patients (84 males, 36 females) actively receiving treatment through the community health services as either inpatients (67%) or outpatients (33%) were interviewed (Ussher et al., 2007). The average age of the sample was 42 ($SD = 16$) years, and included patients with several different psychiatric disorders including schizophrenia ($n = 36$), depression ($n = 20$), and bipolar disorder ($n = 18$). Preferences, however, were only provided for the group in its entirety. The authors reported that walking was the preferred activity listed by 70% of the group, with no other exercise being ranked as the most preferred by more than 3 participants. In line with this finding, there was an overwhelming preference for exercise to be performed in a home-based setting (90% agreement), since no specialist equipment or facilities are required and typically home-based activities do not require active participation of others (Brunet et al., 2014). However, there was also no clear consensus regarding the type of people with whom patients preferred to exercise. The majority reported no preference (43%) whereas an equal amount preferred to exercise alone (31%) or with others (30%). Further, despite the preference for home-based exercise, the majority of respondents (52%) believed that they would do more exercise in a controlled environment such as a gym or local fitness centre.

In order to assess whether the preferences of patients with mental illness differed from the general population, Carpiniello and colleagues (2013) conducted a cross sectional examination that replicated the work of Ussher by comparing a cohort of 138 patients with psychiatric illness (age: 50 ± 11 years) to a gender- and age-matched control group (age: 48 ± 12 years). The clinical group comprised a mix of psychiatric illness, with the majority of diagnoses being schizophrenia and related psychotic disorders ($n = 40$), MDD ($n = 38$), and bipolar disorder ($n = 35$). Walking was again selected as the preferred form of activity for both the clinical group (57%) and the control group (46%). In contrast to the findings from Ussher et al. (2007), there was a clear preference for exercise to be performed in the company of others, reported by both the clinical (49.6%) and the control (48.9%) when compared to exercising alone (~20%) or not having a particular preference either way (~31%). Interestingly, only 11 patients and 14 control participants reported exercise in the home setting as their preference. This figure of 9% is only one tenth of that reported by Ussher and colleagues. However, the result was likely influenced by the fact that home exercise was not examined based on location (i.e., home vs gym), but was included as a type of activity to be selected against more specific activities such as walking, jogging, dancing, and cycling. In this context, the meaning is less clear and may not be comparable to previous findings. Nonetheless, both the clinical cases (67%) and controls (72%) agreed that exercising in a gym setting would encourage them to be more active than exercising at home.

Importantly, these authors also extended the initial findings and examined whether clinical diagnosis influenced the response provided by the patient group (Carpiniello et al., 2013). The patient groups tended to show similar preferences, with the only difference reported for those suffering anxiety disorders preferring to exercise in a controlled environment ('facility') and perform daily activities, such as housework, as a form of exercise.

3.4 Discussion

It is evident by the lack of available literature that much remains to be learned about the exercise preferences of depressed individuals. The two studies that have addressed this question, only examined patients' preferred activity, setting, and location and, within these limited results, some equivocal findings were presented. Importantly, no information was presented that related to within-session preferences, such as exercise intensity, timing of exercise, and whether supervision is desired, all of which were available for numerous studies

examining cancer survivors. From the evidence presented above, only one definitive conclusion can be made. Walking is the most preferred exercise activity selected by a multitude of cancer survivors or depressed patients treated either as in- or out-patients at psychiatric hospitals.

The intensity at which any exercise is performed is one of the most important prescriptive variables to elicit physiological adaptation (Kraemer et al., 2002). In most instances, light activity will have minimal impact on the physical health and well-being of an individual. Therefore, physical activity guidelines only include the amount of time recommended for moderate and vigorous exercise (Garber et al., 2011). In accordance with these recommendations, and others specifically targeting cancer survivors (Hayes et al., 2009; Schmitz et al., 2010), it was encouraging to see that approximately 60% of the cancer survivors preferred exercise at or above moderate intensity. The preferred intensity for depressed patients has not been assessed, but other research suggests that low intensity is preferable (Callaghan, Khalil, Morres, & Carter, 2011). It was reported that a cohort of 19 depressed women self-selected a lower intensity for aerobic exercise compared to a randomly allocated control group that received exercise at a higher intensity in line with national exercise guidelines (Callaghan et al., 2011). Despite exercising at a lower intensity, the women in the self-selected group responded better to training, statistically exceeding the control group on all psychological outcomes, including reduced levels of depression and increased self-esteem. Further, adherence to exercise was improved when participants selected their own intensity illustrated by a significantly greater number of sessions attended (8.2 ± 3.6 vs 5.9 ± 4.2 , $p = .04$) compared to the control group (Callaghan et al., 2011).

Not only is there a lack of information available to compare exercise preferences, but the characteristics of the two clinical populations are largely different. Only 35% of the 6002 cancer survivors were male, with the entire cohort averaging in excess of 60 years old. The characteristics of the samples including depressed patients were both younger (50 ± 11 and 43 ± 16) and included a larger proportion of males (45%) than the cancer survivor population. However, the greatest limitation is that the preferences reported were for the entire psychiatric sample ($n = 258$), but only a minority ($n = 58$) were cases of depression. This is problematic since other psychiatric mental illnesses such as psychosis and schizophrenia are associated with an increased number of comorbid health complications (Pelletier, Nguyen, Bradley, Johnsen, & McKay, 2005) and more severe side-effects of pharmacotherapy such as weight gain,

metabolic dysfunction, and insomnia (Pearsall, Smith, Pelosi, & Geddes, 2014) all of which could influence exercise preferences. Therefore, there is a need to examine a larger cohort of people living with depression and determine their specific preferences.

Within the studies that examined exercise preferences of cancer survivors, not only have the overall results been presented, but many performed regression analyses to examine relationships between the outcomes (Karvinen et al., 2007; Vallance et al., 2006). These analyses illustrated that not only do differences exist between cancer types, but that, even within each cancer group, personal circumstances (e.g., past treatment, socio-economic status) or personal characteristics (e.g., age, body mass, gender) can influence exercise preferences. Therefore, exercise preferences used for prescription may need to be more individualised, rather than being specific to cancer type or treatment. At this individualised level, psychosocial factors are more likely to be an important consideration and indicate the need to examine preferences not only for cancer survivors and depressed individuals but also people living with cancer and comorbid depression.

Although the intention of this review was to examine the preferences for exercise, initiating successful programs also relies on program designs that limit established barriers to participation (Ussher et al., 2007). This is an extensive topic in itself, and is beyond the scope of the current review. Briefly however, fatigue and lack of motivation to exercise are commonly reported by both cancer survivors and people experiencing depression (Carpiniello et al., 2013; Milne et al., 2007; Ussher et al., 2007). Lack of time is another limitation that has been suggested as a reason for not commencing exercise, or being sufficiently active, in both cancer survivors and the general population (Carpiniello et al., 2013; Milne et al., 2007). Time seems to be less of a consideration for psychiatric patients, reported by only 24% compared with 55% of participants in the control group in the study by Carpiniello et al. (2013).

In summary, the findings to date provide a solid foundation for understanding preferences for exercise in different groups of cancer survivors. However, no research has examined the exercise preferences of depressed cancer survivors and insufficient information is available regarding exercise preferences of people living with depression. These two groups are likely to obtain considerable benefits from exercise that improves both physical and mental health, yet are also likely to be less tolerant towards exercise. Therefore, any measures to increase exercise uptake in these groups, such as creating programs that are based around individualised

preferences, are certainly worthwhile. Nonetheless, several research trials with cancer survivors and depressed individuals have not considered client preferences and have managed to attract participants and elicit favourable outcomes. This suggests that there is also a need to examine the exercise protocols that have previously been successful to ensure that both patient preferences are considered along with applied and proven best practice.

CHAPTER FOUR

Physical activity levels and exercise preferences of depressed and non-depressed cancer survivors

4.1 Introduction

People living with cancer are more likely than those in the general population to experience depression (this term will be used for both clinically diagnosed depression and elevated depressive symptoms measured using self-rating scales), with prevalence rates as high as 50% (Massie, 2004). However, the prevalence of depression is not uniform amongst all cancer patients. It has been established that cancer site can influence depression, with newly diagnosed lung (17.6%), colorectal (10.5%), prostate (4.0%), and breast cancer survivors (5.3%) showing different proportions of depressed cases (Sellick & Edwardson, 2007). Nonetheless, the consequences of depression are common and impact negatively on quality of life (Moller, 2008; Singh et al., 2005), which may further impact upon adherence to medical treatment and therefore exacerbate disease outcomes (Jehn et al., 2006; Pasquini & Biondi, 2007). Cancer survivors with depression have been reported to have increased recurrence rates of cancer and higher rates of mortality (Miller et al., 2008) and this outcome is similar for both clinical diagnosis or elevated depressive symptomology (Pinquart & Duberstein, 2010). However, many cancer survivors suffer with symptoms of depression but are not diagnosed, and, therefore have limited access to professional assistance (Sellick & Crooks, 1999). Hence, there is a need to reduce depression at all levels, not only clinically-diagnosed depression. The development of tailored interventions to reduce, prevent or treat depression in cancer survivors is imperative.

Physical exercise may provide a unique opportunity in the treatment of depressed cancer survivors. Exercise is acknowledged to have a therapeutic effect in reducing depression, reportedly as effective as either pharmacological treatments or psychotherapy (Blake 2012; Brosse et al., 2002; Rimer et al., 2012). Moreover, the importance of exercise for cancer survivors is well established. The most recent consensus statement by the American College of Sports Medicine declares that exercise is safe for cancer survivors and that physical inactivity should be avoided at all times, including during active treatments (Schmitz et al., 2010). It is known that exercise can improve muscle strength, cardiovascular fitness, and improve physical function (Garber et al., 2011) and may even decrease the likelihood of cancer recurrence (Siegel et al., 2012). Despite the differences in depression prevalence in different cancers, exercise is likely to provide similar benefits to cancer survivors regardless of disease stage or site of the cancer (Adamsen et al., 2004; Courneya, Friedenreich, Sela, et al., 2003).

Unfortunately, side-effects and health complications caused by cancer and its treatment often make exercising difficult (Ferrer et al., 2011). Fatigue, as well as physical side-effects such as decreases in muscle mass and strength (Schmitz et al., 2010), negatively affect the functional abilities and daily activities of cancer survivors (Mock et al., 2001). These functional/physical declines may result in increased likelihood of developing additional comorbidities such as hypertension, diabetes, sarcopaenia and osteoporosis (Galvao et al., 2008), all of which can be reversed or delayed by exercise. Therefore, depressed cancer survivors could improve their physical and mental health if they commence or continue to exercise following a cancer diagnosis.

When prescribing exercise to depressed individuals, adherence is an especially important consideration, as this group is typically less physically active and more socially withdrawn (Derntl et al., 2011). To date, only two papers have examined the exercise preferences of people with mental illness and in those studies, only a minority (22%) were diagnosed with depression ($n = 58$) (Carpiniello et al., 2013; Ussher et al., 2007). Ussher et al. (2007) interviewed 120 psychiatric patients (67% inpatients, 33% outpatients) and found that walking was the preferred method of activity for 70% of the group. There was no obvious preference for exercising alone or with others; however, an overwhelming majority reported a preference for home-based exercise (90%) (Ussher et al., 2007). A randomised controlled trial by Callaghan and colleagues (2011) reported that women who chose to exercise at a low self-selected intensity had better overall outcomes, including decrements in depression, compared to a group exercising at a prescribed higher intensity. This finding, along with others, indicates that the psychological benefits of exercise can occur independent of physiological improvements such as an increase in aerobic capacity (Brosse et al., 2002; Courneya et al., 2009). It remains unknown, however, whether the optimal exercise prescription for depression requires activity to be performed at a level that is associated with physiological changes (Wolff et al., 2011) in cancer survivors. Perhaps the most important factor to consider is the preferences of the individual, as engaging in a preferred regime is likely to increase exercise adherence, which is necessary for long term physical and psychological adaptations (Perraton et al., 2010).

Recent research has examined the exercise preferences of cancer patients with the aim of finding suitable modes of exercise delivery to this population, which both increases adherence and provides positive exercise benefits (Lowe et al., 2010). Research available for various cancer populations including breast, prostate, colorectal, lung, and brain, provides a solid

foundation for understanding exercise preferences in cancer survivors (Karvinen et al., 2006; Karvinen et al., 2007; Stevinson et al., 2009; Vallance et al., 2006). Only one study, to date, has considered depressive symptoms when examining exercise preferences and reported that there were no differences between depressed and non-depressed head and neck cancer survivors (Rogers, Malone, et al., 2009). It is known that this cancer population suffers with severe treatment side-effects and compromised mental health, indicated by the high proportion (44%) of depressed cases (Rogers, Malone, et al., 2009) and, therefore, these findings may not be generalizable to other cancer survivors. Additionally, all previous outcomes have been reported for Canadian (Belanger et al., 2012; Jones & Courneya, 2002), American (Rogers, Malone, et al., 2009), or European (Blaney et al., 2011; Maddocks, et al., 2011) cancer survivors. Therefore, there is a need to confirm whether these outcomes are similar in Australian cancer survivors. Preferences for Australian survivors may vary to those previously reported due to different environmental and climatic conditions as well as potential differences in health promotion messages relayed through the media and healthcare system. These are important research questions as cancer survivors with depression are likely to be less tolerant and show lower adherence to exercise. Moreover, it has previously been reported that Australian cancer survivors exhibit more mental health complications than the general population (Atlantis, Chow, Kirby, & Singh, 2004) suggesting that depression may be a common comorbid condition for this clinical population.

The primary aim of this cross-sectional study was to examine the exercise preferences of Australian cancer survivors and compare the findings between depressed and non-depressed survivors. A second aim was to determine whether the exercise preferences of Australian cancer survivors are similar to previously reported findings from international groups.

4.2 Methods

4.2.1 Overview and participants

A total of 1799 Australian cancer survivors, aged 18 years or older, were sent a questionnaire pack designed to determine demographic characteristics, cancer history, levels of depression, physical activity levels, and preferences for exercise. Eligible participants included 490 cancer survivors who had registered with the Cancer Council of New South Wales 'Join a Research Study' database, which is a resource for willing patients to express interest in being involved in research trials. A further 1309 cancer patients were contacted by invitation from their

medical specialist (oncologist or surgeon) affiliated to St John of God Hospital, Subiaco, Western Australia (WA) and Joondalup Health Campus, Joondalup, WA. The research was approved by the Human Research Ethics Committee of Edith Cowan University (Ref No. 7909 LEVIN), the St John of God Health Care Ethics Committee (Ref No. 544), and the Human Research Ethics Committee of Joondalup Health campus (Ref No. 1313).

The questionnaire packs (Appendix A) were distributed by mail and each pack included a cover letter, an information sheet explaining the purpose of the research, and a reply-paid, return envelope. For confidentiality purposes all personal details (name and address) were omitted from data collected. Instead, each questionnaire (Appendices B and C) was labelled with a unique number that allowed the researchers to track which participants had completed and returned these questionnaires. Therefore, returned questionnaires were taken to indicate informed consent, and the information letter to the participants clearly stipulated that participation was voluntary. The questionnaires were presented in the following order: demographics, cancer history, physical activity habits, exercise preferences, depression and anxiety measurements. The participants from Western Australia also received a cover letter from their medical specialist (Appendix D and E). Similar to previous studies, if no response was received five weeks after the initial mail out, a second questionnaire pack was sent to the participant (Stevinson et al., 2009). Following the second mail out, no further correspondence was initiated. If no response was obtained ten weeks after initial contact, it was determined that the participant had declined involvement.

4.2.2 Measures

4.2.2.1 Demographics and cancer history

The first sections of the questionnaire were designed to collect demographic information such as age, gender, highest level of education achieved, employment status, and nationality. Height and body mass were obtained through self-reported measures provided by the participants. Cancer-specific medical history was obtained through questioning of cancer type and time since diagnosis.

4.2.2.2 Depression

Determination of depression status was assessed using three criteria to improve accuracy without requiring the participants to undertake a clinical diagnostic interview. First, each

survey pack included two specific questions that asked “Have you previously been diagnosed with depression by a medical professional?” and “Are you currently being treated for depression?” The second question was used to determine whether a participant was currently depressed, and therefore included in the depressed patient group.

Second, depressive symptoms were also assessed using the Hospital Anxiety and Depression Scale (HADS) (Zigmond & Snaith, 1983). The HADS is well validated as a measure of depression in clinical populations (Bjelland et al., 2002), has previously been used as a screening tool in cancer patients (Sellick & Edwardson, 2007), and does not include somatic symptoms of depression (Tylee & Gandhi, 2005), which is important as these can often overlap with cancer-related disease and treatment side-effects. The score for the depression subscale of the HADS can range from 0 – 21 and depression was considered likely if the participant scored at least 11 (Sellick & Edwardson, 2007).

Third, to assess participants for current levels of depressive symptoms, a self-rated scale of depression (SRDS) was also included. Based on the nine symptoms used to characterize a major depressive episode according to the Diagnostic and Statistical Manual (DSM-IV-TR) participants were classified as ‘depressed’ if they responded in the affirmative to at least one of the first two questions and also reported experiencing at least four of the remaining seven symptoms over the past two weeks (Diagnostic and Statistical Manual of Mental Disorders (4th Edition), 2000). The SRDS can be considered to have construct validity, since it was based on the ‘gold-standard’ diagnostic assessment and also demonstrated a high degree of concurrent validity with the HADS-D ($r = .681$; $p < .001$).

For the purpose of analysis, participants were considered depressed if they met any of the three criteria above. Although some depressed cases were asymptomatic, but still currently receiving treatment for depression, they were included in this group because their treatment is considered usual care for depression and does not negate the fact that they were clinical cases, at least at some point (Strong et al., 2008).

4.2.2.3 Physical activity

Current levels of physical activity were determined using a modified version of the Godin Leisure Time Exercise Questionnaire (GLTEQ) (Godin & Shephard, 1985), which was

embedded into the overall questionnaire. Briefly, participants were asked to record how often in the past week they performed exercise and to categorize the intensity of each session as mild, moderate or strenuous. Two modifications were made to the original questionnaire. First, participants were asked to record sessions with a minimum duration of 10 minutes or more, as opposed to 15 minutes, which was the minimum time set in the original GLTEQ (Godin & Shephard, 1985). Ten-minute durations were chosen to be in accordance with current exercise guidelines suggested by the American College of Sports Medicine (Garber et al., 2011). A second modification was that participants were asked to record the average duration of each session. This additional information was used to determine whether participants were meeting international physical activity guidelines for cancer survivors (Schmitz et al., 2010).

4.2.2.4 Exercise preferences

Specific preferences for exercise were assessed by asking 10 forced-choice questions (Table 4.3) adapted from previous studies that have assessed exercise preferences for cancer survivors (Karvinen et al., 2006; Karvinen et al., 2007; Stevinson et al., 2009). Some of the specific preferences examined included: 1) type of exercise that participants would be most interested in performing; 2) who they wanted to exercise with; 3) preferred intensity for exercise training; and, 4) whether they preferred supervised or unsupervised exercise sessions.

4.2.3 Data analysis

To examine the primary aim of this study, participants were classified into depressed and non-depressed groups based on the criteria described above. Demographic characteristics of age, height, body mass, and time since diagnosis were assessed using one-way analysis of variance. Multiple analyses, using independent group *t*-tests, were performed to compare level of depression and to examine the physical activity outcomes. In all cases when *t*-tests were used, 95% confidence intervals (CI) are also reported. Descriptive and categorical statistics, such as frequencies and percentages, were calculated to provide summary results for some characteristic measures of the groups (sex, education, etc.) as well as the proportion of depressed cases per cancer site, and the exercise preference outcomes. For these variables, chi-squared tests were used to assess whether differences between the depressed and non-depressed groups were statistically significant. Fisher's exact test using Markov Chain Monte Carlo simulation was used when Chi-squared assumptions were violated.

For a complete analysis of the exercise preferences, responses were, in some instances, combined to dichotomize results (e.g., 'yes' and 'maybe' combined to compare against 'no'). This was done to match analysis methods of previous research (Karvinen et al., 2006; Karvinen et al., 2007).

All statistical analyses were performed using PASW v18 for Windows (SPSS Inc., Chicago IL, USA) with the criterion for statistical significance set at an alpha of .05. It is acknowledged that the examination of multiple dependent variables, without any adjustment of alpha presents an increased likelihood of the family-wise Type I error rate, which is to find a significant difference where no difference exists. These multiple comparisons should be considered by the reader and results can be interpreted with caution. Nonetheless, since no previous research has examined the exercise preferences of depressed and non-depressed cancer survivors, and very little is known in this field, the risk of a Type I error was considered less detrimental than the risk of a Type II error. In the situation of limited previous research having been conducted, missing detecting an effect might have the untoward effect of preventing future researchers from investigating potentially useful findings.

To examine the second aim of this study, the sample was split according to the type of cancer diagnosis, without accounting for depressed status. Data were presented for each cancer type where more than 10 cases were present, and previous findings had been reported in the literature. No statistical analyses were performed, however, descriptive comparisons with previous findings were provided.

4.3 Results

4.3.1 Participant recruitment and demographics

The initial mail out of 1799 questionnaires resulted in a response rate of 50.6%. However, 88 respondents did not provide any data and a further 14 provided insufficient data to determine depression status. Therefore, 420 females and 388 males provided sufficient data to be used for analysis (Figure 4.1). The majority of the demographic characteristics and the time, in months, elapsed since diagnosis were similar between groups. Differences were found, however, that indicated depressed cancer survivors were younger, and less likely to be living in a committed relationship (Table 4.1).

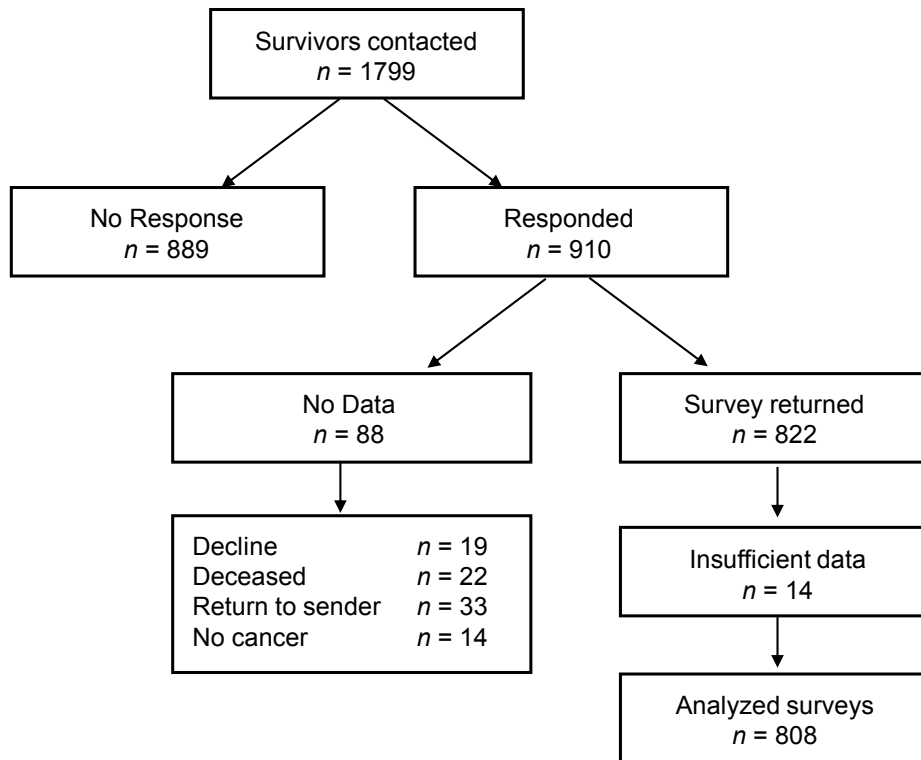


Figure 4.1. Flow diagram of recruitment and responses.

Table 4.1
Demographic characteristics of the depressed ($n = 158$) and non-depressed ($n = 650$) groups

	Depressed Mean (SD)	Non-depressed Mean (SD)	<i>P</i>
Age (years)	61.3 (10.6)	64.4 (12.2)	.002
Height (cm)	169.1 (9.3)	169.5 (15.7)	.741
Body mass (kg)	78.5 (18.3)	76.4 (15.3)	.177
Body mass Index	27.3 (5.4)	26.6 (4.8)	.127
Time since diagnosis (months)	46.5 (65.0)	50.0 (65.2)	.552
	<i>n</i> (%)	<i>n</i> (%)	
Sex			.297
Male	70 (44.3)	318 (48.9)	
Female	88 (55.7)	332 (51.1)	
Level of education			.688
Schooling	53 (33.8)	218 (33.9)	
Trade	16 (10.2)	53 (8.2)	
Certificate/Diploma	46 (29.3)	181 (28.1)	
Bachelor degree	31 (19.7)	124 (19.3)	
Higher degree	11 (7.0)	68 (10.6)	
Marital status			< .001
Partner	96 (60.8)	488 (75.1)	
No partner	62 (39.2)	162 (24.9)	
Employment status			.254
Employed	64 (41.3)	300 (46.4)	
Unemployed	91 (58.7)	347 (53.6)	

In accordance with the group allocation, based on depression, the depressed group exhibited significantly greater depression scores measured using both the HADS-D and the SRDS (Table 4.2). A total of 105 participants were included in the depressed group, regardless of their level of depressive symptoms, since they were actively receiving treatment for depression. The remainder entered based on their elevated depressive symptoms.

Table 4.2
Levels of depression of depressed (n = 158) and non-depressed (n = 650) cancer survivors

	Depressed Mean (SD)	Non-depressed Mean (SD)	Mean Difference (95% CI)	p
HADS-D	7.5 (4.5)	2.5 (2.4)	-5.0 (-5.7, -4.3)	<.001
SRDS	4.6 (2.7)	0.9 (1.4)	-3.7 (-4.1, -3.3)	<.001

HADS, Hospital Anxiety and Depression Scale; HADS-D, Depression subscale score; SRDS, Self-rated depression scale

Including multiple primary or secondary cancers resulted in 881 confirmed cancer diagnoses reported for the 808 participants. Fifty-three non-depressed and 12 depressed participants reported more than one cancer with a further three non-depressed and one depressed participant reporting three independent diagnoses. There were 158 participants in the depressed group (19.6%) and 650 in the non-depressed group (81.4%). Prevalence of depression differed according to the site of the cancer and ranged from 6% for melanoma to as high as 27% for both skin and brain cancers (Table 4.3).

Table 4.3
Number of cancer diagnoses in the sample and percentage of depressed cases per site

	Non-depressed (n = 708*)	Depressed (n = 171*)	% Depressed	p
Cancer type				.254
Brain	8	3	27.3	
Skin	19	7	26.9	
Kidney	27	9	25.0	
Breast	185	59	24.2	
Other	35	10	22.2	
Bladder	29	8	21.6	
Hematological	29	7	19.4	
Prostate	197	42	17.6	
Thyroid	14	3	17.6	
Gynecological	25	5	16.7	
Lung	17	3	15.0	
Colorectal	94	13	12.1	
Melanoma	29	2	6.5	

* Number of cases exceed number of participants due to individuals with multiple diagnoses

4.3.2 Current physical activity

Depressed survivors engaged in significantly less total physical activity, calculated as minutes per week, compared with the non-depressed group (Table 4.4). However, when each of the three intensity bands were compared individually, only strenuous activity exhibited a between-groups difference ($p = .009$).

Table 4.4
Physical activity differences between depressed and non-depressed cancer survivors

	Depressed Mean (SD)	Non-depressed Mean (SD)	Mean Difference (95% CI)	<i>p</i>
Mild	106.35 (240.27)	122.69 (182.09)	16.33 (-17.58, 50.24)	.345
Moderate	83.35 (101.55)	101.55 (134.46)	18.20 (-5.18, 41.58)	.127
Strenuous	19.45 (54.35)	33.36 (77.97)	13.91 (3.49, 24.32)	.009
Total	209.16 (280.86)	257.60 (242.24)	48.44 (22.19, 4.87)	.029

Fewer depressed survivors were engaging in at least 150 minutes of weekly physical activity and a greater number were completely inactive compared to non-depressed participants (Table 4.5). Two further indicators of access to exercise revealed no statistical difference between the percentage of depressed ($n = 28$, 17.7%) and non-depressed ($n = 111$, 17.3%) survivors that reported being members of a local health club or exercise centre (17.4%; $p = .898$), or that owning at least one piece of exercise equipment (e.g., treadmill) ($p = .912$).

Table 4.5
Categorical measures of the physical activity for depressed and non-depressed groups

	Depressed <i>n</i> (%)	Non-depressed <i>n</i> (%)	<i>p</i>
All physical activity > 150 min/week	81 (51.3)	416 (64.0)	.003
Meet exercise guidelines for activity	45 (28.5)	257 (39.5)	.010
Performing some physical activity			< .001
0 minutes reported	38 (24.1)	77 (11.8)	
1 minute or more reported	120 (75.9)	573 (88.2)	

4.3.3 Exercise Preferences

Approximately 82% of all cancer survivors reported that they felt capable ('yes' or 'maybe') of exercising, with no difference found between the two groups. There was, however, a significantly greater proportion of depressed cancer survivors who expressed their desire to definitely or maybe commence an exercise program (78.5% vs 72.2%; $p = .044$). The specific preferences revealed significance for three other exercise programming variables. First, more

depressed cancer survivors reported a preference for exercise sessions to be supervised, by a health professional or qualified exercise instructor (mean difference +18.5%, $p < .001$) (see Appendix B for supervision choices). Second, exercising at a local fitness centre was more appealing to depressed cancer survivors, despite the fact that the majority of participants in both groups reported home-based exercise as their primary preference for location (+7%, $p = .049$). The final significant preference difference between groups was that depressed cancer survivors were less interested in cycling as a form of exercise. However, activity preference produced the most number of comparisons between groups, for a single measure, and is therefore at the highest risk of Type I error. More importantly, it should be acknowledged that most of the exercise preferences were not significantly different between the groups (Table 4.6).

Table 4.6
Exercise preferences for depressed and non-depressed cancer survivors

	Depressed <i>n</i> (%)	Non-depressed <i>n</i> (%)	<i>p</i>
Would you be interested in an exercise program?			.044
Yes	84 (53.2)	273 (42.3)	
No	34 (21.5)	183 (28.4)	
Maybe	40 (25.3)	189 (29.3)	
Would you be able to participate in an exercise program?			.391
Yes	84 (53.2)	313 (48.8)	
No	23 (14.6)	122 (19.0)	
Maybe	51 (32.3)	207 (32.2)	
What type of exercise are you most interested in?			#
Aerobics	25 (15.8)	80 (12.3)	.239
Cycling	24 (15.2)	149 (22.9)	.034
Jogging	13 (8.2)	54 (8.3)	.974
Strength training	64 (40.5)	221 (34.0)	.125
Swimming	40 (25.3)	144 (22.2)	.395
Walking	94 (59.5)	406 (62.5)	.491
Yoga	37 (23.4)	112 (17.2)	.072
Other	33 (20.9)	100 (15.4)	.094
Not interested	17 (10.8)	65 (10.0)	.777
When would you prefer to start an exercise program?			#
Before	25 (15.8)	125 (19.2)	.323
During treatment	14 (8.9)	59 (9.1)	.932
Immediately after treatment	30 (19.0)	97 (14.9)	.208
3 to 6 months after	24 (15.2)	93 (14.3)	.777
1 year or more after	28 (17.7)	90 (13.8)	.216
Do not want	24 (15.2)	96 (14.8)	.894
Who would you prefer to exercise with?			#
Alone	57 (36.1)	205 (31.5)	.274
Friends	32 (20.3)	121 (18.6)	.637
Family	16 (10.1)	85 (13.1)	.315
Other cancer survivors	23 (14.6)	71 (10.9)	.201
No preference	42 (26.6)	177 (27.2)	.869
Do not want	15 (9.5)	63 (9.7)	.940

	Depressed <i>n</i> (%)	Non-depressed <i>n</i> (%)	<i>P</i>
Where would you prefer exercise to take place?			#
Home	61 (38.6)	229 (35.3)	.435
Fitness centre	41 (25.9)	123 (18.9)	.049
Cancer fitness centre	20 (12.7)	61 (9.4)	.219
No preference	36 (22.8)	151 (23.2)	.905
Other	14 (8.9)	72 (11.1)	.418
Do not want	16 (10.1)	83 (12.8)	.364
What time of day would you prefer to exercise?			#
Morning	76 (48.1)	297 (45.8)	.597
Afternoon	26 (16.5)	82 (12.6)	.203
Evening	16 (10.1)	86 (13.2)	.292
No preference	21 (13.3)	89 (13.7)	.895
Do not want	18 (11.4)	80 (12.3)	.752
What intensity would you prefer to exercise at?			.292
Light	22 (13.9)	76 (12.0)	
Moderate	56 (35.4)	254 (40.2)	
Progressive starting light and building up	50 (31.6)	164 (25.9)	
Heavy	7 (4.4)	40 (6.3)	
No preference	6 (3.8)	12 (1.9)	
Do not want	17 (10.8)	86 (13.6)	
Would you prefer the same or different activities each session?			.252
Same	55 (35.3)	177 (28.5)	
Different	81 (51.9)	358 (57.6)	
Do not want	20 (12.8)	87 (14.0)	
Would you prefer your sessions to be supervised or unsupervised?			< .001
Supervised	99 (63.9)	283 (45.4)	
Unsupervised	40 (25.8)	267 (42.8)	
Do not want	16 (10.3)	74 (11.9)	

multiple responses were allowed and therefore each response has been compared between groups individually

4.3.4 Cancer specific exercise preferences

Exercise preferences for various cancer types were collated for all cases when at least 10 cases were present (Table 4.7). No statistical analysis was conducted, however the information enables descriptive comparisons to be examined between Australian cancer survivors and previously reported results of international studies. Within the current study, only two preferences, i) morning exercise sessions and ii) walking as the most preferred exercise modality, showed consistency across all cancer sites.

Table 4.7

Exercise preferences reported as percentage for each cancer site

	Breast <i>n</i> = 244	Prostate <i>n</i> = 239	Colorectal <i>n</i> = 106	Lung <i>n</i> = 20	Hematological <i>n</i> = 35	Gynecological <i>n</i> = 30	Brain <i>n</i> = 11	Bladder <i>n</i> = 37	Kidney <i>n</i> = 36
Would you be interested in an exercise program?									
Yes	46.9	40.7	46.7	35.0	50.0	63.3	63.6	37.8	54.3
No	21.4	29.2	25.2	35.0	22.2	20.0	18.2	35.1	28.6
Maybe	31.7	30.1	28.0	30.0	27.8	16.7	18.2	27.0	17.1
Would you be able to participate in an exercise program?									
Yes	53.5	45.7	50.9	30.0	47.2	60.0	45.5	43.2	41.2
No	14.4	18.8	16.0	30.0	13.9	13.3	18.2	27.0	32.4
Maybe	32.1	35.5	33.0	40.0	38.9	26.7	36.4	29.7	26.5
What type of exercise are you most interested in?									
Aerobics	19.3	10.0	15.9	5.0	8.3	16.7	9.1	10.8	8.3
Cycling	15.2	28.9	19.6	20.0	13.9	16.7	36.4	13.5	22.2
Jogging	8.6	7.1	8.4	5.0	11.1	6.7	18.2	5.4	13.9
Strength	36.1	35.1	34.6	20.0	33.3	36.7	45.5	18.9	33.3
Swimming	25.4	21.8	21.5	25.0	19.4	16.7	27.3	16.2	27.8
Walking	70.9	54.8	58.9	65.0	58.3	60.0	63.6	59.5	58.3
Yoga	32.8	5.4	23.4	15.0	25.0	23.3	9.1	5.4	8.3
Other	6.6	7.9	13.1	20.0	13.9	6.7	9.1	21.6	19.4
None	23.0	12.1	17.8	15.0	16.7	43.3	18.2	13.5	11.1
When would you prefer to start an exercise program?									
Before	12.3	23.8	16.8	5.0	16.7	33.3	18.2	32.4	8.3
During	10.2	5.0	15.0	0.0	16.7	16.7	45.5	10.8	5.6
After	59.8	38.1	43.9	40.0	41.7	30.0	45.5	18.9	33.3
Who would you prefer to exercise with?									
Alone	32.0	35.1	25.2	15.0	41.7	50.0	9.1	21.6	19.4
Company	43.9	31.0	27.1	25.0	44.4	36.7	45.5	27.0	30.6

	Breast <i>n</i> = 244	Prostate <i>n</i> = 239	Colorectal <i>n</i> = 106	Lung <i>n</i> = 20	Hematological <i>n</i> = 35	Gynecological <i>n</i> = 30	Brain <i>n</i> = 11	Bladder <i>n</i> = 37	Kidney <i>n</i> = 36
Where would you prefer exercise to take place?									
Home	39.1	38.5	24.3	25.0	47.2	37.9	36.4	40.5	27.8
Fitness centre	32.0	28.5	30.8	15.0	19.4	30.0	36.4	16.2	22.2
Other	10.2	11.3	9.3	5.0	8.3	16.7	9.1	8.1	5.6
What time of day would you prefer to exercise?									
Morning	61.3	52.3	55.1	45.0	55.6	62.1	36.4	54.1	36.1
Afternoon	13.5	15.5	8.4	0.0	16.7	13.3	18.2	10.8	8.3
Evening	11.9	13.0	11.2	5.0	11.1	13.3	18.2	8.1	16.7
What intensity would you prefer to exercise at?									
Light	14.5	12.2	11.9	28.6	31.3	22.2	20.0	7.4	8.3
Moderate	46.4	47.4	34.5	42.9	50.0	44.4	0.0	59.3	45.8
Progressive	34.5	29.6	45.2	14.3	18.8	33.3	80.0	33.3	37.5
Heavy	4.5	10.7	8.3	14.3	0.0	0.0	0.0	0.0	8.3
Would you prefer the same or different activities each session?									
Same	35.0	43.5	26.8	50.0	25.0	11.5	30.0	31.0	36.0
Different	65.0	56.5	73.2	50.0	75.0	88.5	70.0	69.0	64.0
Would you prefer your sessions to be supervised or unsupervised?									
Supervised	65.3	43.3	61.2	64.3	51.5	67.9	80.0	57.1	55.6
Unsupervised	34.7	56.7	38.8	35.7	48.5	32.1	20.0	42.9	44.4

4.4 Discussion

This study is the first to investigate the exercise preferences of Australian cancer survivors, and to report the preferences of cancer survivors with depression or elevated depressive symptoms separately to non-depressed survivors. In the sample of 808 cancer survivors, it was established that 19.6% had elevated levels of depression, or were currently being treated for depression. This is far greater than the point prevalence rate for depression for the general population, reported to be between 2% and 9% (Andersen, Thielen, Bech, Nygaard, & Diderichsen, 2011; NICE, 2007), but in line with point prevalence reported in other cancer research (Philip et al., 2013). Physical characteristics or time since diagnosis were not able to discriminate depressed from non-depressed survivors. However, depressed cancer survivors tended to be younger, on average, and were more likely not to be in a committed relationship.

When examining the current level of physical activity of the cancer survivors, it was noted that only 29% of depressed survivors performed exercise sufficient to meet the aerobic component of current exercise guidelines (Garber et al., 2011). These findings are in agreement with others that depressed cancer survivors are not performing sufficient physical activity required for health benefits. Approximately 40% of the non-depressed group were exceeding physical activity thresholds and therefore, the Australian sample is generally consistent with previous findings that only 30-50% of cancer survivors meet physical activity guidelines (Blanchard, Courneya, & Stein, 2008). There were very few cases of complete inactivity with over 82% and 90% of depressed and non-depressed survivors, respectively, reporting performing at least one minute or more of exercise per week. Peeters and colleagues (2009) previously reported that almost 40% of the 66 breast, prostate, and colorectal cancer survivors that they examined were performing no physical activity. However, this difference may be due to the time since diagnosis as these lower levels of activity were reported in patients less than six months post-treatment (Peeters et al., 2009). The finding that the depressed group was less physically active than the non-depressed group may confirm that, in cancer survivors, similar to the general population, exercise has a protective effect against depression (Mossner et al., 2007). However, this must be interpreted with caution due to the cross-sectional nature of this study.

The results above found that 85% of depressed survivors believed that they would be able to exercise and 76% were interested in an exercise program. This outcome is similar to others that have examined various cancer groups (Belanger et al., 2012; Karvinen et al., 2006; Karvinen

et al., 2007; Vallance et al., 2013). Whereas there was no difference in perceptions of ability to exercise, more depressed survivors were interested in commencing exercise, and preferred a supervised program delivered either in the home setting or in a fitness centre. This finding is contrary to suggestions that home-based exercise may be more desirable for depressed individuals because the activities can be performed without the involvement of others (Brunet et al., 2014). The desire for supervised exercise, and impartiality to exercising with others, are important outcomes from this study that should be used to inform future exercise prescription for cancer survivors with depression.

Importantly, these results were attained using a large and diverse sample which increases the generalizability of the findings, compared to the only previous study that examined the exercise preferences and accounted for depression in a small sample ($n = 90$) of head and neck cancer survivors (Rogers, Malone, et al., 2009). The results also show some similarity with newer findings for people with depression (Carpiniello et al., 2013) and elevated distress (Khan, Brown, & Burton, 2013), which may suggest that people living with mental illness lack confidence to manage their own exercise and feel a need for additional support relating to exercise advice, monitoring and increased motivation (Khan et al., 2013).

When examining the preferred exercise activities, only cycling showed a significant difference between the groups, with fewer depressed survivors engaging in this activity (23% vs 15%, $p = .34$). However, both the inflation of type 1 error rate associated with the multiple analyses and the relatively low percentage of interest in cycling suggest that this result may not be practically relevant despite its statistical significance. Indeed, the depressed and non-depressed groups both ranked walking (~60%) as their most preferred exercise activity followed by strength training (35%). Therefore these two modalities of exercise, which are also most commonly used when prescribing exercise programs (see Chapter 2), should be considered before any other activity, including cycling.

The interest in strength training may also be unique to Australian cancer survivors with only one previous study reporting a similar amount of interest (36%) (Blaney et al., 2011). Several others however, have reported as few as 3% to 10% expressing interest in resistance exercise (Belanger et al., 2012; Jones & Courneya, 2002; Rogers, Malone, et al., 2009; Rogers, Markwell, Courneya, McAuley, & Verhulst, 2009). This finding has considerable importance as previous research in older adults with depression has demonstrated resistance training to be

particularly effective for alleviating depressive symptoms (Singh et al., 2005). Future research should consider whether these benefits are replicated for depressed cancer patients.

As mentioned previously (see Table 3.2) exercise preferences for cancer survivors appear to vary both within and between different cancer site subgroups. The findings reported above (Table 4.4) present the first data on exercise preferences for Australian cancer survivors, and in most cases are the first time outcomes for several cancer types (e.g., kidney, bladder, and colorectal cancer) have been replicated. It is apparent that supervised exercise seems more preferable in Australia with interest ranging from 43% for prostate cancer survivors up to 80% for brain cancer survivors. This contrasts with many previous reports that reported less than 25% of participants being interested in supervised exercise (Lin et al., 2013; Maddocks et al., 2011; Rogers, Malone, et al., 2009; Rogers, Markwell, Courneya, et al., 2009). Comparing directly between certain cancer types, far fewer kidney (27% vs 52%) and colorectal (24% vs 56%) cancer survivors showed a preference for the home-based setting than reported by others (McGowan et al., 2013; Trinh et al., 2012). Similarly, the results presented above for the 20 lung cancer survivors are much more aligned with previous findings reported with other Western lung cancer survivors (Philip et al., 2014) compared to exercise preferences from lung cancer survivors living in Taiwan (Lin et al., 2013). These findings, together with previous literature, should be used as a foundation upon which exercise delivery models can be built. However, this should not be done at the expense of ignoring the preference of each individual.

A possible limitation of these results is that approximately half of all the participants in this study had previously joined a research database managed by the NSW Cancer Council. Therefore, these individuals may be considered more proactive than other cancer survivors, and this may have influenced their exercise preferences. Similarly, the remaining participants were contacted through local cancer clinicians affiliated to a private hospital, which indicates increased socioeconomic status of the survivors, and could also have influenced the results reported above. However, the findings are exploratory in nature and mention has been made of the fact that individual preferences for exercise differ even within homogeneous sub-populations.

Lastly, it is important to consider that this study has focussed only on the exercise preferences of participants that were able to, and interested in, exercising. Further research should investigate more particularly the barriers to exercise and the reasons why more than 15% of

survivors report that they perceive that they are unable to exercise. Addressing these barriers and associated issues is likely to increase exercise uptake and lead to the design of programs that are more appropriately tailored to the needs of all cancer survivors.

In summary, it is suggested that depressed cancer survivors are interested in the opportunity to exercise and indicates that they would be capable of being involved in an exercise program. However, there are some key differences in exercise preferences between depressed and non-depressed cancer survivors. Depressed survivors are likely to prefer exercise sessions that are supervised and take place at home or in a fitness centre, and similar to non-depressed survivors, tend to be most interested in walking and strength training. These findings suggest that depressive status should be assessed before prescribing an exercise program for cancer survivors and that future research should examine whether exercise programs based on these cancer subgroups or individual preferences are able to increase adherence without compromising the effectiveness of exercise to reduce depression and improve physical outcomes.

CHAPTER FIVE

Depression and Physical Activity of Urban and Regional Cancer Survivors in Australia

5.1 Introduction

As discussed in previous chapters, the diagnosis of cancer is a life changing event and often results in feelings of distress and depression (Zabora, BrintzenhofeSzoc, Curbow, Hooker, & Piantadosi, 2001). It has been reported that up to 50% of all cancer patients suffer with depression (Holland & Alici, 2010) which itself has many negative effects and may result in reduced treatment success due to lower adherence rates (Jehn et al., 2006; Pasquini & Biondi, 2007). Psychosocial support is therefore becoming increasingly important and more common for cancer survivors (Vodermaier, Linden, & Siu, 2009).

However, access to support services is not equally distributed and cancer survivors that live in rural or remote regions often have inadequate access to health care services (Rogers, Malone, et al., 2009) and typically have higher rates of morbidity and mortality (Rogers, Markwell, Courneya, et al., 2009). A large population study ($n > 10,000$) found that more than 60% of Australians who reported affective disorders had utilised health care services within the preceding year (Parslow & Jorm, 2000). However, location of residence was found to relate negatively with the use of services for specialised mental health professionals, such that those people living in remote communities reported less support from psychiatrists and psychologists, but not from GP's (Parslow & Jorm, 2000). This finding is consistent with the knowledge that fewer than 10% of Australian psychiatrists have their offices located outside a metropolitan area and this trend is similar for psychologists (Judd & Humphreys, 2001). Since it has already been reported that there are no differences in the rate of depression between urban and regional residents (Judd et al., 2002), more research is needed into understanding and caring for non-metropolitan residents in the areas of cancer care and mental health (Bettencourt, Talley, Molix, Schlegel, & Westgate, 2008).

Due to reduced number of services providing psychological support in regional locations, one possible option for cancer survivors suffering from depression may be to recommend exercise to alleviate the condition. Exercise has been suggested as an effective means of treating depression (Brosse et al., 2002; Rimer et al., 2012) and, furthermore, it is recommended that cancer survivors commence or continue to exercise after diagnosis (Schmitz et al., 2010). Yet, in order for exercise to be effective it is important that people are able to perform their preferred activity since this will increase their motivation and adherence. For example, Callaghan and colleagues (2011) reported that when women were allowed to exercise at their preferred intensity they had greater improvements in quality of life and other psychological outcomes

compared to a group that were prescribed higher intensity, non-preferred exercise. Further, it has been suggested that individual attitudes towards exercise are much more important than the physical or social environment in which a person resides (Giles-Corti & Donovan, 2002).

Previous research that examined the differences between urban and rural breast cancer survivors living within Australia reported no differences for anxiety or depression based on location (Girgis, Boyes, Sanson-Fisher, & Burrows, 2000). However, a significant difference between groups was found for the amount of assistance required to perform physical and daily activities with rural survivors having increased needs (Girgis et al., 2000). Similarly, a study that assessed the exercise preferences of head and neck cancer survivors found that there were no differences in preferences depending on either location or depression status (Rogers, Malone, et al., 2009). However, the authors stated that they drew their sample from only small cities and rural locations and did not include any larger areas. Therefore, there is a need for additional research into incidence of depression and exercise participation in cancer survivors comparing differences between metropolitan and regional/rural areas. Furthermore, the study above is the only paper that has reported exercise preferences of cancer survivors and associations with depression and location, but it was limited to only head and neck cancer and a relatively small sample size ($n=90$) (Rogers, Malone, et al., 2009). These results may not be generalizable and, therefore, further research with other cancer types is needed. Furthermore, within Australia many different areas such as farmland, holiday precincts, and mining ‘cities’ are all classified as regional or rural locations (Francis, 2012) and may not be addressed by the work of Rogers and colleagues (2009) who examined exercise preferences of rural breast cancer survivors within the United States. However, no research to date has examined the perceived benefits of exercise in cancer survivors and compared whether there are differences between metropolitan and regional survivors. This information would supplement specific preferences when prescribing effective exercise programs.

This cross-sectional study, a secondary analysis of a subset of the data contained in Chapter 4, will first assess whether there is a difference in the incidence of depression for cancer survivors that live in metropolitan versus those that live in rural localities. Second, this research examines the current level of physical activity and perceived benefits and limitations to exercise between cancer survivors that live within these two different localities.

5.2 Methods

5.2.1 Overview and participants

Questionnaires were distributed to 490 cancer survivors, 18 years or older, who had previously registered with the Cancer Council of New South Wales expressing interest to be involved in research studies. Questionnaires were sent by mail and collected data on demographic information, cancer history, physical activity participation, and level of depression. Participants were allowed five weeks after the initial mail out to respond, after which a second questionnaire pack was sent to the participant (Stevinson et al., 2009). If no response was obtained in the following five weeks, it was determined that the participant had declined to be involved. The research was approved by the Human Research Ethics Committee of the university (Ref No. 7909 LEVIN) and the letter to participants clearly stated that participation was voluntary. To ensure confidentiality, all postal responses were only re-identifiable, with no names required, and therefore returned questionnaires equated to written consent. Regional classification was obtained using postcode analysis according to the criteria set by the Australian Bureau of Statistics, Remoteness Structure (Australian Bureau of Statistics, 2011). Respondents were found to come from only three of the six classification zones. These were 1) Major cities of Australia, 2) Inner regional Australia, and 3) Outer regional Australia. The two regional zones were combined to reflect only two subgroups; metropolitan residents and regional residents.

5.2.2 Measures

Demographic information collected included age, gender, height, weight, highest level of education achieved, employment status, and nationality. Medical information relating to the cancer diagnosis included cancer type and time since diagnosis. Address, including postcode, used for analysis was obtained from the participant list provided by the Cancer Council NSW “Join a Research Study” team.

Depression was assessed using three separate methods with the aim of improving accuracy without performing a detailed psychological interview. First, two specific questions were “Have you previously been diagnosed with depression by a medical professional?” and “Are you currently being treated for depression?” These questions were able to provide accurate information on past diagnosis and current treatment. Two subjective scales were also included for assessment. The first of these was the Hospital Anxiety and Depression Scale (HADS) which is well validated (Bjelland et al., 2002) and has previously been used as a screening tool

in cancer patients (Sellick & Edwardson, 2007). The score for the depression subscale of the HADS can range from 0 – 21 and depression was considered likely if the participant scored at least 10 or above (Sellick & Edwardson, 2007). The second self-rated questionnaire of depression was based on the current Diagnostic and Statistical Manual (DSM-IV-TR) criteria for major depressive episode. Consistent with the DSM, depression was considered if participants endorsed the first two questions which assessed the mandatory symptoms, as well as experiencing at least four of the remaining seven symptoms regularly over the past two weeks (*Diagnostic and Statistical Manual of Mental Disorders (4th Edition)*, 2000). For the purpose of analysis, participants were considered depressed if they met any of the three criteria above (i.e., they had received a formal diagnosis and/or were receiving treatment for depression, or they satisfied minimum cut-offs of the self-rated subjective scales).

A modified version of the Godin Leisure Time Exercise Questionnaire (GLTEQ) was used to determine physical activity levels (Godin & Shephard, 1985). The GLTEQ asks participants to record in the past week how often they performed exercise and to categorize the intensity of each session as either mild, moderate or strenuous. Two modifications were made to the original questionnaire in order to more accurately quantify exercise activity. First, the minimum time requirement was lowered from 15 to 10 minutes, which is more in line with current exercise guidelines suggested by the American College of Sports Medicine (Garber et al., 2011). Second, the average duration of each session was reported. These changes allowed for the determination of whether an individual was meeting international physical activity guidelines for cancer survivors (Schmitz et al., 2010). Furthermore, two open-ended questions asked participants to “list any benefits you believe you would get from being involved in an exercise program” and to “list any reasons you feel may exclude you from being involved in an exercise program”. These questions have been used previously when examining exercise preferences of cancer survivors (Karvinen et al., 2006; Karvinen et al., 2007; Stevinson et al., 2009).

5.2.3 Data analysis

The focus of analyses was to compare results between the two groups based on location. Demographic variables as well as depression scores and physical activity were assessed using one-way analysis of variance. Descriptive statistics, such as frequencies and percentages, were calculated for categorical variables and chi-squared tests were used to assess significance. All

statistical analyses were performed using PASW v18 for Windows (SPSS Inc., Chicago IL, USA) with an alpha value set at $p \leq .05$ as the criterion for statistical significance. Similar to Chapter 4, statistical analysis produced an increased likelihood of the family-wise Type I error rate, which was addressed above (see 4.2.3).

5.3 Results

5.3.1 Participant recruitment and demographics

A total of 490 questionnaires were sent to the last known address of the cancer survivors registered on the NSW Cancer Council database. Approximately 15% of the surveys were unaccounted for at the conclusion of the research trial. Of the remaining 415 responses, 12% were unable to be used for analysis. Therefore, 366 usable responses were returned and collated for analysis (Figure 5.1).

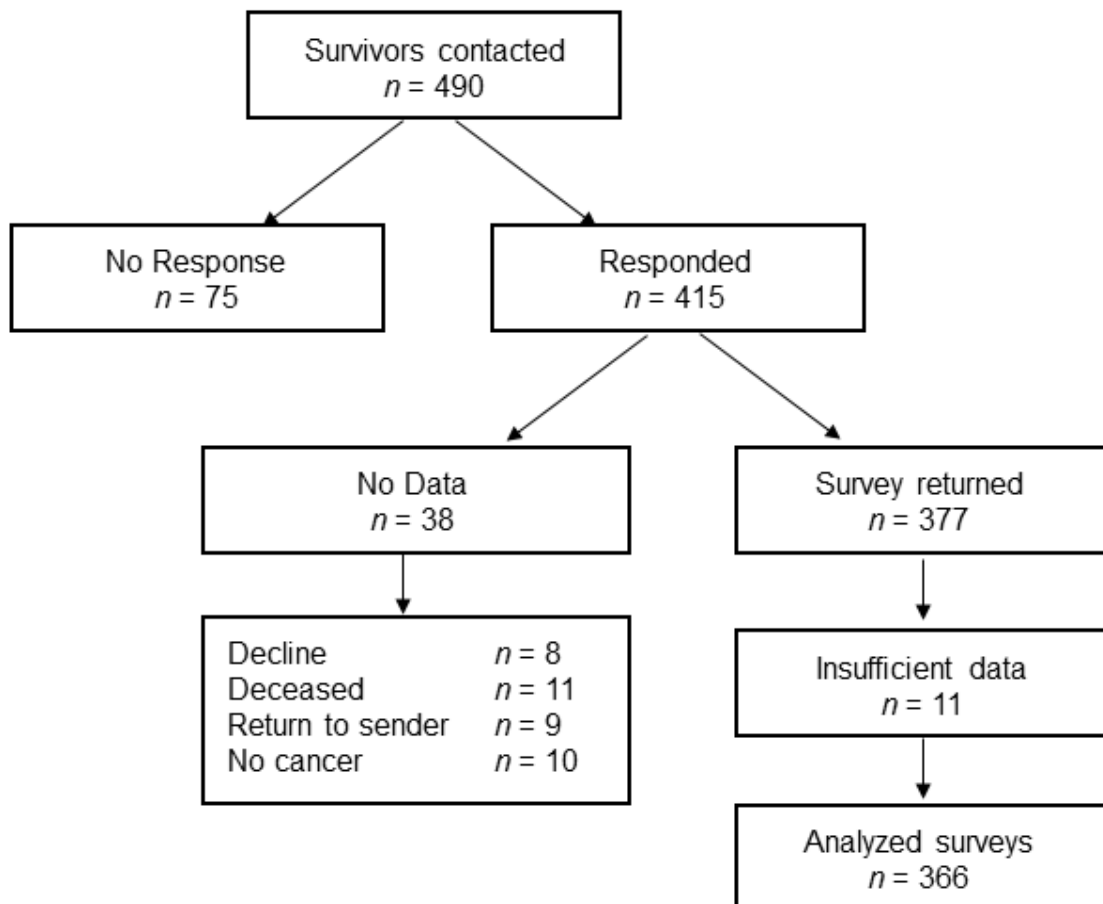


Figure 5.1. Flow diagram of recruitment and responses.

Comparisons based on location are presented in Table 5.1. The only significant difference between the groups was found for education level with the metropolitan group having more degree-qualified participants compared to the regional (39.0% vs. 23.1%). The five most prevalent cancer diagnoses are listed in Table 5.1. However, taking into account people with multiple diagnoses, there were 396 confirmed diagnoses across 34 different cancer types.

Table 5.1
Characteristics, time since diagnosis, and levels of depression of depressed and non-depressed cancer survivors

	Metropolitan (n = 236)	Regional (n = 130)	p
Age (yr)	63.3 (12.9)	64.2 (11.6)	.516
Height (cm)	167.0 (9.4)	166.7 (8.4)	.788
Weight (kg)	75.4 (16.8)	74.7 (16.2)	.696
Body mass index	27.0 (5.7)	26.8 (5.1)	.712
Time since diagnosis (months)	70.1 (80.6)	78.3 (77.8)	.347
HADS total	9.2 (6.6)	9.7 (7.9)	.565
HADS-D	3.7 (3.4)	3.9 (4.0)	.715
HADS-A	5.5 (4.1)	5.8 (4.5)	.514
SRDS	1.8 (2.2)	1.8 (2.4)	.993
Sex	n (%)	n (%)	.927
Male	81 (34.3)	44 (33.8)	
Female	155 (65.7)	86 (66.2)	
Level of education			.034
Primary	5 (2.1)	4 (3.1)	
Secondary	61 (25.8)	40 (30.8)	
Trade	17 (7.2)	11 (8.5)	
Certificate/Diploma	61 (25.8)	43 (33.1)	
Bachelor degree	58 (24.6)	22 (16.9)	
Higher degree	34 (14.4)	8 (6.2)	
Marital status			.830
Partner	148 (62.7)	83 (63.8)	
No partner	88 (37.3)	47 (36.2)	
Employment status			.124
Employed	94 (40.0)	39 (30.0)	
Unemployed	141 (60.0)	91 (70.0)	
Diagnosed depression*			.812
Yes	60 (25.4)	32 (24.6)	
No	157 (66.5)	89 (68.5)	
Cancer type			.280
Breast	82 (31.9)	44 (31.9)	
Prostate	33 (12.8)	25 (18.1)	
Colorectal	23 (8.9)	18 (13.0)	
Skin	17 (6.6)	7 (5.1)	
Melanoma	15 (5.8)	10 (7.2)	
Other	87 (33.9)	34 (24.6)	

HADS, Hospital Anxiety and Depression Scale; HADS-A, Anxiety subscale score; HADS-D, Depression subscale score; SRDS, elf-rating depression scale; NS, Not significant ($p > .05$)

* 19 missing responses for metropolitan

While a slightly higher percentage of respondents from the regional areas met criteria for depression compared to metropolitan survivors (23.1% vs. 20.8%), no significant difference was found for the incidence of depression according to location ($p = .607$; Figure 5.2).

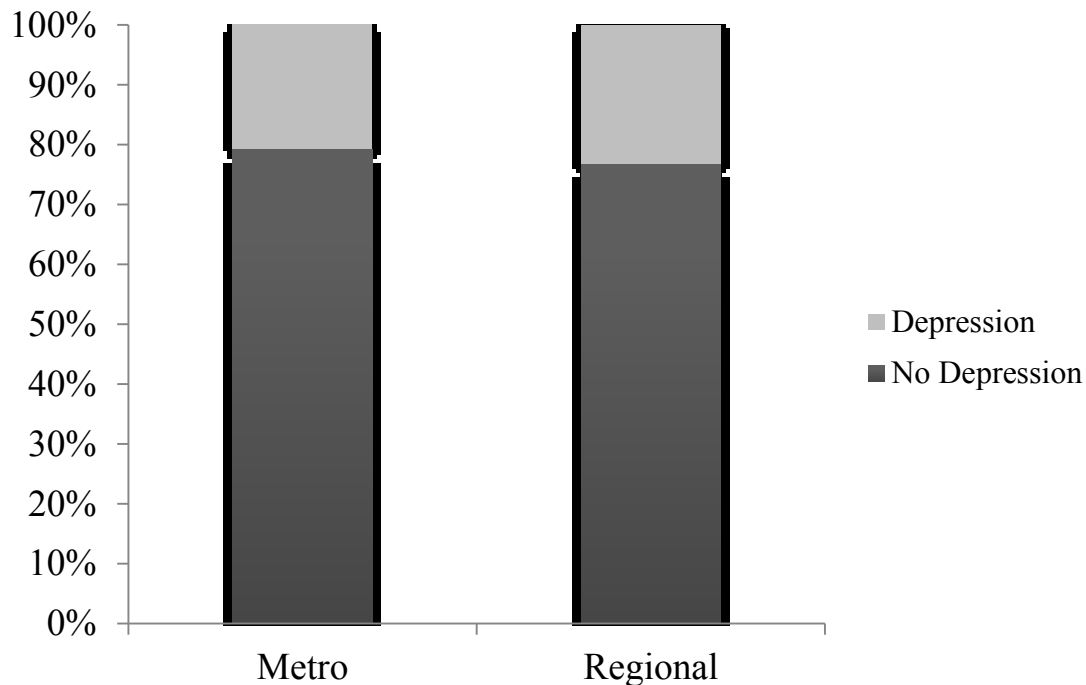


Figure 5.2. Incidence of depression relative to location of residence.

Approximately 60% of the participants were not meeting the minimum standards for physical activity of at least 150 minutes of moderate exercise per week (Garber et al., 2011). The physical activity habits were analyzed using three different cut-offs and in all cases there were no differences found between locations (Table 5.2).

Table 5.2
Physical activity differences between metropolitan and regional cancer survivors

	Metropolitan <i>n</i> (%)	Regional <i>n</i> (%)	<i>p</i>
Moderate PA > 150 min/week	84 (35.6)	54 (41.5)	.261
All PA > 150 min/week	153 (64.8)	87 (67.4)	.615
Performing some physical activity			.880
0 minutes reported	26 (11.0)	15 (11.5)	
1 minute or more reported	210 (89.0)	115 (88.5)	

5.3.2 Benefits and limitations

The metropolitan and regional participants reported similar benefits and limitations to exercise (Table 5.3). In total there were 769 benefits and 346 exclusions listed by all participants. No differences between groups were found for limitations to exercise, with pre-existing medical conditions ($n = 80$) listed as the most common reason. A majority of the benefits reported as attainable from exercise were similar between groups. The most common benefit for both groups was increasing cardiovascular fitness ($n = 108$). Significant between group differences favouring the metropolitan group were noted for the potential of an exercise program to increase strength and also to enhance muscular functioning such as improved balance and range of motion ($p = .041$).

Table 5.3
Perceived benefits and limitations to starting a new exercise program (N = 366)

	Metropolitan n (%)	Regional n (%)	p
Benefits of exercise			
Improve cardiovascular fitness	72 (30.5)	36 (27.7)	.572
Improve health	56 (23.7)	31 (23.8)	.980
Weight control / weight loss	58 (24.6)	27 (20.8)	.409
Improve mental health and mood	51 (21.6)	28 (21.5)	.987
Increase strength	47 (19.9)	15 (11.5)	.041
Improve balance and movement	47 (19.9)	15 (11.5)	.041
Social Interaction	39 (16.5)	20 (15.4)	.776
Feeling of wellbeing	27 (11.4)	20 (15.4)	.280
Other	19 (8.1)	17 (13.1)	.122
Increase exercise adherence	23 (9.7)	12 (9.2)	.873
Feeling more energetic	23 (9.7)	11 (8.5)	.685
Higher self-esteem	18 (7.6)	11 (8.5)	.777
Distraction from cancer / treatment	12 (5.1)	9 (6.9)	.469
Sleep quality improve	10 (4.2)	1 (0.8)	.063
Limitations from exercise			
Pre-existing medical illness	53 (22.5)	27 (20.8)	.708
Lack of time	47 (19.9)	17 (13.1)	.099
Lack of desire	25 (10.6)	10 (7.7)	.366
Excess Fatigue	17 (7.2)	10 (7.7)	.864
Active enough	17 (7.2)	9 (6.9)	.920
Other	14 (5.7)	10 (7.7)	.515
Logistics of travel / location	10 (4.2)	12 (9.2)	.054
Cost	12 (5.1)	10 (7.7)	.315
Unable to keep up / age	18 (7.6)	4 (3.1)	.080
Cancer related side-effects	9 (3.8)	10 (7.7)	.109

5.4 Discussion

The aims of this study were to determine whether a difference in incidence of depression existed between metropolitan and regional cancer survivors and to explore the physical activity habits and beliefs of these two groups. These novel findings are important as they may be useful in understanding how to prescribe best practice care for cancer patients based on location, taking into account mental distress and depression. Since exercise has been reported to be useful in the management of depression (Rimer et al., 2012), it is possible that this may be a viable first line treatment strategy especially in regional settings where access to medical and psychological support services is often limited (Judd & Humphreys, 2001).

No difference was found in the rate of depression between metropolitan and regional cancer survivors with a point prevalence rate of 21% for all participants. This finding is consistent with the results of a review by Judd and colleagues (Judd et al., 2002), which reported that rates of depression in rural and urban residents were not significantly different. However, the review only referred to three well-constructed studies and there continues to be a dearth of literature examining the differences in mental health between urban and regional or rural residents (Caldwell, Jorm, & Dear, 2004). Furthermore, very few studies have assessed depression in cancer survivors living in regional areas. A study by Rogers et al. (Rogers, Malone, et al., 2009) found that 44% ($n = 90$) of head and neck cancer survivors met criteria for depression according to the Centre for Epidemiological Studies Depression Scale. Despite the focus being on rural cancer survivors, the authors did not report the proportion of depressed participants relative to location even though only 27% were considered to be living in 'more rural' areas (Rogers, Malone, et al., 2009). The cross-sectional results obtained in this study are the first to our knowledge to report that incidence of depression between metropolitan and regional cancer survivors does not differ. This is of particular interest, especially since there were almost no differences between the two groups, even when examining cancer type.

This finding should perhaps not come as a surprise since Judd and colleagues concluded that location of residence was less predictive of depression than other more personal attributes such as age, socioeconomic status, marital status, and social support (Judd et al., 2002). Nonetheless, regional residents that do suffer with depression have less access to support services (Judd & Humphreys, 2001) and, therefore, non-traditional sources of treatment such as exercise may be an effective first line treatment option. Furthermore, the majority of mental health treatment is provided by general practitioners (Judd & Humphreys, 2001; Parslow & Jorm, 2000) and,

therefore, a GP-recommended exercise program may be an effective strategy to target depression before more specialised treatment or individualised exercise programs are prescribed.

There were also no differences found between the groups when examining current physical activity habits. Only 40% of participants were meeting physical activity minimum criteria according to the guidelines of the American College of Sports Medicine (Garber et al., 2011). This finding is in accordance with previous population data collected by the US Department of Health and Human Services (King et al., 2000) and the Australian Institute of Health and Welfare (Armstrong, Bauman, & Davies, 2000), both of which reported approximately 60% of the population were insufficiently active. In order to effectively promote physical activity and exercise participation, targeted prescription that increases adherence is necessary. It is suggested that there is little difference in anticipated benefits of exercise relative to location, but that metropolitan residents were more likely to refer to increases in strength, range of motion and improved balance as possible outcomes of an exercise program. It is likely, therefore, that these benefits are either more valued by city dwelling residents or perhaps just that urban residents are more aware of the benefits of resistance training. The current finding suggests that first line exercise prescription for regional residents could be based around purely aerobic activity targeting cardiovascular fitness. In addition, however, health promotion and education for rural cancer survivors should be included in any program with the aim of increasing awareness of the benefits of resistance training for cancer, depression, and related treatment side-effects.

A possible limitation of this research is that the definitions used to determine locality were drawn directly from the Australian Bureau of Statistics Remoteness Structure and are very broad. For example, regional or rural areas can be very diverse and include farmland, tourist destinations, or mining precincts (Francis, 2012). Judd and colleagues (2002) have recommended that a broader understanding of the environment, including social, cultural, and economic conditions, are required when examining determinants of depression, as opposed to broad categorical terms used in this study. In fact, the current sample displayed differences for the highest level of education attained ($p = .034$; Table 5.1), which is often used to infer socio-economic status (SES) (King et al., 2000). SES itself has been shown to be positively related to physical activity (Parks, Housemann, & Brownson, 2003) and a lower SES increases mortality and morbidity (Adler & Ostrove, 1999). Therefore, it is possible that regional cancer

survivors, who are economically disadvantaged, especially those with depression will have poorer long-term prognosis. This, however, was not the focus of the current research, but future research should address longitudinal health outcomes and the effect of exercise in improving health-related outcomes for this population.

In summary, this is the first study that has assessed differences in depression, current levels of physical activity and perceived benefits and limitations to exercise in a cohort of cancer survivors living in both metropolitan and regional Australia. The results indicate that there is little difference in cancer diagnosis, incidence of depression, and current levels of physical activity between metropolitan and regional survivors. With growing evidence suggesting that exercise is beneficial for management and treatment of depression combined with the restricted access to psychological and other medical services in regional and rural locations it is recommended that regional cancer survivors suffering with depression could be prescribed exercise as a first line treatment before seeking elevated levels of assistance.

CHAPTER SIX

The Effect of Exercise on Depression, Quality of Life, and Physical Performance in Depressed Cancer Survivors

6.1 Introduction

The area of psycho-oncology is a rapidly emerging field as practitioners and researchers alike look to provide best practice care models for cancer survivors (Pirl, Jacobsen, & Deshields, 2013). However, psychological distress and depression remains an unsolved problem, with many survivors not receiving appropriate psychological care (Pirl et al., 2013). Cancer patients and survivors are more likely than the general population to become depressed (Satin et al., 2009), with rates of clinically disruptive depression reportedly three times higher than the non-cancer population (Li et al., 2012; Ramasubbu et al., 2012). Comorbid depression has been linked with increased mortality (Pinqart & Duberstein, 2010; Satin et al., 2009), decreased adherence to treatment (Jehn et al., 2006), and reduced quality of life (Hopwood et al., 2000). Persistent depression is also associated with an increased risk of cancer recurrence (Miller et al., 2008). Results from a meta-analysis conducted to examine the effect of depression on mortality in cancer survivors revealed a 25% increase in all-cause mortality for depressed cancer survivors, despite no relationship between depression and disease progression (Satin et al., 2009). This appears to indicate that the increased mortality rate is due to adverse health hazards stemming from depression, and not due to the cancer disease state. Given all of this, the treatment and management of depression in cancer survivors is an important area that requires further attention.

Traditionally, depression has been treated using pharmacotherapy, however the prescription of additional medications in cancer patients and survivors can exacerbate adverse treatment effects and, in certain cases, is known to negatively interact with curative chemotherapy treatments (Craft et al., 2012; Palesh et al., 2013). Evidence has begun to emerge that exercise may be an effective alternative means to treat or manage depression (Mead et al., 2009). An early, randomised controlled trial (RCT) examined the effect of aerobic exercise on major depressive disorder and compared the outcomes to the prescription of antidepressant medication in 156 older adults (Blumenthal et al., 1999). It was found that exercise produced clinically significant reductions of equal magnitude to pharmacotherapy (Blumenthal et al., 1999). A more recent RCT, from the same research group, also found that individuals diagnosed with major depressive disorder, by clinical interview according to the criteria from the Diagnostic and Statistical Manual (IV), were able to decrease depression to a similar extent by performing either home-based exercise or supervised aerobic exercise for 16 weeks (Blumenthal et al., 2007). Despite these positive outcomes, limited research has examined whether exercise reduces depression in cancer patients with co-morbid depression. Based on

the evidence that suggests physical exercise can decrease depression in clinically depressed patients (Rimer et al., 2012; Singh, Clements, & Fiatarone, 1997a; Singh et al., 2005), it is feasible that similar effects could be found with depressed cancer survivors.

The most seminal guidelines for exercise and cancer produced by the American College of Sports Medicine (ACSM) were based on the results of 85 research trials (Schmitz et al., 2010). Only eight trials reported outcomes for depression, however, the level of depression at baseline was very low and fell within an expected range for normal function. Therefore, results to date should be cautiously considered when inferring how exercise may manage depression in depressed cancer survivors. Regardless, it has been reported that exercise is well-tolerated in both male and female cancer survivors and also may be effective at managing moderate and severe depression in this population (Craft et al., 2012). However, in making these claims, the authors acknowledged that no research was available that had examined the role of exercise in reducing depression in cancer survivors with clinically-diagnosed or elevated subsyndromal depression (Craft et al., 2012).

An added benefit of exercise for the treatment of depression is that enhancements in quality of life beyond improvement in affective state can be obtained. Secondary outcome measures, such as physical functioning or health-related quality of life have been used to demonstrate this effect (Rapaport, Clary, Fayyad, & Endicott, 2005). Since it is known that quality of life is diminished in people living with depression (Rodin et al., 2007), this subjective outcome provides an important indication of improvement obtained from the exercise program (Rapaport et al., 2005).

Other outcomes closely related to depression that can be used to indicate improved daily physical and psychological functioning include sleep quality (Tang, Liou, & Lin, 2010) and generalised and cancer specific self-efficacy (Beckham, Burker, Lytle, Feldman, & Costakis, 1997; Manne et al., 2006). Poor sleep quality is a common problem experienced by many cancer survivors and is exacerbated by depression, which is known to disrupt sleep by itself (Palesh et al., 2013). Previous findings have demonstrated that aerobic exercise can improve sleep quality for cancer survivors (Payne et al., 2008; Tang et al., 2010). Since the relationship between depression and sleep disturbance is bi-directional (Palesh et al., 2013), any improvement in either sleep quality or a reduction in depression is likely to have a positive effect on the other.

Self-efficacy is related to the ability to cope and adjust to different situations and stressors (Manne et al., 2006). It has been demonstrated that cancer survivors with higher levels of self-efficacy have increased quality of life and lower levels of psychological distress (Kreitler, Peleg, & Ehrenfeld, 2007). Therefore, there appears to be an inverse relationship between depression and self-efficacy. Philip et al. (2013), explored the relationship between coping self-efficacy, measured using the Cancer Behaviour Inventory, and depression, using the CES-D, in a sample of cancer survivors. They found coping self-efficacy related strongly to depression, accounting for almost 50% of the variance (Philip et al., 2013).

While exercise appears clinically beneficial, important questions regarding the mechanisms by which exercise reduces depression remain unanswered, along with the type of training or intensity necessary for this purpose (Lawlor & Hopker, 2001; Mead et al., 2009). Previous literature has suggested that decrements in depression can be attained from exercise even when the exercise program fails to elicit an increase in measured strength or aerobic fitness (Blumenthal et al., 2007; Callaghan et al., 2011; Courneya et al., 2009). However, others have suggested that increased exercise intensity, which results in physical or functional adaptations, is required before clinically meaningful changes in depression can occur (Singh et al., 2005). It is possible that when no physiological response is apparent, benefits may stem via psychological mechanisms such as enhanced self-efficacy, increased feelings of mastery, or distraction associated with the initiation of exercise.

Since no research to date has examined exercise interventions on depression outcomes with depressed cancer patients, the aim of this study was to examine the effect of two commonly prescribed/utilised exercise training protocols on depression and the associated physical, psychological and functional outcomes. Furthermore, in order to elucidate the impact of the two different exercise alternatives (supervised training or self-directed home-based exercise), these were compared to a usual care control group and to one another. This study used a pragmatic design and therefore the two programs were not matched for the exercise selection or intensity.

6.2 Method

6.2.1 Study design and protocol

A repeated measures study, was conducted between November 2012 and September 2013, to examine the effect of exercise on depression in cancer survivors. Prior to the commencement of the intervention, potential participants were screened (Western Australian cohort from Chapter Four, see section 4.2.1), to ensure that only cancer survivors presenting with elevated depressive symptoms or established clinical depression were invited to participate.

Twelve medical professionals (oncologists and surgeons) affiliated with one of two private hospitals, in Perth, Western Australia, (St John of God, Subiaco and Joondalup Health Campus) supported the research and agreed to allow their patients to be contacted for initial screening. All patients ($n = 1309$) contacted were over 18 years of age and had made at least one visit to their referring specialist in the past 36 months. Mail packs were posted to the last known address of each patient and contained a letter from the referring specialist inviting them to participate in a research study that was examining the relationship between physical activity and depression in cancer survivors (Appendices D & E). The letter explained that, based on their response to the initial questionnaire, some participants may be eligible for involvement in an exercise program. The mail pack also contained a participant information letter, the Hospital Anxiety and Depression Scale (HADS), a self-rated depression scale (SRDS, Appendix C) based on the nine items used to diagnose depression according to the Diagnostic and Statistical Manual for Mental Disorders (DSM-IV-TR), and a modified Godin Leisure Time Questionnaire. Furthermore, two specific questions “have you previously been diagnosed with depression by a medical professional (GP, psychiatrist, clinical psychologist)” and “are you currently being treated for depression? (e.g., taking antidepressant medication or treatment from a clinical psychologist or psychiatrist)” were used to identify patients with established clinical depression.

These three measures were used together to confirm eligibility. The HADS has been used previously as a screening tool in studies recruiting cancer patients with depression (Strong et al., 2008), and it has been suggested that a score greater than 10 on the depression-specific subscale (HADS-D) is indicative of elevated depressive symptoms (Korstjens et al., 2010). Therefore, a score of 11 or greater was selected as the cut-off for eligibility in this study. The SRDS was assumed to have construct validity, since it was based on the DSM criteria, however

empirical testing of the validity and reliability of this scale has not been conducted. For participants to be eligible according to SRDS responses, they were required to meet similar criteria to that of a clinical diagnosis responding 'yes' to at least four depressive symptoms, along with meeting one of the primary criteria of major depressive disorder: anhedonia or continual feeling of depressed state. Lastly, the depression-specific questions were able to easily and accurately determine respondents that had a current clinical diagnosis according to evidence-based treatment guidelines (Wang, Berglund, & Kessler, 2000) and individuals who responded in the affirmative to currently being treated for depression were considered eligible even if they scored below the thresholds on the other two scales. Research has indicated that the negative effects of depression are evident even for subsyndromal depression (Rodin et al., 2007). Therefore, these three criteria for eligibility were considered stringent enough to produce a treatment effect. Furthermore, by including those survivors with elevated depression or clinically-diagnosed and current depression the outcomes would be applicable to best practice management for depressed cancer patients, regardless of antidepressant treatment status. It is acknowledged however, that this pragmatic approach does restrict the homogeneity of the sample and may limit the generalizability of results across these independent groups.

All eligible participants were contacted by telephone or email (based on contact details provided by the participant; if both were included contact was initiated by phone) and informed that they had been identified as having current depression or elevated depressive symptoms and invited into the exercise intervention study. Those participants that expressed interest and met eligibility criteria of being able to speak and understand written English as well as being able to walk 400m unassisted. were mailed a second information and recruitment pack containing an introductory letter, detailed information sheet, informed consent sheet, medical consent form (all included in Appendix F), and health history questionnaire (Appendix H). Prior to enrolment and baseline testing, participants were required to obtain consent from their GP confirming that they had no musculoskeletal, cardiovascular, or neurological limitations that would exclude them from involvement in an exercise program. Participants that entered the study were randomly allocated into one of two different exercise groups, stratified for current depressive treatment and baseline levels of physical activity. One group performed home-based aerobic exercise whereas the second group were allocated into a supervised aerobic and resistance exercise program performed twice weekly in a local exercise clinic. A third group of eligible participants that had declined participation in the exercise intervention,

were invited to participate as the usual care control cases (appendix G) and were required to complete only the written outcome assessments.

6.2.2 Participants

A response rate of 38% (492/1309) was achieved from the initial mail out, with 89% ($n = 439$) of responses providing enough information to enable the participants to be considered for eligibility based on depression or depressive symptoms. A total of 78 participants met the eligibility criteria ($n = 17$ for HADS; $n = 52$ for current depression; $n = 47$ for SRDS). Forty-eight participants met eligibility based on only one of the criteria ($n = 2$ for HADS; $n = 29$ for current depression; $n = 19$ for SRDS), whereas 18 met two of the three criteria ($n = 5$ for HADS and SRDS; $n = 13$ for SRDS and current depression), and 10 participants were eligible based on their results for all three eligibility criteria. Thirty-two of the eligible participants (41%) agreed to participate in the intervention study. It was intended that participants would be randomised to one of the three intervention groups (supervised exercise, home-based exercise, and usual care), however only 18 consented to randomization. These 18 participants were allocated into the two intervention groups, stratified for current treatment of depression ('yes' or 'no'), but not accounting for whether that treatment was pharmacological or psychological, and baseline levels of physical activity (150 minutes of exercise per week). A further 14 participants agreed to act as a usual care control group, only completing the questionnaire component of the study via post. The recruitment flow chart is depicted in Figure 6.1.

All 32 participants provided informed consent and were aware that participation was voluntary and that they could withdraw at any point without prejudice. The 18 participants that presented for testing provided written consent, whereas the 14 control participants were informed that returning questionnaires indicated written consent. The research study was approved by the Human Research Ethics Committee of Edith Cowan University (Ref No. 7909 LEVIN), the St John of God Health Care Ethics Committee (Ref No. 544) and the Human Research Ethics Committee of Joondalup Health campus (Ref No. 1313).

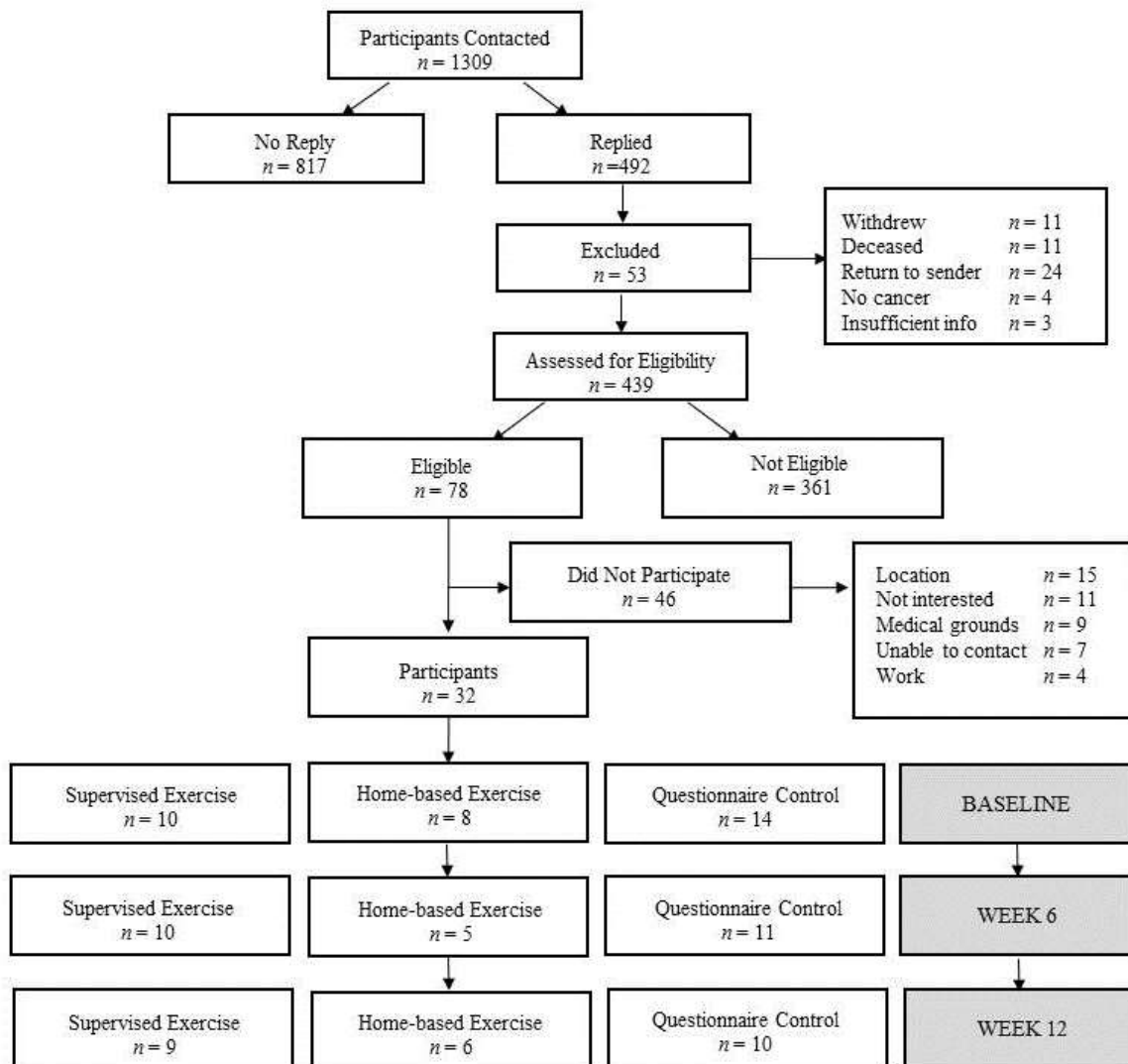


Figure 6.1. Flow diagram illustrating the recruitment and retention of participants.

Allocation into the exercise groups was randomised and stratified (as detailed above) according to the results from the screening questionnaires (depressed status and physical activity). Since there was a delay between screening and allocation due to the recruitment process, and participants needing to visit their GP to acquire medical consent, new baseline measures were recorded and used for analysis of the intervention. The screening results were therefore not used other than for the purposes of eligibility and stratification. Demographic details of all participants are displayed in Table 6.1.

Table 6.1*Demographic characteristics of the participant representing the intention-to-treat samples*

	Supervised (n = 10)	Home-based (n = 8)	Control (n = 14)	All (n = 32)	p
Age (y)	53.3 (10.4)	61.9 (8.6)	61.2 (7.9)	58.9 (9.4)	.072
Height (cm)	170.8 (9.8)	171.5 (5.8)	173.6 (11.0)	172.2 (9.4)	.772
Mass (kg)	83.3 (22.9)	90.4 (19.9)	82.6 (14.3)	84.8 (18.4)	.617
BMI	28.2 (5.4)	30.7 (6.1)	27.4 (3.9)	28.4 (5.0)	.269
Number of medicines	3.3 (1.9)	1.9 (1.7)	3.5 (2.7)	3.0 (2.3)	.337
Time since diagnosis (months)	47.3 (54.4)	25.0 (18.4)	27.2 (17.1)	32.9 (34.0)	.279
% Male	40.0%	62.5%	64.3 %	56.3%	
Current depression treatment	60.0%	50.0%	50.0%	53.1%	
Active cancer treatment	20.0%	25.0%	35.7%	28.1%	
Cancer site					
Breast	3	2	5	10	
Brain	2	–	1	3	
Bowel	–	1	1	2	
Bladder	2	1	1	4	
Prostate	1	4	6	11	
Kidney	2	–	–	2	

Over the course of the 12-week intervention nine participants were lost to follow-up and the demographic characteristics of three groups without these participants included are reported below (Table 6.2).

Table 6.2*Demographic characteristics of the participant representing the per-protocol samples*

	Supervised (n = 9)	Home-based (n = 5)	Control (n = 9)	All (n = 23)	p
Age (y)	52.7 (10.8)	63.6 (10.1)	61.3 (9.6)	58.4 (10.8)	.112
Height (cm)	170.7 (10.4)	170.2 (7.0)	174.0 (10.5)	171.9 (9.6)	.714
Mass (kg)	80.9 (22.9)	93.1 (22.5)	80.8 (14.3)	83.5 (19.6)	.480
BMI	27.3 (5.0)	32.0 (6.5)	26.5 (2.9)	28.0 (5.0)	.124
Number of medicines	3.1 (1.9)	1.6 (1.5)	3.8 (3.1)	3.0 (2.4)	.288
Time since diagnosis (months)	46.0 (57.5)	19.8 (11.7)	20.3 (9.0)	30.2 (37.7)	.291
% Male	33.3 %	60.0 %	66.7 %	52.2 %	
Current depression treatment	55.6 %	60.0%	55.6 %	56.5 %	
Active cancer treatment	22.2 %	20.0%	44.4 %	30.4 %	
Cancer site					
Breast	3	1	3	7	
Brain	2	–	–	2	
Bladder	1	1	1	3	
Prostate	1	3	5	9	
Kidney	2	–	–	2	

6.2.3 Exercise intervention

The two exercise programs, supervised exercise or home-based exercise, were performed for a 12-week period. Twelve weeks was selected, as it is representative of the length of many previous training studies in the area of exercise and depression (Blumenthal et al., 1999; Dunn, Trivedi, Kampert, Clark, & Chambliss, 2005; Mather et al., 2002). Moreover, training twice weekly for 12-weeks ensured that the supervised group completed 24 exercise sessions, which

replicates the number of sessions that were used by Singh and colleagues in their key paper on resistance training and depression (Singh et al., 2005).

The supervised exercise group performed two 60-minute exercise sessions per week consisting of both resistance and aerobic training. All sessions were conducted in a local fitness centre or an exercise clinic and were supervised by an accredited exercise physiologist (GTL, the student). Each session comprised approximately 20 minutes of aerobic exercise, 30 minutes of resistance training, and a five-minute warm-up and cool-down (see Appendix J for a copy of the 24 session exercise program). Resistance exercises targeted the upper and lower body including the following: chest press, leg press, lat pull, leg extension, seated row, leg curl, step-up, bicep curl, and triceps pushdown. Participants were encouraged to work within specific repetition maximum ranges to ensure an optimal training stimulus. The number of sets and repetitions were manipulated over the course of the intervention commencing with 2 sets of 12 repetitions and ending with 4 sets of 6 repetitions (Galvao et al., 2010). Aerobic exercise was performed on a variety of machines (stationary bike, treadmill, elliptical trainer) at a heart rate of between 65% and 90% of estimated heart rate maximum (calculated according to the formula – “220 beats per minute minus age of participant”). Exercise intensity was monitored and maintained by an accredited exercise physiologist using measures of perceived exertion and heart rate monitors. Participants in this group were also encouraged to complete additional aerobic exercise outside of the prescribed exercise sessions to ensure that they met national activity guidelines of 150 minutes of aerobic activity per week. Each participant was provided with a training log to assist them to record additional exercise. These were returned at the completion of the study.

Participants that were allocated to the home-based training group received an exercise information booklet (Appendix K) at the conclusion of their baseline testing session and were informed that they were required to complete at least 150 minutes of aerobic exercise per week in sessions of 10 minutes or more. Participants were also informed that, in order to assist them in adhering to the exercise, they would receive weekly telephone calls, during which time they could discuss their exercise activity and any related questions with the researcher (Segal et al., 2001). The exercise booklet provided to the participants contained only generic information about physical activity, health benefits of exercise, depression-specific effects of exercise, methods of measuring exercise intensity including the Borg CR-10 scale, and a log book section used to record all exercise sessions performed over the 12-week period. However, no

specific exercise prescription was provided either in the booklet or verbally during follow-up telephone calls.

6.2.4 Assessment of outcomes

Testing sessions were conducted before the commencement of the program (baseline), halfway through (Week 6) and after the completion of the intervention (Week 12). The assessments for the exercise groups were performed at least 24 hours after their previous training session and the final assessment was conducted no more than seven days after the last training session. This ensured sufficient recovery to minimize fatigue from the preceding exercise session, without compromising the exercise adaptations. The control group were contacted and requested to complete all questionnaires exactly six and twelve weeks from baseline.

The following measures were recorded at each testing session for all three groups.

6.2.4.1 Primary Outcome

Depression: The depression subscale (HADS-D) of the HADS (Zigmond & Snaith, 1983) was used to assess depression. The HADS-D does not include somatic measures of depression commonly experienced by cancer patients and, therefore, has been extensively used with cancer patients and survivors (Craft et al., 2012). Seven specific questions are used to measure depression; each having three alternate responses which are scored from 0 to 3, giving a total range of 0 to 21 for the entire assessment. It has been suggested that a score of greater than 10 represents elevated depressive symptoms (Korstjens et al., 2010). As depression was the primary outcome of this study, a clinical interview to assess clinical depression would have been the ideal measure. However, since this was not possible, the HADS-D was considered the best alternative and has been shown to be a valid, reliable, and sensitive test to examine depressive symptoms (Bjelland et al., 2002).

6.2.4.2 Secondary Outcomes

Anxiety: Anxiety was assessed according to the anxiety subscale (HADS-A) of the HADS (Zigmond & Snaith, 1983). Similar to the depression subscale, anxiety is measured using the total score calculated from a 7 item subscale, with a total possible score ranging from 0 to 21. A score of 11 or greater is considered to represent a level of anxiety exceeding normal functioning (Korstjens et al., 2010). Again, anxiety was measured using subjective assessments

and the questionnaire is indicative of a clinical diagnosis, but cannot substitute the diagnostic requirements.

Total psychological distress: The two subscales of the HADS when scored together assess total distress. A total HADS score of 16 or more has been suggested as an indicative marker of elevated distress (Sellick & Edwardson, 2007). Further it has been reported that a score of 16 or greater has a negative predictive value of 86% for any mental health disorder according to the Composite International Diagnostic Interview (CIDI) (Reuter & Härter, 2001). Although the HADS is a single 14 question scale, research continues to support the use of the subscales to assess either anxiety or depression (Annunziata, Muzzatti, & Altoe, 2011).

Quality of life: Quality of life was recorded using the Short Form-36 v2™ (SF-36) (Ware, Kosinski, & Dewey, 2002). The questionnaire has eight subscales that are averaged to produce two composite scores relating to physical health (PHC) and mental health (MHC). The questionnaire was administered manually before item scores were entered into custom software (Health Outcomes Scoring Software 4.5, QualityMetric Inc.) for calculation of the results. The scale has been standardised and composite scores are presented for comparison to the mean *T*-score of 50 and a standard deviation of 10 (Maruish & Turner-Bowker, 2009). This generic measure of quality of life was preferred to a cancer-specific measure, as previous trials comparing home-based and supervised exercise for cancer survivors have reported that the SF-36 was more sensitive than cancer-specific scales (Segal et al., 2001).

Satisfaction with life: The Satisfaction With Life Scale (SWLS) (Diener, Emmons, Larsen, & Griffin, 1985) is a brief questionnaire consisting of five questions that are answered using a Likert rating scale from 1 ‘strongly disagree’ to 7 ‘strongly agree’ to determine an individual’s subjective satisfaction with their life at a particular point in time. The maximum score is 35 with a minimum possible score of 5. Categorical scoring zones have been provided by the authors, with each 5-point block (e.g. 5-9, 21-25) representing an increased level of satisfaction with life (Diener et al., 1985). A score of ‘20’ is classified as neutral threshold value for this scale (Pavot & Diener, 1993).

Self-efficacy: The ability to manage living with cancer was measured using the Lewis Cancer Self-Efficacy Scale (CASES) (Kershaw et al., 2008; Northouse et al., 2007). This questionnaire comprises 17 items (e.g., “I am able to manage what is being asked of me despite the cancer”)

that are scored on an 11-point Likert scale ranging from '0 – not at all confident' to '10 – very confident'. In accordance with the authors' instructions, participants were asked to rate their level of confidence to manage or cope with cancer related problems for that particular day. Higher scores represent increased self-efficacy.

Physical exercise: Physical activity was determined using a modified version of the Godin Leisure Time Exercise Questionnaire (GLTEQ) (Godin & Shephard, 1985). Participants were asked to record how often over the past seven days they performed exercise, and to categorize the intensity in line with three pre-set levels: mild, moderate, or strenuous. Two minor changes to the original questionnaire were made. First, the minimum session duration was reduced from 15 to 10 minutes (Godin & Shephard, 1985). Ten-minute durations were chosen to be in accordance with current minimum session duration suggested by the American College of Sports Medicine (Garber et al., 2011). A second modification was that participants were also asked to record the average duration of each session. This additional information allows for the calculation of overall exercise duration as well as duration in each intensity bracket, which was used to determine whether participants were completing 150 minutes or more of moderate physical activity per week in accordance with international exercise guidelines (Garber et al., 2011).

Sleep quality: The Pittsburgh Sleep Quality Index (PSQI; Buysse, Reynolds, Monk, Berman, & Kupfer, 1989) is a self-rated scale which measures sleep outcomes over the previous one-month period. The questionnaire consists of nine sleep-specific questions, which, when scored, are converted to seven component measures by grouping the responses to certain questions. Each component is scored on a 4-point scale ranging from 0 to 3 and, therefore, the maximum score of 21 represents the greatest sleep disturbance while lower scores represent better sleep quality. A cut-off score of five or greater represents poor sleep quality (Singh et al., 1997b; Tang et al., 2010).

The following additional measurements were recorded for the exercise participants that presented for physical and physiological assessments (Appendix I).

Muscle strength: Maximal concentric muscle strength was assessed for the chest press and the leg press. Participants performed a graded warm-up consisting of one set of six repetitions at a light weight, followed by a second set of three lifts at a heavier weight. Thereafter, single lift

sets were performed commencing at the perceived one repetition maximum (1-RM), for baseline test, or at a weight approximately the same as the previous successful maximum effort for follow-up tests (Galvao et al., 2010). If participants were able to complete the lift correctly, additional resistance was added and the test repeated until the maximal lift was established. In accordance with previous suggestions, all 1-RMs were determined within five attempts.

Aerobic fitness: A submaximal test was selected as a measure of aerobic fitness to control for the confounding factors such as fatigue or existing musculoskeletal problems which can limit accurate assessment of maximal aerobic capacity (Noonan & Dean, 2000). Participants completed the long-distance corridor walk test, a timed 400m walk, as a measure of physical function and aerobic fitness (Simonsick, Fan, & Fleg, 2006). The test requires participants to walk 400m as quickly as possible, without running or jogging, covering the distance by walking laps around markers placed 20m apart. Participants were required to walk completely around each cone without stopping and completed ten 40m laps (up and back). The time taken to complete the long-distance corridor walk test has been shown to relate well to maximal aerobic capacity, physical functioning and mobility, and mortality (Newman et al., 2006).

Body composition: Total body muscle and fat mass was measured by dual energy X-ray absorptiometry (DXA, Hologic Discovery A, Waltham, MA). This assessment also provided the percentage of body fat for each participant. Body composition results were automated using up-to-date software installed by the manufacturer.

6.2.5 Statistical analysis

This exploratory study was an examination of the therapeutic effect of exercise for depression (measured using the HADS-D) in depressed cancer patients, as well as several secondary physical and physiological outcomes associated with the intervention. Therefore, multiple dependent variables were assessed which presents a number of statistical confounds that are acknowledged and explained below.

Analysis was performed to examine equivalence of the three groups at baseline. One-way analysis of variance (ANOVA) tests with Bonferroni adjustment were used for ratio and interval data and Chi-squared tests were used to compare categorical data.

In order to test the first hypothesis, two sets of analyses were performed. Mixed model, two-factor ANOVA was conducted comparing the three groups (between subjects) across the three assessment times (within subjects). Outcomes that produced a significant interaction effect were examined further by comparing the change in means over time for each of the three groups using a one-way ANOVA with *Scheffé post hoc* tests. The one-way ANOVA was used to explain where the significance occurred in the 3 x 3 results. To further examine the effect of exercise, analyses were performed comparing the results of a single exercise group (results of both exercise intervention groups combined) to the usual care control group. This was also performed using a two-factor ANOVA comparing the two groups across the same three time points. If interaction effects were found, a one-way ANOVA with *Scheffé post hoc* testing was performed and, effect sizes were calculated using Cohen's *d* (Hopkins, 2003).

To test the second hypothesis, the results of the two exercise groups were compared to each other following the same procedures reported above. All results were analysed using both the intention-to-treat (ITT) with the last measure carried forward method in order to account for drop-out and missing data (missing at random) and per-protocol (PP) analysis to explain the actual changes for those that completed the entire intervention (not missing at random). Both of these analyses were performed because no previous research in this area has been conducted, and therefore it was not possible to determine whether missing data were random or not. The use of both ITT and PP analyses throughout also avoids any outcome bias, however, due to the small sample size PP results are likely more stringent within this feasibility study.

Standardised effect sizes were used to determine the magnitude of the effect as small (0.2 – 0.5), moderate (0.5 – 0.8), or large (> 0.8). Effect size calculations were performed using a custom designed MS Excel template (Hopkins, 2003) and all statistical analyses were performed using PASW v18 for Windows (SPSS Inc., Chicago IL, USA).

The use of multiple analyses of the dependent variables leads to an increased likelihood of a Type I error and it is acknowledged that this could have been overcome by performing planned comparisons and correcting for the alpha value (set at $\alpha = .05$) when comparing between different groups. Secondly, initial analyses could have been conducted using a Multivariate ANOVA (MANOVA) because there were multiple dependent and independent variables.

MANOVA would have initially been more stringent. However, if significance were found then *post hoc* analysis similar to the method employed above would have been necessary. Furthermore, the MANOVA would not have been as suitable for the exploratory results, for which a Type I error is more acceptable than a Type II error, and may have excluded some valuable information attained through examining the influence of the intervention on each dependent variable.

The exploratory nature of the research also suggests that initial analysis which is exposed to the likelihood of a Type I error is more beneficial than data analysis that could result in a Type II error. Keppel (1991) suggests that replication of results, across multiple trials, is more indicative of a significant and meaningful difference than the outcomes of a single study. Therefore, it was felt that the risk of increased Type I error was acceptable and would not result in disadvantage, or the presentation of erroneous data, and would provide greater benefit than the reporting of a Type II error, failing to reject a false null hypothesis, as this may convince future researchers not to continue examining this area. The scope of this study suggests that future research should be performed which would be able to support or refute the findings below.

Prior to commencing the trial, an initial power calculation was performed to consider changes in depression from the HADS-D. The sample size was calculated for an expected 60% reduction of depressive symptoms in the intervention groups and a 30% reduction in the usual care group. Assuming a drop out of ~20% which can be expected in exercise intervention studies with depressed participants (Stathopoulou et al., 2006), a total of 90 participants, 30 per group, was required. This took into account the attrition rate, but maintained a power of 80% at an alpha level of .05. Due to difficulty with recruitment and the limited time available, target recruitment was not met and, therefore, the study may be underpowered. Despite the limited sample size, and unbalanced groups, results reported below elucidate useful and significant findings which contribute to the literature through this feasibility trial.

6.3 Results

In this section, initial results are presented to display the changes that occurred over the course of the intervention for all three groups. Results are then presented examining the outcomes for the combined exercise group and the control group. Lastly, the results comparing the outcome

measures between the two exercise groups are presented. These multiple comparisons replicate data, and it is acknowledged some of the data presented in the tables below can be considered redundant. However, for the convenience of the reader, all measurement outcomes are reported in tabular format for each analysis.

6.3.1 Participant characteristics and group differences

No statistical differences were found when comparing the demographic characteristics of the three groups for either the ITT or PP analyses (Tables 6.1 and 6.2, above). One-way analysis of variance indicated that the greatest mean difference was found for the age difference of the groups, however the result was not significantly different ($p = .072$ for ITT and $p = .112$ for PP). Some differences that were constant for the per-protocol and intention-to-treat samples include the supervised group being younger and having the greatest time since diagnosis, the home-based exercise group having the largest body mass index, and taking the least amount of prescribed medications, and the supervised group also being the most heterogeneous group with only 50% of the sample comprising breast and prostate cancer survivors, compared to the home-based group (75%) and the control group (78%). Analysis comparing the combined exercise groups (All Ex) to the control group also revealed no significant differences (Table 6.3).

Table 6.3
Characteristics of the combined exercise groups compared to control, for both the intention-to-treat analyses and the per-protocol sample

	Intention-to-treat			Per-protocol		
	All Ex (<i>n</i> = 18)	Control (<i>n</i> = 14)	<i>p</i>	All Ex (<i>n</i> = 14)	Control (<i>n</i> = 9)	<i>p</i>
Age (y)	57.1 (10.3)	61.2 (7.9)	.228	56.6 (11.5)	61.3 (9.6)	.315
Height (cm)	171.2 (8.0)	173.6 (11.0)	.478	170.5 (9.0)	174.0 (10.5)	.409
Mass (kg)	86.5 (21.3)	82.6 (14.3)	.565	85.3 (22.7)	80.8 (14.3)	.601
BMI	29.3 (5.7)	27.4 (3.9)	.296	29.0 (5.8)	26.5 (2.9)	.254
Number of medicines	2.7 (1.9)	3.5 (2.7)	.344	2.6 (1.9)	3.8 (3.1)	.256
Time since diagnosis (months)	37.4 (42.9)	27.2 (17.1)	.410	36.6 (47.4)	20.3 (9.0)	.325
% Male	50.0 %	64.3 %		42.9 %	66.7 %	
Current depression treatment	55.6 %	50.0%		57.1 %	55.6 %	
Active cancer treatment	22.2 %	35.7%		21.4 %	44.4 %	

There were no significant differences at baseline between participants that completed the study and those that withdrew (Table 6.4). Despite the magnitude of differences producing no statistical significance, closer examination of effect sizes revealed greater level of depression ($d = 0.52$), a consistent trend for decreased mental health ($d = 0.43 - 0.63$), and lower physical

activity levels in the group that did not complete the trial. This pattern of results, but lack of significance, is likely due to the low power associated with the small sample size. Nonetheless, these results suggest that participants who failed to complete the program may have differed from those who completed the entire intervention.

Table 6.4
Mean (SD) baseline results compared for participants that did and did not complete the 12-week program

	Completed (n = 23)		Withdrew (n = 9)		p	d
Age (y)	58.4	(10.8)	60.1	(4.5)	.659	0.21
Height (cm)	171.9	(9.6)	173.0	(9.3)	.766	0.12
Mass (kg)	83.5	(19.6)	88.2	(15.4)	.529	0.25
BMI	28.0	(5.0)	29.5	(5.2)	.460	0.30
Number of meds	3.0	(2.4)	2.9	(1.8)	.860	0.07
Time since diagnosis (months)	30.2	(37.7)	39.9	(22.3)	.479	0.28
HADS-D	6.9	(3.7)	8.9	(4.0)	.194	0.52
HADS-A	8.6	(3.3)	10.6	(3.0)	.131	0.60
HADS-T	15.5	(5.9)	19.5	(6.5)	.110	0.63
SF36 MHC	42.8	(9.2)	37.2	(11.4)	.158	0.56
SF36 PHC	48.7	(6.4)	48.8	(6.9)	.978	0.01
SWLS	19.3	(8.6)	16.6	(8.3)	.442	0.14
PSQI	9.9	(4.4)	11.8	(3.9)	.264	0.45
CASES	127.3	(32.7)	112.8	(36.1)	.282	0.43
Total exercise (min/wk)	194.5	(207.6)	136.1	(152.3)	.451	0.30

The two point higher score for depression reported for participants that withdrew equated to a categorical shift, with the mean score 8.9 exceeding the maximum level of “7” set as normal range for depressive symptoms (Zigmond & Snaith, 1983). Similarly, the group of participants that did not complete the intervention presented with a mean distress score (HADS-T) exceeding 16 which has been suggested as indicative of clinically elevated levels of distress (Sellick & Edwardson, 2007). Anxiety, quality of life (mental health composite), satisfaction with life, and sleep quality all favoured the group that completed the intervention. However, unlike depression and distress, the groups did not differ in symptom severity according to cut-off scores. Further, cancer self-efficacy was lower in the group that withdrew suggesting that this may be related to adherence. Exercise engagement represented as minutes per week was 43% greater for the group that completed the entire program compared to those that did not. An even larger (66%) disparity in activity was noticed when comparing the amount of time spent performing exercise at a moderate intensity or above between the group that completed (119.0 ± 153.1 min) and the group that did not complete the program (71.1 ± 135.4 min).

6.3.2 An examination of outcomes between the three groups

A summary of the interaction effects found when comparing the psychological and subjective self-reported outcomes for the three groups is reported below (Table 6.5). The primary outcome of depression produced significant group by time interactions in both intention-to-treat and per-protocol analysis. Secondary outcomes closely related to mood and depression also displayed significance, whereas self-reported physical activity, physical well-being and cancer self-efficacy did not show an effect for the three groups over the 12-week intervention.

Table 6.5
Statistical summary for the interaction effects (group x time) of all three groups

	Intention-to-treat			Per-protocol		
	<i>F</i>	<i>df</i>	<i>p</i>	<i>F</i>	<i>df</i>	<i>p</i>
<u>Primary outcome</u>						
HADS-D	4.343	4	.004	4.021	4	.008
<u>Secondary outcomes</u>						
HADS-A	3.003	4	.025	1.836	4	.141
HADS-T	4.275	4	.004	3.296	4	.020
SF-36 MHC	4.785	4	.002	4.378	4	.005
SF-36 PHC*	0.514	3.589	.706	0.454	4	.769
SWLS	6.646	4	< .001	5.238	4	.002
PSQI	1.465	4	.225	5.356	4	.141
CASES	0.950	4	.442	0.530	4	.714
Godin (total duration)*	0.364	3.581	.813	0.501	4	.735
Godin (moderate and strenuous)	1.411	4	.242	1.291	4	.290

*Sphericity violated, Huynh-Feldt correction employed

6.3.2.1 Depression

A significant group by time interaction effect was found for the primary outcome of depression ($p = .004$) for the intention-to-treat results. There was a trend for depression to decrease consistently over time in both exercise groups; whereas the control group experienced an initial decrease followed by an increase resulting in their final depression score being higher than the baseline level (Figure 6.2 A). The one-way ANOVA analysis to examine the interaction effect revealed that the greatest interactions occurred between the control group and the supervised exercise group over the entire 12-week period ($p = .002$). The change from baseline to the 6-week assessment was also significant ($p = .027$) and favoured the supervised exercise group compared to the control group. A significant effect was also found between the home-based group and the control group for changes in depression over the 12-weeks ($p = .016$).

The per-protocol responses of the participants that completed each testing session (Figure 6.2 B) reveal similar patterns to the ITT results with a significant interaction effect ($p = .008$). Again there was a significant difference between the supervised group and the control group for the change in depression ($p = .021$) over the entire program. There was an even greater interaction favouring home-based exercise in reducing depression ($p = .006$) over the 12-weeks. Notably, the response to supervised exercise appeared to occur towards the end of the program with significant differences found between the control and the supervised groups for change in depression ($p = .032$) during the last six weeks of the program. The data for depression is reported in Table 6.6.

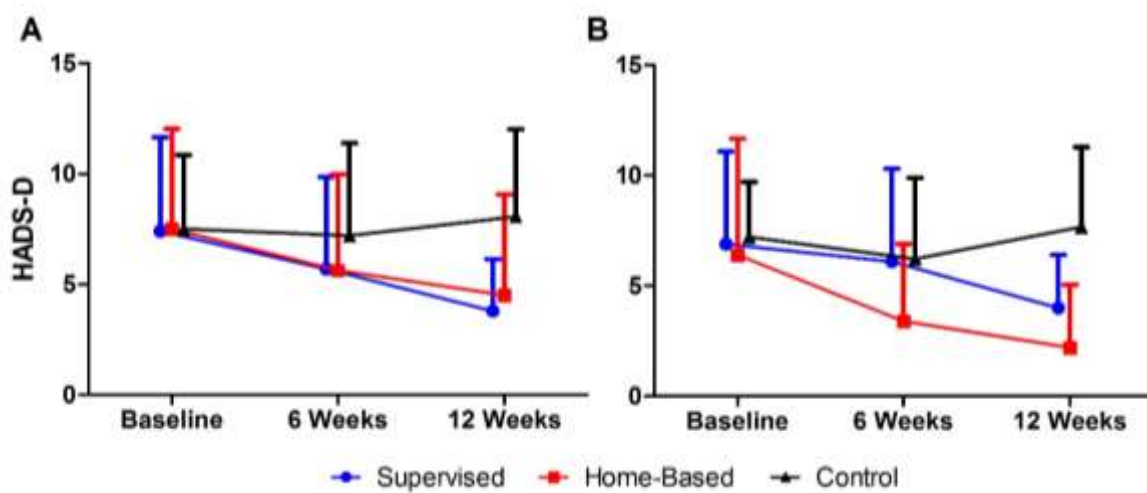


Figure 6.2. Changes in depression according to results from the HADS-D. Intention-to-treat results are represented in A and per-protocol results depicting only those participants that completed the 12-week program are represented in B.

Table 6.6
Mean (SD) results for HADS-D for all three study groups

	Intention-to-treat			Per-protocol		
	Supervised	Home-based	Control	Supervised	Home-based	Control
Baseline	7.40 (4.27)	7.50 (4.54)	7.50 (3.35)	6.89 (4.20)	6.40 (5.27)	7.22 (2.49)
Week 6	5.70 (4.16)	5.63 (4.34)	7.21 (4.19)	6.11 (4.20)	3.40 (3.51)	6.22 (3.67)
Week 12	3.80 (2.35)	4.50 (4.57)	8.07 (3.95)	4.00 (2.40)	2.20 (2.86)	7.67 (3.61)

6.3.2.2 Anxiety

Intention-to-treat analysis revealed a significant group by time interaction effect for the HADS-A outcome ($p = .025$). Anxiety decreased at each time point for the two exercise groups whereas

the control group had no noticeable change to their level of anxiety (Figure 6.3 A, Table 6.7). Further analysis revealed that the significant interaction was due to the change in anxiety between the supervised and control groups over the entire 12-week period ($p = .014$). No other significant interactions were found. Per-protocol results (Figure 6.3 B) also revealed no significant interaction effect for HADS-A ($p = .141$). Therefore, no further analysis was conducted. However, difference between the ITT and PP results indicates that the participants that did not complete the trial did influence the outcome for anxiety, despite baseline scores not being significantly different (see 6.3.1 above).

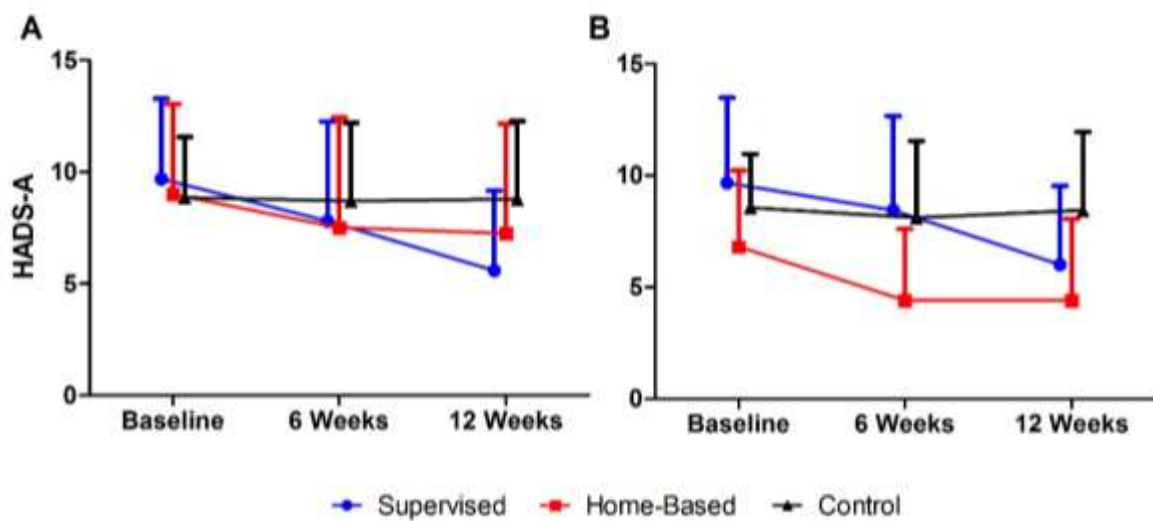


Figure 6.3. Changes in anxiety according to results from the HADS-A. Intention-to-treat results are represented in A and per-protocol in B.

Table 6.7
Mean (SD) results for HADS-A

	Intention-to-treat			Per-protocol		
	Supervised	Home-based	Control	Supervised	Home-based	Control
Baseline	9.70 (3.59)	9.00 (4.04)	8.86 (2.71)	9.67 (3.81)	6.80 (3.42)	8.56 (2.40)
Week 6	7.80 (4.47)	7.50 (4.96)	8.71 (3.50)	8.44 (4.22)	4.40 (3.21)	8.11 (3.44)
Week 12	5.60 (3.57)	7.25 (4.92)	8.79 (3.49)	6.00 (3.54)	4.40 (3.65)	8.44 (3.50)

6.3.2.3 Total distress

Analysis of total distress revealed similar statistical outcomes and a significant group by time interaction effect for both the intention-to-treat ($p = .004$) and per-protocol ($p = .020$) results. For both analyses it was found that significance occurred only for the change in mean distress

score between the control and supervised groups over the 12-week period ($p = .002$ for ITT; $p = .021$ for PP). The response to supervised exercise appeared to occur towards the end of the program with significant differences only found during the last six weeks of the program between the control and the supervised groups for change in distress ($p = .033$ for ITT; $p = .045$ for PP). This outcome is due to the sustained decrease in distress for the supervised group, whereas the home-based group appears to demonstrate the greatest response to exercise in the first period of the intervention (Figure 6.4, Table 6.8).

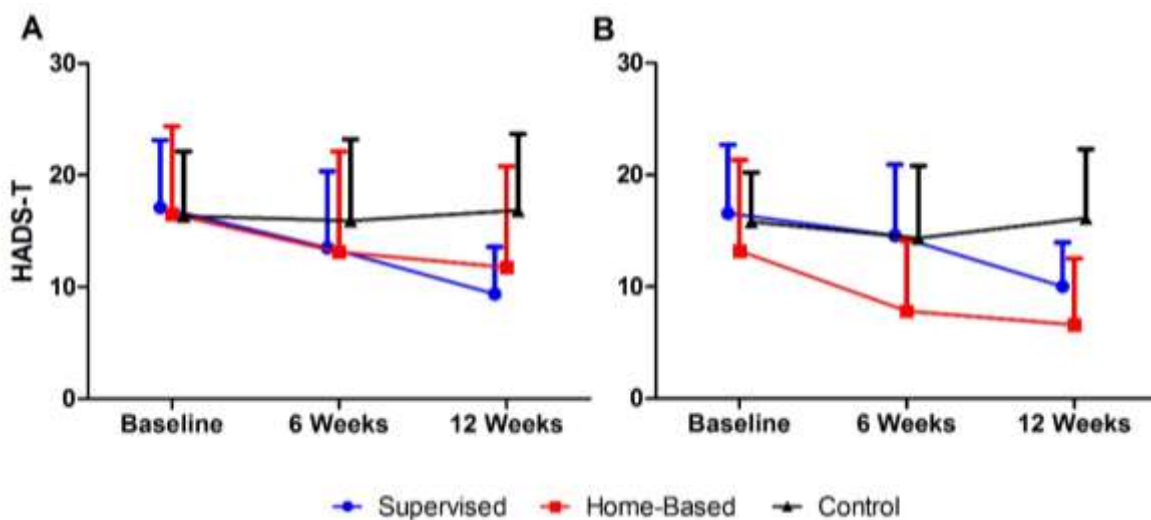


Figure 6.4. Changes in total distress according to results from the HADS. ‘A’ represents analysis of the intention-to-treat results and ‘B’ represents per-protocol results.

Table 6.8
Mean (SD) results for HADS-T

	Intention-to-treat			Per-protocol		
	Supervised	Home-based	Control	Supervised	Home-based	Control
Baseline	17.10 (6.03)	16.50 (7.89)	16.36 (5.77)	16.56 (6.13)	13.20 (8.14)	15.78 (4.44)
Week 6	13.50 (6.87)	13.13 (8.98)	15.93 (7.27)	14.56 (6.36)	7.80 (6.34)	14.33 (6.48)
Week 12	9.40 (4.20)	11.75 (9.07)	16.86 (6.85)	10.00 (3.97)	6.60 (5.90)	16.11 (6.21)

6.3.2.4 Quality of life

The SF-36 provided quality of life measures using the physical (PHC) and mental health composite (MHC) scores. There were no interaction effects for the PHC score with minimal changes over the entire intervention for any of the three groups for either ITT or PP analyses (Figure 6.5A and B, Table 6.9). Conversely, MHC displayed significant interaction effects for

ITT ($p = .002$) and per-protocol results ($p = .005$) (Figure 6.5C and D). Over the 12-week period, both training groups increased MHC scores whereas the control group demonstrated a decrease. Significance was due to the change in mean scores over the entire intervention between the supervised group and the control group for both ITT ($p = .006$) and per-protocol ($p = .036$) analyses. Moreover, the first 6-weeks in the per-protocol analysis resulted in an increase in MHC (39.72 ± 12.90 to 45.55 ± 12.84) for the home-based group and the decrease for the control group (43.23 ± 8.33 to 41.67 ± 10.84) which produced a significant effect ($p = .029$). However, the decrease in MHC reported by the home-based group at the end of the intervention eradicated the statistical effect.

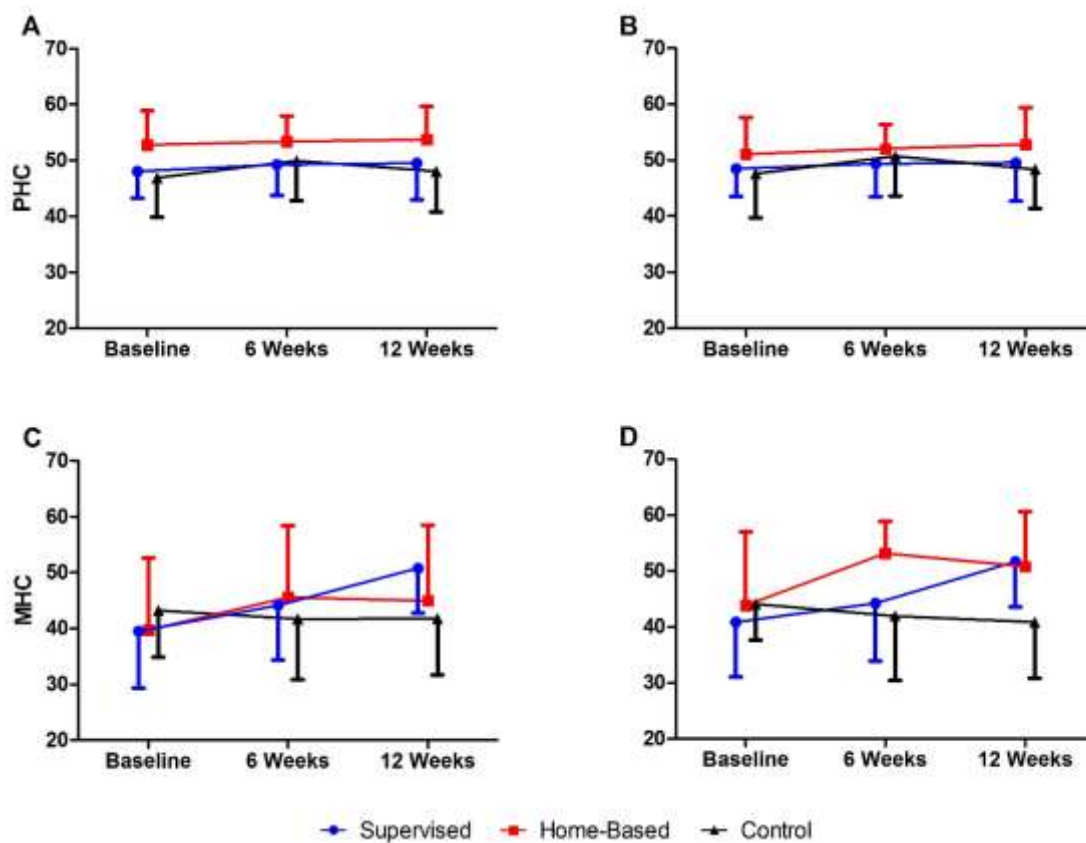


Figure 6.5. Physical (PHC) and Mental (MHC) Health Composite scores from the SF-36. ITT results displayed in A and C, per-protocol results displayed in B and D.

Table 6.9

Mental health composite (MHC) and physical health composite (PHC) for all three groups represented as mean (SD) for both intention-to-treat (ITT) and per-protocol (PP) analyses

	PHC			MHC		
	Supervised	Home-based	Control	Supervised	Home-based	Control
Baseline	48.08 (4.85)	52.79 (6.05)	46.88 (6.99)	39.53 (10.17)	39.72 (12.90)	43.23 (8.33)
ITT						
Week 6	49.28 (5.54)	53.40 (4.51)	49.95 (7.14)	44.13 (9.75)	45.55 (12.84)	41.67 (10.84)
Week 12	49.50 (6.51)	53.71 (5.88)	48.07 (7.26)	50.78 (8.07)	44.92 (13.55)	41.76 (10.09)
PP						
Baseline	48.48 (4.97)	51.08 (6.61)	47.62 (7.88)	40.86 (9.82)	43.84 (13.13)	44.09 (6.46)
Week 6	49.35 (5.88)	52.06 (4.33)	50.73 (7.11)	44.23 (10.34)	53.16 (5.75)	41.94 (11.53)
Week 12	49.58 (6.90)	52.80 (6.59)	48.36 (6.97)	51.63 (8.07)	50.78 (9.87)	40.85 (10.04)

6.3.2.5 Satisfaction with life

A significant group by time effect was found for satisfaction with life for both intention-to-treat ($p < .001$) and per-protocol ($p < .001$) analyses. A similar trend was also noticed for both analyses, whereby the supervised group increased their SWLS score at each testing session, whereas the home-based group showed an initial improvement followed by a decrease. The control group produced fairly consistent results, but displayed a slight decrease over the duration of the program (Figure 6.6, Table 6.10). This resulted in the supervised group displaying the greatest scores for satisfaction with life at the conclusion of the study, despite starting with the lowest scores in both cases.

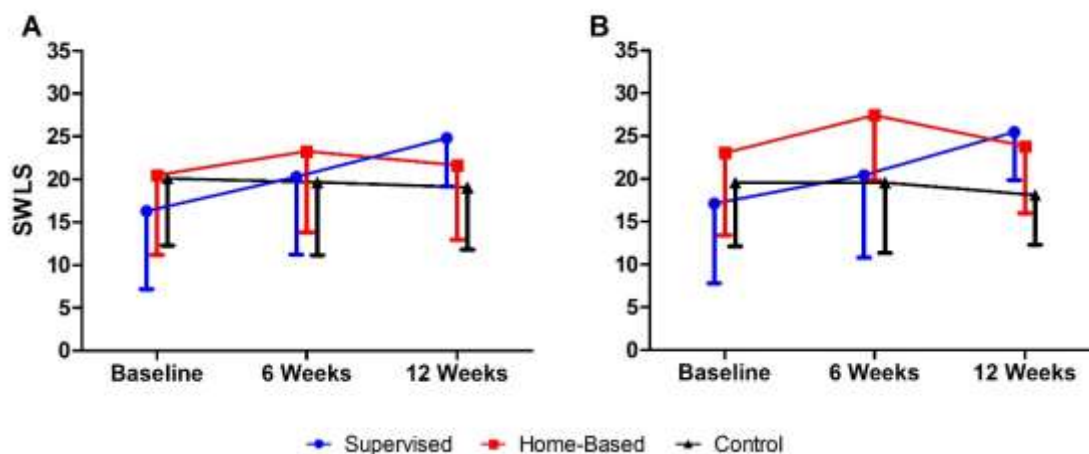


Figure 6.6. Satisfaction with Life Scales mean results for all three intervention groups. ‘A’ represents analysis of the intention-to-treat results and ‘B’ represents per-protocol results.

Further analysis revealed several significant interactions for the ITT analysis. The supervised exercise group displayed a large increase in satisfaction with life (mean change +8.5) compared with the small change attained by the home-based group (mean change +1.1) and decrease (mean change -1.0) of the control group over the entire 12-weeks. This resulted in significant interactions between the supervised exercise and the control groups ($p < .001$) as well as between the supervised and home-based exercise groups ($p = .008$). The interaction between the supervised and control groups was already significant at the 6-week assessment ($p = .037$). Per-protocol analysis displayed a significant interaction only between the supervised exercise and control groups over the entire 12-week duration ($p = .003$).

Table 6.10
Mean (SD) results for Satisfaction with Life Scales

	Intention-to-treat			Per-protocol		
	Supervised	Home-based	Control	Supervised	Home-based	Control
Baseline	16.30 (9.15)	20.50 (9.35)	20.07 (7.82)	17.11 (9.32)	23.00 (9.59)	19.56 (7.43)
Week 6	20.30 (9.12)	23.25 (9.44)	19.64 (8.51)	20.44 (9.66)	27.40 (7.64)	19.56 (8.23)
Week 12	24.80 (5.65)	21.63 (8.70)	19.07 (7.30)	25.44 (5.59)	23.80 (7.79)	18.11 (5.82)

6.3.2.6 Sleep quality

No significant effects were found for sleep quality over the course of the 12-week intervention (Figure 6.7, Table 6.11). There was a trend for improvement in both exercise groups, but the overall mean score was still well above the cut-off of ‘5’ for normal sleep quality.

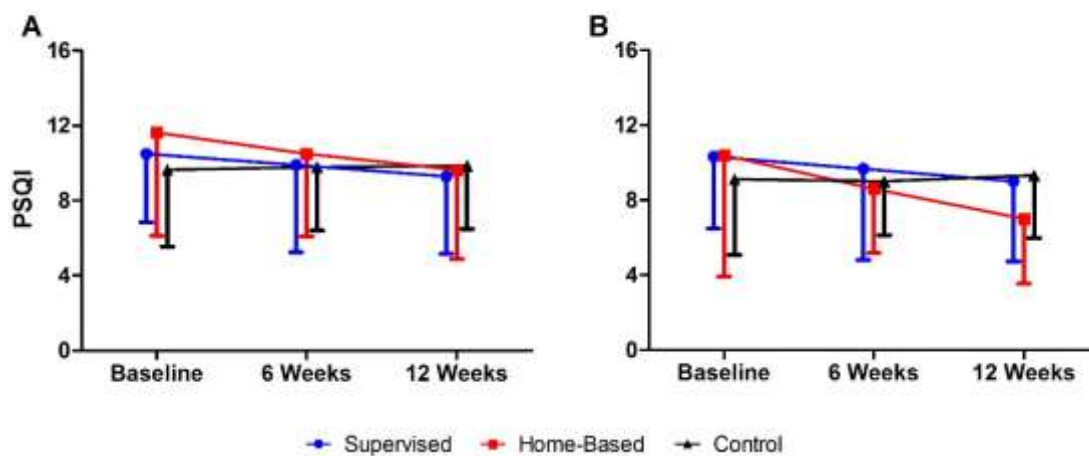


Figure 6.7. Pittsburgh Sleep Quality Index (PSQI) mean results for all three intervention groups. ‘A’ represents analysis of the intention-to-treat results and ‘B’ represents per-protocol results.

Table 6.11

Sleep quality scores for the three intervention groups tested at all three time points. Results shown as mean (SD) are presented for both ITT analysis and per-protocol analysis

	Intention-to-treat			Per-protocol		
	Supervised	Home-based	Control	Supervised	Home-based	Control
Baseline	10.50 (3.66)	11.63 (5.50)	9.64 (4.09)	10.33 (3.84)	10.40 (6.47)	9.11 (4.04)
Week 6	9.90 (4.65)	10.50 (4.14)	9.79 (3.38)	9.67 (4.87)	8.60 (3.44)	9.00 (2.87)
Week 12	9.30 (4.14)	9.63 (4.75)	9.86 (3.72)	9.00 (4.27)	7.00 (3.46)	9.33 (3.35)

Lower scores indicate less sleep disturbance

6.3.2.7 Cancer self-efficacy

No significant group by time interactions were noted for changes in cancer self-efficacy over the duration of the intervention for either the intention-to-treat analysis or the per-protocol analyses. The non-significant result may be due to the small sample size or large variability, since the two exercise groups appear to increase by greater margins than the control group in both analyses (Figure 6.8, Table 6.12).

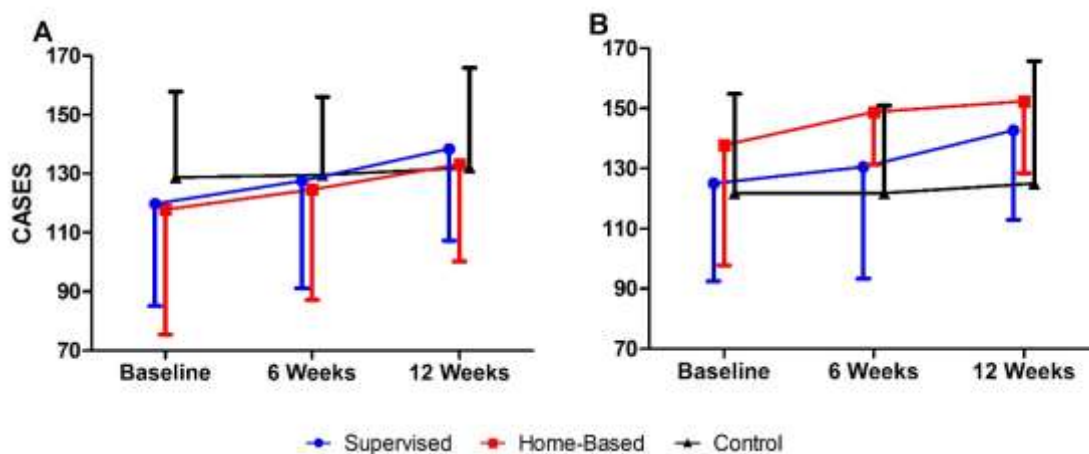


Figure 6.8. Cancer Self-Efficacy Scale (CASES) mean results for all three intervention groups. ‘A’ represents analysis of the intention-to-treat results and ‘B’ represents per-protocol results.

Table 6.12

Cancer Self-Efficacy Scale results represented as mean (SD) over the duration of the 12 week intervention for all groups

	Intention-to-treat			Per-protocol		
	Supervised	Home-based	Control	Supervised	Home-based	Control
Baseline	119.80 (34.76)	117.75 (42.39)	128.71 (29.13)	125.00 (32.48)	137.80 (40.02)	121.75 (33.11)
Week 6	127.50 (36.45)	124.63 (37.47)	129.57 (26.53)	130.56 (27.28)	148.80 (17.51)	121.75 (29.25)
Week 12	138.40 (31.07)	133.13 (32.93)	132.00 (33.89)	142.67 (29.68)	152.40 (23.94)	125.00 (40.71)

6.3.2.8 Physical activity

A consistent trend was found whereby all three groups reported an initial increase in total exercise engagement followed by a decrease in the second 6-week period of the intervention. This resulted in no significant group by time effects. A similar trend was also found for exercise performed at a moderate level or above (Figure 6.9, Table 6.13). Interestingly, only the control group was performing fewer minutes of high intensity exercise at the conclusion of the program than they were at baseline.

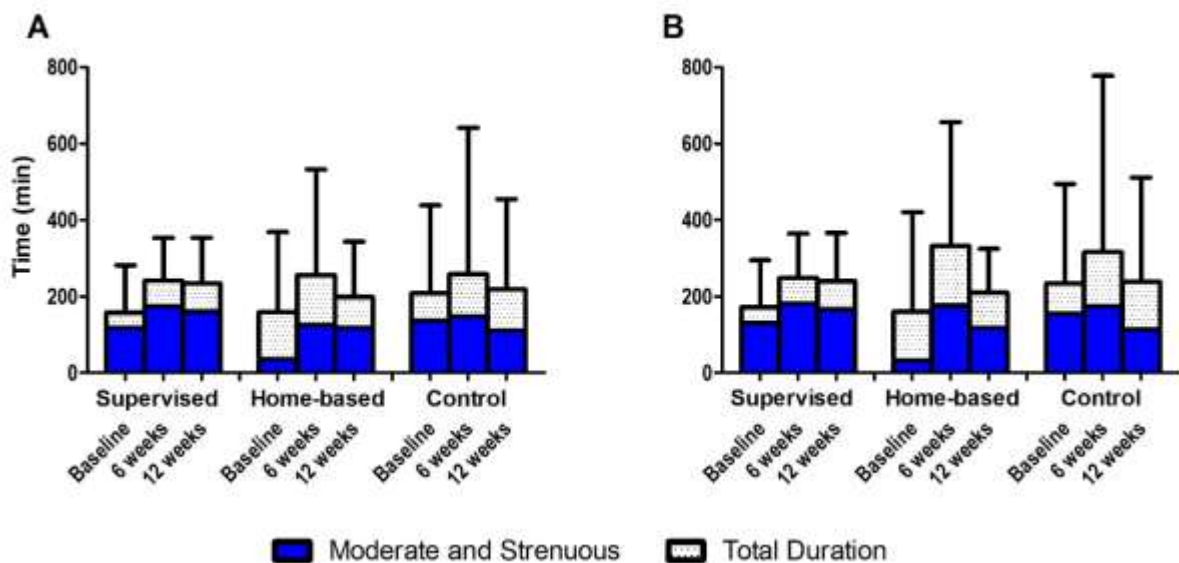


Figure 6.9. Total minutes of leisure time physical activity performed per week including the proportion of time spent performing moderate and strenuous activity for all three groups during the intervention. Results are presented for both intention-to-treat analysis (A) and per-protocol analysis (B).

Table 6.13

Mean (SD) for the total amount of leisure time physical activity reported by all three groups for both intention-to-treat (ITT) and per-protocol (PP) analyses

	Total Duration			Moderate and Strenuous		
	Supervised	Home-based	Control	Supervised	Home-based	Control
Baseline	158.00 (123.90)	149.38 (209.39)	208.82 (229.90)	118.00 (128.48)	35.63 (54.34)	136.86 (186.74)
ITT						
Week 6	241.50 (111.71)	256.56 (276.01)	258.57 (383.18)	175.00 (96.52)	125.31 (88.60)	147.50 (292.96)
Week 12	234.00 (119.53)	198.75 (145.25)	218.93 (236.12)	161.50 (85.90)	118.75 (118.13)	110.36 (157.67)
Baseline	172.22 (122.45)	161.00 (259.09)	235.39 (258.57)	131.11 (128.98)	33.00 (52.39)	154.56 (200.97)
PP						
Week 6	248.33 (116.24)	332.50 (323.96)	316.11 (461.63)	181.11 (181.11)	176.50 (51.04)	174.44 (174.44)
Week 12	240.00 (125.17)	210.00 (114.46)	238.89 (272.47)	166.11 (166.11)	118.00 (53.10)	113.33 (113.33)

6.3.3 An examination of the results combining both exercise groups to compare the effect of any exercise against a control group

6.3.3.1 Depression

When the two exercise groups were combined and compared to the control group, there was a significant interaction effect over the 12-week period for both ITT outcomes ($p < .001$) and per-protocol results ($p = .003$) (Figure 6.10, Table 6.14). When results were examined comparing the responses at each time point, significance was only found for the entire 12-week period ($p < .001$ for ITT; $p = .001$ for per-protocol), or the change in levels of depression during the final 6-week period ($p = .006$ for ITT; $p = .008$ for per-protocol).

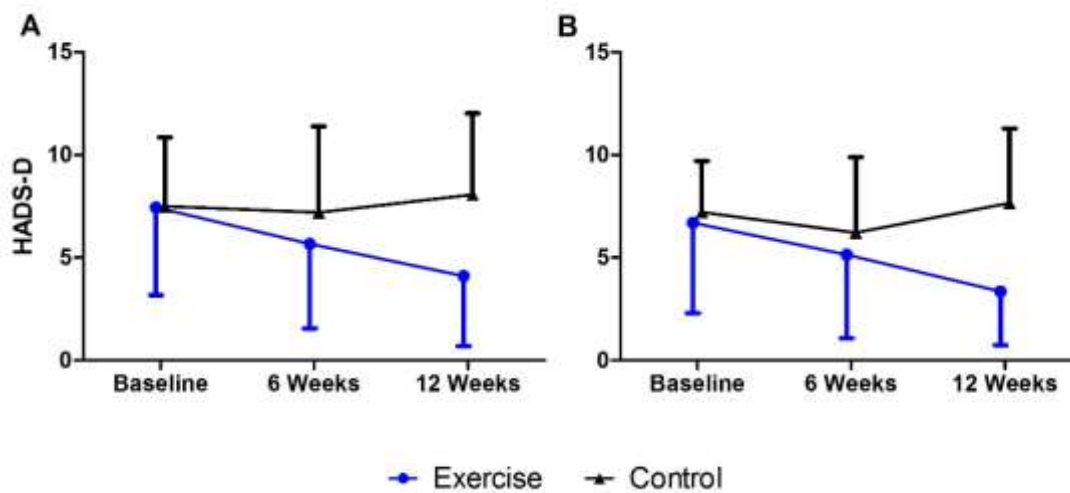


Figure 6.10. Depression mean results for the combined exercise group and the control group over the 12-week intervention. ‘A’ represents analysis of the intention-to-treat results and ‘B’ represents per-protocol results.

Table 6.14

HADS-D results for the combined exercise and control groups presented as mean (SD)

	Intention-to-treat		Per-protocol	
	Exercise	Control	Exercise	Control
Baseline	7.44 (4.26)	7.50 (3.35)	6.71 (4.41)	7.22 (2.49)
Week 6	5.67 (4.12)	7.21 (4.19)	5.14 (4.05)	6.22 (3.67)
Week 12	4.11 (3.41)	8.07 (3.95)	3.36 (2.62)	7.67 (3.61)

Statistical significance was confirmed using effect size calculations for the difference between the groups at each time point (Table 6.15). There was little difference between the groups at baseline and a large effect favouring the exercise group at the completion of the intervention.

The greatest changes were noted for the second half of the program during which time the exercise group continued to decrease depression whereas the control group increased their level of depression.

Table 6.15

Cohen's effect sizes comparing the combined exercise group to the control group for the duration of the 12-week intervention. Week 0 represents baseline scores. Negative scores favour the supervised group

Week/s	0	0 to 6	0 to 12	6 to 12
Intention-to-treat	-0.01	-0.39	-1.02	-0.63
Per-protocol	-0.14	-0.15	-1.02	-0.87

6.3.3.2 Anxiety

The influence of exercise in decreasing anxiety was less strong than for depression as statistical significance was only found for the between groups interaction using intention-to-treat analysis ($p = .020$), but not for the per-protocol interaction. Further, when the change in mean was analysed for the different time points, neither the first or last six-week period were significant on their own ($p = .141$ and $.132$). However, the total change from baseline to week 12 remained significant ($p = .013$) (Figure 6.11, Table 6.16).

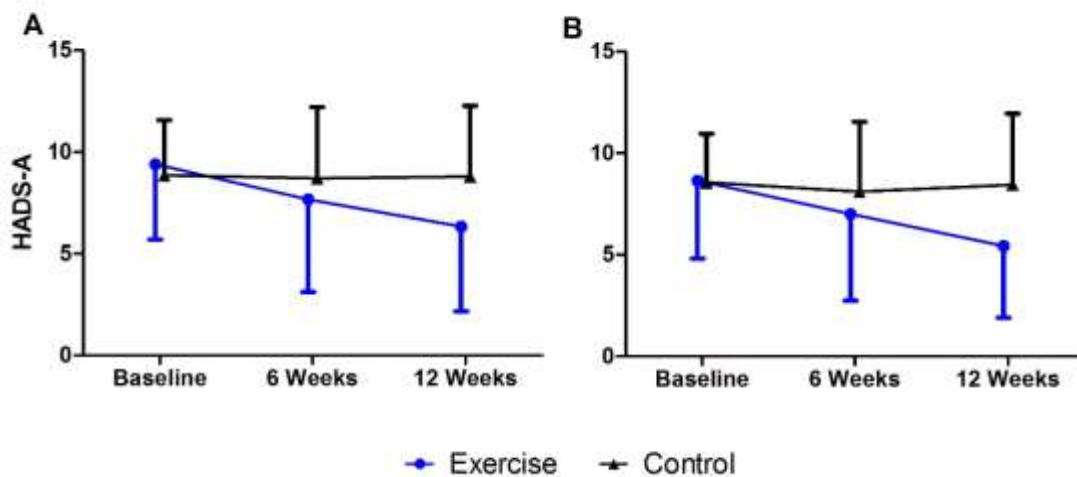


Figure 6.11. Anxiety mean results for the combined exercise group and the control group over the 12-week intervention. 'A' represents analysis of the intention-to-treat results and 'B' represents per-protocol results.

Table 6.16

HADS-A results for the combined exercise and control groups presented as mean (SD)

	Intention-to-treat		Per-protocol	
	Exercise	Control	Exercise	Control
Baseline	9.39 (3.70)	8.86 (2.71)	8.64 (3.82)	8.56 (2.40)
Week 6	7.67 (4.55)	8.71 (3.50)	7.00 (4.26)	8.11 (3.44)
Week 12	6.33 (4.17)	8.79 (3.49)	5.43 (3.52)	8.44 (3.50)

Cohen’s effect sizes confirm the significance of the statistical results from the ITT analysis, showing that the greatest effect was found for the entire 12-week period. Conversely to the statistical results, effect sizes for per-protocol analyses were as large as the intention-to treat results, which suggests that there was also a difference between groups in this condition (Table 6.17).

Table 6.17

Cohen’s effect sizes comparing the combined exercise group to the control group for the duration of the 12-week intervention. Week 0 represents baseline scores. Negative scores favour the supervised group

Week/s	0	0 to 6	0 to 12	6 to 12
Intention-to-treat	0.16	-0.48	-0.91	-0.43
Per-protocol	0.03	-0.37	-0.95	-0.58

6.3.3.3 Total distress

Total distress displayed a similar response to the results obtained for depression (Figure 6.12, Table 6.18). Both the intention-to-treat ($p = .001$) and per-protocol ($p = .007$) analyses produced statistically significant interactions between the two groups. The initial change over the first 6-week period was not significant between groups, however the mean difference increased from week 6 to week 12 due to an increase in distress reported by the control group and a further improvement for the exercise group. This resulted in significance for both ITT ($p = .022$) and PP ($p = .026$) analyses. Overall the change from baseline to completion was similar for ITT and PP ($p = .001$ and $.002$ respectively).

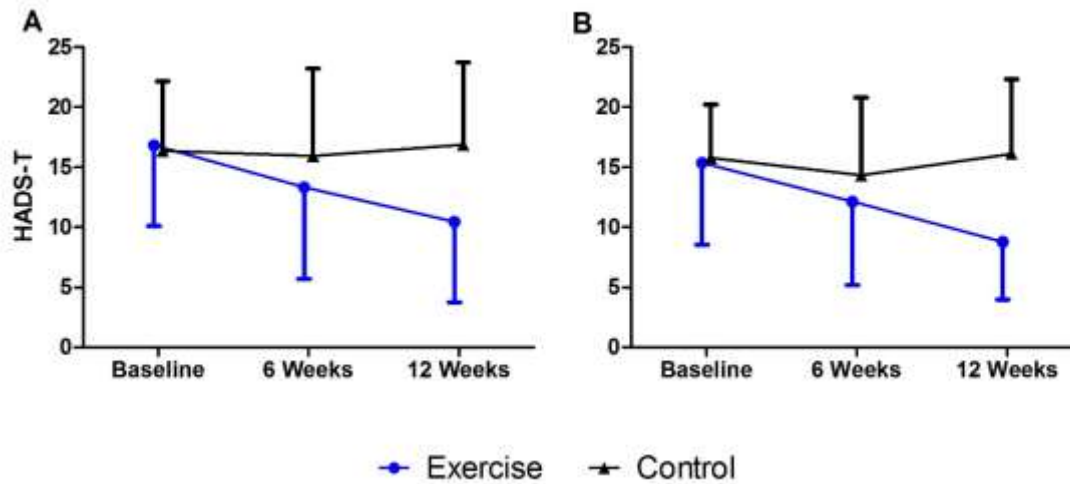


Figure 6.12. Mean total distress reported for the combined exercise group and the control group over the 12-week intervention. ‘A’ represents analysis of the intention-to-treat results and ‘B’ represents per-protocol results.

Table 6.18

HADS-T results for the combined exercise and control groups presented as mean (SD)

	Intention-to-treat		Per-protocol	
	Exercise	Control	Exercise	Control
Baseline	16.83 (6.71)	16.36 (5.77)	15.36 (6.80)	153.78 (4.44)
Week 6	13.33 (7.63)	15.93 (7.27)	12.14 (6.97)	14.33 (6.48)
Week 12	10.44 (6.68)	16.86 (6.85)	8.79 (4.82)	16.11 (6.21)

Cohen’s *d* revealed small to moderate effects for each six-week block period favouring the exercise group. However, the combined effect of these two 6-week periods resulted in an overall large effect indicating a very likely, and clinically significant, response to exercise (Table 6.19).

Table 6.19

Cohen’s effect sizes comparing the combined exercise group to the control group for the duration of the 12 week intervention. Week 0 represents baseline scores. Negative scores favour the supervised group

Week/s	0	0 to 6	0 to 12	6 to 12
Intention-to-treat	0.08	-0.49	-1.11	-0.61
Per-protocol	-0.07	-0.30	-1.17	-0.87

6.3.3.4 Quality of life

When the results of the two exercise groups were combined and examined compared to the control group, it was found that a significant interaction effect existed for the mental health composite (MHC) for ITT ($p = .002$) and PP ($p = .005$) analyses. However, the physical health composite score (PHC) did not display any statistical differences. Mean (SD) results for the two groups are reported in Table 6.20. It is noticeable that MHC mean score increased at each measure for the exercise group, whereas the control group showed an initial decrease before a plateau; the same pattern occurred for both ITT and PP results. This trend resulted in significant differences found for the initial 6-week period ($p = .009$ for ITT; $p = .010$ for PP), where the mean change was greater than the second half of the program and did not result in statistical significance. Nonetheless, effect sizes favouring exercise were found for each 6-week period of the intervention ($d = 0.33 - 0.83$) and large effect sizes were found for the entire 12-week intervention ($d = 1.00$ for ITT; $d = 1.38$ for PP).

Table 6.20

Quality of life (SF-36) results comparing mental health composite (MHC) and physical health composite (PHC) outcomes between the combined exercise group and control group for both intention-to-treat (ITT) and per-protocol (PP) analyses

		PHC		MHC	
		Exercise	Control	Exercise	Control
	Baseline	50.17 (5.78)	46.88 (6.99)	39.62 (11.10)	43.23 (8.33)
ITT	Week 6	51.11 (5.39)	49.95 (7.14)	44.76 (10.90)	41.67 (10.84)
	Week 12	51.37 (6.43)	48.07 (7.26)	48.18 (10.91)	41.76 (10.09)
	Baseline	49.41 (5.50)	47.62 (7.88)	41.92 (10.70)	44.09 (6.46)
PP	Week 6	50.32 (5.37)	50.73 (7.11)	47.42 (9.78)	41.94 (11.53)
	Week 12	50.73 (6.73)	48.36 (6.97)	51.33 (8.38)	40.85 (10.04)

6.3.3.5 Satisfaction with life

The exercise program resulted in a significant and moderately beneficial increase in satisfaction with life when compared to the control group ($p = .007$ for ITT; $p = .026$ for PP). Continued improvement in satisfaction with life over time for the exercise group is illustrated in Figure 6.13, whereas the control group decreased slightly at each testing session (Table 6.21). Over the course of the 12-week intervention this resulted in moderate to large effect sizes favouring the exercise group ($d = 0.73$ for ITT; $d = 0.83$ for PP).

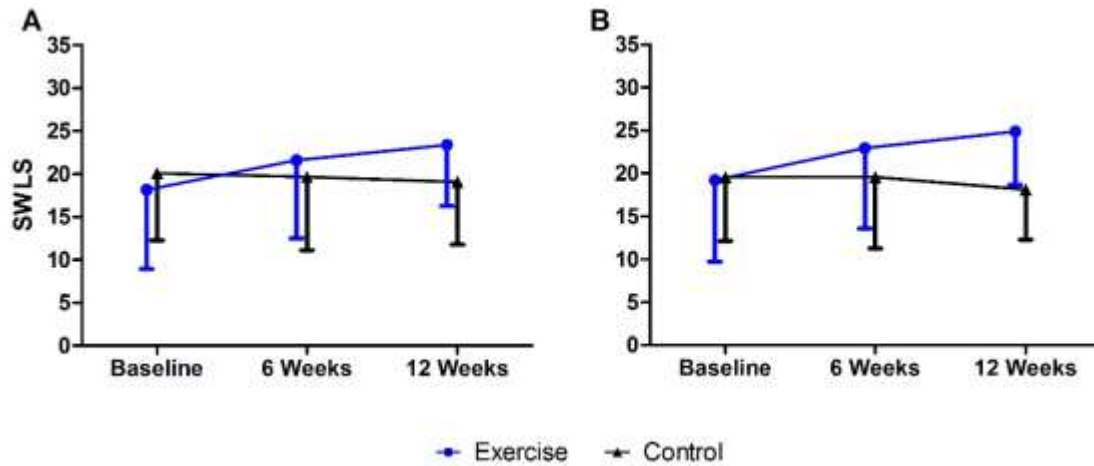


Figure 6.13. Satisfaction with life scales results represented for the combined exercise group and the control group for the intention-to-treat (A) and for the per-protocol outcomes (B).

Table 6.21

Satisfaction with life scales results for the combined exercise and control groups presented as mean (SD)

	Intention-to-treat		Per-protocol	
	Exercise	Control	Exercise	Control
Baseline	18.17 (9.22)	20.07 (7.82)	19.21 (9.50)	19.56 (7.43)
Week 6	21.61 (9.11)	19.64 (8.51)	22.93 (9.34)	19.56 (8.32)
Week 12	23.39 (7.12)	19.07 (7.30)	24.86 (6.21)	18.11 (5.82)

6.3.3.6 Sleep quality

Despite a trend for sleep quality to improve in the exercise group and decrease in the control group, no statistically significant interaction effects were found (Figure 6.14, Table 6.22). Nonetheless, the pattern of change justified further examination of difference between the groups using the effect size measures. Exercise provided a small to moderate enhancement to sleep over the duration of the 12-week intervention ($d = 0.41$ for ITT; $d = 0.52$ for per-protocol), according to the effect size calculations.

Table 6.22

Sleep quality for the combined exercise and control groups presented as mean (SD)

	Intention-to-treat		Per-protocol	
	Exercise	Control	Exercise	Control
Baseline	11.00 (4.46)	9.64 (4.09)	10.36 (4.68)	9.11 (4.04)
Week 6	10.17 (4.31)	9.79 (3.38)	9.29 (4.30)	9.00 (2.87)
Week 12	9.44 (4.29)	9.86 (3.72)	8.29 (3.99)	9.33 (3.35)

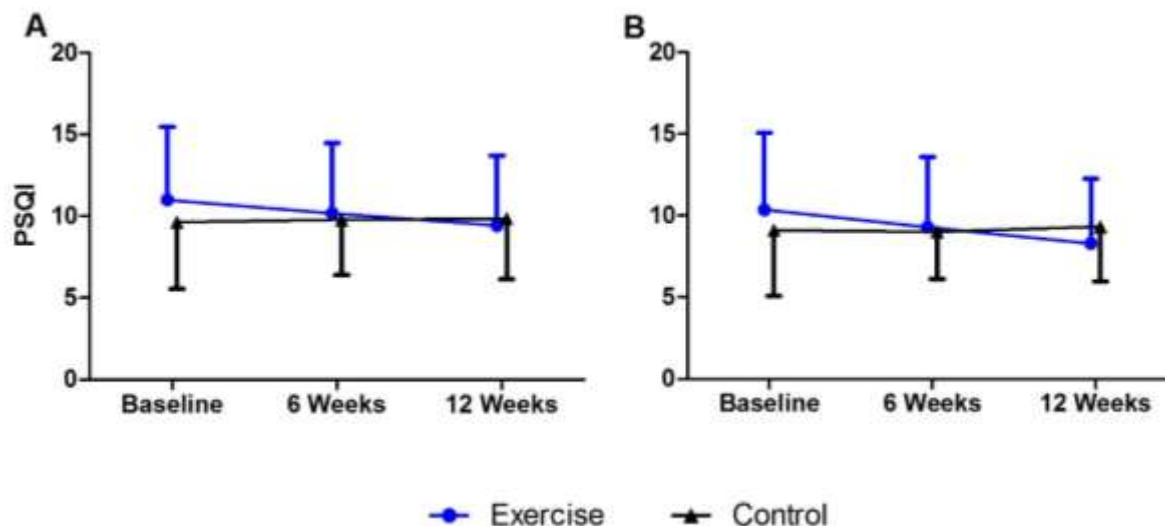


Figure 6.14. Changes in sleep quality according to the Pittsburgh Sleep Quality Index (PSQI) for the combined exercise group and the control group. Results are displayed for both intention-to-treat analysis (A) and per-protocol analysis (B). Lower scores represent improved sleep quality.

6.3.3.7 Cancer self-efficacy

Examination of self-efficacy between the combined exercise group and the control group also revealed no group by time interaction effect (Table 6.23). Self-efficacy increased in the exercise group and did not change in the control group over the 12-week period (Figure 6.15). Interestingly, the magnitude of change over the period did not vary between the intention-to-treat and per-protocol analysis, however the baseline values shifted 11 points higher for the exercise group (118.89 ± 37.16 to 129.57 ± 34.39) and seven points lower for the control group (128.71 ± 29.13 to 121.75 ± 33.11) from the ITT to the PP results. Cohen's effect size suggested that exercise provided a small to moderate benefit in increasing self-efficacy over the 12-week intervention when compared to usual care control ($d = 0.41$ for ITT; $d = 0.40$ for per-protocol).

Table 6.23

Cancer Self-Efficacy Scale results for the combined exercise and control groups presented as mean (SD)

	Intention-to-treat		Per-protocol	
	Exercise	Control	Exercise	Control
Baseline	118.89 (37.16)	128.71 (29.13)	129.57 (34.39)	121.75 (33.11)
Week 6	126.22 (35.83)	129.57 (26.53)	137.07 (32.13)	121.75 (29.25)
Week 12	136.06 (31.06)	132.00 (33.89)	146.14 (27.24)	125.00 (40.71)

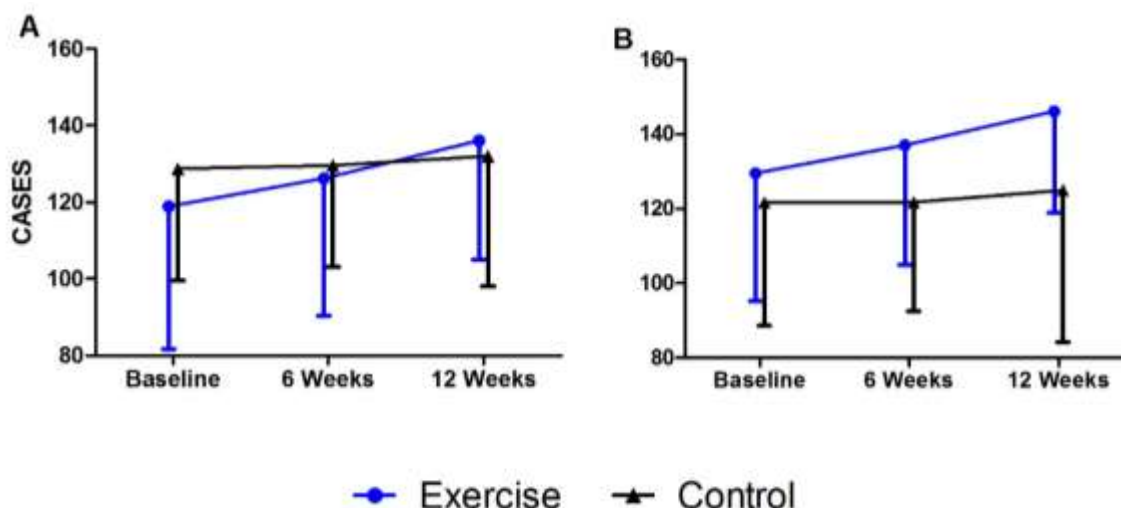


Figure 6.15. Cancer self-efficacy scale results represented for the change over time comparing the combined exercise group and the control group for intention-to-treat (A) and per-protocol (B) analysis.

6.3.3.8 Physical activity

Comparing the combined exercise group to the control group revealed no significant interactions for total exercise engagement or for the exercise performed at a moderate intensity or above (Table 6.24). Effect size calculations resulted in a net increase in higher intensity exercise of 88 minutes favouring the exercise group for both the ITT ($d = 0.59$) and per-protocol ($d = 0.61$) analyses.

Table 6.24

Exercise engagement as minutes per week for the total duration and the amount that was performed a moderate or strenuous intensity for the combined exercise group and the control group. Results are presented as mean (SD) for both the intention-to-treat (ITT) and per-protocol (PP) analyses

		Total duration		Moderate and strenuous	
		Exercise	Control	Exercise	Control
ITT	Baseline	154.2 (161.9)	208.82 (229.90)	81.4 (108.3)	136.86 (186.74)
	Week 6	248.2 (195.0)	258.57 (383.18)	152.92 (93.9)	147.50 (292.96)
	Week 12	218.3 (128.8)	218.93 (236.12)	142.5 (100.7)	110.36 (157.67)
PP	Baseline	168.2 (173.0)	235.39 (258.57)	96.0 (116.0)	154.56 (200.97)
	Week 6	278.4 (205.8)	316.11 (461.63)	179.5 (83.7)	174.44 (174.44)
	Week 12	229.3 (117.9)	238.89 (272.47)	148.9 (80.0)	113.33 (113.33)

6.3.4 An examination of results comparing both exercise groups

There was little statistical difference found when comparing the outcomes between the two exercise groups for both the intention-to-treat and per-protocol analyses. Depression decreased throughout the intervention and this trend was similar for all other subjective measures of mental health, whereby any exercise had a positive influence. Only two variables (satisfaction with life and leg press strength) displayed significant group by time interaction effects. However, due to the small sample size, effect size changes are reported below. These effects highlight that in certain instances the overall effects of exercise were no different, but the time course response varied according to the type of exercise undertaken.

6.3.4.1 Depression

Visual trends were noticeable for differences between the groups whereby the final level of depression was lower for the home-based group using per-protocol analysis, which was not supported in the intention-to-treat results, despite no difference at baseline between groups for either condition (Table 6.25). Per-protocol analysis found that the initial six-week period produced greater decreases in depression ($d = 0.50$) in the home-based group. This trend was reversed in the second six weeks of the program with greater decrements in depression seen for the supervised group ($d = 0.21$). Overall the results suggest that there was a small effect favouring home-based training to decrease depression over the entire 12 weeks ($d = 0.30$).

Table 6.25
HADS-D results of the two exercise groups presented as mean (SD)

	Intention-to-treat		Per-protocol	
	Supervised	Home-based	Supervised	Home-based
Baseline	7.40 (4.27)	7.50 (4.54)	6.89 (4.20)	6.40 (5.27)
Week 6	5.70 (4.16)	5.63 (4.34)	6.11 (4.20)	3.40 (3.51)
Week 12	3.80 (2.35)	4.50 (4.57)	4.00 (2.40)	2.20 (2.86)

6.3.4.2 Anxiety

Intention-to-treat analysis revealed that there was a moderate effect size ($d = 0.64$) favouring the supervised exercise group (9.70 ± 3.59 to 5.60 ± 3.57) compared to the home-based group (9.00 ± 4.04 to 7.25 ± 4.92) for reducing the severity of anxiety measured over the entire intervention (Table 6.26). This was largely due to the continued decrease in anxiety reported by the supervised group during the second half of the program, compared to the home-based

group which did not show any further improvements beyond the first 6-weeks ($d = 0.53$). This result was consistent with the per-protocol analysis, which again showed a greater improvement for the supervised group to decrease anxiety ($d = 0.64$) after the first 6-week period. However, there was a small effect that favoured the home-based group initially ($d = 0.31$); indicating that time effects may be present. Nonetheless, over the entire 12-week intervention, there was a small effect favouring supervised exercise ($d = 0.33$).

Table 6.26

HADS-A results of the two exercise groups presented as mean (SD)

	Intention-to-treat		Per-protocol	
	Supervised	Home-based	Supervised	Home-based
Baseline	9.70 (3.59)	9.00 (4.04)	9.67 (3.81)	6.80 (3.42)
Week 6	7.80 (4.47)	7.50 (4.96)	8.44 (4.22)	4.40 (3.21)
Week 12	5.60 (3.57)	7.25 (4.92)	6.00 (3.54)	4.40 (3.65)

6.3.4.3 Total distress

Distress results mirrored the outcomes from anxiety and depression indicating that, as the duration of the intervention increased, the outcome became more favourable for the supervised group (Table 6.27). There was a small to moderate effect for both the ITT ($d = 0.41$) and per-protocol analysis ($d = 0.49$) for reduced distress in favour of the supervised group for the second half of the program. The first 6 weeks showed variable responses, with no difference in the mean change according to ITT results and a moderate effect favouring the home-based group ($d = 0.50$) according to PP results.

Table 6.27

HADS-T results of the two exercise groups presented as mean (SD)

	Intention-to-treat		Per-protocol	
	Supervised	Home-based	Supervised	Home-based
Baseline	17.10 (6.03)	16.50 (7.89)	16.56 (6.13)	13.20 (8.14)
Week 6	13.50 (6.87)	13.13 (8.98)	14.56 (6.36)	7.80 (6.34)
Week 12	9.40 (4.20)	11.75 (9.07)	10.00 (3.97)	6.60 (5.90)

6.3.4.4 Quality of life

There was a moderate to large difference at baseline for the physical health composite between the two exercise groups ($d = 0.81$ for ITT; $d = 0.47$ for PP) with the home-based group reporting higher scores (Table 6.28). However, the magnitude of change due to the intervention was no

different with effect sizes ranging from 0.02 to 0.11. The effect of the exercise program did influence the mental health composite (MHC), which displayed a similar trend to the other psychological measures demonstrating that the home-based group had a greater initial improvement due to exercise. Intention-to-treat results showed an increase of 5.83 for the home-based group compared to an increase of 4.60 for the supervised group ($d = 0.11$). However, per-protocol results demonstrated a greater positive response for the home-based group increasing from 43.84 (13.13) at baseline to 53.16 (5.75) at the mid-point testing session compared to the supervised group, which increased from 40.86 (9.82) to 44.23 (10.34) ($d = 0.56$). The supervised exercise group continued to improve their MHC from week 6 to 12 whereas the home-based group decreased their MHC. Results were similar between ITT and per-protocol analyses and resulted in the supervised group completing the program with a higher MHC score in all conditions (ITT: 50.78 ± 8.07 vs 44.92 ± 13.55 ; per-protocol: 51.63 ± 8.07 vs 50.78 ± 9.87). This shift in results favouring the supervised exercise group resulted in a moderate to large effect ($d = 0.66$ for ITT; $d = 0.91$ for per-protocol) from week 6 to week 12.

Table 6.28

Mental health composite (MHC) and physical health composite (PHC) for the two exercise groups represented as mean (SD) for both intention-to-treat (ITT) and per-protocol (PP) analyses

		PHC		MHC	
		Supervised	Home-based	Supervised	Home-based
	Baseline	48.08 (4.85)	52.79 (6.05)	39.53 (10.17)	39.72 (12.90)
ITT	Week 6	49.28 (5.54)	53.40 (4.51)	44.13 (9.75)	45.55 (12.84)
	Week 12	49.50 (6.51)	53.71 (5.88)	50.78 (8.07)	44.92 (13.55)
PP	Baseline	48.48 (4.97)	51.08 (6.61)	40.86 (9.82)	43.84 (13.13)
	Week 6	49.35 (5.88)	52.06 (4.33)	44.23 (10.34)	53.16 (5.75)
	Week 12	49.58 (6.90)	52.80 (6.59)	51.63 (8.07)	50.78 (9.87)

6.3.4.5 Satisfaction with life

The two training groups produced statistically significant interaction effects for both the ITT analysis ($p = .020$) and per-protocol analysis ($p = .035$) (Figure 6.16, Table 6.29). Further analysis indicated that the mean change over the 12 weeks was significant for both ITT and PP analyses ($p = .011$ for ITT; $p = .046$ for PP) and was only a significant effect between week 6 and week 12 in the per-protocol analysis ($p = .044$). Effect sizes revealed a moderate to strong influence of supervised exercise increasing SWLS greater than home-based training over the entire 12-week period ($d = 0.80$ for ITT; $d = 0.79$ for PP). Despite both groups increasing their

SWLS from baseline, the magnitude and rate of change illustrate that during the last six weeks the supervised group continues to improve whereas the home-based group reduced their satisfaction, but remained marginally above baseline levels ($d = .66$ for ITT; $d = 0.90$ for PP).

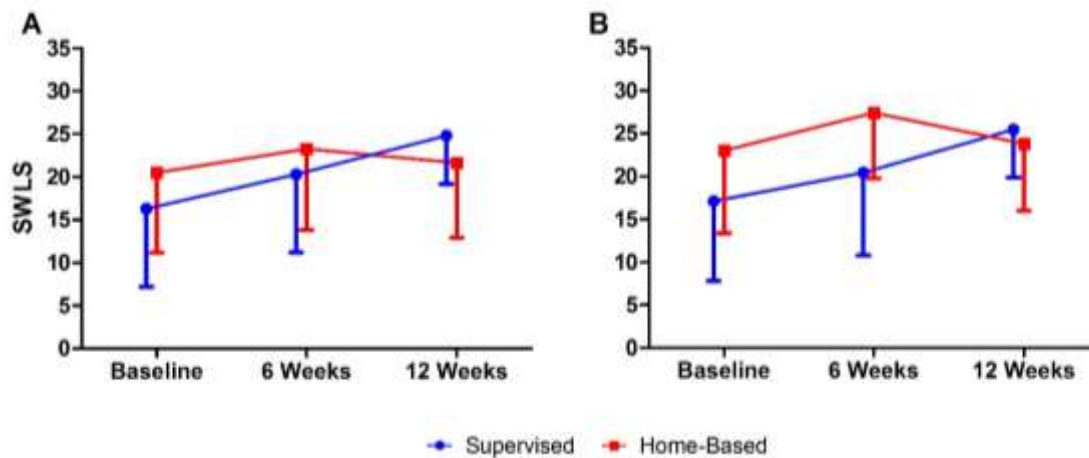


Figure 6.16. Satisfaction with Life Scales results for the two exercise groups. ‘A’ represents analysis of the intention-to-treat results and ‘B’ represents per-protocol results.

Table 6.29

Satisfaction with life scales outcomes for the two exercise groups presented as mean (SD)

	Intention-to-treat		Per-protocol	
	Supervised	Home-based	Supervised	Home-based
Baseline	16.30 (9.15)	20.50 (9.35)	17.11 (9.32)	23.00 (9.59)
Week 6	20.30 (9.12)	23.25 (9.44)	20.44 (9.66)	27.40 (7.64)
Week 12	24.80 (5.65)	21.63 (8.70)	25.44 (5.59)	23.80 (7.79)

6.3.4.6 Sleep quality

Both exercise groups improved their sleep quality over the course of the intervention and therefore no significant interaction effects were found (Table 6.30). Similarly, the effect size differences in the intention-to-treat analysis were negligible ($d = .006 - 0.18$). However, there was a small effect in the per-protocol analysis favouring the home-based group ($d = 0.44$) at the conclusion of the intervention.

Table 6.30

Sleep quality scores for the two exercise groups presented as mean (SD)

	Intention-to-treat		Per-protocol	
	Supervised	Home-based	Supervised	Home-based
Baseline	10.50 (3.66)	11.63 (5.50)	10.33 (3.84)	10.40 (6.47)
Week 6	9.90 (4.65)	10.50 (4.14)	9.67 (4.87)	8.60 (3.44)
Week 12	9.30 (4.14)	9.63 (4.75)	9.00 (4.27)	7.00 (3.46)

6.3.4.7 Cancer self-efficacy

No effects were found for changes in self-efficacy between the exercise groups (Table 6.31). Indeed the change over time was almost identical across the groups with no effect sizes exceeding 0.25.

Table 6.31
Cancer self-efficacy scale results for the two exercise groups presented as mean (SD)

	Intention-to-treat		Per-protocol	
	Supervised	Home-based	Supervised	Home-based
Baseline	119.80 (34.76)	117.75 (42.39)	125.00 (32.48)	137.80 (40.02)
Week 6	127.50 (36.45)	124.63 (37.47)	130.56 (27.28)	148.80 (17.51)
Week 12	138.40 (31.07)	133.13 (32.93)	142.67 (29.68)	152.40 (23.94)

6.3.4.8 Physical activity

The two groups performed very similar amounts of physical activity at baseline, yet the supervised group was noticeably performing more high intensity activity ($d = 0.76$ for ITT; $d = 0.85$ for PP) (Table 6.32). Cohen’s effect sizes confirmed that over the 12-week intervention the total exercise volume increased equally in both groups, however, the home-based group increased their proportion of high intensity exercise (+36% for both ITT and PP); whereas the supervised group decreased their proportion of high intensity activity relative to total duration (-6% for ITT; -7% for PP). These changes resulted in a small effect size, suggesting that home-based exercise increases moderate and strenuous exercise engagement more ($d = 0.37$ for ITT; $d = 0.43$ for PP).

Table 6.32
Total exercise engagement as minutes per week and the amount of activity that was performed at either a moderate or strenuous intensity per week for the two exercise groups. Results are presented as mean (SD) for both the intention-to-treat and per-protocol analyses

	Total duration		Moderate and strenuous	
	Supervised	Home-based	Supervised	Home-based
Baseline	158.00 (123.90)	149.38 (209.39)	118.00 (128.48)	35.63 (54.34)
ITT				
Week 6	241.50 (111.71)	256.56 (276.01)	175.00 (96.52)	125.31 (88.60)
Week 12	234.00 (119.53)	198.75 (145.25)	161.50 (85.90)	118.75 (118.13)
Baseline	172.22 (122.45)	161.00 (259.09)	131.11 (128.98)	33.00 (52.39)
PP				
Week 6	248.33 (116.24)	332.50 (323.96)	181.11 (181.11)	176.50 (51.04)
Week 12	240.00 (125.17)	210.00 (114.46)	166.11 (166.11)	118.00 (53.10)

6.3.4.9 Exercise sessions during the intervention

The number of exercise sessions completed during the intervention by the two exercise groups are reported in Table 6.33. No statistical differences were found between groups for the number of sessions performed during either six-week period for either ITT or PP analyses. The mean number of sessions completed by each group using ITT analysis was very similar at both time points. There was, however, a greater disparity when per-protocol results were analysed, indicating that the home-based group performed more than one additional exercise session per week in the initial six-week period ($d = 0.63$) and, despite both groups completing an average of almost 29 sessions in the second half of the program, this was an increase in number of sessions completed by the supervised group, whereas it represented a decrease of almost one session per week for the home-based group ($d = 0.61$).

Overall, the supervised group completed a total 21.3 (4.0) of the 24 scheduled sessions for the entire 12-week program. However, removing the participant that withdrew after 6-weeks improved the overall adherence to 22.4 (1.8) of the 24 sessions (range: 19 – 24). The number of supervised sessions completed after the initial 6-weeks was 11.0 (1.1), with no participants withdrawing before completing their mid-point testing.

Table 6.33

Mean (SD) number of exercise sessions completed at each time point during the 12 week intervention for both exercise groups. Analyses are presented for intention-to-treat (ITT) and per-protocol (PP) results

	Week 6		Week 12	
	ITT	PP	ITT	PP
Supervised	25.1 (9.8)	26.7 (9.0)	50.8 (23.2)	55.2 (19.7)
Home-based	24.8 (17.6)	33.0 (11.5)	46.9 (33.7)	61.8 (22.7)

6.3.4.10 Body composition

All three measures of body composition, collected using dual energy X-ray absorptiometry, were very stable throughout the entire intervention, despite effect sizes indicating that some differences in body fat were present at baseline ($d = 0.31$ for ITT; $d = 0.59$ for PP). Over the course of the entire 12-week period, the groups responded almost identically to the exercise intervention and fluctuations in mass did not exceed 0.9 kilograms at any time point (Table 6.34). There was, however, an interesting trend whereby the initial response to exercise resulted

in a decrease of muscle mass. This trend was reversed during the second half of the intervention, with muscle mass returning to baseline levels.

Table 6.34

Body composition represented as muscle mass, fat mass, and percentage body fat for the two exercise groups. Results are presented as mean (SD) for both the intention-to-treat (ITT) and per-protocol (PP) analyses

		Muscle mass		Fat mass		Body fat %	
		Supervised	Home-based	Supervised	Home-based	Supervised	Home-based
	Baseline	50.9 (15.6)	53.4 (7.2)	30.5 (7.5)	34.3 (16.8)	36.7 (3.8)	36.3 (10.9)
ITT	Week 6	50.0 (15.4)	53.0 (6.7)	30.3 (7.8)	33.9 (16.7)	36.8 (3.8)	36.2 (10.8)
	Week 12	50.8 (16.0)	53.2 (7.2)	30.0 (8.1)	33.6 (16.1)	36.3 (4.2)	36.0 (10.4)
	Baseline	49.4 (15.8)	53.4 (16.2)	29.7 (7.5)	36.9 (18.0)	36.7 (4.0)	38.1 (10.1)
PP	Week 6	48.5 (15.5)	52.8 (7.3)	29.4 (7.8)	36.3 (18.0)	36.9 (4.0)	37.9 (10.0)
	Week 12	49.3 (16.2)	53.6 (8.6)	29.1 (8.0)	35.6 (17.3)	36.3 (4.4)	37.3 (9.4)

6.3.4.11 Maximal strength

Maximal upper and lower body strength increased over the duration of the intervention for both groups (Figure 6.17, Table 6.35). Chest press results showed an inconsistent pattern for the home-based participants, with an increase of 8.5% from the intention-to-treat analysis ($32.8 \pm 16.7\text{kg}$ to $35.6 \pm 15.2\text{ kg}$) being much lower than the per-protocol change of 18.5% ($27.0 \pm 10.5\text{kg}$ to $32.0 \pm 10.1\text{kg}$). Nonetheless, no group interaction effect was found. There was a more consistent pattern of results for the leg press outcomes with the supervised group increasing by 29.4% and 30.3% according to ITT and PP analyses, respectively. This exceeded the increase in leg strength of the home-based group, which improved by 9.9% and 14.0%. Furthermore, a statistically significant interaction was presented for the ITT leg press outcomes ($p = .048$), but not for the PP results. This was due to the initial training response, which resulted in a significantly superior strength (+10.9kg) for the supervised group over the first 6-week period ($p = .046$). It should be noted, however, that one participant allocated to the supervised group was unable to perform the maximal leg press on medical advice. Effect sizes agreed with the statistical results and found small to moderate benefits for supervised training to increase maximal lower body strength more than home-based training over the entire 12-week intervention ($d = 0.53$ for ITT; $d = 0.40$ for PP).

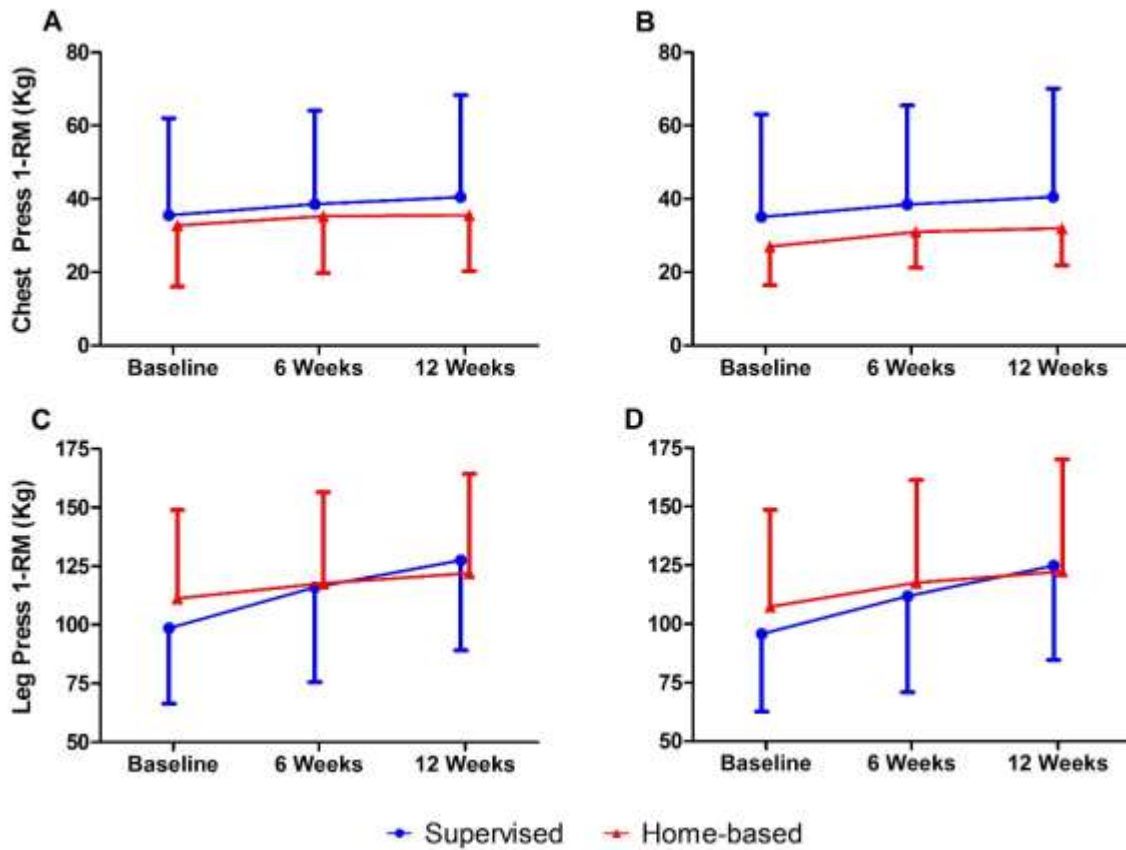


Figure 6.17. Maximal chest and leg press strength for the supervised and home-based exercise groups. Results are presented for intention-to-treat (A and C) as well as per-protocol (B and D) analyses.

Table 6.35

Maximal chest and leg press strength results for the two exercise group for both intention-to-treat (ITT) and per-protocol (PP) analyses

		Chest press (kg)		Leg press (kg)	
		Supervised	Home-based	Supervised	Home-based
ITT	Baseline	35.6 (26.4)	32.8 (16.7)	98.6 (32.2)	111.3 (37.6)
	Week 6	38.6 (25.5)	35.3 (15.5)	116.0 (40.4)	117.8 (38.8)
	Week 12	40.5 (27.8)	35.6 (15.2)	127.6 (38.5)	122.0 (42.3)
PP	Baseline	35.1 (28.0)	27.0 (10.5)	95.8 (33.2)	107.3 (41.3)
	Week 6	38.5 (27.0)	31.0 (9.8)	111.8 (40.9)	117.6 (43.7)
	Week 12	40.6 (29.5)	32.0 (10.1)	124.8 (40.2)	122.3 (47.9)

6.3.4.12 Aerobic fitness

Time to complete the 400m walking test showed a steady decrease in both groups which resulted in no interaction effect from the two different exercise programs (Figure 6.18, Table 6.36). Per-protocol results differed by 6.2% at baseline ($236.65 \pm 40.43s$ vs $251.39 \pm 20.63s$).

However, this did not influence the rate or magnitude of change throughout the intervention. The intention-to-treat results indicate that after the 12-week intervention the supervised group improved their mean time by 18.64 seconds whereas the home-based group only decreased the time to complete the walking test by 11.84 seconds. This 6.8 second difference represented a small effect favouring the supervised group for improvement in aerobic fitness ($d = 0.20$).

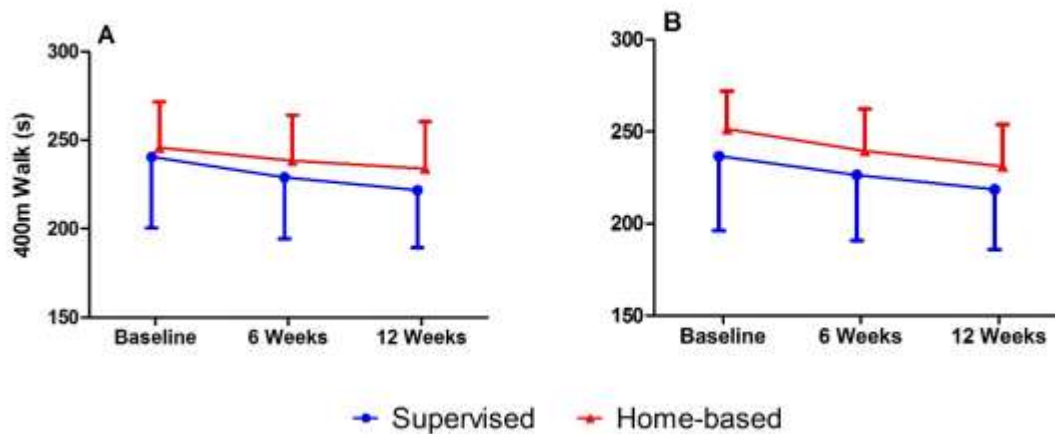


Figure 6.18. Time to complete the 400m walk for the supervised and home-based exercise groups. Results are presented for intention-to-treat (A) and per-protocol (B) analyses.

Table 6.36

Time (s) to complete the 400m walk test for the exercise groups presented as mean (SD)

	Intention-to-treat		Per-protocol	
	Supervised	Home-based	Supervised	Home-based
Baseline	240.51 (40.02)	245.79 (25.88)	236.65 (40.43)	251.39 (20.63)
Week 6	229.00 (34.54)	238.40 (25.80)	226.48 (35.65)	239.55 (22.77)
Week 12	221.87 (32.60)	233.95 (26.54)	218.57 (32.75)	231.01 (22.88)

6.4 Discussion

These are the first reported data that suggest exercise is beneficial for alleviating depression in already depressed cancer survivors, irrespective of cancer type, stage, or other medical and lifestyle factors. This finding confirmed the first hypothesis and also demonstrated improvement in several of the other secondary psychological outcomes. The second hypothesis examining the physical and psychological outcomes between two different exercise prescriptions revealed that there were very few differences over the 12-week intervention, with the most prominent difference reflected in lower body strength. This finding suggests that both of the exercise programs were able to elicit positive and clinically-relevant responses in a

relatively short time frame. However, the rate of change was variable, with home-based exercise typically displaying more rapid initial improvements before slowly declining; whereas the supervised group steadily continued to increase over the entire intervention.

6.4.1 Depression

Over the 12-week intervention period there was a 44.8% decrease in the mean depression score for the combined exercise group compared to a 7.6% increase for the control group according to the ITT analysis. Similarly, the per-protocol results showed a 49.9% decrease in level of depression for the exercise group, whereas the control group increased by 6.2%. Although no previous research has examined the effect of exercise on depressed cancer survivors, the results are in line with other findings that have reported 40-55% decrease in depressive symptoms compared to only 20-30% decrements in control groups (Dunn et al., 2005; Knubben et al., 2007; Singh et al., 2005). While the decrease in depressive symptoms is similar for the intervention groups, the control group in the current study did not show any decrease over time which may be attributable to living with cancer, which in many cases is a terminal and progressive illness, or the fact that the control group in the current study was not engaged in any “placebo” activity, and, therefore, had no benefit from social interactions with other participants or health care providers (Singh et al., 2005) or did not perform a low intensity stretching type program as employed by others (Dunn et al., 2005; Knubben et al., 2007).

A large effect ($d > 1.0$) was found to favour exercise compared to no intervention and only usual care. However, when per-protocol analysis was employed to examine the effect on depression, the location, level of supervision, and type of activity performed influenced the results attained. It was found that, during the first six weeks of the intervention, there was a more rapid and greater decrease in depression ($d = 0.5$) for the participants that were allocated to the home-based exercise group. Although the trend reversed after the initial 6-week period, whereby the supervised group showed greater improvements, this may have been due to a floor effect, with little room for improvement in the home-based group (mean HADS-D after 6 weeks = 4.40). This was indicated by the level of depressive symptoms still being higher after 12 weeks in the supervised group (6.00) than it was after 6 weeks in the home-based group. Since this result was not replicated in the ITT analysis, there is an indication that, although home-based training was an effective exercise modality, it may also likely result in a higher dropout rate, especially for those patients with the most severe levels of depression. However,

further research is needed to confirm this finding. Previous research has indicated that a considerable and rapid reduction in depression (-41%) was possible after completing a brief 10-day aerobic exercise intervention (Knubben et al., 2007). This reduction in depression is in line with the results above, particularly for the initial component of the home-based program.

The 6-week findings appear to contradict Brown and colleagues (2012), who suggested, in a recent meta-analysis, that supervision during exercise is associated with lower depression scores. However, it is possible that inclusion in either exercise group may have satisfied conditions associated with improvements due to supervision, as participants in the home-based group maintained communication through weekly telephone calls during which exercise routines and exercise engagement was discussed. Indeed, it has previously been reported that breast cancer survivors were able to achieve similar exercise outcomes regardless of whether the program was delivered in a face-to-face manner or via telephonic communication (Hayes et al., 2013). However, depressive symptoms were not examined in the above study with only 4 of the 194 participants meeting clinically relevant cut-offs for depression according to the Greene Climacteric Scale at baseline (Hayes et al., 2013). Therefore, the finding that depression can also be successfully managed and improved through both supervised and home-based exercise for cancer survivors is important and clinically relevant.

The results are also supported by research examining depression and exercise in the non-cancer setting. For example, Blumenthal and colleagues (2007) found no significant differences between home-based exercise and supervised aerobic training for reducing depression in depressed individuals measured using the Hamilton Depression Rating Scale (Blumenthal et al., 2007). The groups in the Blumenthal (2007) study were, however, prescribed identical training stimuli (intensity, frequency, exercise modality), whereas the current study did not attempt to match stimulus or intensity, rather focusing on a pragmatic approach that examined two commonly prescribed exercise alternatives. More interestingly, the findings that depressive symptoms improved in both groups appears to conflict with previous findings that suggested intensity was proportional to decrements in depression when resistance training is included as part of an exercise program (Singh et al., 2005). The supervised group performed resistance exercise in the range of 6 to 10-RM similar to the 80% intensity used by Singh and colleagues to train their high intensity group, compared to the 20% 1-RM to train the low intensity group (Singh et al., 2005). Although no specific home-based resistance exercise was prescribed or recommended in the current study (see Appendix K), many of these participants (60%)

commenced or continued with resistance type exercise (results not reported above). Nonetheless, the intensity of this home-based resistance training was much lower than the supervised group (e.g., use of lightweight hand-held dumbbells reported by the participants) and, therefore, in accordance with previous findings, this component of the training, should not have been as beneficial. The optimal type and intensity of exercise to manage depression remains unclear. However, low intensity resistance training supplemented with aerobic exercise provided a significant benefit to depressed cancer patients, similar to the enhancement attained through supervised sessions of higher intensity.

Lack of differences between the two exercise groups may suggest that psychological mechanisms were responsible for the improvement in depression, rather than physiological or physical changes such as strength or aerobic fitness gains. One possibility for improvement in depression in either exercise group could be due to social comparison, as participants became aware that other cancer survivors were experiencing similar depressive symptoms and therefore were able to normalize their situation by comparing themselves to others (Campbell, Phaneuf, & Deane, 2004). Social comparison is more likely to have provided some initial benefit at decreasing depression and distress, since Philip et al. (2013) found that social support was not a strong predictor of depression in cancer survivors that have completed treatment and are in the later stages of survivorship. This suggests that the difference in depression outcomes between the two exercise groups within this study are not related to emerging social relationships and new friendships experienced by the supervised exercise group, who had the ability to interact with other participants. Indeed, it was the more isolated home-based group that displayed more rapid decreases in depression over the initial 6-week period.

The home-based group may have exhibited this initial response due to an increased sense of mastery, an increased sense of self-empowerment and increased motivation. In order to fulfil the requirements of accumulating 150 minutes of exercise per week in a non-supervised, environment the home-based group needed to be more self-motivated and schedule their own sessions. Adding structure and encouraging depressed individuals to adhere to commitments are techniques that have been used successfully to manage depression and are referred to as behavioural activation (Hopko et al., 2011). Moreover, commencing an exercise program results in rapid neuromuscular and cardiovascular adaptation, which results in repeated exercise of a similar intensity feeling progressively easier. When individuals notice that practice and performing a task results in improvement they feel a sense of mastery, and this

feeling of mastery may have resulted in the initial decrease, and short-term benefits, of depression in the home-based group. Yet, exercise adherence decreased over the entire intervention for the home-based group and this may represent a levelling off of improvements and a decrease in interest causing a reduction in effort and motivation, and therefore possibility the inability to maintain these results. Nonetheless, previous findings illustrate that a short 10-day exercise intervention (Knubben et al., 2007) was able to produce an equivalent decrease in depression as a much longer 16-week intervention (Blumenthal et al., 2007). Similarly, exercise used to improve quality of life in cancer survivors has been reported to display greater benefits when short duration interventions are used compared to longer time frames (Ferrer et al., 2011).

One of the proposed mechanisms of exercise to reduce depression is through the distraction associated with engagement in a novel task (Craft, 2005; Craft & Perna, 2004). A reduction in depression is achieved by causing an attentional shift away from the depression, and ruminating thoughts, and towards the exercise task at hand. This principle of distraction may be even more effective in depressed cancer survivors because they are not only distracted from their negative mood but also from the cancer and the adverse treatment effects. For example, it has been reported that cancer survivors enrolled in a group exercise program created a sense of community based on their unifying characteristics as members of an exercise program, and less on the fact that they were cancer survivors (Midtgaard et al., 2006). The power of exercise to cause a distraction has also been found with palliative cancer survivors, reporting that exercise helped distract them from feelings of sickness and made them feel more positive (Paltiel et al., 2009).

Although depression was considered the primary outcome in the current study, it is known that many of the other variables are also influenced by exercise and may also influence depressive status. For example, Payne and colleagues (2008) examined the effect of a 14-week, home-based, exercise intervention on a group of 20 breast cancer patients. Four 20-minute walking sessions per week improved sleep quality in the exercise group, but did not decrease depression, measured using the CES-D. However, the authors acknowledged that none of the participants had elevated depressive symptoms at baseline (Payne et al., 2008). Nonetheless, the relationship between sleep quality and depression was demonstrated in a 10-week resistance training program that found significant improvements in sleep were correlated with improvements in depression (Singh et al., 1997b). Therefore, it is important to examine how

other physical and psychological outcomes responded to the exercise intervention, as it is likely that there is a relationship between these changes and the change in depression status.

6.4.2 Other psychological outcomes

Intervention effects were also found for changes in anxiety and total distress, both measured according to subjective responses on the HADS. A similar pattern of outcomes was observed to those found for depression, but, particularly for anxiety, there were some noticeable differences.

It has been reported that anxiety is even more prevalent than depression in cancer patients (Korstjens et al., 2010). This appears to be reflected not only in the prevalence, but also in the severity of the scores obtained from the HADS-A in the current study. Despite recruitment targeting elevated depression, the mean score for anxiety at baseline was 9.15 (SD = 3.26) which exceeded the mean score for the HADS-D and also exceeded the cut-off score of 7 which represents the upper limit for 'normal' functioning (Zigmond & Snaith, 1983). This elevated baseline score illustrates that the outcomes reported herein should be considered clinically relevant, even though the HADS-A is not intended to be used as a diagnostic tool, as it has low sensitivity, despite high specificity (Stark et al., 2002).

Similar to depression, physical activity appears to have a protective and therapeutic effect on anxiety (Carek et al., 2011). A recent systematic review, that examined eight randomised controlled trials, published details on the effectiveness of exercise therapy for clinically diagnosed anxiety disorders (Jayakody, Gunadasa, & Hosker, 2014). Due to many methodological differences and a low number of trials, the authors were unable to provide a definitive answer. Nonetheless, it was reported that exercise appears to be beneficial in reducing clinical anxiety, but to a lesser extent than pharmacotherapy (Jayakody et al., 2014).

The current results are in agreement with the available evidence, illustrated by the interaction effect for all three groups ($p = .025$ for ITT). Both exercise groups reduced anxiety levels compared to the control group, which remained constant. The PP results did not replicate this finding, with no significance found. This is likely due to the smaller sample size and the baseline characteristics of the participants that did not complete the trial. Although no significant differences were noted between baseline characteristics of the participants that

withdrew and those that completed the intervention, a moderate effect size calculation ($d = 0.60$) confirms that individuals with higher levels of anxiety withdrew. When the two exercise groups were combined and compared against the usual care control, results for the 12-week intervention matched those reported above. Intention-to-treat analysis illustrated a significant decrease in anxiety in favour of the exercise group ($p = .02$) whereas per-protocol analysis approached significance ($p = .078$). The non-significant result did not influence the effect size calculations, displaying a large effect favouring the exercise ($d = 1.02$) for both analyses.

Similar results have been reported previously in a trial which examined the effectiveness of a 12-week program of either exercise alone or exercise and cognitive behavioural therapy on cancer patients' mental health outcomes (Korstjens et al., 2010). The HADS was used to examine change over time and it was found that in the sample of 147 participants, a total of 43 participants were classified as distressed (i.e., exceeding a score of 10 for either the depression or anxiety subscale of the HADS). The authors reported that both intervention arms were effective at reducing anxiety in the distressed group from a score of approximately 13.1 to 7.5 (Korstjens et al., 2010). This reduction of 43% compares favourably to the outcome for the combined exercise group in the current study (32% for ITT; 37% for PP), considering that the distressed group within the study by Korstjens et al. (2010) had higher baseline levels of anxiety and also received an additional two hours of exercise training per week.

When comparing the two exercise groups to each other, effect size calculations indicated that supervised training was more effective at reducing anxiety ($d = 0.64$ for ITT; $d = 0.33$ for PP). Yet, similar to depression, the home-based group showed a more rapid improvement in anxiety within the initial 6-weeks ($d = 0.31$). Nonetheless, that gain was completely reversed in the second training period. This difference in effect size is largely due to the change in baseline HADS-A score (9.00 to 6.80) for the home-based group, due to the withdrawn participants, but nonetheless confirms that supervised training provided a greater benefit to decrease anxiety.

Although it has been suggested that there is a close relationship between anxiety and depression (Reidy & Keogh, 1997), the results described above suggest that using exercise for these affective disorders likely requires a targeted approach. Depression responded most favourably to home-based exercise, whereas anxiety responded best to supervised exercise, particularly over the first half of the intervention. Since there has been considerably less research examining

the effect of exercise on anxiety, particularly in cancer survivors, these results provide a useful addition to the current body of knowledge in this field.

The results for depression and anxiety from the HADS when combined together can be reported as a single measure of psychological distress. Within the current study, distress results mirrored depression outcomes, when results were analysed relative to the control group. However, when comparing between the two modes of exercise delivery, the influence of anxiety becomes more apparent. Effect size calculations favoured supervised training for the ITT analysis ($d = 0.44$), but showed no effect for the PP analysis because the two independent variables of depression (home) and anxiety (supervised) responded better to different exercise modalities.

The mental health composite (MHC) score (SF-36) reflected positive responses to exercise initiation for both exercise groups, whereas the control group declined over the 12-week intervention. There was similar increase in MHC scores between the two exercise groups, which may suggest that the commencement of, and commitment towards, any exercise program is able to produce positive mental health benefits. These findings are similar to other researchers that have shown an improvement in mental health for a heterogeneous cancer population suffering sleeping difficulties after an 8-week, home-based walking program (Tang et al., 2010). Tang and colleagues (2010) reported baseline scores of 49.17 ± 11.34 for the exercise group and 45.79 ± 13.29 for their usual care control group and found that after a two month intervention, with exercise prescribed 3x/week (24 sessions) the intervention resulted in a significant between group change (net change of 10.48) with a large increase in the exercise group and a slight decline in the control group (-1.77).

The baseline MHC scores reported by Tang et al. (2010) are very similar to the participants in the current study (39.53 – 43.84) and indicate that both sleep disturbance and depression compromise mental health in cancer patients. However, after the exercise intervention, mental health improved and exceeded the normative T-value, set at 50 ± 10 (Maruish & Turner-Bowker, 2009) and approaches, or exceeds, the mean MHC score of 53.2, previously reported for a large cohort of 22,370 heterogeneous cancer survivors (Weaver et al., 2012).

In line with previous studies reporting compromised sleep quality for cancer patients (Palesh et al., 2013; Payne et al., 2008; Tang et al., 2010), the sleep quality of the participants within the current study was also compromised. This was unsurprising due to other research indicating

that sleep disturbance is a common side-effect of depression (Tylee & Gandhi, 2005) and is one of the diagnostic criteria used to assess major depressive disorder according to the Diagnostic and Statistical Manual for Mental Disorders. Therefore, the improvement in depression was expected to be associated with improved sleep quality. After the 12-week intervention, sleep quality improved for the combined exercise group and remained unchanged in the control group resulting in a small to moderate effect favouring exercise ($d = 0.41$ for ITT, $d = 0.52$ for PP). However, this difference was not large enough to result in statistical significance.

Tang and colleagues also examined sleep quality (PSQI) in their exercise study with cancer survivors who had reported high levels of sleep disturbance and found that a home-based walking exercise program improved sleep quality (13.42 ± 2.27 to 9.78 ± 3.06) over 24 exercise sessions performed 3x/week for eight weeks. This improvement was statistically significant ($p < .001$) compared to their delayed care control group that showed no change in sleep quality (13.17 ± 3.11 to 13.11 ± 2.89) (Tang et al., 2010). The current findings are similar to those reported by Tang and colleagues (2010) which suggests that the lack of statistical significance may have been due to the small sample size, which was not sufficiently powered to detect a change in this secondary outcome.

A similar study by Payne and colleagues (2008) examined the effects of a 14-week, home-based exercise program for breast cancer patients with high levels of self-reported fatigue. A randomised control trial found that 20 minutes of walking performed four days per week had a positive effect on sleep quality (PSQI) for the exercise group and an increase in sleep disturbance for a usual care group. The exercise intervention did not have any significant effect on depression (CES-D) within or between groups. However, the authors acknowledged that none of the participants in the study met cut-off levels for depressive symptoms (Payne et al., 2008). Others (Singh et al., 1997b) have however reported that improvements in sleep are correlated with improvements in depression and, therefore, this relationship should continue to be explored.

Potential underlying pathophysiological mechanisms, such as cytokine and metabolic regulation, which regulate sleep quality are also closely linked with the potential to induce depression (Dantzer et al., 2008). However, there is potential for the relationship between depression and sleep to be bi-directional, since poor sleep quality and duration can stimulate

the release of pro-inflammatory cytokines (Palesh et al., 2013). Although no biomarkers were measured in the current study, at no stage did sleep quality results average below a score of 5 that indicates good sleep quality (Singh et al., 1997b). Therefore, the improvements above may not have been large enough to be considered clinically meaningful and, because sleep quality did not decrease below the threshold for normal function, it is possible that the positive primary outcome of the intervention (reduction in depression) may not have been sustained once the exercise program was terminated. No follow-up measures were recorded to confirm this suggestion, however, a previous study suggests that exercise treatment does reduce the likelihood of relapse of depression even in clinically diagnosed patients, but only if exercise is maintained beyond the period of intervention (Babyak et al., 2000).

The current findings indicate that exercise has a positive effect of satisfaction with life, confirming the first hypothesis of this trial. Satisfaction with life is a global measure, and, in contrast to many other scales, does not provide any anchors upon which measurement is predicated. Instead the individual is asked to assess their life as a whole (Pavot & Diener, 1993). The beneficial results obtained from exercise therefore indicate that overall well-being was increased with exercise, and that positive mood adjustments transcended into other aspects of life. The group by time interaction comparing all three groups was significant ($p < .001$), and this was mostly attributable to the increase in satisfaction with life for the supervised exercise group and the decrease of satisfaction for the control group over the entire 12-week intervention ($p < .001$ for ITT; $p = .003$ for PP).

This was confirmed when the two exercise groups were compared to one another with outcomes favouring the supervised group, over the 12-week period ($p = .020$, $d = 0.80$ for ITT; $p = .035$, $d = 0.79$ for PP). Initially, the home-based group showed a similar increase in satisfaction with life, but thereafter decreased close to baseline levels. This finding opposes the second hypothesis of the study and is consistent with the outcomes for depression, anxiety, and distress suggesting that the longer the duration of the exercise program, the more important supervision and structure becomes at achieving positive psychological outcomes and further confirms that the exercise environment does influence psychological outcomes. Indeed, only the supervised group were able to make a categorical shift for 'slightly dissatisfied' (score between 15 and 19) to 'slightly satisfied' (score between 21 and 25) according to the criteria set for the SWLS (Pavot & Diener, 1993).

Nonetheless, both exercise groups increased their level of satisfaction with life over the course of the intervention, whereas the control group decreased over the same period. Therefore, when the exercise groups were combined there was a significant and moderately beneficial effect found ($p = .007$; $d = 0.73$) for the ITT analysis and stronger effect found for the PP analysis ($p = .026$; $d = 0.83$). These findings differ to those reported from an exercise intervention with colorectal cancer patients, who had recently completed resection surgery, which found no change in SWLS after a 16-week home-based aerobic program (Courneya, Friedenreich, Quinney, et al., 2003). Despite their recent surgery, the participants ($n = 93$) in that trial reported higher SWLS scores (~ 26.2) at baseline (Courneya, Friedenreich, Quinney, et al., 2003) than those in the current study. This reflects the fact that satisfaction with life is a subjective measure that does not always match objective assessments (i.e., people recently completing surgery could be expected to be less satisfied with life due to health problems, but this is not the case) and that mental illness is the most likely cause for decreased satisfaction with life (Daig, Herschbach, Lehmann, Knoll, & Decker, 2009). It is likely that the decrease in depression, and anxiety, resulting from the exercise was able to enhance satisfaction with life in the current study.

The baseline scores for the self-efficacy measure (CASES) for the entire sample in this study (123.2 ± 33.7) was much lower than previously reported results for treatment-resistant recurrent (140.8 ± 27) or advanced prostate cancers with metastatic disease (140.3 ± 28) (Northouse et al., 2007). It has been reported that measuring coping specific self-efficacy is an indicator of a cancer survivor's ability to manage their life around the disease and is also closely related to feelings of hopelessness (Kershaw et al., 2008). Therefore, any improvement in coping self-efficacy should be considered a positive outcome. The current intervention resulted in a non-significant interaction between all three groups, but a significant time effect, with all groups increasing cancer self-efficacy over a 12-week period. It is necessary to consider that the participants in this trial were recruited based on depression, but the depression was not necessarily a consequence of being a cancer survivor. Nonetheless, when the exercise groups were combined and compared to the control group, effect size calculations revealed a small, but favourable result for exercise ($d = 0.40$), suggesting that engagement in exercise may result in increased coping self-efficacy in depressed cancer survivors. The precise mechanisms for this effect are unknown but one reason may be that the exercise alleviated feelings of distress (depression and anxiety, see section 6.3.2.3). Further, significant correlations indicated that increased self-efficacy over the 12-weeks, for the entire cohort ($n = 32$), independent of group

allocation, was related to a decrease in depression ($r = -.573, p < .01$), anxiety ($r = -.574, p < .01$) and total distress ($r = -.637, p < .01$). Although this finding does not demonstrate causality, it is consistent with the idea that self-efficacy mediates mood and distress in cancer survivors. Similarly, Philip and colleagues (2013) found that self-efficacy, measured using the Cancer Behaviour Inventory, was the primary predictor of depression (CES-D), accounting for 43% of its variance in a study that examined 124 heterogeneous cancer survivors. The correlation results within this trial and previous literature suggest that exercise may be an effective means to increase generalised self-efficacy, and thereby reduce depression, even when self-efficacy is not a specific goal of the exercise program.

6.4.3 Body composition, strength, fitness, and physical health

The strength, fitness and body composition results were recorded to validate the exercise program and explore how the two exercise groups differed. Completing an exercise program should influence these variables in a positive manner, and it should be expected that supervised training in a specialised exercise facility would be more beneficial for physical and physiological enhancements. The supervised program monitored the intensity of the aerobic exercise to ensure participants were exerting themselves, and included resistance-based exercise focussing on strength gains and muscular hypertrophy.

Commencing an exercise program results in rapid neuromuscular adaptations as neural activation is increased to recruit additional muscle fibres during the excitation-contraction coupling (Gabriel, Kamen, & Frost, 2006). The type of exercise commenced will influence the specific adaptations along, with other prescriptive factors such as intensity, duration, and recovery. Furthermore, these adaptations do not always occur simultaneously, as described above, resistance training will result in a neural response before any muscle hypertrophy, which may take up to eight weeks before increases are observable (Folland & Williams, 2007). Certain medical treatments can also moderate the effects of exercise training on body composition changes in cancer survivors. For example, it is known that chemotherapy and hormonal therapies influence the ability of a patient to control their body weight (Schmitz et al., 2010). Interestingly, the results of the current study found that, after the initial 6-week training period, whole body muscle mass decreased, albeit slightly for both groups. Despite the expected decline in body fat, the overall composition for the supervised group regressed such that the total percentage of body fat was higher, whereas the home-based group slowly declined

their percentage of body fat as expected. By the conclusion of the intervention, muscle mass had returned to baseline and fat mass continued to be slightly lower thereby improving body composition outcomes. These small and non-significant changes are in line with expectations as it has been reported that exercise alone is unlikely to alter body composition when it is performed only twice a week and is not performed in conjunction with other health modifications such as a calorie-controlled diet (Miller et al., 1997).

No measures of body composition were recorded for the control group. However, based on the known metabolic dysfunction and sleep disturbances, both of which are associated with increased adiposity, it is likely that the influence of exercise may be underestimated in this study had it been compared with the non-exercise control group. For example, Courneya and colleagues (2007) reported an increase in percentage of body fat (+1.0%) and fat mass (+1.2kg) in a control group of women undergoing chemotherapy for breast cancer, whereas the two exercise intervention groups performing either aerobic or resistance training three times per week for the duration of their treatment maintained their baseline level of percentage body fat, by increasing muscle mass, despite increasing their overall fat mass (+0.7kg for resistance; +0.5kg for aerobic). Further, previous research suggests that cancer survivors commencing exercise, derive favourable alterations in body composition, particularly decreased fat mass, when compared to a non-exercising control group (Courneya, Friedenreich, Sela, et al., 2003).

Strength has been reported to increase by approximately 20-30% after a combined aerobic and resistance training exercise intervention in sedentary, but otherwise healthy, individuals (Chtara et al., 2008). This type of concurrent exercise has also previously resulted in increased leg press (+36.8%) and chest press (+11.0%) maximal strength and cardiovascular enhancements (+4.5%) in cancer survivors (Galvao et al., 2010). The changes reported in the current study are similar in magnitude to those reported by Galvao and colleagues (2010), who examined exercise outcomes in prostate cancer patients undergoing androgen deprivation therapy, following a very similar exercise protocol to that of the current study. The current study found that maximal chest press strength increased between 8.5% and 18.5% (depending on the analysis and the exercise group), and maximal lower body strength increased between 9.9% and 30.3%. In accordance with the principle of specificity, the smaller increases in strength were found in the home-based groups, that did not undertake supervised strength training (Smith, 2003). However, it is not uncommon for strength gains to be found after aerobic exercise training and the increases reported here are similar in magnitude to a previous

aerobic exercise group that displayed an increase of 13.7% for lower body strength and 11.8% increase for upper body strength (Courneya et al., 2007).

An explanation for the increased strength of the home-based group may be due to the fact that 60% of the group performed several sessions of resistance training throughout the 12-week intervention. In particular, two home-based participants were able to increase their chest press strength by 31% and 83% after performing 22 and 35 resistance training sessions during the intervention. Furthermore, within the supervised resistance training, only one exercise was performed with the goal of increasing chest strength. This single exercise may not have evoked a training response great enough to exceed the upper body strength benefits obtained by the home-based group. Lower body adaptations consistently favoured the supervised group and can be explained by the greater number of lower body exercises performed during each session (leg press, leg curl, leg extension, and step up) all of which can contribute to neuromuscular requirements leading to increased leg-press strength.

Aerobic exercise was performed by both groups, and, therefore, an improvement in cardiorespiratory fitness was expected for both groups. However, the ability to set and monitor the intensity for the aerobic component during the supervised sessions, provided justification to hypothesise that the supervised group would exhibit a greater training response. This hypothesis was not confirmed and it was found that both exercise groups improved their fitness and physical functioning equally (5% to 8%). The magnitude of improvement was again very similar to the 5% improvement reported when the same 400m walk test was used to assess aerobic fitness in prostate cancer survivors (Galvao et al., 2010).

Although the 400m walk test employed has been validated as a submaximal test that can accurately predict maximal aerobic capacity, the test was designed for an aged population (Simonsick et al., 2006) and, therefore, may not be sensitive enough to determine maximal changes in the current study. The average age of the sample was 58.9 years, which is more than 11 years younger than other studies that have used the same test to examine aerobic capacity and cardiovascular health (Newman et al., 2006; Simonsick et al., 2006). In fact, the mean time to complete the test fell well within the lowest quartile of scores from a sample of 1,761 participants that completed the test as part of a large cohort study examining longitudinal health outcomes (Newman et al., 2006). The proficient performance of the participants, all of whom had received GP consent to commence an exercise program, along with specific instructions of

the assessment (participants are only to walk and cannot jog or run), may have limited the ability of this test to indicate a training response. Therefore, a limitation of the current study was the lack of a graded exercise test to volitional exhaustion. Consideration was given to include a maximal test within the assessment protocol, but was not feasible due to the need to have a medical practitioner present at each testing session.

Similar to the body composition assessments, the control group did not perform the strength and functional tests, therefore the results presented may be compromised. It is speculated that a greater net gain would have been found by assuming that the control group would have decreased strength and function. A longitudinal decrease can be considered very likely for a usual care control group, because it is well established that aerobic capacity and functional ability decline with a sedentary lifestyle and the increased levels of fatigue and reduced activity associated with depression (Brunet et al., 2014; Nabkasorn et al., 2006).

Subjective measures of physical health (PHC) were recorded for all three groups, using the physical health composite of the SF-36. No significant responses were found when comparing all three groups or between the combined exercise group and the control group. This finding is in accordance with previous research illustrating that exercise programs may not influence the physical health component of health-related quality of life (Tang et al., 2010). Only the composite scores were examined and presented, however closer examination of the subscales that comprise this overall measure may be more revealing.

The lack of difference in strength, aerobic and functional performance between the two different exercise groups, along with the non-significant responses reported for PHC suggest that the exercise settings were equally effective at eliciting physical and physiological enhancements. However, since the physiological results could not be compared to a non-exercising control group, it is important to not rule out psychological factors as also contributing to positive mental health outcomes. Some possible mechanisms, which were not examined within this research, for the improvement in depression independent of physical or physiological outcomes may be that mental health and quality of life increase in cancer survivors who feel more in control of their lives (Bloom et al., 2007), and those patients and survivors who take positive action to deal with their cancer diagnosis and treatment-related effects have better mental health outcomes (Roesch et al., 2005). The act of commencing or enrolling in the program may be sufficient to elicit feelings of self-empowerment and

proactivity (Emslie et al., 2007; McGrath, Joske, & Bouwman, 2011; Milne et al., 2007), which could translate to improvements as reported above.

6.4.4 Exercise uptake and adherence

It is known that individuals diagnosed with depression accumulate less physical activity than the non-depressed population (Ussher et al., 2007). One reason for this may be attributed to social withdrawal that is common in depression, which could exacerbate an already sedentary lifestyle. Therefore, there is a need to encourage this group to engage in activity, not only for their depression, but also to reduce the risk of other chronic illness such as obesity, type 2 diabetes, and cardiovascular disease.

Group by time results revealed no significant interaction effect for either the total amount of time spent exercising or the relative intensity of the activity performed. This suggests that positive changes reported above, favouring the exercise group/s compared to the control group, occurred independently of any change in physical activity. Therefore, psychological mechanisms such as mastery, distraction, or increased self-esteem are likely responsible for these changes (Strohle, 2009). However, due to the small sample size within the current study, future trials would be necessary to confirm this finding.

Nonetheless, the results indicate that both exercise groups increased their total amount of physical activity over the intervention and that this increase coincided with a greater amount of higher intensity exercise. Effect size calculations were marginally favourable for an increase in total exercise time favouring the combined exercise group compared to the control ($d = 0.28$), but larger ($d = 0.60$) favouring the combined exercise groups' increase in intensity of physical activity. This confirms that intensity can be increased independently of increasing the total duration and provides some rationale to suggest that the positive outcomes related to psychological mechanisms may also depend on an increase in exercise intensity. It may, therefore, also be possible that physiological changes do mediate these outcomes, but this cannot be confirmed since the control group were not subjected to the same test battery.

The total number of exercise sessions performed over the 12-weeks was similar between the two groups, indicating that exercise adherence and uptake was not impacted for those participants that were allocated to the home-based group. Nonetheless, this required more

motivation, as the participants in that group did not have the routine of a regular commitment. It was noticeable that the number of sessions completed decreased for the home-based group for the second 6-week block, whereas the supervised group increased the total number of sessions (Table 6.33). This trend appears to relate to the stagnation or deterioration in positive outcomes found for the home-based group for the second half of the intervention, whereas the supervised group continued to display positive adaptations. Unfortunately, due to the small sample size and variable exercise programs that were performed, it is not possible to examine this relationship more closely.

Although many issues were encountered with recruitment and engaging eligible participants to enrol in the research program (discussed below), once the participants commenced the program, adherence was high and there were not many withdrawals during the intervention period, particularly for the two exercise groups. Only one participant withdrew from the supervised program, reporting that he was not enjoying the sessions, and there were no adverse events reported due to training. Including the participant that withdrew, a total of 21.3/24 supervised sessions were adhered to, which represents an 88.8% compliance rate. Excluding the participant that withdrew after completing 11 supervised sessions in the initial 6-week period, there was a 93.3% compliance with supervised training. Of the eight home-based participants, two withdrew based on allocation as they were only interested in participating if they were allocated to the supervised arm, and the third participant lost to follow-up remained in the program, but was unable to attend testing sessions due to personal circumstances, and could therefore not be included in the results. Most participants ($n = 5$, 36%) lost to follow up were in the control group, however, since all communication was via post, no reasons were collected when they withdrew. The small sample size resulted in each individual representing a large net percentage of their entire group. Therefore, despite only 3 participants being lost to follow-up in the home-based group, this represented 37.5% of the group. These low numbers may skew the ability to compare retention rates in this study with others that have employed a much larger sample.

6.4.5 Recruitment and adherence

Eligibility into the study was assessed by multiple methods to ensure that only cancer survivors with co-morbid depression were enrolled. This involved initial contact with 1309 patients identified by their specialist (oncologist, surgeon, and urologist). A total of 492 replies were

received, including 53 excluded cases, which represented a 38% response rate. This was in line with an expected 40-60% response rate reported by others that have performed questionnaire-based research with cancer survivors (Penson et al., 2003; Sharpley, Bitsika, & Christie, 2009; Sharpley & Christie, 2009). Screening identified 78 eligible participants, out of the 439 responses, that were able to be assessed for depression. This represents a point prevalence for depression of 17.8%, which is in line with a recently published study that examined 124 heterogeneous cancer patients and found that 19% could be considered depressed based on the clinical cut-off of the CES-D (Philip et al., 2013).

Enrolling cancer survivors into exercise studies presents many challenges and enrolment rates, relative to the number of cases screened, are typically quite low. For example, Payne and colleagues (2008) were able to enrol only 20 of 58 (35%) eligible breast cancer survivors receiving hormone therapy and experiencing elevated levels of fatigue. Logistical issues, such as travel arrangements, and time commitments, were provided for not entering the study (Payne et al., 2008). This was similar to the 34% enrolment (242 of 736) of breast cancer patients initiating chemotherapy treatment into a randomised controlled exercise trial (Courneya et al., 2007). Reasons provided for refusing participation were a lack of interest in exercise or other logistical reasons such as distance, time, and travel arrangements (Courneya et al., 2007). Accounting for all eligible participants that enrolled into the current study ($n = 32/78$), there was an uptake of 41%, which is slightly higher than the trials reported previously, but lower than others that have reported enrolment of eligible cancer survivors between 58% and 63% (Galvao et al., 2010; Thorsen et al., 2005). These uptake rates are variable and largely depend on the level of screening performed and the method of recruiting participants before eligibility is confirmed. When eligibility is not set against a specific physical or psychological disorder, more participants are able to be considered. However, this increases the number of exclusions that are based on lack of interest or a refusal to participate with no further comment provided (Segal et al., 2001).

These results, along with other findings, suggest that it may not be the exercise activity that limits uptake of cancer patients into voluntary and structured programs, but rather a lack of desire to commit themselves to any fixed activity. A nurse-led, psycho-education intervention program for the management of depression in cancer patients resulted in the enrolment of 220 patients screened for depression, representing only 52% of the eligible sample (Strong et al., 2008). Many of the participants that refused enrolment speculated that the program would not

be of benefit to them ($n = 83$), and 75 additional patients were excluded by the researchers due to a combination of logistical, communication, and medical reasons (Strong et al., 2008).

Therefore, it appears that the lack of uptake in the current exercise program was more likely related to the recruitment of cancer survivors and less likely due to their depression status. Despite depression being known to be associated with increased reclusive behaviour and withdrawal from social activities (Brunet et al., 2014), the uptake of exercise in previous research trials recruiting depressed participants has been much greater than reported for cancer survivors. For example, Krogh and colleagues (2009) assessed 293 clinically depressed patients for eligibility and reported that only 14 (less than 5%) participants refused involvement in the trial. In a second comparable study, approximately 19% of eligible participants with diagnosed major depressive disorder declined involvement in a randomised controlled trial examining the effect of exercise and pharmacotherapy on depression (Blumenthal et al., 2007). These examples indicate a superior enrolment rate compared to exercise studies for cancer survivors. One possible reason for this may be that lifestyle intervention programs for depressed individuals have used specific and targeted recruitment for clinical depression, compared to programs for cancer survivors who may be experiencing a broad range of adverse effects, or indeed may not have any.

Recruitment was plagued by many challenges. However, adherence to the program presents a second challenge to the integrity of the research. It was notable that some secondary outcomes were influenced by the analyses used, with different significance reported when intention-to-treat was compared to per-protocol outcomes. This occurred despite no statistical differences in baseline results compared between the ITT and PP samples. Due to the small sample size, the last known result carried forward does not appear to provide accurate representations of the outcomes. This is especially true for the depression and anxiety results, as indicated in a previous study that examined the psychological profiles of oesophageal cancer survivors over a 12-month period (Dempster et al., 2011). The authors found that, one year after a baseline screening survey was performed, not a single individual improved their psychological status. More than three-quarters (76%) of the 189 survivors surveyed displayed elevated levels of depression and 55% also reported higher rates of anxiety (Dempster et al., 2011). Therefore, in the current study, those participants that were lost to follow-up are more likely to suffer with deteriorating mental health, than to maintain the previously reported outcome.

6.4.6 Limitations

Certain limitations of the study have been acknowledged throughout. However, it is important to reiterate two main drawbacks on the generalizability of the current findings. First, despite imposing strict recruitment measures to ensure a sample of cancer survivors with comorbid depression, the determination of depression was adapted from self-rated questionnaires and no clinical examination was performed. The screening protocol used in the present study has not been validated against “gold standard” clinical diagnostic assessment and, therefore, the sample may not all have met diagnosis for clinical levels of major depressive disorder. Further, due to the different entry criteria for this study, it was not possible to run secondary analyses examining the number of participants that no longer met clinical caseness after completing the intervention. Only 17 participants entered with a HADS-D score exceeding the caseness cut-off of greater than 10. However, the results from this instrument indicate that the two exercise groups reduced the number of overall depressive symptoms. This finding would likely translate to a positive effect favouring exercise.

One opinion relating to diagnosis of depression suggests that the predetermined threshold for diagnosis according to the DSM may not always be representative of the patient’s actual emotional state (Maj, 2011). If depression does indeed occur along a continuum then stipulating a strict definition to determine severity may lead to ‘misdiagnosis’ in many individuals suffering severely, but displaying an inadequate number of these symptoms. A strict medical definition may be required for purposes of pharmaceutical prescription or other treatment methods, but this is not necessary for the prescription of exercise, which is available to all individuals. Therefore, measuring depression and change in depressive status along a continuum may be the best option for allied health professionals who can refer patients on to appropriate professionals should they notice that depression increases.

Second, the number of participants within this study did not meet initial sample size estimates based on preliminary power calculations. It was expected that 30 participants would be required in each of the three groups to have sufficient power to detect a worthwhile change. However, even with only 32 participants that were eventually recruited, significant findings were achieved for many key variables, including the primary outcome of depression. Due to this low sample size, the results should be interpreted with caution and the study should be considered as a feasibility study with a larger randomised controlled trial required to confirm results reported herein.

Other important factors to consider include a non-randomised control group that did not complete any physical or physiological testing. Therefore, it remains unclear whether there is a relationship between exercise outcomes (such as muscle size and strength and cardiorespiratory fitness) and affective states. Similarly, as reported above, several of the participants allocated to the home-based group performed resistance training. Therefore, these results can only be used to infer differences, as stated, between supervised clinic-based and non-supervised home-based exercise, but not between resistance training and aerobic training. Furthermore, it has been suggested that a genetic effect may account for the relationship between habitual physical activity behaviour and depression (De Moor, Boomsma, Stubbe, Willemsen, & de Geus, 2008). This may infer that, despite the similarity in baseline measures for all three groups, the control group, which did not consent to the exercise component, may not have responded either psychologically or physiologically in a similar fashion to a cohort of depressed individuals willing to exercise. Therefore, the encouraging results displayed above would need to be confirmed with future trials that impose stricter controls around recruitment and randomisation.

Lastly, this study also did not examine any biomarkers related to mood, exercise, or cancer progression. However, there is emerging research to suggest that depression and cancer are linked through a relationship with pro-inflammatory cytokines and that exercise may be able to mediate this relationship. Therefore, future studies should consider including specific inflammatory markers such as interleukins and tumour necrosis factor alpha amongst others to gain a better understanding of the physiological mechanisms responsible for changes in depression due to exercise.

6.5 Conclusion

This was the first study to examine the effect of exercise on depression in a cohort of cancer survivors recruited with elevated depression levels or already diagnosed with depression. The main outcomes were that either supervised, clinic-based or unsupervised, home-based exercise were effective at reducing depressive symptoms and improving secondary measures of mental health, such as anxiety and satisfaction with life. By the end of a 12-week exercise intervention, most outcomes favoured the supervised training group. However, the rate at which these improvements were attained varied and in most cases the earlier responses were seen in the home-based group.

It appears as though supervision may become increasingly necessary to obtain or maintain mental health benefits as the duration of an exercise program increases. Some suggestions that have been provided to explain the initial and rapid improvements in mental health outcomes due to exercise include the mastery effect, distraction, and increased self-efficacy. However, when the exercise program becomes repetitive and lacks immediate positive feedback, such as improving performance, these mechanisms may fail to remain effective. The results reported in this thesis confirmed that the home-based group performed a greater number of exercise sessions than the supervised group in the first 6 weeks, but failed to maintain their level of motivation. Consequently when the number of exercise sessions began to decline, the positive responses were reversed or plateaued. This inability to effectively self-manage an exercise program over an extended period of time resulted in outcomes favouring the supervised group at the conclusion of the 12 weeks and suggests that self-managed programs may require an additional educational component to support the development of stronger self-regulatory skills.

Unfortunately, the results are confounded by the fact that the control group did not perform any of the physical or functional assessments. This limitation (addressed in chapter 2 of the thesis) resulted in the inability to thoroughly examine the effectiveness of the exercise intervention using objective measurements. Nonetheless, while these outcomes for the control group remain unknown, the intervention groups displayed increases in muscle strength and aerobic capacity (main effects for time, not reported above). Further, the magnitude of these enhancements were sufficiently large, and similar to previously reported outcomes from other exercise studies, to dispute that they occurred as a result of the exercise intervention.

A notable strength of the current study was that no adverse effects were reported as a result of the exercise interventions. Since correctly prescribed exercise is unlikely to cause any physical or psychological harm, and may indeed be beneficial, there appears to be sufficient evidence to include physical exercise within the management plan of all cancer survivors, especially those with elevated levels of depression. However, encouraging the uptake of exercise in cancer survivors presents a great challenge. Within this study only 23% of eligible participants agreed to enrol into the exercise program. Therefore, future research should consider how to ensure depressed, and non-depressed, cancer survivors 'buy-in' to and engage with exercise programs developed to meet their unique needs.

In summary, many cancer survivors suffer high levels of distress and depressive symptoms at some stage throughout survivorship. The most seriously affected will require specialist treatment, from clinical psychologists, psychiatrists, or other health professionals. However, many more may be able to receive adequate treatment through effective and targeted exercise prescription. This three-arm feasibility study was the first to examine the effect of exercise in a cohort of cancer survivors with comorbid depression and, despite the small sample size, results unequivocally supported the beneficial effects of either a supervised clinic-based or home-based exercise program to decrease depressive symptoms compared to usual care. The results also confirmed that the exercise program variables (e.g., activity, intensity, frequency) influence both the overall outcomes attained and the time response to achieve these results. Therefore, when prescribing exercise for mental health outcomes, it is no less important to adhere to the principle of specificity, than it is for physical adaptations. Furthermore, some participants lost to follow-up expressed that they withdrew because they were dissatisfied with their group allocation. Therefore, in order to increase exercise uptake and adherence, the type of exercise prescribed should also account for individual preferences.

CHAPTER SEVEN

Concluding Discussion and Future Research Recommendations

7.1 Concluding discussion

This chapter summarises the findings from the two literature reviews and results from the original research studies undertaken in this thesis. Further, the importance of translating these findings into practice is addressed and suggestions for future research in this area of enquiry are provided.

The work conducted in this thesis was designed to address gaps within the research relating to the role of exercise to improve depression for depressed cancer survivors. At the time when these original research studies (Chapters 4, 5, and 6) were designed, the American College of Sports Medicine had recently published the seminal exercise guidelines for cancer survivors (Schmitz et al., 2010). It was identified that there were an insufficient number of RCTs that had included any measure of depression as an outcome. Further, it was identified that there was a lack of understanding relating to the exercise preferences of cancer survivors with depression, which could limit the ability to translate research findings with non-depressed survivors to those with comorbid depression, a condition experienced by many cancer survivors.

The combined effects of cancer and depression can severely impact upon both quality and quantity of life and, therefore, efforts have been made to examine ways of decreasing depression in cancer survivors. Recent interest has focussed on the therapeutic effect of exercise for depressed cancer survivors and the first literature review (Chapter 2) of this thesis critically examined 12 randomised controlled trials, conducted to date, that reported on the effectiveness of an exercise intervention for cancer survivors. Although none of these trials set out to examine the effects of exercise on depression in depressed survivors, they are the only twelve RCTs examining exercise with cancer survivors that have reported outcomes for depression and included an objective outcome measure that could be used to quantify the success of the intervention itself.

Only four of the studies, providing five comparisons between exercise and non-exercising groups, reported that the exercise produced significant reductions in depression compared to a control group. The critical analysis reported in this thesis found that, for nearly all cases, the mean level of depression at baseline was too low for these outcomes to have any clinical relevance. For those trials that did report elevated depression at baseline, positive changes in depressive status were noted when exercise was able to increase aerobic capacity and was performed under supervision. Further, the results of this critical review highlighted the

considerable differences in exercise programs that have been delivered to date and argued that the exercise variables are of critical importance, but appear to have been overlooked in previous research reviews. Therefore, suggestions for future research were provided which recommend that that exercise programs are well addressed in the reporting of future research and reviews. Secondly, it was recommended that all future RCTs include objective physiological outcome measures that can be used to explain whether the benefits of exercise are related to physiological changes, to psychological mechanisms, or to a combination of both.

The diversity of the exercise programs suggested that there may be scope to include the individualised preferences into the program design. Preference-based programs would likely create a favourable exercise environment and, therefore, should increase uptake and could also improve adherence and retention. Given this, the examination of the exercise preferences of depressed and non-depressed cancer survivors was the focus of the second review (Chapter 3).

A total of eighteen studies were included in the review that had previously surveyed cancer survivors about their preferred exercise. In total, 6002 cancer survivors were included in these studies spanning a range of cancer types (e.g., breast, prostate, kidney, and bladder) and at various phases throughout the cancer continuum. Further, since no research had been conducted with depressed cancer survivors, the review examined exercise preferences for people with depression who were not diagnosed with cancer. Only two published studies were found to have reported on exercise preferences for people with severe mental illness, including, but not exclusive, to depression. The most definitive exercise preference was that both cancer survivors and depressed individuals consistently rated walking as their most preferred activity, with the vast majority of cancer survivors also preferring an unsupervised, self-managed program. The review points to the fact that, not only were there differences between groups, but that preferences for exercise also differed within the homogeneous groups (Table 3.2). Therefore, it was concluded that the results of the review should provide guidance to researchers and health practitioners when designing exercise programs for these clinically important groups. For example, exercise prescribed for survivors of kidney cancer should be based on a walking with family or friends, whereas breast cancer survivors who have completed treatment are more likely to show interest in a supervised exercise program in a fitness centre. An even more individualised approach could be centred on designing programs for each individual based on their own preferences. This method may increase exercise uptake and adherence to an even greater extent.

Since no studies reviewed in this thesis included Australian cancer survivors, and limited information was available for the preferences of depressed cancer survivors, the first research study (Chapter 4) was a cross-sectional examination, performed to determine current physical activity habits and exercise preferences of depressed and non-depressed cancer patients. A total of 808 (420 female; 388 male) Australian cancer survivors responses to a survey were analysed comprising 158 (16.6%) who met criteria for depression. Whilst most preferences were consistent between the two groups, depressed cancer survivors were more interested in the opportunity to commence an exercise program (+6.9%, $p = .044$) under guided supervision (+18.5%, $p < .001$). These two significant findings were both contrary to expectations that depressed cancer survivors would prefer to remain inactive, and, if choosing to commence exercise, would prefer to exercise alone. The second aim of the review was to compare the preference of Australian cancer survivors to previously reported results from international trials. It was found that there was a higher acceptance of resistance training and a greater interest in supervised programs for all Australian cancer survivors, regardless of depressive status. These novel outcomes extend those reported in the previous review (Chapter 3) and provide the first indication of exercise preferences for depressed cancer survivors, and other Australian cancer survivors. Further, the greater acceptability of resistance training suggests that, in congruence with the ACSM exercise guidelines for cancer, resistance training could be included within a cancer survivors exercise program. However, future research should be performed to validate these outcomes, particularly with depressed cancer survivors and to determine whether prescribing exercise programs based on these preferences does indeed increase exercise uptake and adherence.

A second cross-sectional analysis (a secondary analysis of the data) was performed with a particular interest in regional cancer survivors (Chapter 5). Since evidence suggests that physical exercise is effective at reducing depression and cancer survivors in regional and rural Australia lack access to psychological support services, the beneficial effects of exercise may be even more important for this distinct population. Therefore, this study compared the incidence of depression, levels of physical activity, and perceived benefits and limitations to exercise in cancer survivors living in either metropolitan or regional Australia. It was found that the proportion of survivors meeting criteria for depression (~21%) was not different in regional residents ($n = 130$) than it was for metropolitan cancer survivors ($n = 236$). The levels of physical activity participation was also similar between metropolitan and regional sites, with only 40% of participants meeting national exercise guidelines. The only significant difference

found when examining the perceived benefits of exercise was that metropolitan residents were more interested in increasing strength and improving functional capabilities ($p = .041$). The trial did not include details about access to psychological services, however it has previously been reported that limited services are available in regional locations. Therefore, the results suggest that exercise therapy should be considered as a first line treatment option to manage depression in regional cancer survivors.

The aim of the final study (Chapter 6) was to examine the therapeutic effect of exercise on depressed cancer survivors, or those with elevated symptoms of depression. No previous trials have been conducted with depressed cancer survivors, as this was the first study to recruit participants based on their affective status. Contact was initiated with 1309 cancer survivors to screen for depression. Eventually, thirty-two participants were allocated to either a clinic-based, supervised exercise program ($n = 10$), an unsupervised, home-based program ($n = 8$), or a usual care control group ($n = 14$). Assessment outcomes were completed three times throughout the study, at baseline, after 6 weeks and again after completing the 12-week intervention. A significant difference was found for the primary outcome of depression, measured using the HADS-D. The exercise groups showed a large decrease in depression (-44.8%) over the duration of the intervention compared to an increase in depression (+7.6%) reported by the control group. The outcomes for the two exercise groups were similar after 12 weeks, however there was a notable difference in the time course responses for the changes between the two different exercise interventions. The home-based exercise showed a more rapid reduction in depression, measured after only 6 weeks. However, at the conclusion of the intervention the supervised clinic-based exercise group outperformed home-based exercise for decreased level of depression.

An important finding of this feasibility study was that no adverse effects to exercise were noted. However, two participants randomised to the home-based group withdrew from the study because the group allocation did not match their preference. This outcome confirms the importance of understanding exercise preferences, and suggests that controlled trials may need to include pragmatic allocation based on preference in future studies to avoid drop-out. Other secondary outcomes measures were examined to supplement and explain the antidepressant effect of exercise. Results were that satisfaction with life increased for either exercise group compared to a decreased reported by the control group ($p < .01$). No effects were evident for measures of sleep quality, coping self-efficacy, or self-reported measures of physical activity.

Further, at each assessment, the two exercise groups, but not the control group, performed maximal strength tests, aerobic function test, and body composition was examined. Strength and function were improved, whereas no responses were seen for body composition.

The finding that two different exercise programs were able to elicit antidepressant effects in depressed cancer survivors is extremely important, since this was the first study to recruit only depressed participants. Despite the small sample size the results of this feasibility trial suggests that, similar to non-cancer populations with depression, exercise does provide an antidepressant effect and could be integrated into clinical practice. However, as this was only a feasibility trial with a small sample, further research should be done to confirm the outcomes of this study.

7.2 Translation of findings and practical applications

Evidence continues to emerge regarding the beneficial effects of exercise, yet many professionals and organisations, such as the National Comprehensive Cancer Network (National Comprehensive Cancer Network, 2014), still view exercise only as an adjuvant form of treatment for patients with depression. There are several reasons why exercise should be considered as a possible first line treatment, and integrated into professional practice.

Many cancer survivors suffer with symptoms of depression without receiving a clinical diagnosis. The normalisation of their depressive symptoms reduces their access to professional psychiatric or psychological support, many of which need specialist referrals for consultations. It has been acknowledged that distress screening is important for cancer survivors and therefore more people may be provided with the opportunity to seek help (Bultz & Carlson, 2006). However, some individuals do not wish to receive psychological counselling or in certain cases this psychiatric and psychological support may not be consistent with religious beliefs. Therefore, using exercise as an alternative therapeutic option for depression would provide these individuals with access to acceptable and affordable treatment.

Second, well managed exercise delivered by professional allied health practitioners has repeatedly been shown to negate the risk of adverse effects, presenting opportunities for all cancer survivors to engage in, and benefit from, exercise. Along with improved mood state, exercise is also the only treatment available that can nullify, or delay, the onset of secondary co-morbidities related to cancer treatment toxicities or depression, such as cardiovascular

disease. Therefore, exercise as management for cancer survivors adheres to the principle of ‘do no harm’ and, even if no antidepressant effects result from commencing exercise, it is likely that other beneficial physiological outcomes will arise.

Finally, some regional and rural cancer survivors may lack access to necessary health service providers that are trained to deliver psychological support. However, the findings above suggest that a short-term, home-based exercise program may be able to provide significant antidepressant effects, with minimal resources required. The home-based participants in the intervention study received a booklet about exercise for depression, which included an exercise diary component. Place of residence does not provide any restrictions on the potential to recommend self-managed home-based exercise.

In summary, the results of these three studies, combined with previous findings summarised in the literature reviews, suggest that exercise for depressed cancer survivors is beneficial but that effective programs are needed which account for individual preferences while also ensuring that prescription and delivery are targeted not only to enhance psychological outcomes, but also to elicit physiological adaptations. Therefore, specialized exercise instructors such as exercise physiologists should be included in multidisciplinary management teams to lead the effective delivery of exercise for mental health in cancer survivors.

7.3 Limitations of this thesis

It has been acknowledged several times throughout this thesis that the term depression has often been used interchangeably to refer to clinically-diagnosed depression or people presenting with elevated symptoms of depression. The three research studies presented determined depression using multiple, yet related, measures (HADS-D, SRDS, targeted questioning). The participants may not, however, have met criteria for clinical-diagnosis and this should be considered by the reader. However, the research studies undertaken were intended to have applied results that could easily be translated to clinical practice, and the recruitment and eligibility criteria effectively capture cancer survivors who would be in need of treatment for symptom relief or required secondary management of current clinical-depression.

The focus on practical and applied outcomes resulted in the underlying mechanisms of change not being included within this research. It was acknowledged, in Chapter 2, that cytokine and endocrine activity may be associated with depression and that exercise may be able to resolve these homeostatic imbalances. However examining these responses was beyond the scope of this research, but should be considered in the future. The interaction of depression and cancer may inhibit the responses which have been seen in non-cancer populations, and it has been suggested that it is important to assess the influence of exercise on these markers in cancer survivors and to understand the mechanisms of change.

Another limitation addressed within each relevant chapter is that the statistical analyses performed allowed for an increased Type I error rate. Since the research presented was novel in nature and understudied to date, the risk of Type II errors were considered to be greater than the risk of making a Type I statistical error. However, the findings presented within this thesis provide a foundation of knowledge that should be considered in future trials when examining the role of exercise for depression in cancer survivors.

7.3 Suggestions for future research

The results of this thesis extend the knowledge base relating to exercise for cancer survivors and provided the first exercise intervention for depressed cancer survivors. Several questions have been addressed regarding exercise interest, preferences and outcomes. The prospective feasibility study which examined the effectiveness of exercise to reduce depression in already depressed cancer patients provided extremely encouraging results that warrant further investigation and validation in larger controlled trials.

This was the first trial to recruit a cancer group comprising only depressed survivors and it has been acknowledged that more research is needed in this area (Craft et al., 2012). No long-term follow-up measures were recorded and, therefore, it remains unknown whether the immediate benefits would continue beyond the length of the exercise intervention. Since it is known that sleep disturbances can result in compromised mental health, and no beneficial effects were reported for sleep quality in this trial, it is feasible that participants may have regressed post-intervention. Previous research in clinically depressed individuals (not cancer survivors) reported that exercise was associated with a reduced likelihood of relapse into depression 6-months after completing an exercise program, but only if positive lifestyle changes continued

(Babyak et al., 2000). Therefore, there is a need to examine whether depressed cancer survivors are able to sustain lifestyle modifications over the longer term.

In line with the recommendation of exercise matching individualised preferences, future research using a pragmatic trial could examine the effects of self-selected exercise on depression in depressed survivors. Allowing participants to select and modify their own program may increase uptake and adherence to the exercise, whilst providing a program platform that could easily be translated into practice. Further, previous research has reported that when patients are able to self-select into an exercise program, motivation to exercise is increased along with the perceived benefits that will arise (Courneya et al., 2008), both of which could result in greater psychological enhancements.

A pragmatic research design which compares exercise to an alternative cross-disciplinary intervention, such as psycho-education or mindfulness-based therapy, should be considered in future in preference to delayed exercise or a usual care group design. This design would be able to more accurately determine whether the benefits are associated with exercise itself or related to physiological or psychological responses. For example, learning to play a musical instrument may present the participant with the similar opportunities for distraction, or enhance self-efficacy and increase task-mastery, without obtaining the physiological effects of aerobic or resistance exercise. These pragmatic studies can elucidate the adjunctive or primary treatments that may be most optimal and most desirable for depressed cancer survivors.

A final avenue that should be explored is a health economic analysis of the costs of exercise used to treat depression in cancer survivors. The debilitating effects of depression can exacerbate health problems or cause further comorbidities which places a burden on the health care system. It is possible to speculate that exercise will be found to be extremely cost effective and this outcome alone is likely to have the greatest influence in changing medical practice.

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Appendix A

Cover letter and information sheet for exercise preference studies

*(Sent to participants from the New South Wales Cancer Council
Join a Research Study database)*

<DATE>

Exercise preferences of depressed and non-depressed cancer survivors and current levels of activity

Dear _____

I have recently been provided with your contact details by the Join a Research Study project team at Cancer Council NSW. You have previously consented to be approached by ethically approved studies to do with cancer for which you appear to be eligible. I am a current PhD student at Edith Cowan University, Western Australia and I am examining exercise preferences of depressed and non-depressed cancer survivors and current levels of physical activity. I invite you to participate in my study but remind you that you are under no obligation to accept this invitation. Participation in this research study is completely voluntary.

I would sincerely appreciate if you could complete the enclosed questionnaires and return them as soon as possible using the enclosed postage paid reply envelope. The questionnaires are very brief and should take no longer than 10 minutes to complete.

Further information can be obtained by reading the included information letter, which provides greater detail about the purpose of this study and the expected outcomes that will be gained.

Please complete all questionnaires to the best of your ability answering each question. The questionnaires are completely confidential and do not ask for your name or any other information which could be used to identify you. Therefore the pack is safe to be sent in the post. However, each survey has a unique number which will allow me to track how many questionnaires are returned and who has completed the surveys.

If you have any questions, please do not hesitate to contact me at your convenience using the details provided below. Thank you for your assistance and I look forward to receiving your completed questionnaires.

Best regards,

Gregory Levin, MSc
PhD Candidate
Edith Cowan University
School of Exercise and Health Sciences

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Supported by the Cancer Council WA

Information Letter to Participants

Exercise preferences of depressed and non-depressed cancer survivors and current levels of activity

As specified in the initial letter, the purpose of this document is to provide further information and clarification about this research study. Please read this document carefully, making sure that you understand all the information below. If you are unsure or need further clarification feel free to contact the researchers. This research is being undertaken as part of the requirements of a PhD at Edith Cowan University.

Research Team

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Purpose of the Study

Exercise preferences of various cancer populations have already been established (Emslie et al., 2007; Karvinen et al., 2006; Karvinen et al., 2007; Stevinson et al., 2009; Vallance et al., 2006) but no research has examined the preferences of cancer survivors that are also suffering from depression or depressive symptoms. Since it has been reported that up to 50% of survivors may suffer from depression, specific exercise preferences for this group are important. Therefore, the purpose of this study is to anonymously collect data on depressed and non-depressed cancer survivors' current physical activity levels, preferences for exercise, as well as their demographics and cancer history. Results of this research will be used to identify preferences for exercise which can be applied in clinical settings and professional practice. Understanding current levels of physical activity and preferences for all cancer survivors will allow clinicians to prescribe physical activity that is compatible with cancer survivors as well as those who are also suffering with depression.

Participant Involvement / Eligibility

We require at least 200 completed surveys. This will comprise at least 100 surveys from depressed cancer survivors and 100 from non-depressed survivors. To be eligible participants must therefore have been diagnosed previously with cancer.

Contact from the Researchers

Following this initial contact, the researchers will mail out a reminder letter should no response be collected within 4 weeks from the date of postage. If this second contact fails to result in a response a second survey and reminder letter will be posted 8 weeks after the initial pack. If no response is forthcoming four weeks after posting the second survey it will

be assumed that the participant has withdrawn or not consented to be involved in the research. No further contact will be made at this time

Measures

Exercise preferences and current levels of physical activity will be assessed for depressed cancer survivors using the enclosed questionnaire.

Two further questionnaires are included to determine levels of depression. These questionnaires should not be used by you to diagnose depression and neither will the researchers use them as a diagnosis. However, if you feel depressed or anxious after completing the questionnaires it is advised that you visit your GP or talk to a support service such as the Cancer Council Helpline (13 11 20) or Lifeline (13 11 14) if required.

Risks

No significant risks are posed to you through your involvement in this study. There is a risk however that the questionnaires on depression can cause some distress. As outlined above, if this is the case you should contact your GP for further information. As an initial source of support it is advised that you contact the Cancer Council Helpline (131120) or Lifeline (131114) if required.

In cases where participants indicate that they are not being treated for depression, results from the depression questionnaires will be assessed by the research team. If it is noticed that you meet criteria which suggests you may be suffering with depression, the research team will follow up with a letter informing you of your results and include a recommendation for a referral from a clinician.

Informed Consent

In order to ensure that all information is de-identified, completion and return of the questionnaire will equate to your consent to be involved in this research study. This means that you have read and understood this document, as well as the other documents that have been delivered to you. Furthermore, you understand that all research data will be treated as confidential and agree to participate in this study with the understanding that you can withdraw at any time without prejudice. Lastly, you agree that research data gathered for the study may be published provided that you cannot be identified as a participant.

Research Ethics and Contact Person

This study has been approved by Human Research Ethics Committee at Edith Cowan University. If you have any concerns or complaints and would like to contact an independent person, please contact the university ethics officer, Ms Kim Gifkins via telephone (+61 8 6304 2170) or Email (research.ethics@ecu.edu.au).

Appendix B

Exercise preference questionnaire

(For participants recruited in New South Wales and Western Australia)

PHYSICAL ACTIVITY LEVELS OF CANCER SURVIVORS AND EXERCISE PREFERENCES

The following section is asking about your current personal and demographic details:

1)	What is your age?	_____		
2)	Are you male or female?	_____		
3)	What is your height?	_____		
4)	What is your current weight?	_____		
5)	What is the highest level of education that you have completed? (please circle)			
	Primary	Secondary	Trade	Certificate/Diploma
	Bachelor degree	Higher degree	Other	_____
6)	Are you currently employed? (please circle)			
	Yes / No (if yes, please provide status)			
	Working status			
	Full time	Part Time	Casual/Contract	
7)	What is your marital status? (please circle)			
	Single	Married	De Facto	
	Separated	Divorced	Widow/Widower	
8)	Are you an Australian citizen?			
	Yes / No			
9)	Were you born in Australia?			
	Yes / No			
	If no, please list the country where you were born _____			

The following section is asking about your cancer status:

- 1) What type of cancer were you diagnosed with? _____
- 2) How long (in months) since you were diagnosed with cancer? _____ months

If you know these details

- 3) What stage and grade was the tumor at diagnosis?
Stage _____ Grade _____

The following section is asking about your physical activity levels:

During a typical 7-Day period (a week), how many times on the average do you do the following kinds of exercise for more than 10 minutes during your free time (write on each line the appropriate number).

	Times per week	Duration of each session (min)
a) Strenuous Exercise (heart beats rapidly) (e.g., running, jogging, field sports, squash, vigorous swimming, vigorous cycling)	_____	_____
b) Moderate Exercise (not exhausting) (e.g., fast walking, tennis, easy bicycling, volleyball, badminton, easy swimming, dancing)	_____	_____
c) Mild Exercise (minimal effort) (e.g., yoga, archery, fishing from river bank, bowling, golf, easy walking)	_____	_____

The following section is asking about your preferences for exercising:

- 1) Would you be interested in an exercise program? (please circle)
Yes / No / Maybe
- 2) Would you be able to participate in exercise program? (please circle)
Yes / No / Maybe
- 3) What type of exercise are you most interested in? (please circle)
Aerobics Cycling Jogging Strength training Swimming
Walking Yoga Not interested in exercise
Other (please list) _____

4) When would you prefer to start an exercise program? (please circle)

Before treatment	3 to 6 months after treatment
During treatment	1 year or more after treatment
Immediately after	I do not want to exercise

5) Who would you prefer to exercise with? (please circle)

Alone	Friends	Other cancer survivors
No preference	Family	I do not want to exercise

6) Where would you prefer exercise to take place? (please circle)

Home	No preference
Cancer fitness centre	Other (e.g. bowls club, golf, sailing)
Fitness centre	I do not want to exercise

7) What time of day would you prefer to exercise? (please circle)

Morning	Afternoon	Evening
No preference	I do not want to exercise	

8) What intensity would you prefer to exercise at? (please circle)

Light	No preference
Moderate	Progressive starting light and building up
Heavy	I do not want to exercise

9) Would you prefer the same or different activities each session? (please circle)

Same	Different	I do not want to exercise
------	-----------	---------------------------

10) Would you prefer your sessions to be supervised or unsupervised? (please circle)

Supervised	Unsupervised	I do not want to exercise
------------	--------------	---------------------------

If supervised by whom? (please circle)

Exercise physiologist	Fitness instructor	Medical professional
-----------------------	--------------------	----------------------

Nurse	Physiotherapist	Other (please list) _____
-------	-----------------	---------------------------

11) Would you prefer scheduled sessions or a flexible arrangement? (please circle)

Set

Flexible

I do not want to exercise

12) Do you own any exercise equipment (please circle, choose all relevant options)

Treadmill

Exercise bike

Cross trainer/elliptical

Stepper machine

Rowing machine

Abdominal machine

Free weights

Exercise bench

Home gym

I do not own any equipment

Other (please list) _____

13) Are you a current member of a health club/local gym? (please circle)

Yes / No

The following section asks you to provide detailed answers for the last two questions:

List any benefits you believe you would get from being involved in an exercise program.

List any reasons you feel may exclude you from being involved in an exercise program.

Appendix C

Self-rating depression scale

(Used to assess depression status in the preference study and to determine eligibility of participants for the intervention study)

A self-rating scale of depression

Part 1

The two questions below are intended to establish if you have ever been diagnosed with or treated for depression and to establish whether you are currently depressed. Please answer **both** questions.

- | | | |
|---|--|----------|
| 1 | Have you previously been diagnosed with depression by a medical professional (GP, psychiatrist, clinical psychologist)? | YES / NO |
| 2 | Are you currently being treated for depression?
(e.g. taking antidepressant medication or treatment from a clinical psychologist or psychiatrist) | YES / NO |

Part 2

The following nine statements relate to clinically diagnosed depression. Please indicate if you have been experiencing these symptoms over **the past two weeks**.

You should only select "yes" only if you experience the symptom for large amounts of time, for example almost every day.

Symptom	Did you experience this nearly every day over the past two weeks?
1 Feeling depressed or sad or being told by others that you seem depressed.	YES / NO
2 Lack of interest in pleasure or doing pleasurable activities which you enjoy.	YES / NO
3 A large change in your body weight, either increasing or losing weight, without being on a planned diet.	YES / NO
4 Either being unable to sleep or sleeping excessively throughout the day.	YES / NO
5 Both extremely restless and fidgety or feeling very lethargic and unable to move properly.	YES / NO
6 Tired or lacking energy	YES / NO
7 Feeling unimportant and like you are a burden to yourself and others.	YES / NO
8 Unable to pay attention, concentrate or make decisions.	YES / NO
9 Thinking about dying and/or the possibility of suicide	YES / NO

Appendix D

Invitation letter from clinician – Example 1

(Example letter from the patient's clinician sent to Western Australian cancer survivors inviting them to participate in the exercise preference and intervention study)

Research Study Information Letter

Effects of exercise on depression, quality of life, and physical performance in depressed cancer survivors

22 April 2013

Please find enclosed information about a research study which is being conducted by Edith Cowan University. You have been sent these documents as a past patient of Dr David Ransom at The Bendat Cancer Centre, St John of God Hospital, Subiaco.

The study is supported by the Cancer Councils of Western Australia and New South Wales and has already commenced in NSW. The purpose of the research is to examine the relationship between exercise and depression in cancer survivors. Previous research has shown that being physically active may limit depression, but it is not known if this is also the case for people after they develop cancer.

In order to assist in this research all you need to do is fill out the enclosed questionnaires and mail them to Greg Levin (PhD Student) using the reply-paid envelope provided.

Based on your results the researchers may also notice that you will be eligible to be involved in a second part to this study. The second phase of the study will be led by the research team, and if you are eligible they will contact you directly.

Lastly, I would like to remind you that your participation is voluntary and should you not wish to participate this decision will be respected.

Sincerely,

Greg Levin
PhD Candidate
Edith Cowan University
School of Exercise and Health Sciences

Tel: 6304 3971

Appendix E

Invitation letter from clinician – Example 2

(Example letter from the patient's clinician sent to Western Australian cancer survivors inviting them to participate in the exercise preference and intervention study)

6 February 2013

<Name>
<Address Line 1>
<Address Line 2>

Dear <Name>,

RE: Exercise Study for Patients from SJOG

Please find enclosed information about a research study which is being conducted jointly by St John of God Hospital, Edith Cowan University and the Marian Centre. I believe that you would be a good candidate to be involved in this program.

The study is supported by the Cancer Councils of Western Australia and New South Wales and has already commenced in NSW. The purpose of the research is to examine the relationship between exercise and depression in cancer survivors. Previous research has shown that being physically active may limit depression, but it is not known if this is also the case for people after they develop cancer.

In order to assist in this research all you need to do is fill out the enclosed questionnaires and mail them to Greg Levin (PhD Student) using the reply-paid envelope provided.

Based on your results the researchers may also notice that you will be eligible to be involved in a second part to this study. The second phase of the study will be led by the research team, and if you are eligible they will contact you directly.

Lastly, I would like to remind you that your participation is voluntary and should you not wish to participate this decision will be respected. However, I encourage you to help with this beneficial research.

Yours Sincerely,

Dr Jerard Ghossein
MBBS, FRACS (Urological Surgeon)

Appendix F

Cover letter and information package for the intervention study

(Sent to participants from Perth that were eligible and interested in being considered for the exercise intervention study.)

12 December 2012

Dear <NAME>

Thank you for your interest in this important research, "Effects of exercise on depression, quality of life, and physical performance in depressed cancer survivors."

Please find attached:

1. A "Participant Information Sheet" outlining all aspects of the study;
2. A "Statement of Informed Consent" which you will be required to sign before participating in the study;
3. A "Medical Doctor Consent Form" for your doctor;
4. A "Demographic Information and Health History Questionnaire"; and
5. A map of the Joondalup Campus

All volunteers are required to obtain their doctor's approval prior to participation – please take the Medical Doctor Consent Form to your doctor (GP) and have them complete and sign the consent form (you may also want to show them the Participant Information sheet). Following approval from your doctor, please contact me to arrange a meeting where an orientation to the study will be provided and baseline measurements will commence. At this meeting, please bring with you;

1. "Medical Doctor Consent Form"
2. "Demographic Information and Health History Questionnaire" and
3. "Statement of Informed Consent."

If you have any questions, please don't hesitate to contact me.

I look forward to hearing from you.

Best regards,

Gregory Levin, MSc
PhD Candidate
Edith Cowan University
School of Exercise and Health Sciences

Phone: 6304 3971

Email: g.levin@ecu.edu.au

PARTICIPANT INFORMATION

Effects of exercise on depression, quality of life, and physical performance in depressed cancer survivors

The purpose of this document is to provide you with information and clarification about the current research study. Please read this document carefully. If you are unsure or need further clarification feel free to contact the researchers. This research is undertaken as part of a PhD at Edith Cowan University.

Research Team

PhD Student: Greg Levin, MSc	Email: g.levin@ecu.edu.au	Phone: 6304 3971
Professor Robert Newton, PhD	Email: r.newton@ecu.edu.au	Phone: 6304 5037
Professor Ken Greenwood, PhD	Email: k.greenwood@ecu.edu.au	Phone: 6304 3420

The research team is happy to answer any questions you may have. If you have any queries in the future please do not hesitate to contact any one of the team listed above.

Purpose of the Study

Recent guidelines on exercise and cancer have been published which show that exercise is safe and beneficial. Furthermore, exercise has been reported to be an effective method of reducing depression but there has been no research which has examined the effect of exercise with depressed cancer survivors. Therefore, this trial will assess the effectiveness of exercise to decrease depression and increase quality of life in depressed cancer survivors. This study will assess depressed cancer survivors before and after an intervention period, during which they will be randomised to one of three groups: 1) typical aerobic and resistance exercise program conducted in an exercise clinic; 2) home-based aerobic exercise; or 3) a delayed exercise group.

Participant Involvement / Eligibility

We require ninety cancer survivors who are also suffering with depression to enrol in the current study. You have been assessed as an eligible participant based on your responses from the initial questionnaires. Participants will also be required to obtain consent from their doctor (GP) before participating in the study. This will ensure that people with acute illness or musculoskeletal, cardiovascular, or neurological disorders are not put at risk of injury or illness through the exercise testing or program. For example, you will need to be able to walk 400m unassisted.

Procedures

Prior to being allocated to one of three different groups all participants will undergo a series of test measurements (listed below). There will also be testing sessions at the halfway point (6 weeks), and after completing the 12 week program. Participants who are allocated to the two exercise groups will also be required to complete all survey questionnaires at the end of the first exercise session.

All testing sessions will be performed at Edith Cowan University, Joondalup. Each testing session should last between 60-90 minutes.

Exercise Sessions

- *Exercise in an exercise clinic (Group 1)*

Sessions will take approximately 60 minutes and will be conducted in the Vario Wellness Clinic at Edith Cowan University (ECU) or at the Floreat Surf Life Saving Club. Twice weekly exercise sessions, for 12 weeks, will commence with a warm up followed by resistance exercises that target the major upper and lower body muscle groups (chest press, seated row, leg press, leg extension, leg curl, lat pulldown). The rest period between sets will be 1 minute. To ensure the progressive nature of the training program, participants will be encouraged to work past the specific intensity prescribed. The workload will be increased by 5-10% increment for the next set/training session if participants are able to perform more repetitions than the RMs specified. Intensity will be manipulated ranging from 6-12 RM using 2-4 sets per exercise. In addition, each clinic session will include 20 minutes of aerobic exercise using various modes such as walking or jogging on a treadmill, cycling, rowing a stationary ergometer, or exercising on a cross training machine. Target intensity will be 65-90% estimated maximum heart (220 – age). In addition to the clinic training, participants from this group will be encouraged to undertake additional home-based aerobic activity for the duration of the study.

All exercise sessions will be conducted in small groups of no more than 10 participants to ensure adequate level of supervision. All sessions will be supervised by an Accredited Exercise Physiologist or graduate from a BSc (Sports Science) course or equivalent level of qualification.

- *Home-based aerobic exercise (Group 2)*

This group will perform non-supervised home-based exercise similar to the additional activities to be completed by participants in Group 1. Aerobic exercise, in the form of walking, will be prescribed for a period of 12 weeks and will be performed twice per week. Each session will be between 30 and 60 minutes in duration.

- *Delayed exercise group (Group 3)*

This group will be tested at the same time points as the other two groups but will receive no exercise prescription for an initial 12 week duration. Participants will be asked to maintain their customary physical activity. Following the delay period participants will receive the same exercise prescription as Group 2 (above).

Measurements

- **Body Composition**
 - Height, weight, waist and hip circumference will be measured.
 - Body composition (fat mass and lean mass) will be measured by dual x-ray absorptiometry (DXA). You will lie on a specially designed table for approximately 5 minutes and a scanning arm will move above your total body. A low-dosage x-ray will pass from underneath the table to the scanning arm. The total radiation dose for the scans undertaken during the study is very low only a little more than normal background radiation and much less than, for example, an international aeroplane flight.
- **Depression, Quality of Life, and other Questionnaires**
 - Standard questionnaires will be used to determine psychological outcomes as well as overall quality of life these include:
 - BSI-18 and HADS (depression and anxiety)
 - SF-36 and EORTC QLQ-30 (quality of life)
 - SWLS (satisfaction with life)
 - CASES (self-efficacy)
 - PSQI (sleep quality)
 - Initially you will be asked to complete a health history questionnaire along with demographic / personal details. You will also be asked to complete a questionnaire relating to physical activity at each testing session.
- **Muscle Strength**
 - Maximal muscle strength will be determined for both the upper and lower body (chest press and leg press) using weight-training machines. The maximal strength is the most weight that can be lifted one time using correct technique.
- **Aerobic Capacity**
 - Time to complete a 400 metre walk will be determined using a standard corridor walking test. You will be asked to walk 20 metres in a corridor, turn around a marker, and return to the starting position and repeat the sequence another nine times. Performance will be assessed as the time taken to complete the task.
 - Aerobic capacity will be measured by expired air analysis during a staged walking test on a motorised treadmill. Cardiovascular efficiency will be determined based on direct expired air gas analysis and heart rate achieved during exercise. You will be asked to walk in a staged progressive walking test on a motorised treadmill under direct supervision of an exercise physiologist.

Risks

- Initial response to exercise and in particular resistance training can result in discomfort and muscle soreness. However, in order to avoid this all sessions are supervised and will commence with a warm up and conclude with a cool down period. The risk of discomfort and muscle soreness will also be minimised by a gradual increase in exercise intensity. In the event that an emergency occurs, medical assistance will be obtained from the University Health Service according to our established emergency procedures.
- There is a small risk associated with the treadmill walking for the cardiovascular testing especially when people are unfamiliar with treadmill walking. However, to minimise this risk participants will be instructed to walk safely and will be closely monitored during the test. The maximal walking speed does not exceed 4kph which should be within the easy capacity of all participants. The mouthpiece that is used to collect expired air for this test can be uncomfortable but does not present any risks or prevent normal breathing.
- In some cases the use of questionnaires regarding depression and psychological distress can further exacerbate these conditions. In order to minimise any harm participants are encouraged to report if this occurs so that they can be referred by a clinical psychologist to the most appropriate clinician or support agency.
- Risks will be further minimised as the researchers are all first aid qualified.

Benefits

- All study activities, including exercise instruction and training as well as all assessments are provided at no cost to you. On completion of the 12 week program a summary of your results will be made available and upon completion of the entire study the findings will be reported to the group.
- You will gain information relating to exercise, depression, and cancer and how these areas link together.
- It is possible that you may have no direct benefits from your involvement in the study, however the knowledge gained from your participation is most likely going to benefit others in the future. This study has the potential to change clinical practice for the benefit of cancer survivors with depression.

Confidentiality of Information

All information provided by you will be treated with full confidentiality. Your contact information will only be accessible by the Chief Researcher during the period of the study. The information and data gathered from you during the study will be used to answer the research question of this study. People who will have access to the raw information for this study are only limited to the researcher and the Supervisors. Data collected will be stored in a password-protected computer and is only available to the researchers. Hard copy data (paper etc.) will only be kept in the researcher's office and locked in a specific drawer/filing cabinet. All data will be stored according to ECU policy and regulations following the completion of the study.

Results of the Research

The results of this study are intended for completion of a PhD thesis and may be presented in conferences/seminars and published in peer-reviewed journals, as articles, as part of a book section, or as a report. Published results will not contain information that can be used to identify participants unless specific consent for this has been obtained. A copy of any published results can be obtained from the investigator upon request

Voluntary Participation

Your participation in this study is voluntary. No monetary reward will be provided. No explanation or justification is needed if you choose not to participate. Your decision if you do not want to participate or continue to participate will not disadvantage you or involve any penalty. Furthermore, you are free to withdraw your consent at any time. You also have the right to withdraw any personal information that has been collected during the research with your withdrawal.

Research Ethics and Independent Contact Person

This study has been approved by Human Research Ethics Committee at Edith Cowan University. If you have any concerns or complaints and would like to contact an independent person, please contact the university Human Research Ethics Officer via telephone (+61 8 6304 2170) or Email (research.ethics@ecu.edu.au).

Statement of Informed Consent

Effects of exercise on depression, quality of life, and physical performance in depressed cancer survivors

- I have read and understood the information sheet and this statement of informed consent for this study.
- The nature and possible effects of the study have been explained to me.
- I understand that the study involves the following procedures:
 - I will be required to obtain my doctors approval to undertake the study before any measures or training can take place
 - I will be required to complete a medical history before the training program commences.
 - I will be randomly assigned to one of the following three groups for a 12 week period: (1) a combined aerobic and resistance training program in an exercise clinic (2) an exercise program based on preferences from my peers (3) a delayed exercise group.
 - I will be required to have my height, weight, body composition, cardiorespiratory capacity, and maximal strength measured before, during, and at completion of the study.
 - I will be required to complete questionnaires regarding quality of life, depression and anxiety, and self-efficacy before, during, and at completion of the study.
- I understand that all research data will be treated as confidential.
- Any questions that I have asked have been answered to my satisfaction.
- I agree to participate in this study freely and without coercion.
- I agree to participate in this study and understand that I can withdraw at any time without prejudice or penalty.
- I agree that research data gathered for the study may be published provided that I cannot be identified as a subject.

This study has been approved by Human Research Ethics Committee at Edith Cowan University. Should there be any concerns relating to the project the Ethics Committee can be contacted by telephone (+61 8 6304 2170) or Email (research.ethics@ecu.edu.au).

Participant:

_____	_____	_____
Name	Signature	Date

Witness:

_____	_____	_____
Name	Signature	Date

Medical Doctor Consent Form for Exercise Study

Effects of exercise on depression, quality of life, and physical performance in depressed cancer survivors

Dear Doctor,

A research study into the effects of exercise on improving the quality of life of cancer survivors with depressive symptoms and examining biomarkers related to depression is being undertaken as part of the requirements of a PhD at Edith Cowan University. The intervention program will run for 12 weeks, entailing combinations of progressive resistance (strength/weight) training, and aerobic exercises. This type of exercise has been shown to be safe for cancer survivors as well as being effective in reducing depressive symptoms. However, no study has assessed the effects of exercise on depression in cancer survivors. Furthermore, since it has been reported that up to 50% of cancer survivors experience depressive symptoms this study could provide both physical and mental health benefits.

For the purposes of this study we require ninety depressed cancer survivors assessed using the Hospital Anxiety Depression Scale. Participants may have pre-existing co-morbidities that do not exclude them from exercising. However, participants should not have any signs or symptoms of dementia or a life expectancy of less than six months.

There will be three groups into which participants will be randomly assigned. These are: 1) typical aerobic and resistance exercise program conducted in an exercise clinic; 2) home-based aerobic exercise; or 3) a delayed exercise group.

All resistance training will take into consideration any pre-existing musculoskeletal injuries and will be modified accordingly. However, it is anticipated that exercise will target both upper and lower body and target all major muscle groups.

Exercise sessions will commence with a warm-up and conclude with a cool-down period that includes stretching. The exercise sessions will be undertaken at Edith Cowan University Health and Wellness Institute, using traditional resistance training machines to ensure participant safety. The aerobic component of the training session will incorporate 20 minutes of aerobic exercise at an intensity of 65-85% of heart rate maximum. All sessions will be conducted in small groups of up to 10 participants under direct supervision of an Accredited Exercise Physiologist to ensure proper technique and minimize the risk for injury. The total time to complete the exercise session will be about 60 minutes.

Outcome measures in the study include muscle strength, aerobic capacity and endurance, and body composition which are all standard measures in studies of cancer survivors. Measures of psychological wellbeing and quality of life will also be recorded using standardised questionnaires.

Participants must meet all the following criteria to participate:

- (1) suffer from depressive symptoms
- (2) previously diagnosed with cancer
- (3) able to speak and understand English
- (4) able to walk 400m unassisted
- (5) able to undertake an exercise program that will run for 12 weeks.

Participants will be excluded if they meet any of these conditions:

- (1) suffer from dementia
- (2) have a musculoskeletal, cardiovascular, or neurological disorder which would inhibit them from exercising or place them at risk from exercise
- (3) in situations where the GP believes that the exercise program could have a negative impact.

The study has been approved by the Human Research Ethics Committee at Edith Cowan University and participants will be free to withdraw from the study at any time. The concern of the principle investigators are of past and/or present medical conditions that may compromise the individual's ability to participate in the intervention or put them at risk of injury or illness, whether they be musculo-skeletal, neurological, cardiovascular, etc. in origin. For these reasons all potential participants have been asked to seek their medical doctor's approval prior to involvement in the study.

Should you require further information, please feel free to contact me by phone (6304 3971) or by e-mail (g.levin@ecu.edu.au).

Sincerely,

Greg Levin, MSc, AEP (MESSA)

_____ is in sufficient health to participate in the above intervention study.
(Participant)

(Doctor's signature)

(Date)

Please stamp your practice stamp here for contact details and authenticity



Supported by the Cancer Council WA

Appendix G

Cover letter for control participants

*(Sent to control group participants of the intervention trial
who received all correspondence via post)*

17 September 2012

Dear <Name>,

Thank you for agreeing to assist my research by completing the questionnaires included in this pack. If possible, it is preferable that you take about 20 minutes to complete all the questionnaires at one time. Many of the pages are printed on both sides so please also ensure that you answer each question to the best of your ability.

Please find attached the following 10 documents:

- 1) Health History Questionnaire
- 2) Hospital Anxiety and Depression Scale
- 3) Brief Symptom Inventory 18
- 4) "Your Health and Well-Being" Questionnaire
- 5) EORTC QLQ-C30
- 6) CASE Scale
- 7) Godin Leisure-Time Exercise Questionnaire
- 8) The Satisfaction with Life Scale
- 9) Pittsburgh Sleep Quality Index
- 10) Depression Thermometer

Once you have completed all questions please place them inside the reply-paid envelope and return the pack to me via post. You may notice that some of the questions across the documents are quite similar so I apologise for the repetition but this is necessary as I am using established questionnaires. This means I cannot cut out any questions, so once again please answer all questions honestly and to the best of your ability.

Lastly, before commencing please ensure that you read the instructions for each new questionnaire and each question as these may relate to different time frames (1 week, 4 weeks, today).

If you have any questions, please don't hesitate to contact me. Thank you very much for contributing to research into depression and cancer. I greatly appreciate your efforts.

Best regards,

Gregory Levin, MSc
PhD Candidate
Edith Cowan University
School of Exercise and Health Sciences
Phone: 6304 3971
Mobile: 040 313 8765
Email: g.levin@ecu.edu.au

Appendix H

Health history questionnaire

(Completed by all participants that entered into the intervention study)

EFFECTS OF EXERCISE ON DEPRESSION, QUALITY OF LIFE, PHYSICAL PERFORMANCE AND BIOMARKERS OF DEPRESSION IN CANCER SURVIVORS

Demographic Information and Health History Questionnaire

_____	_____	
First Name	Last Name	
_____	_____	_____
Date of Birth	Age	Sex

Postal Address		
_____	_____	_____
Home Phone	Mobile Phone	Email Address

Family Physician (GP) Name		GP Contact Number

Emergency Contact

_____	_____	_____
Name	Contact Number	Relationship

Demographics

10) What is your current marital status? (please circle)

Single Married De Facto Separated Divorced Widowed

11) What is the highest level of education that you have completed? (please circle)

Primary Secondary Trade Certificate/Diploma
Bachelor degree Higher degree Other (please specify) _____

12) What is your current employment status? (please circle)

Retired Unemployed Casual Full time Part Time

If employed, what is your current occupation? _____

Medical History

Please Circle

- 1) **Are you or have you ever been a daily smoker?** Yes No
If yes:
Are you a past or current smoker? _____
Age you started smoking: _____
Age you quit smoking (for past smokers only): _____
Average number of cigarettes smoked per day: _____
- 2) **How many alcoholic drinks do you usually have per week?** _____
- 3) **Has your weight fluctuated more than a few kilos in the last 12 months?** Yes No
If yes:
Did it increase or decrease? _____
How much change has there been? _____
- 4) **Do you experience shortness of breath while walking with others of your age?** Yes No
- 5) **Do you experience sudden tingling, numbness, or loss of feeling in arms, hands, legs, feet, or face?** Yes No
- 6) **Do you experience swelling of your feet and ankles?** Yes No
- 7) **Do you get pains or cramps in your legs?** Yes No
- 8) **Do you experience any discomfort in your chest?** Yes No
- 9) **Have you ever been told that your cholesterol or triglyceride level was high?** Yes No
- 10) **Have you ever been told that your blood pressure was abnormal?** Yes No
If yes, please describe
(e.g. high / low / high during pregnancy) _____
- 11) **Do you have diabetes?** Yes No
If yes, how is controlled?
Insulin only; Tablets only; Insulin and tablets
Diet only; Exercise only; Diet and exercise;
Medication with diet and/or exercise _____
- 12) **Do you have epilepsy** Yes No

13) **Do you have any known blood disorders?** Yes No
 If yes, please describe
 (e.g. hemophilia) _____

14) **Have you ever had any medical surgery not related to cancer diagnosis or treatment?** Yes No
 If yes, please provide details of each surgery

Cancer Specific Medical History

1) **What type of cancer have you been diagnosed with?** _____

2) **How long (in months) since you were diagnosed with cancer?** _____ months

3) **Have you been diagnosed with a secondary cancer?** Yes No
 If yes, please specify _____

4) **If you know these details, what stage and grade was the tumor at diagnosis?**
 Stage _____
 Grade _____

5) **Which types of treatments have you undertaken or are you currently undertaking?**

Surgery	Yes	No
Radiation Therapy	Yes	No
Chemotherapy	Yes	No
Hormone Therapy	Yes	No
Other (please specify)	Yes	No

6) **Please specify the start date, duration, and other important details of each treatment.**

Depression Specific Medical History

- 1) **Have you been clinically diagnosed with depression?** Yes No
 If yes, how long (in months) since you were diagnosed? _____ months
- 2) **Which types of treatments have you undertaken or are you currently undertaking for your depression?**
- | | | |
|-------------------------------------|-----|----|
| Seen a psychologist | Yes | No |
| Seen a psychiatrist | Yes | No |
| Antidepressant medication | Yes | No |
| Managed by my GP without medication | Yes | No |
| Other (please specify) _____ | Yes | No |
- 3) **Did depression become an issue for you before or after your cancer diagnosis?**
- Before _____
- After _____
- 4) **Please specify the start date, duration, and other important details of each treatment.**
-
-
-
-
-
-

Medication List

Please list below any **prescription** medications you are currently taking. Fill out **every** column for each medication you list.

Medication Name	Frequency	Duration	Reason for taking (what medical condition does this treat)
Lipitor (EXAMPLE)	2x / day	Since May 2009	Cholesterol medication

Do you have any other medical conditions not mentioned above, or are there any other health related issues that the researcher should know which could limit your ability to exercise?

Appendix I

Exercise intervention recording sheet for testing

(Used to ensure all tests were completed at each assessment point throughout the 12-week intervention)

PhD Study - Testing Sheet

Participant # _____ Date _____

Baseline 6 week 12 week

Height _____ cm Hip: _____

Weight _____ Kg Waist: _____

Depression Thermometer _____

DXA

Aerobic Capacity Testing

	Speed	Gradient	HR	RPE
REST				
Min 1	0.0 kph	10%		
Min 2				
Min 3				
Stage 1				
Min 4	2.7 kph	10%		
Min 5				
Min 6				
Stage 2				
Min 7	4.0 kph	12%		
Min 8				
Min 9				

Notes

Recovery / Questionnaires

P.T.O



Questionnaires

Given

Received

Health History Questionnaire
HADS
BSI-18
SF-36
QLQ-C30
CASES
Godin
SWLS
PSQI

Strength Tests

(,)	<input type="checkbox"/> 1-RM Chest Press	_____	_____	_____	BEST	
()	<input type="checkbox"/> 1-RM Leg Press	_____	_____	_____		

Functional Walking Test

400m 1 2 3 4 5 6 7 8 9 10 Time: _____ : _____ : _____

↓

HR Start _____	HR Finish _____
----------------	-----------------

Appendix J

Exercise training templates

*(Used to monitor exercise session for all participant allocated into the supervised exercise group arm of the intervention study
&
home-based training diary used to record additional activity throughout the week)*

Name: _____

Session	1	2	3	4	5	6	7	8	9	10	11	12
Date												

Warm up												
---------	--	--	--	--	--	--	--	--	--	--	--	--

Resistance training Exercise

	2x12	2x12	2x12	2x12	3x10	3x10	3x10	3x10	3x10	3x10	3x10	3x10
Chest press												
Leg Press												
Lat Pulldown												
Leg Extension												
Seated Row												
Leg Curl												
Lateral raise												
Step Up												
Biceps curl												

Aerobic (20 minutes)

Upright Bike												
Treadmill												
Rower												
X-trainer												
Recumbent Bike												

Other

Cool Down												
Stretches												

Session RPE												
-------------	--	--	--	--	--	--	--	--	--	--	--	--

Comments / Reasons for Missing a Session

Name: _____

Session	13	14	15	16	17	18	19	20	21	22	23	24
Date												

Warm up												
---------	--	--	--	--	--	--	--	--	--	--	--	--

Resistance training Exercise

	3x8	3x8	3x8	3x8	3x8	3x8	4x6	4x6	4x6	4x6	4x6	4x6
Chest press												
Leg Press												
Lat Pulldown												
Leg Extension												
Seated Row												
Leg Curl												
Lateral raise												
Step Up												
Biceps curl												

Aerobic (20 minutes)

Upright Bike												
Treadmill												
Rower												
X-trainer												
Recumbent Bike												

Other

Cool Down												
Stretches												

Session RPE												
-------------	--	--	--	--	--	--	--	--	--	--	--	--

Comments / Reasons for Missing a Session

Appendix K

Home-based exercise training booklet

(Copy of the exercise booklet provided to the intervention study participants allocated to the home-based training group)

Effects of exercise on depression, quality of life, and physical performance in depressed cancer survivors

Home-Based Exercise Training Booklet

Contact details

Gregory Levin

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(Provided as part of a PhD study)

Introduction

This booklet is designed to inform you on the importance of physical activity and exercise and provide you with an easy to follow exercise programme for the next 12 weeks. Starting to exercise should not be intimidating and this booklet will take you step by step through everything you need to know to be able to exercise for health and lifestyle benefits in your own home.

Recent findings have shown that exercise is extremely beneficial during all stages of treatment for cancer and that adhering to an exercise programme can improve not only your strength and physical fitness but also your overall quality of life and mental health.

An Introduction to Physical Activity

Physical activity is a term that relates to all movements that we perform throughout the day. This term includes all unstructured forms of movements such as walking within your house from the bedroom to your kitchen and cycling to the train station on your way to work. Although this type of activity would not be strenuous or long enough to count as structured exercise, enough physical activity on its own is still associated with health benefits.

The recommended physical activity guideline according to the American Heart Association is to achieve 2 ½ hours of activity per week. This equates to 30 minutes of activity on five days of the week. However, this is only a recommended minimum and more activity is usually associated with additional health and lifestyle improvements.

Key Guidelines

- At least 150 minutes of physical activity
- If this is too much start with something more manageable
- More is better
- Adding strength exercise for muscle and bone health

Exercise Training

Exercise is slightly different from physical activity because it is something that is planned and usually follows a specific programme. It is important to realise that exercising is not something that is difficult or should be seen as a burden; it is something that should become a part of your lifestyle in order to remain physically active and healthy. For the purpose of this study we will be focussing on aerobic exercise.

Aerobic Training

Aerobic exercise encompasses any activity that uses large muscle groups over a sustained period of time. In general sessions should last between 20 minutes to an hour and can be either continuous or intermittent in nature. However a minimum bout of 10 minutes is suggested in order to attain health benefits. There are many different ways to perform aerobic exercise, the most common ways are walking, jogging, cycling, running and swimming. It is however important that you find an activity which is enjoyable and keeps you motivated. Some other examples of ways to perform aerobic exercise include: hiking, rowing, dancing, skipping, boxing, and playing sports.

Some benefits of aerobic exercise are that it may: 1) decreases body fat, 2) improve insulin sensitivity, 3) reduces risk factors for cardiovascular disease, 4) improves cardiorespiratory capacity, and 5) reduce blood pressure.

Monitoring your Training

Two forms of monitoring your own exercise training are by measuring your heart rate, or quantifying your rate of perceived exertion (RPE). Both are explained in more detail below.

Heart Rate

Recording your heart rate during exercise sessions enables you to ensure you are working at an adequate intensity without causing excessive fatigue. The most common method is to calculate the percent of maximal heart rate (maxHR) at which you are working. Maximal heart rate is determined using the formula: $220 - \text{your current age}$. The proposed maxHR

intensity range to cancer patients and survivors during cardiovascular activities is 60% to 90% of maxHR. For example, a 40 year old should have a maxHR of 180. Therefore the target training heart rate is between 108 to 162 beats per minute.

The simplest method to determine your heart rate is to measure the pulse rate at the wrist counting the number of beats for 15 seconds and then multiplying that by four to calculate beats per minute. However, electronic heart monitors are available, relatively inexpensive and very convenient.

Rate of Perceived Exertion

RPE is a subjective measurement used to determine how you feel at any given time. It is usually taken whilst performing or shortly after completing exercise and is a valuable instrument because it has been well correlated with intensity and effort during and after exercise. RPE can be used in lieu of heart rate in individuals who have difficulty with HR palpation and especially in cases where medications alter HR responses to exercise (e.g. Beta Blockers). The RPE scale below is a typical Borg Scale and exercise intensity should be targeted to fall between 5 and 7 on this scale. To use the scale as yourself this question:

“How hard does this exercise feel now?”

Rating	Descriptor
0	Rest
1	Very, Very Easy
2	Easy
3	Moderate
4	Somewhat Hard
5	Hard
6	–
7	Very Hard
8	–
9	–
10	Maximal

Exercise and Depression

In the last few years there have been a series of research studies that have assessed the effect of exercise on depression. The major findings have been:

1. Regular physical activity decreases the severity of depressive symptoms.
2. These improvements occur after as little as 8 to 16 weeks of exercise training.
3. Home based exercise is as effective as being in a gym or clinic setting.
4. Exercise seems to be at least as effective as medication in reducing depression.
5. Both aerobic and resistance exercise are effective.
6. The positive benefits are long lasting even if the exercise is stopped

Summary

In summary, there is a clear need to increase levels of physical activity within our daily lives. Sufficient activity, typically suggested as 150 min/week or 30 minutes five days per week is regarded as the minimum amount of activity required to attain these physical and psychological benefits. Although we can accumulate enough activity by living a healthy lifestyle and choosing to be active adding structured exercise into our lifestyle is an optimal way to make sure that we remain active and healthy.

Aerobic Exercise – Home Programme

Aim: to complete 150 minutes of home based aerobic exercise per week

This may be done in as many sessions as you want (4 x 30; 6 x 20 etc.). You can also do more than one session per day. Each session must be 10 or more minutes at a time to count towards the target.

Date	Type of Exercise	Start Time	Finish Time	Ave Heart Rate / RPE	Intensity	General Comments
<i>Example</i>	<i>Walking</i>	<i>7:30 am</i>	<i>8:30 am</i>	<i>143 / 7</i>	<i>strenuous</i>	<i>Morning walk around river</i>

Aerobic Exercise – Home Programme (continued)

Date	Type of Exercise	Start Time	Finish Time	Ave Heart Rate / RPE	Intensity	General Comments
<i>Example</i>	<i>Walking</i>	<i>7:30 am</i>	<i>8:30 am</i>	<i>143 / 7</i>	<i>strenuous</i>	<i>Morning walk around river</i>

Aerobic Exercise – Home Programme (continued)

Date	Type of Exercise	Start Time	Finish Time	Ave Heart Rate / RPE	Intensity	General Comments
<i>Example</i>	<i>Walking</i>	<i>7:30 am</i>	<i>8:30 am</i>	<i>143 / 7</i>	<i>strenuous</i>	<i>Morning walk around river</i>

Aerobic Exercise – Home Programme (continued)

Date	Type of Exercise	Start Time	Finish Time	Ave Heart Rate / RPE	Intensity	General Comments
<i>Example</i>	<i>Walking</i>	<i>7:30 am</i>	<i>8:30 am</i>	<i>143 / 7</i>	<i>strenuous</i>	<i>Morning walk around river</i>

Aerobic Exercise – Home Programme (continued)

Date	Type of Exercise	Start Time	Finish Time	Ave Heart Rate / RPE	Intensity	General Comments
<i>Example</i>	<i>Walking</i>	<i>7:30 am</i>	<i>8:30 am</i>	<i>143 / 7</i>	<i>strenuous</i>	<i>Morning walk around river</i>

Aerobic Exercise – Home Programme (continued)

Date	Type of Exercise	Start Time	Finish Time	Ave Heart Rate / RPE	Intensity	General Comments
<i>Example</i>	<i>Walking</i>	<i>7:30 am</i>	<i>8:30 am</i>	<i>143 / 7</i>	<i>strenuous</i>	<i>Morning walk around river</i>

Aerobic Exercise – Home Programme (continued)

Date	Type of Exercise	Start Time	Finish Time	Ave Heart Rate / RPE	Intensity	General Comments
<i>Example</i>	<i>Walking</i>	<i>7:30 am</i>	<i>8:30 am</i>	<i>143 / 7</i>	<i>strenuous</i>	<i>Morning walk around river</i>

“It always seems impossible until it’s done”

- Nelson Mandela