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SUPERVISED EXERCISE FOR OLDER WOMEN RECENTLY DIAGNOSED WITH BREAST CANCER: A PRAGMATIC PILOT RANDOMISED CONTROLLED TRIAL

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A thesis submitted to the University of Huddersfield in partial fulfilment of the requirements for

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Abstract

Background: There is compelling evidence of the benefits that women with breast cancer can experience by participating in physical activity during or post cancer treatment. However, research in this field has been largely conducted with younger women with breast cancer (aged up to 60 years). Evidence from older women with breast cancer is very limited, despite the higher incidence of diagnosis and lower survival rates in this population. Pilot and feasibility work is considered essential to evaluate the feasibility and acceptability of intervention procedures and trial design especially with an under-researched population and is strongly recommended by the Medical Research Council (MRC) when designing or conducting complex healthcare interventions (Craig et al., 2008). To redress this imbalance, the aim of this research was to conduct a pragmatic pilot randomised controlled study of a supervised exercise intervention for older women (aged 60 years and over) with breast cancer to consider whether a 12-week supervised exercise intervention and home-based exercise programme versus usual care was feasible and acceptable. This was done by assessing trial intervention procedures and outcome measures, along with interviews to consider barriers to and motivators for physical activity, with the aim of informing the viability of progressing to a full-scale randomised controlled trial with this population.

Methods: **Study 1:** a pragmatic pilot randomised controlled trial (RCT) of a 12-week supervised exercise intervention was conducted recruiting participants from two hospital sites and a breast cancer charity. Participants were all women over 60-years old, very recently diagnosed with breast cancer (< 2-years) stage I-III (mean=8.34-months post diagnosis, SD=4.50-months). All participants were post-surgery, but may

have been undergoing or recently completed radiotherapy treatment. Most participants were on hormone treatment (77.1%). Patients were randomly assigned to either the exercise intervention or usual care groups. Outcomes to assess the feasibility and acceptability of trial parameters were: recruitment rates and time-scales, randomisation, adverse events, retention and attrition rates at all follow up time-points. Acceptability of the supervised sessions was assessed using Ratings of Perceived Exertion (RPE), implementation fidelity, verbatim comments from the participants recorded at the time and adherence rates to the intervention. **Study 2:** was a qualitative study design, using a purposive sampling strategy with face to face semi-structured, individual interviews, utilising the framework analysis method (Ritchie and Spencer, 1994). Women over 60-years old (mean=67.3-years, SD=5,.14) were recruited via a national breast cancer charity educational programme (< 11-months since diagnosis) or by attendance at an established exercise class for breast cancer patients at the University of Huddersfield (<5-years since diagnosis).

Results: **Study 1:** Eighty-four women were approached who met the inclusion criteria at two hospital sites and a breast cancer charity resulting in thirty-five breast cancer survivors (BCS) (mean age = 67-years ± 5.02) and were randomly assigned to either a supervised exercise intervention group (n=16) or a usual care control group (n=19). The recruitment rate was 35/84 = 41.6%. (11/33 = 33% from hospital sites; 24/51 = 47% from breast cancer charity). Recruitment lasted 22 months. Attrition rates were 12.5% for the intervention group and 26% for the control group. No adverse events were reported. The questionnaire completion rate was 100% at all time-points, as was the 12-minute walk. Body composition assessment was 96.5% completion at baseline and all follow up points (one participant was claustrophobic and did not undertake body composition

assessments). Intervention adherence to the supervised sessions was 87.5%, although home-based exercise adherence was not monitored. **Study 2:** 15 participants were interviewed, all aged over 60-years old (range 60-77-years, mean 67.3-years, SD 5.14). Interview questions were developed from a topic guide using *a priori* themes from Study 1 and utilising existing behaviour change models and frameworks. Three main themes, and eight sub-themes were identified:

Theme 1: Obstructions affecting physical activity with three sub-themes: accommodating other features of the life world; negative consequences of treatment; environmental influences. Theme 2: Factors enabling physical activity with three sub-themes: perceived health and well-being impact; personal and interpersonal considerations; and environmental influences. Theme 3: Wider environmental context with two sub-themes: timing of exercise advice and family and friendship support.

The main barriers to starting or maintaining a physical activity or exercise programme was related to the negative consequences of breast cancer treatment, such as; joint pain, shoulder mobility problems, fatigue and muscle and joint aches. In addition, not knowing what exercise or how much exercise was safe to do also hindered some from starting to be physically active. The main motivators for starting or maintaining physical activity were also related to the negative consequences of treatment, as women reported how they wanted exercise or physical activity to improve these side-effects, such as, reduce fatigue and increase energy levels, help lose weight, improve joint pain and shoulder mobility and to help recover from treatment.

Conclusions: The strengths of this study were the novel population recruited, considering the age of the participants and how recently they had received a breast

cancer diagnosis. It is the first ever study to only recruit older women (>60 years) very recently diagnosed with breast cancer onto a supervised exercise intervention and longitudinally follow them for 12-months. Air Plesythmography (BOD POD^{TM}) was a novel measurement technology used in the study to assess all participants' body composition using air plethysmography. This was the first study to use this measure with older women with breast cancer and to also follow up participants for nine months after the intervention had finished to assess any ongoing body composition changes. The feasibility and acceptability data collected all add to the knowledge and evidence base with this under-researched population. A number of aspects of the intervention worked well. It appeared that once recruited onto the study, attrition rates were favourable (7/35 = 20%) and the trial outcomes and supervised exercise intervention were acceptable with high adherence rates to the supervised intervention (87.5%) and high completion rates to the whole trial. What appeared to be a useful and novel approach to recruiting this population was through a cancer charity and should be considered as an additional recruitment approach alongside the more traditional methods of a hospital setting. One of the main study limitations was not being able to fully assess the feasibility of the intervention because home-based exercise adherence and additional physical activity (PA) outside of the supervised intervention was not monitored. Therefore, we cannot ascertain how effective the overall programme was. An additional limitation was not being able to assess heart rates during the supervised intervention, although RPE was monitored. This would have provided novel, objective data as to the intensity of the intervention, however, it demonstrated, that assessing heart rates with this population in a group setting may be time-consuming and potentially problematic for an exercise instructor on their own to manage. This pragmatic pilot study

demonstrates the difficulties in recruiting this population, particularly from a hospital setting by breast care nurses (31% of study participants). That the exercise intervention was not local to either hospital site appeared to add a further barrier to recruitment (16/84 reported distance to exercise sessions as a reason for non-participation; 19%). The time taken to recruit the number of participants (22-months) could also question the viability of any larger future trials. The barriers and motivators reported by this population appeared to be specific to breast cancer, with the majority related to the disease or treatment side-effects. It may be possible to reduce some of these barriers by better and more education about the benefits of exercise and physical activity. It is also important to further educate health care professionals (HCPs) and family and friends, as the timing of exercise advice and by whom it is given may play an important role in encouraging physical activity during and after treatment. With only the chief investigator able to deliver the exercise intervention at the University site, the distance for some to travel to the University to participate was also a noticeable barrier. For future trials, stop/go indicators (as suggested by the Medical Research Council [MRC]) should be put in place to further ascertain whether a larger scale trial is feasible. Strategies to improve recruitment from the hospital setting need to be developed and more options for local access to the exercise intervention or outcome assessments (based near both hospital sites) need to be considered.

Dedications and Acknowledgements

I would like to thank my Director of Studies, Dr Serena Bartys, who has helped to guide me through every step of this PhD process from inception to completion and write up of this thesis.

I would also like to thank Professor Felicity Aston and Dr Emma Harris who have provided support and advice at much needed times.

I thank all the breast cancer patients who agreed to take part in this research study as without you it would have not been possible to complete.

To my sons, Harry, Oliver and Isaac, thank you for your patience, support and encouragement to complete this study. Sorry it's taken so long!

Brief overview of each chapter of the PhD thesis

The content of this thesis broadly follows the process of investigation recommmended by the Medical Research Council, (Campbell et al., 2000; Campbell et al., 2007; Craig et al., 2008; Craig et al., 2013), described in the introduction and shown below in Fig. 1. The early **chapters 1-3** introduce the subject of this thesis and provide the theoretical background and rationale for the research. **Chapter 1** provides an introduction which briefly summarises the size and scale of breast cancer, the common side effects that may accompany treatment and introduces the concept of physical activity as an important mechanism that could be used to help treat or prevent some of these treatment-related side effects. The aims and objectives of the thesis are also stated along with a brief overview of the MRC guidelines that have helped to frame this PhD study. **Chapter 2** considers the journey of a breast cancer patient covering referral mechanisms, screening and tests to diagnose breast cancer along with common curative treatments. Finally, the often debilitating side effects that can be experienced from these life-saving treatments are discussed. **Chapter 3** introduces and explores the role that exercise and physcial activity can play in reducing breast cancer treatment-related side effects and the effects of physical activity on the quality of life of breast cancer survivors. The evidence of the role physical activity has in reducing breast cancer recurrence and mortality is explored and the mechanisms underlying this relationship are considered. To conclude this chapter a summary of the exericse literature for older adults *without* cancer is briefly explored to highlight the benefits of exercise and physical activity that older adults without cancer can obtain. **Chapter 4** completes the first stage identified by the MRC guidelines for the development of complex interventions (Phase 0 – pre-clinical/theory) with a rapid evidence review of the quantative literature of

exercise and physical activity with older women with breast cancer, following a recognised and rigourous systematic process, with the aim to reduce the possibility of bias whilst determining what we know about exercise with this specific but under-researched population. This chapter concludes with the rationale for this PhD research project and the aims and objectives of the thesis. **Chapter 5** is a critical appraisal of the philosophical assumptions about the scientific methodology used in this thesis, suggesting why they are considered the most approriate for meeting the research aims and objectives. The chapter will cover the design of the research and the underpining theoretical framework, such as the MRC guidelines for the design and conduct of complex interventions, that has been followed and utilised. Chapters 6 and 7 detail the research studies that have provided new data in this thesis. **Chapter 6** details the feasibility of the intervention procedures and outcome measures, as recommended by the MRC , to be evaluated before a full RCT should be undertaken or considered. This chapter explores the feasibility of recruitment rates and timescales, randomisation procedures, adverse events, retention and attrition rates to the study overall, the acceptability of the intervention and adherence to the intervention outcomes measures were also explored. **Chapter 7** provides further feasibility information to whether a full RCT is warranted by exploring the barriers to and motivators for exercise and physical activity for this population following a diagnosis of breast cancer. The participants in this second study were a mixture of recently-diagnosed women over 60 years old, participants who had been involved in the feasibility trial from either the intervention group or the control group and older **Chapter 8** is a general discussion of the key findings and the contribution of new knowledge that has emerged from both studies reported in this thesis. It concludes this PhD research by summarising the main recommendations

for future research based on the results of the research and interprets the scope, significance and limitations of any findings that have emerged that may contribute to clinical practice and furthering the knowledge of cancer and exercise required by exercise practitioners and medical professionals.
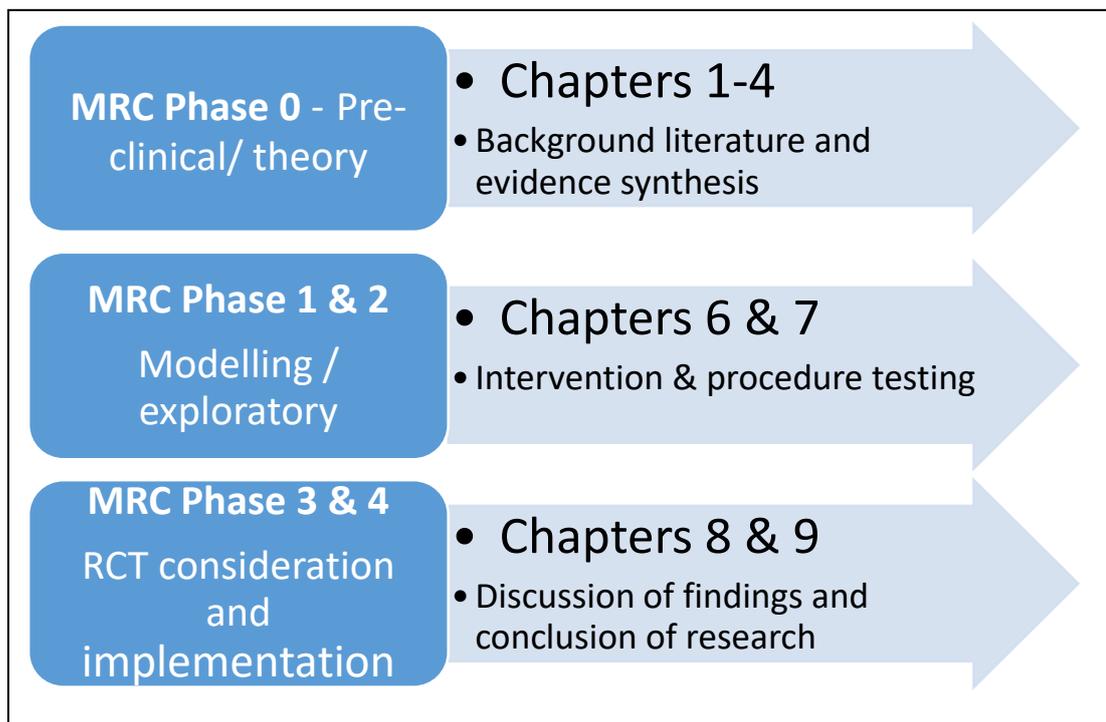
Figure 1: The structure of this PhD thesis according to the Medical Research Council Framework for complex interventions (Craig et al., 2008)

Chapter 1: Introduction

1.1 Introduction

This thesis details an investigation into the feasibility of a 12-week exercise intervention with women aged over 60 years recently diagnosed with breast cancer. Although major advances have been made in managing breast cancer, patients still have to deal with severe side-effects and psychological distress during and after adjuvant therapy (Furmaniak, Menig, & Markes, 2016). Furthermore, many of the adverse side effects are often long-lasting because of the disease and treatments. These may include cancer-related fatigue (CRF), changes in body composition, lymphoedema (swelling of the arm due to an accumulation of lymphatic fluid), osteoporosis (due to accelerated bone mineral loss), anxiety and depression (Demark-Wahnefried et al., 2012; Hormes et al., 2010; Mishra et al., 2012).

Breast cancer is the most frequently-occurring cancer in women in the United Kingdom, with approximately 53,400 women being diagnosed with breast cancer in 2013, although it is rare in men (Cancer Research UK, 2016). Maddams, Utley, and Moller (2012) estimated that by the end of 2008, there were more than 2 million cancer survivors in the UK and it is forecasted that there will be more than 3.2 million people living with and beyond a diagnosis of cancer by 2020. Cancer survivors who have successfully completed their treatment often expect to continue with work and "normal" life at levels similar to those experienced before their diagnosis of cancer; however, whilst cancer treatment can prolong survival it can often be very intensive, leading to a number of negative and unwanted physiological and psychological side-effects that can hinder a cancer survivors return to normal life (Fong et al., 2012)..

Female breast cancer is strongly related to age, with much higher incidence rates with increasing age. In 2011-13 almost half of all breast cancer diagnoses were in women over 65 years old (Cancer Research UK, 2016). These statistics are also strongly related to survival, with advancing age lowering survival rates. However, the generalizability of research findings of exercise and breast cancer may not be applicable to the whole breast cancer population because the majority of cancer survivors (60%) in the UK are aged over 60 years with the mean age of diagnosis between 60-64 years, with 25% of all breast cancer diagnoses made between the ages of 60-69 years (Cancer Research UK, 2016). In the USA, the median age of breast cancer diagnosis among women is 62 years (Howlader et al., 2012). Even with this knowledge, it appears that the majority of women recruited to breast cancer and exercise studies are much younger than this. In a Cochrane review and meta-analysis of exercise and breast cancer, of the 1,042 women from 15 exercise interventions during adjuvant treatment for breast cancer that were included in the review, the mean age of the women was 50 years (Markes, 2009). A series of other large–scale breast cancer and exercise trials and reviews have also reported a similar mean age of 51.7 years with 3,777 women having been recruited and taken part in these trials (McNeeley et al., 2006; Courneya et al., 2007; Mutrie et al., 2007; Kim at al., 2009; Fong et al., 2012).

However, exercise is becoming increasingly recognised as an important treatment for the recovery and rehabilitation of cancer patients (Spence, Heesch, & Brown, 2010), and has long been considered a useful therapy to offset the declines in physical and mental functioning brought on by ageing and long-term medical conditions Courneya et al., 2004). Physical activity has been consistently identified as a fundamental element of rehabilitation for many chronic diseases and disabilities and has been successful in

improving quality of life and reducing all-cause mortality (McNeely et al., 2006). Cancer survivors are at greater risk for other cancers, cardiovascular disease, osteoporosis, diabetes and accelerated function decline, than those who have not had a diagnosis of cancer (Demark-Wahnefried et al., 2006). Therefore, it is even more important that cancer survivors become physically active. The evidence of the benefits of exercise for cancer survivors has been steadily increasing over the past twenty years, specifically in the areas of quality of life outcomes (Maryam, Fazlollah, Eesa, Ebrahim, & Abbas, 2010; McNeely et al., 2006), cancer related fatigue (Schneider, Hsieh, Sprod, Carter, & Hayward, 2007), functional capacity, strength and endurance (Pinto et al., 2005; Cheema et al., 2008; Adamsen et al., 2009) and improved body composition (Courneya et al., 2007; Schmitz et al., 2005)

It appears the existing evidence from older women with breast cancer involved in exercise intervention studies is very limited. Therefore, the focus of this PhD investigation was to examine the feasibility of women aged over 60 years old recently diagnosed with breast cancer being recruited to participate in a 12-week exercise programme. Another research gap identified in the literature is that of long term outcome measures. Thus, follow up of outcome measures over 12-months would also be reported. This in itself appeared to be a relatively simple and straightforward intervention; however, it became apparent that the process of investigation was far more complex, as exercise intervention studies in the UK have not specifically targeted this older breast cancer population before. From an ontological and epistemological standpoint, the author's "worldview" of research paradigms is to consider pragmatism and mixed methods research as the most appropriate approach when conducting this research. The aim of this research is not to solve the methodological differences

between the purist positions (qualitative vs quantitative), but rather to use a method and philosophy that attempts to fit together the insights provided by qualitative and quantitative research into a practical and workable solution (Johnson & Onwuegbuzie, 2004).

1.2 Aims and objectives

From the outset the key aim from which this work evolved was as follows:

"To determine the feasibility and acceptability of a 12-week supervised aerobic and resistance training programme on females over the age of 60 who have very recently been diagnosed with breast cancer and are undertaking treatment or have just finished adjuvant treatment".

The objectives considered during the study were:

1. To assess the feasibility of the recruitment of older women with breast cancer during and immediately after adjuvant therapy;
2. To assess the feasibility and acceptability of the trial intervention;
3. To assess the feasibility and acceptability of the trial outcome measures;
4. To record and report any adverse events from the exercise programme (injury, lymphoedema);
5. To examine barriers to and motivators for exercise after breast cancer diagnosis.

In order to ensure a systematic process of investigation, a step-wise process was proposed following the MRC guidance for the development and evaluation of complex

interventions (Craig et al., 2008). This framework, originally developed in 2000 and later updated in 2008 has helped researchers to adopt appropriate methods to answer the key questions when evaluating complex interventions; are they effective in everyday practice and how does the intervention work: what are the active ingredients and are they effective? (Craig et al., 2008). This framework was used as a guide throughout this study. Campbell et al. (2000) consider complex interventions are those that include several components and evaluation of complex interventions requires the use of both qualitative and quantitative evidence with the aim of considering all the components that are required to enable a well-informed decision before committing to a definitive and much larger RCT with the population.
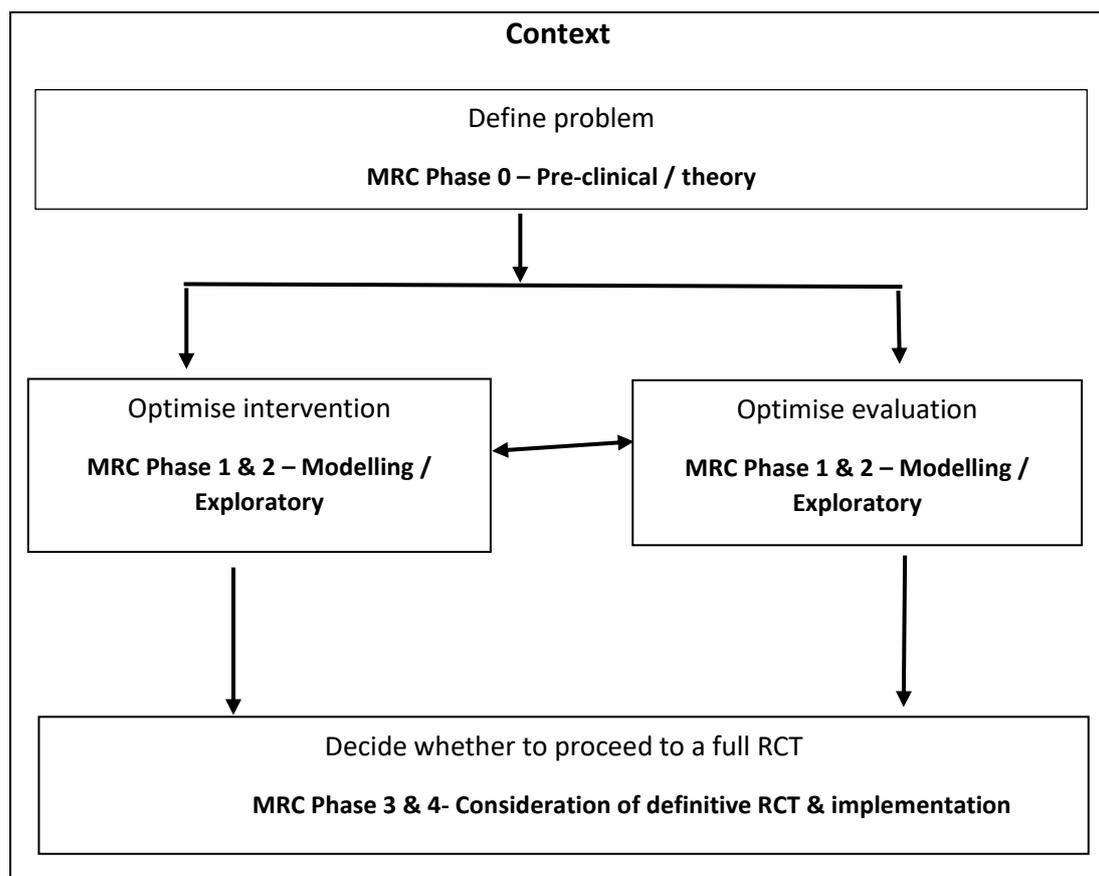
Figure 2: Relationship between context, intervention and evaluation of complex interventions (Craig et al., 2008)

To address the aims and objectives of this PhD thesis, and by following the step-wise process proposed by the MRC framework, this thesis has focussed on the preliminary work required before a definitive RCT could be considered or undertaken. It followed partly the suggestions by Campbell and colleagues (2007) who found it useful to consider phases 0, 1 and 2 of the step-wise approach as part of one larger activity rather than sequential stages (Campbell et al., 2007) and considered it in a parallel approach – pragmatic in nature. This thesis considered the three phases to assess the feasibility and acceptability of trial procedures and outcome measures of a pragmatic pilot RCT and a qualitative study to explore thoughts and feelings about exercising and being more physically active after a recent diagnosis of breast cancer.

Phase 0 – "Pre-clinical or theoretical" stage (why should we do this intervention?); the existing research evidence was synthesised in order to examine and establish what was already known about this older population and exercise after a breast cancer diagnosis and identify what kind of intervention was required. Phase 1 – "Modelling" (how does it work?) and Phase 2 - "Exploratory" stage; a pragmatic pilot RCT to assess the feasibility of the study design, protocol, outcome measures conducted, and to provide important information about the proposed design of the intervention, the subsequent outcomes measures and the evaluation of these methods (Craig et al., 2008). This was followed by a qualitative study to explore the barriers to and motivators for exercise and physical activity for women over 60 after a diagnosis of breast cancer. The experiences of designing and then conducting the intervention and the subsequent interviews of the target population provided valuable research skills for the PhD researcher and helped to generate new knowledge to inform learning and provide lessons regarding how to approach future research with this population and whether or not it would be advisable

to proceed with the implementation of a full-scale RCT (Phase 3 – Definitive randomised controlled trial and Phase 4 – Implementation). This invaluable learning will be discussed in the conclusion of this thesis.

Chapter 2: Diagnosing and treating breast cancer

2.1 Introduction

In 2012, it was estimated that nearly 1.7 million women worldwide were diagnosed with breast cancer, accounting for around 522,000 deaths (Ferlay, Steliarova-Foucher, Lortet-Tieulent et al., 2013). This was an increase in breast cancer incidence by nearly 18% since 2008. It has been predicted that worldwide the incidence of breast cancer will reach 3.2 million new cases per year by 2050. These predicted figures reflect the magnitude of breast cancer, its effect on society worldwide and the urgent need for better preventative and treatment measures (Tao et al., 2014).

Area	Incidence	Mortality	Survival (5 years)
Worldwide	1.68m (2012)	522,000 (2012)	80-90%
Europe	464,000 (2012)	131,000 (2012)	82%
UK	55,222 (2014)	11,433 (2014)	87% (2012-11)

Table 1: Global incidence and survival of breast cancer
(taken from Ferlay, Steliarova-Foucher, Lortet-Tieulent et al., 2013)

Table 1 shows the global incidence, mortality and survival rates for breast cancer. Whilst the mortality rate is significant, progress has been made in terms of prognosis and survival. Although the incidence of breast cancer is increasing, mortality rates from breast cancer have fallen steadily since 1990, having been previously stable or increasing for a number of decades. The fall in mortality rates during this period has been attributed to three key factors. These are: improved screening and detection programmes; a greater public awareness of the early signs and symptoms; and the widespread use of systemic therapies with Tamoxifen (Benson et al., 2009; Berry et al., 2005).

Women are now living longer with a diagnosis of breast cancer than ever before. More than 90% of women diagnosed early with stage 1 breast cancer survive the disease for at least 5 years. Almost 8 in 10 women will now survive for longer than 10 years following diagnosis and almost 70% beyond 20-years (Quaresma, Coleman & Rachet, 2014). These increases in cancer survival rates will have implications for health care required by cancer survivors, with a greater focus on community care and self-management of the long-term effects and consequences of cancer treatments. As the population of cancer survivors increases in both numbers and with advancing age, cancer has now largely become considered a long-term condition. Efficient and effective management by a range of healthcare providers and specialist clinicians will be required to support many more elderly cancer survivors (Maddams et al., 2012).

To continue to improve cancer survival rates the Department of Health published: *Improving Outcomes: A Strategy for Cancer* (DoH, 2011). This strategy has resulted in initiatives such as the National Awareness and Early Diagnosis Initiative (NAEDI), which is a partnership between the Department of Health, National Cancer Action Team, and

Cancer Research UK. The role of NAEDI is to promote the benefits of an early diagnosis of cancer, and involves research to further improve survival from cancer.

2.2 National policies on cancer care delivery

In the UK, cancer treatment is mainly delivered through the National Health Service (NHS). To improve cancer care delivery and to try to reduce inequalities in treatment provision, the NHS Cancer Plan (2000) was a strategy produced to shape and standardise cancer services in England. This has been a priority of the Department of Health since its ten-year Cancer Plan was produced. For the first time this plan provided a comprehensive strategy for bringing together prevention, screening, diagnosis, treatment and care for cancer. Following on from the progress of the NHS Cancer Plan, the Department of Health published its five-year Cancer Reform Strategy (2007) to set out aims of developing cancer services to be among some of the best in the world by 2012. This strategy set out a programme of action across ten areas: six to improve cancer outcomes (preventing cancer, earlier diagnosis, better treatment, living with and beyond cancer, reducing inequalities in cancer care and delivering care in the appropriate setting) and four to ensure delivery (using information to improve quality and choice, better commissioning, improved funding and building for the future). The government and NHS appear committed to ensuring that cancer services "are among the best in the world" Improving outcomes: A strategy for cancer (DoH, 2011) and more recently the Independent Cancer Taskforce published their strategy: Achieving World-Class Cancer Outcomes (2015-2020): Cancer Strategy for England. This sets out how England wants to radically improve the outcomes that the NHS delivers for people affected by cancer. This key report describes provision over the next five years and sets

out six strategic priorities. First, a radical upgrade in prevention and public health, including a new tobacco policy and a national obesity plan. Second, to achieve earlier diagnosis, whereby 95% of patients referred for cancer testing are definitely diagnosed or cancer is excluded within four weeks. Third, to improve patient experience through improving communication and information. Fourth, every person with cancer to have access to elements of a recovery package and follow-up care for common cancer. Finally, to make investments in high quality equipment to be able to deliver faster and more effective services and overhaul the process for commissioning to ensure that it is clearer, establishing Cancer Alliances across the country to bring together key partners to drive and support improvement at a local level.

2.3 Evaluating the effect of cancer care policy

Since the introduction of the NHS Cancer Plan in 2000 and the publication of the five-year Cancer Reform strategy in 2007, significant progress has been made in improving cancer services, with falling mortality rates whilst incidence rates have increased. According to the Cancer Strategy for England (2015) the number of people being diagnosed and living with cancer will continue to grow rapidly even with major improvements in prevention, due to the ageing population and the success of increasing survival. Variations and inequalities in outcomes and access to services persist throughout the country, especially for older patients and particularly those from lower socio-economic groups who are more likely to experience worse outcomes. Furthermore, data for the cost-effectiveness of cancer care have not improved in line with the development of data on cancer treatments and outcomes; it appears that this

lack of cost-effectiveness data restricts commissioners' ability to make fully-informed decisions about which treatments offer the best value for money or whether resources are being used to best effect (NAO, 2015).

The introduction of the Cancer Strategy for England (2015) has resulted in the establishment of a number of Cancer Alliances across the country. Breast cancer survival rates are higher now than those reported for any other cancer afflicting females, but evaluating success purely on length of survival is limited as the quality of life during survival is important. Other measures should be used to assess the quality of life during survival in view of the treatment-related side-effects and long-term consequences of treatment, all of which can be a burden on physical and psychological morbidity.

2.4 Screening and tests to diagnose breast cancer

2.4.1 Referral guidelines

The majority of women attending a specialist breast clinic will have been referred to it by their GP. The Department of Health in 2000 and the National Institute for Health and Clinical Excellence in 2005 (NICE, 2005) published referral guidelines for patients presenting with breast cancer symptoms. These guidelines allow for prompt appointments to be made to ensure urgent referrals are seen by a breast specialist within the national targeted time-frame of two weeks. All patients presenting with breast symptoms should undergo a triple assessment, involving history taking and physical examination, followed by breast imaging (radiological assessment) and pathological assessment.

2.4.2 History and physical examination

The clinical history is important in establishing cancer risk and the presence or absence of symptoms indicative of breast cancer. It should include age at menarche, menopausal status, previous pregnancies, use of oral contraceptives and post-menopausal hormone replacement. In addition, a family history of breast cancer in first-degree relatives should be assessed (Shah, Rosso, & Nathanson, 2014). An estimated risk for breast cancer may be determined by using prediction models which indicate risk followed by physical examination. The most well-known and widely used risk prediction screening tool is the Breast Cancer Risk Assessment Tool (BCRAT), or the Gail model, developed by Dr. Mitchell Gail (Benichou, Gail, & Mulvihill, 1996). Prediction models are used to stratify a person's risk of developing breast cancer based on the presence of known and quantifiable risk factors. The concordance statistic or "c-statistic" of 0.5 indicates that the prediction model is no better than chance at discriminating patients who are at risk from those who are not. The c-statistic of the Gail model has been reported to be between 0.55-0.67 (Rockhill, Spiegelman, Byrne, Hunter, & Colditz, 2001). Other commonly-used prediction model are the Claus model with a c-statistic of 0.56 (Amir, Evans, Shenton, Lalloo, & Moran, 2003) and the Breast Cancer Pro (BRCAPRO), a computer model which assesses a women's risk of developing breast cancer or carrying the BRCA gene mutation. The c-statistic for the BRCAPRO is 0.72-0.92 (Parmigiani, Chen, Iversen, Friebel, 2008). Physical examination will check for skin changes such as dimpling, visible lumps, nipple retraction and peau d'orange with a patient in both sitting and supine position with the cervical supraclavicular and axillary lymph node basins palpated for adenopathy (Osborn & Vaughan-Williams, 2010; Shah et al., 2014).

2.5. Radiological assessment

2.5.1 Mammography

One of the most important advances in the treatment of breast cancer is early detection of non-palpable masses, and mammography remains the mainstay in breast cancer detection and the gold standard for breast imaging (Smetherman, 2013). Mammograms have a sensitivity of up to 90% in women over the age of 50 years. All women in the UK from the age of 50 should have a routine mammogram every three years, although mammograms are not routinely performed in women under the age of 50 because an accurate assessment is difficult due to denser breast tissue. Mammograms are performed in women who have a palpable mass or other symptoms of breast disease, a family history or have been recalled because of an abnormal previous mammogram. Typically, a two-view mammogram of each breast is performed to allow comparison of potential abnormalities between both sides with carcinomas usually presenting as masses, asymmetries and calcifications (Osborn & Vaughan-Williams, 2010; Smetherman, 2013).

2.5.2 Ultrasound

Ultrasound scanning should be used as an adjunct to mammography. It may be used in high-risk patients with dense breast tissue where mammographic sensitivity is lower, allowing the clinician to screen for breast cancers that may have not been detected by traditional mammography, to assess for abnormalities on mammography or magnetic resonance imaging (MRI), problems with breast implants and is particularly useful in the

assessment of discrete lumps (Berg, Blume, Cormack, Mendelson, & Lehrer, 2008; Kelly, Dean, Comulada, & Lee, 2010).

2.5.3 Magnetic Resonance Imaging (MRI)

Breast magnetic resonance imaging (MRI) is an expensive technique which is reserved for certain clinical settings (Bansal & Gower-Thomas, 2010). MRI scanning of the breast is indicated if there has been a discrepancy between the clinical, mammographic and ultrasound measured size of the tumour, if breast augmentation has been considered or mammographic evaluation is limited by augmentation, if the density of the breast tissue is not appropriate for mammography and to assess the size of lobular carcinomas (Osbourne & Vaughan-Williams, 2010). Other uses of breast MRI include evaluation of response to neo-adjuvant chemotherapy with imaging before, during and after treatment and identification of any disease present in patients with positive margins after lumpectomy (Shah et al., 2014). An important application of MRI is in the screening of women with increased familial breast cancer and especially those carrying BRCA1 or BRCA2 genes, in which mammography may be ineffective. With a lifetime risk of 60-85% for developing breast cancer, NICE have published guidelines recommending MRI screening in these women (NICE, 2006; Bansal & Gower-Thomas, 2010). However, the value of pre-operative MRI remains controversial. Although high-quality MRI in a multi-disciplinary setting can help with surgical planning, the concern remains that the lack of specificity in detecting multi-centric lesions could lead to unnecessary mastectomies (Gonzales, Sandelin, Karlsson et al., 2014; Sung, Li, Da Costa et al., 2014;). Furthermore, Harbeck and Gnant, (2017) suggest multicentric tumours need to be properly diagnosed

before surgical planning and mastectomies should not be indicated based solely on an MRI.

2.6 Pathological assessment

2.6.1 Biopsy

A breast mass warrants biopsy with the exception of a simple cyst, a fluid filled mass that may be aspirated and the removal checked by ultrasound or palpation (Pengally, Lambert, Khan, & Groome, 2014). Core biopsy of a breast lump is carried out, preferably under guided imaging via ultrasound or mammography to enhance the accuracy of the technique, and provides an image of the biopsy being performed, which may be useful in the multi-disciplinary team (MDT) meeting (see Section 2.8 below for further discussion) and if conducting further investigations. Biopsy options may include core needle biopsy, fine needle aspiration cytology (FNAC) and incisional or excisional procedures that partially or completely remove the suspicious lesion (Zhang, Wei, Li et al., 2013). Using core biopsy, clinicians are provided with a wealth of information, including cytological information, grade and tumour receptor status, prior to surgery. This is particularly useful in treating elderly women as hormonal therapy may be the primary form of treatment. Core biopsy has become the preferred method to investigate breast abnormalities, allowing the removal of small slivers of tissue and can be undertaken in the clinical setting with little preparation or with ultrasound guidance. Core needle biopsies provide pathological information that can be used for planning local treatment (Zhang et al., 2013). Although it is a relatively invasive procedure requiring local anaesthesia and can lead to extensive bruising it is generally well

tolerated (Osborne & Vaughan-Williams, 2010). The role of FNAC is to obtain cells from a lesion for the histopathology laboratory to analyse. It is a safe and quick procedure to perform, allowing cytology results to be available quickly but does not give much information about the pathological characteristics and does have a high false-negative rate. Open incisional or excisional biopsies are usually performed as follow-up biopsies when the initial biopsy has not provided adequate information to confirm the nature of the lesion.

2.7 Cancer staging

The clinical stage of breast cancer is defined describing the size of tumour in centimetres, presence or absence of axillary node enlargement and involvement, skin involvement and the presence or absence of regional or distant metastatic disease (Lester, 2015; National Cancer Institute, 2015). The patient is clinically staged using the acronym TNM (Tumour, Node, Metastasis) using the American Joint Commission on Cancer (AJCC) guidelines (O'Connell, Maggard, & Ko, 2004). Neo-adjuvant chemotherapy may be given before surgery to help achieve tumour reduction and offer less aggressive surgery, especially in patients presenting with locally advanced breast cancer or in borderline cases where the tumour to breast ratio will not allow for removal and acceptable cosmetic results (American Cancer Society, 2014; Shah et al., 2014). Even if neo-adjuvant chemotherapy is administered the clinical stage (before chemotherapy) is often considered the accurate stage rather than compared to a downgraded outcome subject to effective chemotherapy (Bhoo-Pathy et al., 2015). The histological classification of invasive breast cancers indicates the anatomical source of the

malignancy and includes: infiltrating ductal (70-80%), invasive lobular (8%-10%) and inflammatory (2%) breast cancer, the most lethal form of breast cancer with very fast progression of local tumour and metastasis (Yamauchi, Woodward, Valero et al., 2012; American Cancer Society, 2014).

2.8 Multi-disciplinary teams

Best practice in breast care is provided by a range of breast specialists and form the basis of multi-disciplinary teams (MDT). Therapy concepts and decisions regarding the best and most appropriate treatment are made in conjunction with the patient after discussions and recommendations within a multi-disciplinary team meeting. Prognostic factors, tumour size, nodal involvement, spread of the disease, hormonal status (oestrogen and progesterone receptor status), biological tumour subtypes such as triple negative breast cancer or human epidermal growth factor receptor 2 status (HER2 receptor status) will be carefully scrutinised and considered. Additional factors relating to age, menopausal status, medical history and family history of breast or ovarian cancer will be discussed in the decision-making process. Many patients with early breast cancer require combination adjuvant treatment therapy, making it a complex planning process (Osborn & Vaughan-Williams, 2010; Passant & Borley, 2010; Harbeck & Gnant, 2017).

2.9 Treatment of invasive breast cancer

2.9.1 Surgery

The majority of patients who are diagnosed with breast cancer will undergo surgical treatment. This may be followed by adjuvant chemotherapy, radiotherapy and hormone therapy. Surgical treatment is a primary intervention intended to provide local control by removing the tumour and any visible or microscopic tumour cells and to identify the pathological stage of the disease. Several combinations of surgical procedures may be performed depending on the size and site of the tumour and the clinical stage of the disease (Lester, 2015).

2.9.2 Breast conserving surgery

Breast conservation is established as the intended surgical standard for most clinical situations in breast cancer (McLaughlin, 2013). Conservation surgery represents 75-85% of all breast cancer operations (Veronesi et al., 2005). Developments in surgical techniques and multi-disciplinary approaches (including neo-adjuvant systemic therapy), as well as increased treatment of patients in dedicated breast units have improved women's access to this life-saving treatment (Mansfield, Agrawal, & Cutress, 2013). Patients with a single lesion measuring 4cm or less (either invasive or Ductal Carcinoma in Situ) are suitable for breast-conserving surgery (often known as a lumpectomy or local wide excision). There is no significant difference in local recurrence rates or overall survival when breast-conserving surgery is compared to mastectomy Local recurrence rates with either method should be less than 5% at 5 years (Fisher, Anderson, & Bryant, 2002; Osborn & Vaughan-Williams, 2010). Breast conserving

surgery is contraindicated in women with a history or previous radiation therapy to the chest or breast, current pregnancy, widespread disease, positive margins that were not cleared with a repeat lumpectomy or suspicious microcalcifications (Jorns, Daignault, Sabel, & Wu, 2014).

2.9.3 Mastectomy

Total removal of the mammary gland (mastectomy) may be needed with invasive, extensive, large or inflammatory carcinomas, local recurrence following breast conserving surgery, inherited genetic mutations, a significant family history, tumours which have not been reduced enough by neo-adjuvant chemotherapy or a combination of these factors (Veronesi et al., 2005). Prophylactic mastectomies are performed to take out the breast tissue bilaterally and remove all of the breast tissue. Since the complete removal of all breast cells is virtually impossible, long term follow-up is still necessary (Lester, 2015). Prophylactic contralateral mastectomy is a common request from patients who require a mastectomy on the affected side or in lieu of breast-conserving surgery. According to Berry and Gomez (2010) between 48-52% of patients in the UK undergo a mastectomy to treat their breast cancer, which is considerably higher than figures they report from Paris and Milan (although these are not country-wide statistics). In the United States, Shah et al. (2014) suggests approximately 30% to 40% of patients are eligible for mastectomy or chose to have one. However, according to (Hamelinck et al., 2014; Jatoi & Parsons, 2014) and, the increasing trend of patients being directed to have voluntary bilateral mastectomies is of concern. Although they accept patient choice as important, the increase in the number of these surgeries does not align with the evidence that contralateral mastectomy either lowers mortality or improves survival (Kurian et al., 2014). Published evidence that supports the decision-

making process for this more aggressive treatment is lacking. Hamelinck et al., (2014) conducted semi-structured interviews with nine women who voluntarily elected for contralateral prophylactic mastectomy over other surgical choices. A number of factors that influenced their decision-making process included: personal evaluation of the risks and benefits, future avoidance and worry of further biopsies and cancer assessments, and a desire to maintain or maintain breast appearance. Preferences for this type of surgery may relate to perceptions of disease recurrence and survival and concerns about body image; however, clinicians have a clear ethical responsibility to ensure that patients have all the information about options and consequences of this surgery including the evidence of survival to ensure that patients are not making decisions based on fear alone (Jatoi and Parsons, 2014; Kurian et al., 2014).

2.9.4 Axillary surgery

Axillary node status is the single most important prognostic indicator in breast cancer staging. All patients undergoing surgery to the breast for invasive cancer or extensive, high grade ductal carcinoma in situ (DCIS), requiring mastectomy should have an axillary staging procedure. This test provides prognostic information to guide the use of appropriate adjuvant therapy and provide local disease control (Berry & Gomez, 2010). One of the areas of most significant change in breast cancer management is that complete lymph node dissection (ALND) or removal of level I and II axillary nodes are no longer standard practice. A sentinel lymph node biopsy (SLNB) has superseded both axillary node sampling and axillary node clearance as the initial staging choice due to its much reduced rate of complications (Berry & Gomez, 2014). A sentinel lymph node biopsy can be performed at the time of surgery. It is based on the principle that breast

cancer drains into a chain of lymph nodes. If the first lymph node in the chain (the sentinel node) does not show any sign of cancer, the other nodes should also be free of cancer. If a sentinel lymph node biopsy provides evidence of metastatic spread to the lymph nodes then further axillary treatment will be required.

In one of the very earliest randomised trials into SLNB, Veronesi et al. (2003) randomised 516 patients to receive SLNB followed by routine ALND, or SLNB, followed by ALND only if metastatic disease was found during the SLNB. At 10 year follow-up, no differences were observed between the groups in recurrence of axillary cancer (0% in the SLNB vs 2% in the ALND group) or disease free survival (89.9% vs 88.8%)(Veronesi et al., 2010). These research findings question whether all patients with a positive SLNB require complete ALND. For patients who have node-negative disease, it raised the question whether ALND was required for all patients.

Findings from the American College of Surgeons Oncology Group (ASOCOG Z0011) trial (Caudle et al., 2012) helped to address these questions. Patients identified with T1 and T2 tumours undergoing lumpectomy who were found to have metastatic disease in the sentinel node were randomised to undergo either ALND or no further treatment to the axilla. At 5-years, the local recurrence rate was 1.6% in the SLNB group compared to almost double (3.1%) in the ALND group. There was also no difference in 5-year disease free survival. The results from the trial and at 5-year follow appear to suggest that for select patients with non-positive breast cancer, SLNB alone does not result in inferior survival or inadequate local disease control (Giuliano et al., 2011).

2.10 Adjuvant radiotherapy in the treatment of early breast cancer

Radiation therapy is an essential component of local treatment of the breast and is most commonly administered after lumpectomy, following mastectomy or in those patients with multiple positive lymph nodes (Bauer & Lester, 2014; Marta et al., 2015). Patients who have undergone breast conservation surgery for primary invasive breast cancer are usually treated with post-operative adjuvant radiotherapy, as long-term follow up has confirmed significant increased rates in local recurrence and possible risk of distant disease recurrence when radiotherapy has been omitted, and improved survival in those patients treated with radiotherapy with more aggressive disease(BASO, 2009; Fisher et al., 2002). In a systematic review and meta-analysis of five randomised clinical trials with a sample of 3,190 patients, those who received radiotherapy had a lower relative risk of local recurrence (pooled odds ratio [OR] 0.36; 95% CI 0.25-0.50). The 5-year absolute risk was 2.2% (95% CI 1.6-3.1) among patients who received radiotherapy compared to those who did not (6.5%, 95% CI 5.3-7.9) (van de Water et al., 2014). These results suggest that patients who received radiotherapy had a lower relative risk of local recurrence, the absolute risk was low, and overall survival was no different. Whole breast radiation therapy following lumpectomy has demonstrated similar mortality rates as mastectomy but with fewer long-term consequences of treatment reported (Moran & Truong, 2014; Wobb et al., 2015). Passant and Borley (2013) continue suggesting that radiation to the whole breast reduces local recurrence after wide local excision by two-thirds.

The Early Breast Cancer Trialists Collaborative Group (EBCTCG) demonstrated that radiotherapy gives significantly better control of local recurrence than no radiotherapy but with little effect on mortality within the first 5-years of treatment (Clarke et al., 2005). A relatively new approach to breast radiotherapy following breast conserving surgery is accelerated partial breast irradiation (APBI). This approach reduces the number of days receiving radiation, the area of breast needed to be treated and the overall amount of radiation required. Bauer and Lester, (2014) found that larger and more frequent doses of radiation may be superior to whole breast radiation; however, there are insufficient large scale, prospective, randomised trials to fully assess the value and benefits of APBI to whole breast radiation (Bauer & Lester, 2014; Moran & Truong, 2014).

Patients who have undergone adequate surgical axillary assessment do not usually receive axillary radiotherapy. Axillary node positive patients who have undergone axillary clearance are also not usually treated with radiotherapy unless the MDT suggest high risk of relapse. A further option of a positive sentinel node could be radiotherapy to the axilla; however, the benefits of these dual treatments options have to be considered against the increased risk of lymphoedema (BASO, 2009). Donker et al. (2014) in their AMAROS trial reported that axillary radiotherapy was not an inferior option versus axillary lymph node dissection, although because of the low numbers of level III dissections and wound infections in the surgery group that could have affected the data, caution should be taken when interpreting the results. However, further research and evidence into this radiotherapy approach of targeting the axilla has gained momentum. In a 10-year follow up of the EORTC trial, Bartelink et al. (2007), suggested a 5-year overall survival benefit (82.3% in the nodal radiotherapy group vs 80.7% in the

control group (no nodal radiation)[Hazard Ratio (HR) for death, 0.87, 95% CI 0.76-1.00, p=0.06]). The MA-20 trial suggested the addition of regional nodal radiotherapy to whole-breast radiotherapy did not improve overall survival but did reduce recurrence of breast cancer (Whelan et al., 2015). In a meta-analysis of the above trials (EORTC and MA-20) both overall and metastasis-free survival were significant in the nodal irradiation groups, supporting the increasing promotion of this adjuvant therapy.

2.11 Adjuvant systemic therapies in the treatment of early breast cancer

Even with effective local treatment as described above, Passant and Borley, (2010) consider that micro-metastases are often present with early stage breast cancer because many patients develop metastases over time. Improvements in local control provide only a small decrease in distant metastases. The increasing and improved survival rates for patients with early-stage breast cancer have been achieved by systemic treatments.

2.11.1 Neo-adjuvant systemic therapy

Neo-adjuvant systemic treatment has emerged as a standard of care for treatment when primary breast conservation surgery is not possible because of large, locally advanced or inoperable tumours or inflammatory breast cancer. Both cytotoxic and endocrine therapy are used, and targeted therapy may be used depending on the tumour biology (Teshome & Hunt, 2014). These treatments can down-stage inoperable cancers to be

operable and reduce the size of large cancers so that they can be treated with breast-conserving surgery (Osborn & Vaughan-Williams, 2010).

2.11.2 Adjuvant chemotherapy

In what is considered a landmark study, Bonadonna and his colleagues demonstrated that with post-operative adjuvant chemotherapy consisting of cyclophamide, methotrexate and fluorouracil (CMF) with women with positive axillary lymph nodes that after being given 27 months of treatment decreased the risk of breast cancer recurrence (Bonadonna et al., 1976). Since this trial much research has been conducted to understand the most beneficial chemotherapy agents, combinations of chemotherapy drugs, doses and durations of treatment (Clarke et al., 2005). Adjuvant systemic treatments are offered to patients to reduce their risk of relapse and to improve disease-free survival and overall survival with treatment of breast cancer by surgery and/or radiation alone (Shah, Rosso, & Nathanson, 2014). In general, breast cancer patients with an estimated risk of over 10% of recurrence over the course of 10-years are viewed as potential candidates for adjuvant chemotherapy (Harbeck & Gnant, 2017). Predictive markers are required to select the most appropriate and optimum treatment for each patient. The oestrogen receptor, the progesterone receptor and the human epidermal growth factor receptor 2 (HER2) are considered the best predictive markers. High rates of recurrence are probably related to the presence of micro-metastatic disease in 10-30% of lymph node negative patients and 35%-90% of lymph node positive patients at the time of diagnosis which was not eradicated with surgery or radiotherapy (Jaiyesimi, Buzdar, Decker, & Hortobagyi, 1995).

Adjuvant chemotherapy helps to eliminate residual or distant micro-metastases, but the absolute benefit varies according to disease stage, patient age and underlying prognosis (Passant & Borley, 2013). Our understanding was advanced by research conducted by Bonadonna et al. (1976). They investigated chemotherapy treatment with anthracyclines-based combination regimens (e.g. 5-fluoruracil, epirubicin and cyclophosphamide, given every 3 weeks for six cycles) which were shown to significantly reduce recurrence and breast cancer mortality when compared to cyclophosphamide, methotrexate and fluirouracil (CMF) regimens, and may be used unless there is a contraindication of cardiac dysfunction (Passant & Borley, 2013). Additional research which has focused upon chemotherapy treatment combinations has demonstrated that the addition of taxanes (paclitaxel and docetaxel) to anthracycline-based chemotherapy combinations leads to a 17% reduction in recurrence risk (Henderson et al., 2003; Mamounas et al., 2005). A meta-analysis conducted by De Laurentiis et al. (2008) demonstrated that taxane-based chemotherapy combinations provided disease-free survival and overall survival benefit with an absolute 5-year risk reduction of 5% for disease-free survival and 3% for overall survival when compared to the standard anthracycline regimens. Patients with endocrine-unresponsive breast cancer, with no expression of oestrogen or progesterone receptors, are usually offered chemotherapy for 6 weeks, whereas on the other hand, patients with endocrine-responsive disease are offered adjuvant systemic therapy based on endocrine treatments (Goldhirsch et al., 2003; Harris et al., 2007).

2.12 Adjuvant endocrine therapy

Adjuvant hormone therapy is given to women diagnosed with endocrine-sensitive tumours for a period of 5-10 years (Harbeck and Gnant, 2017). Breast cancer is an oestrogen-dependent cancer in approximately 70% of patients and is thus hormone sensitive. Attempts to disrupt the interaction of the oestrogen hormone and the oestrogen hormone receptor signalling pathways have been demonstrated to cause tumour regression. This can be done by interfering with the oestrogen receptor signalling pathway, in the case of Tamoxifen, or by decreasing the production of oestrogen with ovarian ablation, ovarian suppression or aromatase inhibition (Passant & Borley, 2013).

2.12.1 Pre-menopausal endocrine therapy

In pre-menopausal patients Tamoxifen is the standard endocrine treatment. The responsiveness of breast tumours to hormonal manipulation allows opportunity for targeted therapy via the anti-oestrogen Tamoxifen. Tamoxifen acts by blocking the action of oestrogen by binding to one of the two activating regions of the oestrogen receptor (ER). By doing this it stops both the translocation (joining together) and binding of the oestrogen receptor. Clarke et al., (2005) demonstrated that in women with ER-positive breast cancer who took Tamoxifen for 5-years the annual recurrence rate was decreased by 50%, the rate of contralateral cancers decreased by 41% and breast cancer-related mortality reduced by 31%. They noted a dose-response relationship, with a 5 year course of tamoxifen therapy being more effective than a course of one or two years (Clarke et al., 2005). A later meta-analysis (2011) reported by the same group

(EBCTCG) showed that 5-years of tamoxifen treatment in women with ER-positive disease reduced not only recurrence risk in the first 4 years (RR 0.53, p<0.0001) but also in years 5-9 (RR 0.68, p<0.0001), demonstrating the importance of endocrine therapy for reducing recurrence and mortality long term.

2.12.2 Post-menopausal endocrine therapy

In post-menopausal women the production of oestrogen by the ovaries stops; however, oestrogen can still be produced by other tissues particularly in subcutaneous adipose tissue. (Cohen, 2001). Aromatase inhibitors (AIs) stop the production of oestrogen through this mechanism (Passant & Borley, 2013). AIs represent an important advance in endocrine therapy treatment for breast cancer. These include non-steroidal (anastrazole and letrazole) and steroidal (exemestane) oral agents which are particularly valuable if tamoxifen is contra-indicated, or prescribed as an initial treatment, or as a treatment sequenced after tamoxifen (Lyman et al., 2005). However, for post-menopausal patients, both tamoxifen and aromatase inhibitors are important treatment options, either given in sequence (switching from AI to tamoxifen after 2-3 years to complete 5-years in total) or on their own. The ATAC trial (Baum et al., 2003) compared the use of anastrozole with tamoxifen, either alone or in combination in women with early stage post-menopausal breast cancer. At 10-years, anastrozole as initial therapy was demonstrated to increase disease free survival (HR 0.86, p=5.003), increased time to local or distant recurrence (HR 0.79, P=5.0002, HR 0.85, p=5.02, respectively), and reduced reports of contralateral breast cancer (HR 0.62, p=05.003) when compared to tamoxifen (Cuzick et al., 2010). To date, research has supported the use of aromatase inhibitors for a total of 5 years, either as part of a first line treatment or as extended

adjuvant therapy (Dowsett et al., 2009). However, more recent research has concentrated on longer durations of endocrine therapy of up to 10 years and with different combinations of AIs and tamoxifen, with positive results. Goss et al. (2016) demonstrated that after 5-years of tamoxifen, with letrozole treatment added from 5-10 years, is beneficial in post-menopausal women for a 5-year disease-free survival of 95%, when having letrozole treatment for 10-years vs 91% for women only taking letrozole treatment for 5-years, HR 0.66, p=0.01. Prolonging endocrine use beyond 5-years must be carefully balanced against potential risks, previous use of tamoxifen, side effects and the risk of recurrence (Harbeck & Gnant, 2017).

2.13 Adjuvant management of HER2-positive disease

The increased knowledge about tyrosine-kinase family receptors combined with the growth in the number of bio-molecular markers has led to the development of the first targeted therapies such as trastuzumab (Herceptin). Herceptin is a monoclonal antibody which can localise to a single site on or in a breast cancer cell, blocking the effects of HER2 – a growth factor for breast cancer. Treatment with Herceptin improves disease-free survival rates and overall survival for patients who are HER2 positive with early stage breast cancer, independent of age, oestrogen or progesterone receptor status or node metastases. Although Herceptin is generally well tolerated it can be cardiotoxic, causing heart failure. The risk of cardiac toxicity ranges from 0.5%-4% (Benson et al., 2009).

2.14 Side effects and long-term consequences of breast cancer treatment

In the process of destroying cancerous cells, breast cancer treatments can cause considerable physiological changes, damage and death to normal tissues, organs and body functions, causing many unwanted side effects and psychological distress. This can result in declines in performance and functional status during and after adjuvant therapy (Furmaniak et al., 2016; McNeely et al., 2006). In addition, many of these adverse side-effects can often be prolonged because of the disease and treatments and can hinder a patient's return to normal life (Fong et al., 2012).

2.14.1 Fatigue

The most common problem reported by cancer survivors is cancer-related fatigue (CRF) (Dimeo, Thomas, Raabe-Menssen, Propper, & Mathias, 2004; Dodd et al., 2010; Schwartz, Mori, Gao, Nail, & King, 2001; Velthuis, Agasi-Idenburg, Aufdemkampe, & Wittink, 2010). CRF is differentiated from fatigue or tiredness reported by healthy individuals by its severity, impact on quality of life and the fact that it is not relieved by rest or sleep (Curt et al., 2000; Escalante, 2003). Reported prevalence levels of fatigue are as high as 60-100%; although the actual prevalence of CRF varies across studies, a consensus exists that it is high both during and after treatment and survivors report persistent fatigue lasting months to years after finishing therapy (Curt et al., 2000).

2.14.2 Pain and upper-limb morbidity

Cancer-related pain is one of the most prevalent symptoms reported by cancer survivors attributed to their cancer or its treatment. The aetiology of cancer-related pain can be attributed to a variety of reasons, such as surgery (e.g. damage to nerves and tissues from removal of the tumour, scarring), radiotherapy (e.g. radiation sunburn reaction), chemotherapy (e.g. peripheral neuropathy, damage to nerves from chemotherapeutic agents) (Keating, Nørredam, Landrum, Huskamp, & Meara, 2005; McNeely et al., 2006). Further surgery side-effects may also include shoulder stiffness and a reduced range of movement (ROM) around the shoulder girdle, a weakness of the shoulder muscles and lymphoedema and can impact on everyday functioning and health-related quality of life (Ahmed, Thomas, Yee, & Schmitz, 2006).

2.14.3 Obesity and body composition changes

Weight gain commonly occurs after the diagnosis of breast cancer (Harvie, Campbell, Baildam, & Howell, 2004). Although adjuvant chemotherapy has improved survival, weight gain and unfavourable changes to body composition, with increased fat mass and decreased fat-free mass, are frequently reported following this treatment, even when overall weight gain or an increase in body mass is negligible (W. Demark-Wahnefried et al., 2008). Obesity is a well-established risk factor for a number of cancers, including breast (post-menopausal), colon, kidney, oesophagus and endometrium. Demark-Wahnefried et al. (2012) suggest that 71% of cancer survivors are overweight or obese so it appears to be extremely important for weight management interventions to be developed to respond to this.

2.14.4 Cardiovascular changes

Treatment-related effects can damage all parts of the heart including the muscle, electrical conduction systems and valves. Several chemotherapeutic agents and targeted therapies, including anthracyclines, taxanes and trastuzumab, can cause cardio-toxicities and damage heart muscle, leading to congestive heart failure, arrhythmias, significant electrocardiogram (ECG) changes, cardiomyopathy and death. (Floyd et al., 2005; Hequet et al., 2004). These potential side-effects can occur during treatment, within one year or many years after treatment has ceased (Piccart-Gebhart et al., 2005). Symptoms appear to be reversed following cessation of the treatment (Suter et al., 2004). Radiation to the chest wall can cause cardiotoxicity with increased inflammation in the heart and chest cavity. This can lead to fibrosis and scarring to the heart muscle, resulting in cardiomyopathy, which can cause severe breathlessness. Late cardiomyopathy can present years after treatment (Floyd et al., 2005).

2.14.5 Bone loss

Breast cancer survivors are at increased risk of bone loss, bone fractures, osteopenia or osteoporosis as a consequence of adjuvant hormone therapy and chemotherapy. Pre-menopausal women may experience chemotherapy-induced amenorrhea or ovarian suppression treatment with previous studies demonstrating a 4%-8% lumbar spine bone loss within the first year after menopause (Shapiro & Recht, 2001). In postmenopausal women, aromatase inhibitors accelerate bone loss and increase the risk of fracture, especially during treatment and within the first few years post adjuvant therapy (Lester & Coleman, 2005).

2.14.6 Lymphoedema

It is suggested by Petrek, Senie, Peters, and Rosen (2001) that 49% of breast cancer survivors self-report symptoms of lymphoedema with or without clinical diagnosis. Breast cancer-related lymphoedema is a chronic and progressive swelling of the arms, shoulder, neck or torso as a result of a physical disturbance, damage or removal of the axillary lymphatic vessels from surgery or radiotherapy (Ahmed et al., 2006). Damage cause by cancer treatment interrupts lymph transport in such a way that volume exceeds drainage capabilities leading to an accumulation of tissue fluid including protein, oedema and inflammation within the arm (Ahmed et al., 2006; Schmitz et al., 2009). Physiological changes that may result from lymphoedema are a decreased range of movement and function, decreased muscle strength, a reduction in activities of daily living, discomfort and pain, sleep disturbances and an increased risk of infection and cellulitis (Mortimer, 1998). Significant psychosocial morbidities have also been reported such as depression and anxiety and a reduced quality of life (Velanovich & Szymanski, 1999).

2.14.7 Psychological distress and reduced quality of life

Breast cancer treatment and the combined effects of surgery and adjuvant therapies can cause considerable changes in a woman's physical and psychological well-being. These can cause suffering and distress, all of which can have an influence on how women cope with a diagnosis of breast cancer and on their quality of life (QoL) many years after treatment (Hormes et al., 2010; Kirshbaum, 2007; Mustian et al., 2007; Mutrie et al., 2007; Schwartz et al., 2001). However, often psychological distress and physical symptoms may continue (e.g. joint and muscle pain, fear of recurrence, uncertainty)

beyond the end of treatment and during the transition to survivorship. Therefore, ensuring the quality of that survival becomes a crucial priority (Mishra et al., 2012). Research on the quality of life of cancer patients has increased steadily over the last 15 years, consistent with the recognition that endpoints in addition to survival and disease-free survival are important when considering cancer treatments (Hormes et al., 2010; Kirshbaum, 2007; Mishra et al., 2012). It is no longer just "how long" patients are surviving but research on quality of life addresses the "how well" patients are surviving (Jacobsen & Jim, 2011). Exercise has been identified as an intervention that can support and alleviate the stressors of a cancer diagnosis and subsequent treatments during and after therapy (Knobf, Musanti, & Dorward, 2007).

2.14.8 Endocrine side-effects

Hormone therapy is the mainstay in the long-term management of oestrogen and progesterone receptor positive breast cancer. Tamoxifen has historically been the hormone treatment of choice with reports of a decrease in incidence of recurrence and death from the diseas by 47% and 26%, respectively (EBCTCG, 1998). Tamoxifen (TAM) and aromatase inhibitors (AIs) are the most widely used, although AIs appear to be better tolerated than tamoxifen, they both have different negative consequences that have often not been well publicised in practice (Garreau et al., 2006). The most frequently reported negative consequences of hormone therapy use were hot flushes, weight gain, insomnia and joint aches, musculoskeletal disorders, mood changes, vaginal dryness and fractures (Baum et al., 2002; Goss et al., 2003; Coombes et al., 2004). These negative consequences of these treatments effects goes further with compliance

to the actual treatment being compromised with patients unable to tolerate a full course of therapy.

2.15 Summary

Owing to the ageing of the population, the high incidence of breast cancer and continually-improving survival rates, there is an increasing number of older breast cancer survivors in middle and higher income countries. Optimising the physical functioning of this population is an important public health imperative (Cadmus et al., 2009). Cancer survivors who have successfully completed their treatment now routinely expect to continue with work and normal life at similar levels to those preceding their diagnosis of cancer. However, it has become clear that whilst cancer treatment can prolong survival, it can be very intensive leading to a number of negative and unwanted physiological and psychological treatment side-effects that can hinder return to normal life (Fong et al., 2012). Although physical activity is often considered fundamental in the rehabilitation from many long term conditions to offset declines in physical and mental functioning brought on by ageing and disease progression (Courneya et al., 2004), very little research has targeted this older population and there is a need to explore the efficacy of interventions that can promote a return to normal life and counter the side-effects of treatment.

The next chapter will explore how exercise is now more frequently being recognised as a way to try and reduce the often debilitating consequences of breast cancer treatment (Spence et al., 2010). With breast cancer survivors at greater risk of long-term conditions compared to those without cancer it is very important that breast cancer survivors

become physically active (Demark-Wahnefried et al., 2006). The evidence for the benefits of exercise for breast cancer survivors has been increasing over the last two decades and will be explored in more detail in the next chapter.

Chapter 3: The role of exercise in reducing breast cancer-related morbidity and mortality

3.1 Introduction

Chapter 2 presented the journey that a breast cancer patient would follow, finishing with the most common treatments and the common side-effects, highlighting both the acute and long-term problems that patients may experience during and after treatment. This chapter will consider the role of exercise as rehabilitation during and after breast cancer treatment, as a way of trying to reduce these often debilitating consequences of treatment and improve participation in work and social activities (Spence et al., 2010).

3.2 Exercise guidelines for cancer patients

To date, no formal exercise guidelines specific to cancer survivors have been published in the UK (Campbell, Stevinson, & Crank, 2012). However, exercise guidelines for cancer survivors have been published by the American College of Sports Medicine (Schmitz et al., 2010). These guidelines suggest that cancer survivors should follow the 2008 Physical Activity Guidelines for Americans (US Department of Health & Services, 2008), but that specific exercise programmes may have to be adapted based on an individual's health status, disease trajectory and treatment-related adverse effects (ACSM, 2013). The US Department of Health and Services (2008) guidelines for aerobic activity are a weekly accumulation of 150 minutes of moderate intensity activity or 75 minutes of vigorous activity. Resistance training recommendations are to take part in two to three sessions

per week to include exercises for major muscles, with stretching of the major muscle groups on days that exercise is performed (Haskell et al., 2007; Nelson et al., 2007; US Department of Health & Services, 2008). In the UK, the British Association of Sport and Exercise Science (BASES) published an expert statement on exercise and cancer survivorship (Campbell et al., 2012). They suggest that health-related physical activity guidelines for the general population are appropriate for most cancer survivors and that those with cancer-related complications or co-morbidities that prevent moderate intensity exercise should be encouraged to avoid being sedentary.

A number of RCTs of exercise during and after treatment for breast cancer have reported on any adverse events experienced by participants when exercising, such as injuries or lymphoedema (McGuire, & Kearney, 2005; Courneya et al., 2007; Mutrie et al., 2007; Schwartz, Winters-Stone, & Gallucci, 2007; Campbell, Mutrie, White, Demark-Wahnefried et al., 2008; Cadmus et al., 2009, and all have concluded that exercise was safe.

3.3 Physiological benefits of exercise for breast cancer patients

When assessing physiological changes during and after treatment for breast cancer, physical functioning was found to have been significantly improved (cardiovascular fitness and muscular endurance). Interventions ranged from walking only, home-based exercise programmes, to supervised and structured training programmes in fitness facilities (Courneya et al., 2003; Campbell et al., 2005; Courneya et al., 2007; Nikander et al., 2007; Schwartz et al., 2007; Adamsen et al., 2009; Schmitz, 2010; Speck, Courneya, Mâsse, Duval, & Schmitz, 2010). Resistance training has also demonstrated benefits of

increased strength (upper and lower body), improved bone health and the maintenance of lean muscle (Speck et al., 2010; Winters-Stone et al., 2011, 2012). Myths connecting lymphoedema risk with exercise continue to be a barrier to physical activity (Speck et al., 2010). However, Cheema et al. (2008) reviewed the evidence of resistance training in breast cancer by evaluating 10 trials; four uncontrolled trials, one controlled trial and five RCTs. The authors concluded that no exacerbation of lymphoedema was reported in any of the trials with exercise. Sprod et al. (2010) compared physiological and psychological outcomes in breast cancer patients following 3 months and 6 months of exercise compared to a control group that did not exercise. They found significant differences ($p<0.05$) in cardiovascular endurance, fatigue and depression in those participants in the exercise groups. Additional benefits in pulmonary function and muscular endurance ($p<0.05$) was found in the 6-month exercise group only. This is very similar to Schneider et al.'s (2007) results from a 6-month exercise intervention. The exercise group attended exercise sessions 2-3 times week for the duration of the study. Limitations to this study appear to be the lack of randomisation so those exercising may have been more motivated to begin and continue with the exercise. In addition, as with many exercise studies, the study was not placebo-controlled or blinded, thus participant expectancy and researcher bias may have contributed to the improvements described. Despite the limitations to the study, it demonstrated that motivated BCS can gain a number of physiological and psychological benefits in the short term, with additional benefits gained by continuing to exercise for a longer period of time.

A multi-centred RCT assessing the effects of aerobic and resistance exercise on 242 breast cancer patients during chemotherapy (Courneya et al., 2007) concluded that neither aerobic or resistance training significantly improved quality of life but did

improve self-esteem, physical fitness, body composition and chemotherapy completion rates. The median length of the exercise intervention was 17 weeks. Training sessions were three times per week increasing in duration and intensity as the programme progressed. The intensity of the aerobic training increased at week six and week 12 with duration of sessions increasing by five minutes every three week. Resistance training was increased by 10% when participants completed more than 12 repetitions of an exercise. The effects of the exercise interventions may have been slightly diluted by inadequate adherence or insufficient volume and/or intensity of the exercise. However, whether positive changes to these parameters would have yielded further significant results remains unclear. Although aerobic and resistance exercise training did not significantly improve QoL, fatigue or depression and anxiety, trends did favour the exercise groups. Aerobic training preserved aerobic fitness, an important factor, when chemotherapy can cause anaemia, tachycardia, dehydration and cardiac dysfunction, which can lead to a downward trajectory of aerobic fitness (Jenson et al., 2002). Resistance training significantly improved muscular strength and lean body mass, all important for health.

Campbell et al. (2005) in a pilot study of supervised group exercise during adjuvant treatment reported significantly higher levels of physical functioning and reported higher QoL scores than controls. Changes in reported levels of fatigue and satisfaction with life were positive in the exercise group but did not reach significance. In a follow-up RCT study (Mutrie et al., 2007) 177 women completed the 12-week group exercise programme and responded to a follow up questionnaire 6 months later. They reported significant effects on distance walked in 12 minutes, amount of weekly moderate activity, shoulder mobility and positive mood after the 12-week intervention when

compared with the control group. The benefits to quality of life using a validated breast cancer specific QoL questionnaire (FACT-B) from the intervention only emerged at the 6 month follow up, when most women were post treatment.

Markes et al. (2009) led a Cochrane review of exercise for women receiving adjuvant therapy. Nine trials involving 452 women met the inclusion criteria. Their subsequent meta-analysis of these trials suggested that exercise improves cardiorespiratory fitness (207 participants) but they did not find any significant improvements for fatigue (317 participants) or weight gain (147 participants) when the exercise intervention groups were compared to control groups. They concluded that exercise during adjuvant treatment is beneficial for improving physical fitness and thus the capacity to perform activities of daily living, which could be impaired with de-conditioning due to sedentary behaviour during treatment.

Ahmed et al. (2006) examined the effects of supervised upper and lower body weight training on the incidence and symptoms of lymphoedema in 45 breast cancer patients taking part twice weekly over 6 months. All participants were between 4-36 months post treatment and had axillary dissection as part of their treatment. They found that none of the participants experienced any significant changes in arm circumference > 2.0cm after the 6-month intervention and self-reported incidence of a clinical diagnosis of lymphoedema or symptom changes over 6 months did not vary by intervention. They suggest that additional research to determine whether exercise leads to physiological structural and functional change of the lymphatic system of the affected arm and also the timing of exposure to risk and the incidence of lymphoedema should be conducted.

Kilbreath et al. (2012) examined the effects of progressive upper limb resistance training and stretching exercises on reducing upper limb impairments in women treated for early stage breast cancer. Participants were randomised to an 8-week programme of exercise or to a control group and followed up at 6 months. They concluded that changes in symptoms from baseline were not significantly different between the groups immediately following the intervention or at 6-months post intervention; however, the change in range of movement for flexion (p=0.01) and abduction (p=0.05) and shoulder abductor strength (p=0.04) was significantly greater in the exercise group immediately after the intervention. The exercise intervention group did not report less arm symptoms than the control group, although both groups reported little impairment. A notable finding was that the resistance training programme commencing with low resistance but quickly progressed to what participants considered "Hard" on the Borg Scale did not cause or exacerbate lymphoedema. By the end of three months post-operatively, participants were lifting up to 4kg free weight above their heads without developing lymphoedema. A potential limitation to the study was that the group of participants were younger on average than women diagnosed with breast cancer, although the age range for the study was 24-82 years. This appears to be a common limitation with exercise studies in that that those recruited have a history of exercise and are typically younger (Courneya et al. 2007).

In the Physical Activity and Lymphoedema trial (PAL), an update of a resistance training research protocol carried with breast cancer survivors, Schmitz et al. (2009) agreed with Ahmed et al.'s (2006) suggestion that clinical guidelines which indicate women at risk of lymphoedema should protect the affected arm from overuse can in practise translate into avoiding the use of the affected arm. This may increase the likelihood of injury from

common activities of daily living and poses a severe barrier to remaining or increasing their physical activity levels (Ahmed et al., 2006). Schmitz et al. (2009) hypothesized that a slow programme of resistance training with no upper limit on weight will increase the capacity of the at risk arm/limb, so that activities of daily living become easier and are carried out at a lower percentage of maximal capacity. They continued to suggest that the resistance training programme was safe as no participant was referred for follow-up because of suspected lymphoedema and no-one left the study due to onset or flare up of lymphoedema.

Schmitz et al. (2010, as part of the PAL trial, randomised 154 women whose lymph nodes had been removed but without signs of breast cancer-related lymphoedema into a weight lifting and control group (no exercise). The weight lifting group was instructed for 13 weeks by a certified fitness professional in small groups of 2-6 participants and then continued unsupervised twice weekly to one year. This study found that BCS who performed slowly progressive weight lifting twice weekly for one year were actually less likely to experience clinically significant increases in arm swelling ($p<0.003$) or clinician defined lymphoedema ($p<0.001$) than women in the control group who did no exercise. These findings should be considered clinically significant and help to clarify clinical advice to BCS regarding upper body exercise and should alleviate patients' concerns regarding the safety of resuming or beginning a weight training programme. This study's findings concur with previous RCTs' findings of weight lifting programmes during or post treatment for breast cancer (McKenzie & Kalda, 2003; Johansson et al. 2005; Ahmed et al. 2006; Courneya et al. 2007). This was a well-conducted, large study, delivered in the community setting over a long duration for an exercise intervention (1 year). The applicability of the findings can be useful for primary care staff involved in the

rehabilitation of breast cancer patients by removing concerns that resistance exercise will increase the risk of lymphoedema. These results combined with previous findings suggest that BCS can gain the many health benefits associated with weight training.

In a study utilising both aerobic and resistance training Garner and Erck (2008) examined the effects of exercise and weight bearing activities on maintaining bone health. Maintenance or improvement in bone mineral density (BMD) in the spine and hips is very important for women especially postmenopausal women because a decline of one SD in BMD can be associated with a twofold increase in fracture risk (Waltman et al., 2003). Garner and Erck (2008) reported a 60% improvement in hip BMD and 22% improvement in spine BMD after 8 weeks of aerobic and resistance training. Although this could be an important finding and could further strengthen the importance of resistance exercise and weight bearing activity to BCS to maintain bone health, this was a pilot study of only 11 participants who were not randomised to an intervention or control group but recruited by word of mouth or using flyers. This will limit the applicability of the study's finding although it highlights an important area for further research.

Winter-Stone et al (2013) investigated the effects of resistance training + impact training to improve BMD and body composition in prematurely-menopausal BCS utilising RCT methodology. They recruited 71 BCS (mean age 46.5 years) to either an impact+ resistance training group or to a flexibility only group for 12 months. They reported that the resistance group increased BMD at the hip (p<0.01) and slowed down BMD loss at the spine (p=0.03) when compared to the flexibility only group. An interesting observation was that women who were less than one year past the onset of menopause, the resistance + impact exercise did not appear to affect bone health (BMD or bone

turnover markers). However, the authors suggest that the phase of menopause may have masked the effects and benefits of the exercise. They report that it was only the women who were a year or more post-menopause that the resistance + impact exercise stopped bone loss at the spine and increased BMD at the hips. Conversely, the flexibility only group lost bone at both sites. A possible reason for this lack of improvement in BMD in the very early stages of menopause could be that during oestrogen deficiency, exercise may be competing with the resorptive processes resulting from low oestrogen and therefore at these times exercise may not be able to influence bone remodelling during these periods of high turnover (Dalsky, 1990; Lanyon, 1996). Dalsky further suggests that increases in bone resorption are at the highest in the first 12 months of menopause but much slower thereafter, which may then allow exercise to have a beneficial effect.

Winters-Stone et al. (2011) targeted postmenopausal BCS (mean age 62 years) in an RCT examining whether strength training would stop bone loss and build muscle. This study was the first to target specifically older BCS with resistance training, as previous research (Ahmed et al., 2006; Schmitz et al., 2009; Twiss et al., 2009) has only included older women as part of a broader age range. Thus, these studies cannot evaluate the specific capacity of older BCS to tolerate and respond to resistance training interventions. Primary endpoints were BMD of the hip and spine and whole body bone-free lean and fat mass assessed by Dual Energy X-ray Absorptiometry (DEXA) along with biomarkers of bone turnover [serum osteocalcin (ng/ml) and urinary deoxypyrodiniline cross links (nmol/mmolCr)]. Women in the resistance and impact exercise group preserved BMD at the spine (p=0.001) when compared to the control stretching only group, although no significant effect was seen on BMD at the hips. The resistance only group reported

smaller increases in osteocalcin (p=0.03) and a larger decrease in deoxypryrodine (p=0.06) than controls, suggesting bone resorption was improved in the exercise groups although it did not reach a level of significance. The authors suggest that the intensity of the impact training and modest jump number may have not placed sufficient stress and stimulus on the hip to incur a positive adaptation. They further consider that the hip may also require a longer time period to adapt to the moderate intensity training programme in the study. Snow et al. (2000), utilising a similar exercise programme but for 9 months, reported no effects on hip BMD. In this study, participants were followed up longitudinally at 5 years and the women who continued to exercise preserved BMD compared to reported losses in the inactive women. Therefore, Winters-Stone et als'. (2011) study may have longer-term benefits for women adhering to exercise that may reduce their chance of falls and fractures as they age.

In further analysis of this research intervention with older BCS Winters-Stone et al. (2012) demonstrated significantly improved leg strength (p<0.02) and bench press strength (p<0.02) of women randomly assigned to a 1-year resistance and impact group when compared to a stretching only group. Older BCS appeared to be able to tolerate a moderate-vigorous resistance training programme with good reported compliance rates (85% of participants in the resistance group) although using the study's definition of compliance to the programme as the percentage of participants who completed the study exercises without significant modification for six months or more, 98% were compliant. No injuries or adverse events were reported. This additional analysis demonstrates the benefits BCS can gain from resistance training on lower and upper body strength which may help reduce their fall and fracture rate in older age.

3.4 The benefits of exercise on body composition in breast cancer patients

Weight gain and changes in body composition are common problems amongst women during adjuvant treatment for breast cancer. These are well-established side-effects which are also associated with reduced survival, decreased QoL and increased risk of co-morbidities, such as cardiovascular disease and diabetes and could exacerbate the risk of functional decline and may even contribute to cancer recurrence and cancer-related death (Harvie, Campbell, Baildam, & Howell, 2004; Jones & Demark-Wahnefried, 2006; Ingram & Visovsky, 2007). Harvie et al. (2004) reported significant weight gains of 5.0kg +/-3.8; p<0/01) and body fat (7.1kg +/-4.5; p<0.01) over a year following chemotherapy treatment and there was also a decline in fat free mass of 1.7 +/-2.5kg; however, they found no significant changes in dietary habits or physical activity. According to Demark-Wahnefried et al. (2008) two thirds of studies that have assessed body composition change in cancer patients have observed no improvements in muscle mass but reported losses in muscle mass as body weight and adipose tissue increase. They term this pattern of loss of muscle mass and an increase in fat mass and body weight as sarcopenic obesity. They noted it to be a common side effect of chemotherapy and hormonal therapy and suggest that these recognised common changes in body composition call for interventions that promote exercise, especially resistance training. Demark-Wahnefried et al. (2005) suggest that 71% of cancer survivors are overweight or obese; therefore, it appears to be extremely important for weight management interventions to be developed to respond to this.

A systematic review conducted by Ingram et al. (2006) concluded that despite the recognition of adverse body weight and body composition changes during and post breast cancer treatment, very few studies had focused on these measurements as their primary outcomes. A number of limitations to the studies that have included bodyweight or body composition (pre-2006) could be noted. The length of interventions ranged from 6-26 weeks, with only three studies exceeding 12 weeks in duration. Significant changes to bodyweight and composition take time, something that these shorter duration studies did not allow for. Exercise interventions were different. A number of studies examined aerobic exercise only; however, the type of aerobic exercise was often different (cycling, walking or stepping). A number of studies examined both aerobic and resistance exercise, some were supervised exercise classes (often in a fitness facility) and some were unsupervised (home-based). The frequency of exercise sessions did appear to closely follow the American College of Sports Medicine guidelines specifying three to five times per week; however, the duration of exercise was often different or the time not reported. Intensity of exercise sessions ranged from 40-75% of maximum heart rate, low to moderate or did not include information about exercise intensity. No studies were adequately powered to examine bodyweight and composition and none of the studies specifically tried to recruit overweight or obese BCS or used highly validated and reliable instruments for the estimation of body composition. Studies did not control for dietary intake, which had the potential to be altered during the course of adjuvant treatment of an exercise intervention. Low sample sizes were also noted in the studies; however, high retention rates could be reflective of highly motivated participants as the majority had to attend exercise facilities a number of times each week.

Courneya et al. (2007) in a large RCT of breast cancer patients receiving chemotherapy (n=242) assessed the independent effects of both aerobic and resistance exercise on body composition. The groups were balanced at baseline and the median length of the exercise intervention was 17 weeks (95% CI, 9-24 weeks) and the mean length of treatment was 17 +/- 4 weeks. They found that neither exercise intervention prevented weight gain, but each altered body composition. Aerobic exercise prevented fat gain whilst resistance training added lean body mass. What was interesting was that improvements in body composition resulted in reported improvements in QoL, self-esteem and depression, suggesting that not only will these changes in body composition have physiological benefits, but they may have additional psychosocial social benefits as well. These findings concurred with Schmitz et al. (2005) who noted significant effects of weight training on lean mass and body fat % but not for body weight, BMI, body fat or waist circumference in her study of the effects of twice weekly weight training on bodyweight and composition in BCS who were randomised into an immediate and delayed treatment groups. The immediate treatment group trained for one year whilst the delayed treatment group did not start training until the seventh month of the intervention. Although the changes in body composition were significant between the groups, they may not be considered clinically significant in the short term. It could be suggested that if the BCS continue to weight train over the long term the body composition changes between these exercisers and sedentary BCS may become clinically important by preventing an increase in body fat that often occurs over time during advancing age. However, currently there is no research that has longitudinal data examining these outcomes.

A Cochrane review conducted by Markes et al. (2009) did not find statistically significant results after a meta-analysis of weight change in BCS participating in exercise when compared to non-exercisers. However, this meta-analysis was conducted only on a small number of studies (n=5) and a limited number of participants. A number of different approaches were used for assessing body weight and composition (body weight, BMI, skinfolds and lean muscle mass). Also, there was a considerable degree of clinical heterogeneity between trials regarding adjuvant cancer treatment and exercise interventions. With such potential limitations these results should be interpreted cautiously.

An updated systematic review and meta-analysis by Speck et al. (2010) demonstrated that after pooling data from seven RCTs conducted during treatment, slight increases in lean body mass were noted along with significant reductions in body fat (p=0.04). This was considered to be a small to moderate effect size of physical activity on body weight during treatment. This comprehensive review of 82 studies utilised weighted mean effect sizes (WMES) from 66 high quality studies and applied them to evaluate 60 outcomes. Significant small reductions in body fat were also reported after they pooled the data from 15 RCTs conducted after treatment (p=0.006) and demonstrated increases in muscle mass when five RCTs were pooled on interventions after treatment. A small effect size for body fat and muscle mass post-treatment was noted.

3.5 The benefits of exercise on Health Related Quality of Life (HRQoL) in cancer patients

In a comprehensive Cochrane review of evidence, Mishra, Scherer, Snyder, et al. (2012) evaluated the effectiveness of exercise on overall health-related QoL (HRQoL) and specific HRQoL domains during and at the end of active cancer treatment. They included 56 RCTs and quasi-randomised clinical controlled trials (CCTs), comparing exercise interventions with usual care or other types of non-exercise comparison interventions. A total of 4826 participants were analysed (2286 = exercise intervention and 1985 = control/comparison group). Thirty-six trials were conducted with participants during active treatment and 10 trials were during and post active treatment. The results from the pooling of study data suggested that exercise interventions had a more positive effect on HRQoL and certain HRQoL domains. The modes of exercise interventions and physical activities were heterogeneous across the different trials and included walking, cycling, resistance training and yoga or Qigong (slow flowing movements, breathing and meditation). The methods used to assess HRQoL were also wide-ranging. Exercise interventions demonstrated a positive impact on overall HRQoL when compared to control interventions. These improvements included HRQoL from baseline to 12-weeks follow-up (SMD 0.33, 95% CI 0.12 to 0.55) in physical functioning from baseline to 12-weeks follow-up (SMD 0.69, 95% CI 0.16-1.22), role functioning from baseline to 12-weeks follow-up (SMD 0.48. 95% CI 0.07-0.90), social functioning at 12-weeks follow-up (SMD 0.54, 95% CI 0.03-0.44). Exercise interventions also demonstrated a decrease in fatigue from baseline to 12-week follow-up (SMD –0.38, 95% CI -0.57to -0.18). They also found consistency between the differences in follow up scores and change scores,

further suggesting the robustness of these results. They also found that when examining exercise effects by subgroups, exercise interventions had significantly greater reductions in anxiety when examining breast cancer participants alone. However, they did report greater reductions in depression, fatigue, sleep disturbances and improvements in HRQoL, emotional wellbeing, physical functioning and role functioning for cancers other than breast cancer but not for breast cancer. When examining the intensity of the exercise interventions they reported that a more positive effect on HRQoL and in physical functioning, fatigue, anxiety and better sleep was evident for participants who followed a moderate or vigorous exercise programme compared to a mild exercise programme. However, they reviewed all trials at high risk of performance bias and the majority of trials at high risk of detection, attrition and selection bias; thus, the results of the review should be interpreted with a degree of caution.

In a further Cochrane review examining exercise interventions among adults after completing active cancer treatment, Mishra, Scherer, Geigle, et al. (2012) included all RCTs and CCTs comparing exercise interventions with usual care. They included 40 trials and 3694 participants in their subsequent analysis with 1927 randomised to an exercise group and 1764 in a comparison group of usual care or no-exercise. The modes of exercise interventions included walking, resistance training, cycling, yoga or tai-chi. They found similar results to their other review; exercising post cancer treatment had a positive impact on HRQoL and certain HRQoL domains. Exercise resulted in improvements in global HRQoL (SMD 0.48, 95% CI 0.16-0.81) body image / self-esteem (MD 4.50, 95% CI 3.40-5.60) emotional well-being (SMD 0.33, 95% CI 0.05 to 0.61) and social functioning (SMD 0.45, 95% CI 0.02-0.87) Not only did exercise result in the above described improvements but the exercise interventions also demonstrated decreased

anxiety (SMD -0.26, 95% CI -0.07 to -0.44), a reduction in fatigue at 12-weeks (SMD -0.82, 95% CI -1.50 to -0.14) and between 12 weeks and six months follow up (SMD -0.42, 95% CI -0.02 to -0.83) when compared to the usual care / no exercise group. The review also noted positive trends in favour of the exercise interventions groups for depression and body image, although they did not have many other studies to compare these findings against, therefore, a degree of caution should be used. The limitations to these Cochrane reviews appear to be a common problem in exercise and breast cancer research. Many studies are heterogeneous, using a wide range and variety of assessment tools and modes of exercise and intensity of exercise, which makes it difficult to ascertain what types of exercise or specific duration or intensity of exercise is most beneficial or effective in improving these HRQoL domains. The authors also urged caution when interpreting the results due to risk of bias – detection, attrition and selection bias.

3.6 Exercise and cancer-related fatigue

The most common problem reported by cancer survivors is cancer-related fatigue (CRF) (Schwartz et al., 2000; Dimeo et al., 2004; Dodd et al., 2010; Veltuis et al., 2010). The National Comprehensive Cancer Network defines CRF as a distressing, persistent, subjective sense of physical, emotional and/or cognitive tiredness or exhaustion related to cancer or cancer-related treatment that is not proportional to recent activity and interferes with usual functioning (NCCN, 2009). High levels of fatigue during or after cancer treatment are reported by 60-96% of patients (Lucia et al., 2003). According to Velthuis, Agasi-Idenburg, Aufdemkampe, and Wittink (2010) the rationale for exercise

interventions supporting CRF is based on the theory that the combined effect of the cancer, subsequent adjuvant treatment and a decreased level of activity during treatment cause a reduction in physical capacity. Thus, with this reduced physical capacity the workload of normal daily activities demands a higher percentage of physical capacity, resulting in premature fatigue. Maintaining physical activity of sufficient duration, intensity and frequency throughout treatment and survivorship improves physical capacity through increasing cardiac output, increasing capillarisation, an increased number of mitochondria and mitochondrial activity in the periphery. These beneficial factors may lead to a reduction or even a prevention of CRF (McNeely et al., 2006; Cramp & Daniel, 2008).

Cramp and Byron-Daniel (2012) reviewed 56 RCTs and identified the most appropriate amount of exercise for reducing CRF. This review included not only breast cancer but also studies examining the effects of exercise and CRF with other cancer survivors. They included studies that compared exercise with no exercise (a usual care group) or an alternative treatment or exercise regime for fatigue associated with cancer. All types of physical activity were included; however, studies that investigated multi-dimensional programmes in which the effects of exercise alone could not be determined were excluded. Half of the studies (28) investigated breast cancer only (n = 1671 participants). In total, eighteen interventions provided data for 672 participants in an exercise group and 511 in a control arm were compared. They concluded that aerobic exercise was statistically more effective than the control group for improving CRF (SMD -0.35, 95% CI -0.51 to -0.19) with a moderate level of statistical heterogeneity detected (p = 0.06; I2 = 36%). To find out the most beneficial type of exercise to reduce CRF, Cramp and Byron-Daniel (2012) assessed 22 studies providing data on 832 participants following an

aerobic only intervention and 701 in the control arm. At the end of these programmes, aerobic exercise was statistically more effective that the control arm (SMD -0.22, 95% CI -0.34 to -0.10). When they applied the same analysis to five studies that used resistance training as an intervention to improve CRF, they found that after analysing 237 participants in the resistance groups and 164 in the control arms resistance exercise was not statistically more effective than the control intervention (SMD -0.18, 95% CI -0.39 to 0.19). It appears from these comprehensive meta-analyses that exercise is a beneficial and useful treatment for improving and reducing CRF and aerobic exercise such as walking and cycling is recommended.

3.7 The role of physical activity in reducing breast cancer risk

The role that exercise and physical activity can play in reducing the risk of breast cancer and reducing the risk of breast cancer recurrence and mortality is well established and becoming increasingly convincing with over 100 studies worldwide having examined and investigated some aspect of a cancer and PA association (Friedenreich & Cust, 2008; Li, Wei, Shi, Pang, Qin et al., 2016). Freidenreich & Cust, (2008) reviewed the evidence from 34 case-control and 28 cohort studies examining the impact of different parameters of activity and its effect on the association between PA and breast cancer risk. They found an approximately 25% decrease in the risk of breast cancer between the most physically active women when compared to the least physically active in over 70% of studies and a dose-response relationship in nearly half of the studies. They also reported that all modes of exercise and physical activity were associated with a decreased risk of breast cancer but those women who reported actual recreation activity as opposed to

occupational or household activities had a stronger association with a reduced risk. Ballard-Barbash et al. (2012) within their systematic review of physical activity, biomarkers and disease outcomes in cancer survivors, examined 17 observational studies of physical activity before and/or after diagnosis and the effects on breast cancer-specific and overall survival. Although, the studies demonstrated a high degree of heterogeneity in cohort sizes, length of follow-up, range of sub-group populations, and physical activity assessments and metrics, they summarised, that the strongest evidence of an inverse relationship between physical activity and cancer outcome was for BCS. Nearly all of the breast cancer studies reported an association with physical activity and reduction in breast cancer-specific mortality as well as all-cause mortality. They reported a risk reduction (RR) that was statistically significant in nearly half of the studies and evidence of a dose-relationship response effect of lowering mortality risk with increasing levels of physical activity was demonstrated in half of the studies. Zhong et al. (2014) carried out a meta-analysis of sixteen cohort studies involving a total of 42,602 breast cancer patients examining the association between physical activity and breast cancer mortality. When examining pre-diagnosis physical activity involving 27,805 patients, those patients who participated in moderate to high levels of PA before diagnosis had a RR of 0.82 (95% CI 0.74-0.91, p<0.01) for breast cancer specific mortality when compared to participants reporting low levels of PA. The RRs of breast cancer specific mortality for moderate versus low PA and high versus low PA were 0.83 (95% CI 0.73-0.94, p<0.01) and 0.81 (95% CI 0.72-0.90, p<0.01), respectively. Regarding all-cause mortality from their analysis they determined that pre-diagnosis PA was also associated with a protective effect. Moderate to high levels of PA before diagnosis reported a RR of 0.79 (95% CI 0.73-0.85, p<0.01) for all-cause mortality compared to low levels of PA.

When they further analysed PA levels and all-cause mortality and compared moderate versus low PA and high versus low PA, they reported RRs of 0.80 (95% CI 0.73-0.88, p<0.01) and 0.76 (96% CI 0.69-0.83, p<0.01), respectively. All these studies demonstrate a very strong association between physical activity levels and risk of breast cancer.

3.8 Physical activity to reduce risk of breast cancer recurrence and mortality

Zhong et al. (2014) examined the association of post-diagnosis physical activity on mortality among 23,360 patients. The results suggested that patients who took part in moderate to high levels of PA after breast cancer diagnosis had a RR of 0.71 (95% CI 0.58-0.87, p<0.01) for breast cancer specific mortality compared to those who reported low PA levels. The RRs of breast cancer-specific mortality for moderate versus low PA and high versus low PA were 0.81 (95% CI 0.70-0.94, p<0.01), and 0.68 (95% CI 0.57-0.82, p<0.01), respectively. When they considered all-cause mortality, moderate to high levels of PA reduced all-cause mortality by 43%, RR 0.57, (95% CI 0.45-0.72. p<0.01) when compared to low levels of PA. When they analysed moderate versus low PA and high versus low PA levels, they reported that high moderate and high levels of PA decreased all-cause mortality by 39%, RR 0.61 (95% CI 0.46-0.81, p<0.01) and 48%, RR 0.52 (95% CI 0.43-0.64, p<0.01), respectively.

Li et al. (2016) not only analysed the association of physical activity on cancer mortality in the general population and in cancer survivors but also examined the amount of exercise that was required to have an effect. They found that individuals who

participated in the most physical activity had an HR of 0.83 (95% CI 0.79-0.87) and 0.78 (95% CI 0.74 to 0.84) for cancer mortality in the general population and among cancer survivors, respectively. Their analysis found that in the general population, a minimum of 2.5h/week of moderate intensity activity resulted in a 13% reduction in cancer mortality, whereas cancer survivors who completed approximately five hours a week of physical activity reduced their risk of cancer mortality by 27%. They also found that physical activity post-diagnosis (HR 0.60, 95% CI 0.50-0.71) seemed to offer more of a protective effect than pre-diagnosis physical activity (HR 0.86, 95% CI 0.80-0.92), where the same amount of activity (5 hours/week) decreased the risk by 35% and 21%, respectively. They also confirmed an inverse relationship between physical activity and breast cancer mortality, findings which are consistent with Zhong et al. (2014) who revealed a similar non-linear dose-response relationship.

3.9 Mechanisms underlying the relationship between physical activity and breast cancer

The biological mechanisms that underlie the relationship between physical activity and breast cancer are not completely understood; however, a number of mechanisms have been postulated to explain the inverse association between PA and mortality in breast cancer patients (Zhong et al., 2014). Clarifying the precise biological mechanisms through which physical activity and exercise may exert a protective effect on the risk of breast cancer, recurrence and mortality is very challenging, mainly due to the difficulties in measuring physical activity precisely and the different modes of exercise, duration, intensity and the effects of the exercise on the physiological systems either before,

during or after treatment. A further limitation to understanding these mechanisms is that there are no suitable or very specific biomarkers of exposure or a known biological dose of physical activity to ascertain any changes (Friedenreich & Cust, 2008).

Despite these methodological challenges, experimental and epidemiological data have provided some possible hypotheses of how these biological mechanisms of physical activity may reduce the risk of breast cancer (Ballard-Barbash et al., 2012; Irwin et al., 2009; Payne, Held, Thorpe, & Shaw, 2008; Zhong et al., 2014). The proposed mechanisms can be broadly categorised into the following physical activity effects on: insulin levels and insulin resistance, a reduction in the levels of circulating sex hormones and cumulative exposure to sex steroid hormones, changes and lowering of inflammation markers and immune function, hormonal and cellular metabolic processes and the effects on adiposity and BMI.

Breast cancer has a complex aetiology and it is unlikely that any one mechanism is responsible but that any of these mechanisms could interact at differing stages of the cell cycle during carcinogenesis, including DNA mutations, initiation, promotion and progression of the disease (Rundle, 2005). Also, the potential mechanisms may often differ depending on the type of cancer, hormone sensitivity, the population, age and the mode of exercise, duration and intensity. Evidence regarding steroid hormones is particularly convincing (Berstein, 2009). Oestrogen and progesterone are implicated in breast cancer risk considering that rates increase rapidly during reproductive years but decline after menopause. This link has been supported in a number of studies demonstrating that increases in oestradiol increase mitotic activity in breast epithelial cells and regulation of the cell cycle progression (Friedenreich & Cust, 2008). Several

studies have demonstrated that physical activity is inversely associated with reduced circulating levels of oestrogen and progesterone (McTiernan, Wu, Chen et al., 2006).

There appear to be two postulated mechanisms by which physical activity could reduce exposure to oestrogen and other circulating endogenous hormones. One is that physical activity can maintain energy balance and reduce adiposity, with reduced body fat likely to have a stronger effect on breast cancer risk in postmenopausal women rather than premenopausal women because of the production of oestrogen by the aromatase enzyme in adipose tissue, which becomes the major source of endogenous oestrogen (Key, Appleby, Reeves et al., 2003). The second mechanism by which regular or moderate (and vigorous) physical activity could reduce circulating endogenous hormones and cumulative exposure to these hormones is through altering menstrual function through delayed menache, disruption to menstrual cycles, abnormal luteal function, a loss in the surge of the luteinising hormone and longer menstrual cycle (Tworoger, Missmer, Eliassen et al., 2007; Friedenreich & Cust, 2009). Excess weight is also associated with early menarche and delayed menopause, so physical activity may also have an effect on this.

Exercise has been demonstrated to improve insulin sensitivity, lower fasting insulin levels, improve insulin-like growth factor (IGF-I) and insulin-like growth factor binding protein 3 (IGFBP-3) synthesis, all of which have been related to breast cancer progression, recurrence and mortality among BCS. Insulin is thought to play a role in breast cancer development by indirectly increasing the bioavailability of oestrogen and androgen levels by downregulating sex hormone binding globulin (SHBG) and upregulating sex steroid production (Ligabel et al., 2008; McTiernan et al., 2008; Irwin et al., 2009; Boyle, Boniol, Koechlin et al., 2012). Insulin also increases the synthesis and

bioavailaibity of IGF-I and both insulin and IGF-I and may act directly on mitogenic and anti-apoptotic growth factors involved in malignant breast tissue growth (Lorincz & Sukumar, 2006).

Another potential mechanism that physical activity may exert on reducing breast cancer risk is the reduction in inflammation and inflammatory markers. Evidence suggests that inflammation may up regulate aromatase which could result in a higher production of these circulating endogenous oestrogens (Morris, Hudis, Giri et al., 2011). Physical activity can have a positive effect on the balance of pro- and anti-inflammatory cytokines in the systematic circulation and although strenuous exercise induces increases in the production and concentration of pro-inflammatory cytokines, it appears the body produces more anti-inflammatory cytokines and cytokine inhibitors to control and compensate for this overexpression (Moldoveanu, Shepherd, & Shek, 2001). This balance of inflammatory cytokines may depend on the mode of exercise, duration and intensity and long-term physical activity may enhance natural immunity and a positive cytotoxic activity (Moldoveanu, Shepherd, Shek, 2001; Suzuki, Nakaji, Yamada et al., 2002).

3.10 Summary

There is compelling evidence as to the range of benefits that breast cancer patients can experience by participating in exercise during active treatment or post-treatment. Research involving younger cancer survivors and older "cancer free" adults has demonstrated that exercise plays an important part in maintaining and improving general health and can help with ameliorating the effects of cancer treatment (Courneya

et al., 2004). However, evidence from older cancer survivors appears to be extremely limited with the focus of research with younger patients, despite the higher incidence of diagnosis and lower survival rates among older cancer survivors (Whitehead & Lavelle, 2009). They proposed that further research direction should provide the evidence to refine exercise guidelines and characterise the exercise requirements for this population. Unfortunately, still very little has been done focusing on this population.

There is now a need to build the evidence base for exercise in older women with breast cancer. It is important to understand whether the same benefits from exercise in a younger breast cancer population can be obtained by older women, particularly considering feasibility and acceptability of an exercise intervention, along with the efficacy and any potential risks. The next chapter will present the results of a rapid evidence synthesis of the quantitative literature on exercise for older women with breast cancer. Investigation of these factors will help to further inform the design of an exercise intervention for older women surviving breast cancer.

Although, there are a number of different definitions of old age, there appears to be no consensus for the age at which a person is classified as "old". Without an agreed and acceptable definition for old age, the age at which a person becomes eligible for a statutory retirement pension often has become the default definition. Thus, the ages of 60 and 65 years for women and men respectively are often used, despite their arbitrary nature (Roebuck, 1979; Thane, 1978, 1989). For the purpose of the rapid evidence synthesis, "older breast cancer survivors" will be defined as aged 60 years or older.

Chapter 4: Exercise for older breast cancer survivors: a rapid evidence review of the quantitative literature

4.1 Introduction

The aim of this chapter is to comprehensively review and critically examine the literature on exercise interventions for older breast cancer survivors, following the Medical Research Council Framework guidelines. Craig et al. (2013) as part of the process for developing a complex intervention, (Craig et al., 2008). The previous chapters have examined in detail the background evidence relating to breast cancer treatments and common side effects. The role of exercise and physical activity as a benefit both during and after treatment to support with reducing or ameliorating the consequences of treatment has also been examined. This chapter will focus on identifying and appraising the most relevant literature relating to older women with breast cancer and exercise to gain an in-depth understanding about exercise and physical activity with this population.

4.2 Why it is important to do this review

The benefits of taking part in regular physical activity and exercise in older adults have been extensively researched and studied (M. E. Nelson et al., 2007). In ageing populations, regular physical activity has been demonstrated to reduce the risk of cardiovascular disease, stroke, high blood pressure, high cholesterol, osteoporosis, Type II diabetes, colon and breast cancer and all-cause mortality and improve metal health conditions of anxiety and depression (Haskell et al., 2007; Lim & Taylor, 2005). An

important benefit of exercise particularly for older adults is the substantial evidence that physical activity can prevent falls and fall-related injuries (pooled rate ratio 0.84, 95% CI 0.77-0.91) (Sherrington, Tiedemann, Fairhall, Close, & Lord, 2011).

Older adults can substantially increase their strength with resistance training with reported increases ranging from less than 25% (Carmeli, Reznick, Coleman, & Carmeli, 2000) to over 100% (Ferketich, Kirby, & Alway, 1998). Supervised aerobic exercise programmes of an intensity ($\geq$60% of pre-training VO_{2max}), frequency ($\geq$3/day/week) and length ($\geq$16 week) can significantly increase VO_{2max} in older adults, with the average improvements in VO_{2max} reported of over 16% when compared to non-exercise controls and larger improvements have been demonstrated with longer interventions but not necessarily higher intensities (Huang, Gibson, Tran, & Osness, 2005). Significant improvements in VO_{2max} have also been reported in adults >75 years but the magnitude of improvement is significantly less, although men and women in their 60s and early 70s have shown similar relative increases in VO_{2max} after aerobic training compared to younger adults (Binder et al., 1999; Malbut, Dinan, & Young, 2002).

Reductions in total body fat without dietary modification have been demonstrated with older adults involved in moderated-intensity aerobic training ($\geq$60% of VO_{2max}), with average losses during 2-9 months ranging from 0.4 to 3.2 kg (1%-4% of total body weight) (Kay & Fiatarone Singh, 2006; Toth, Beckett, & Poehlman, 1999) . However, in contrast to the effects on body fat, aerobic training appeared to have no effect on fat free mass, as Tracy et al. (1999) reported in their meta-analysis of 36 studies. Only 8 reported increases in fat-free mass and these increases were less than 1kg. Resistance training has also been demonstrated to improve both fat free mass and decrease body-fat in older adults who participate in moderate or high intensity resistance training

(Hunter, Bryan, Wetzstein, Zuckerman, & Bamman, 2002). There is a substantial amount of evidence of the benefits of exercise and physical activity with older adults without cancer (Nelson et al., 2007; Skelton, Dinan, Campbell, & Rutherford, 2005) and exercise has been demonstrated to be effective in reducing cancer treatment-related side effects in women aged 55 years and younger (Furmaniak et al., 2016). However, to date, very limited research has focused on exercise to manage side effects in older women during or after adjuvant therapy for breast cancer.

The risk of cancer increases significantly with increasing age and functional decline is much more likely with a cancer diagnosis (Demark-Wahnefried, 2003). Thus, maintaining and improving functional capacity in later life is crucial. Relatively little is known about what exercise or physical activity interventions may alleviate symptoms or reduce these side-effects in this older population, or to what extent older BCS may benefit from these interventions (Penedo, Schneiderman, Dahn, & Gonzalez, 2004). As the majority of exercise studies have recruited younger BCS there appear to be limitations to the generalisability of the current exercise and breast cancer research evidence to the whole breast cancer population. Although the age range of participants in many research studies did include some older women (>60 years), the mean age of the women included in a number of large exercise and breast cancer trials and reviews of the evidence was approximately 50 years (Courneya et al., 2007; C.-J. Kim, Kang, & Park, 2009; McNeely et al., 2006; Mutrie et al., 2007). What appears to be a common limitation with exercise studies is that those recruited have a history of exercise and are typically younger (Courneya et al., 2007). In addition to the normal ageing process, older BCS often face the demands and challenges of managing often more than one debilitating condition, which can affect physical and psychological functioning.

Aims

To identify and evaluate the international evidence on exercise or physical activity interventions with women ≥ 60 years old recently diagnosed with breast cancer to answer the following questions:

1. Is it feasible and safe for women aged over 60 years recently diagnosed with breast cancer to participate in an exercise or physical activity intervention?

2. What are the health benefits that women aged over 60 years, recently diagnosed with breast cancer may gain from taking part in a physical activity intervention?

4.3 Methods

4.3.1. Design

This rapid evidence review used a comprehensive and systematic approach (Higgins & Green, 2011) to identify and evaluate internationally published primary research relating exercise and physical activity interventions with older women with breast cancer. Rapid evidence reviews have gained popularity more recently as a way of providing policy makers and healthcare decision makers with information in a timely fashion while still following and trying to maintain the rigour of the systematic review process, but with some components of the process omitted or simplified (Khangura, Konnyu, Cushman, Grimshaw, & Moher, 2012). They provide an evaluated and critical appraisal of what is known about policy or practice issues, using systematic review methods but make concessions to the extent and depth of a full systematic review process by limiting certain aspects of the process (Grant & Booth, 2009). The Government Social Research Service lists this method of review in its Rapid evidence assessment Toolkit (Thomas, Newman, & Oliver, 2013) and the National Institute for

Health and Care Excellence (NICE) has commissioned and used a number of rapid reviews recently to inform care in dementia, disability and frailty in later life (Dementia, 2015). With no exercise or physical activity policies or guidance for older adults with breast cancer this method of review was considered appropriate by providing information and evidence in a timely manner.

4.3.2 Search methods for identification of studies

Relevant studies were identified and considered for inclusion by individually searching the electronic databases AMED (Allied and Complimentary Medicine), CINAHL (Cumulative Index to Nursing and Allied Health Literature), MEDLINE (Medical Literature Analysis and Retrieval System Online) and EMBASE (Excerpta Medica Database) between the years of 2003-2018. The search term dates were set to follow on from the review of exercise issues with older cancer survivors by Courneya et al. (2004), thus, searching from 2003-2018. Limitations were added to the searches if allowed by the database and where possible, which were: non-English language studies were excluded, female only studies, human only studies, only articles published between the dates of 2003-2018 and age groups of middle age, aged 60 - 80 years or aged >80 years to further focus the searches.

Further studies were identified by reviewing reference lists of relevant published clinical trials, reviews and qualitative studies. Search terms included words associated with breast cancer, exercise, physical activity and older adults or the elderly to ensure a wide range of related and relevant studies were identified, which specifically targeted women with breast cancer who were aged over 60 years. Boolean logical operators were

incorporated and used for the search strategy, predominately "AND" or "OR" to search for alternative concepts or synonyms and to combine the different search terms used above. (For a list of the full search terms see Appendix 1).

4.3.3. Screening and selection of studies

All searches were conducted and screened by the researcher (KK) according to the selection criteria. All titles and abstracts of all articles identified by the database and bibliographic search were screened and those that fulfilled the inclusion and exclusion criteria (see Table 2) for this rapid evidence review were selected. All duplicates of the same records were removed. Full-text articles of potentially relevant studies were retrieved for a closer inspection and detailed evaluation. Multiple reports of the same studies were also linked together. Articles included in the final synthesis were also reviewed by SB (researcher supervisor) to avoid selection bias by independently assessing for compliance of studies meeting the eligibility criteria.

4.3.4. Data extraction and synthesis

The main characteristics and methodological details on study design and outcomes from the identified articles were extracted by KK and characteristics of included studies were summarised in Table 4 and study findings reported as narrative. Multiple publications of the same trial were considered together and the most relevant ones that met the aims of the synthesis were included. This information was organised under the headings of: study design, participants (including sample size, ages and date of breast cancer

diagnosis), intervention details (duration, type, intensity) outcome measures (time-points and threats to validity/bias). (McNeely et al., 2006; Kirshbaum, 2007).

4.3.5. Inclusion and exclusion criteria for considering studies for this review

Table 2: Eligibility criteria for article inclusion in the rapid evidence review

PICO Framework	Inclusion criteria
Population	Women ≥ 60 years old with breast cancer during or after adjuvant treatment.
	Early stage, curative breast cancer treatment
Intervention	Randomised controlled trials (RCTs), quasi-controlled trials, non-randomised trials. Home-based and supervised exercise programmes. Mean age ≥ 60 years
	Feasibility and pilot studies
	Studies that were a further analysis of the same population group
Control	Studies with or without a control group
	Studies with a comparison group
Outcome	Feasibility outcomes: recruitment, acceptability, retention, completing and implementation fidelity
	Health, physical and psychosocial benefits of exercise
	Adverse events, safety
Article Type	Full text journal articles written in English published between 2003-2018
	Female only studies
	Quantitative methodology

4.3.6 Methodological quality assessment

The methodological quality of trials included in the review was assessed by KK using the following criteria (McNeely et al., 2006):

1. Was there adequate concealment of allocation?

2. Was the method of randomisation well described and appropriate?

3. Was the outcome assessment described as blinded?

4. Was the method of blinding of the assessment of outcomes well described and appropriate?

5. Was there a description of withdrawals and drop-outs?

6. Was the analysis intention to treat?

7. Were withdrawals and drop outs less than 10%?

8. Was adherence to the exercise intervention (attendance or completion of the exercise intervention) greater than 70%?

All items were scored as positive (Y), negative (N) or unclear (?). Studies were defined as being high quality if they fulfilled four or more of the eight quality criteria (See Table 3).

4.4 Results

The electronic search strategy identified a total of 1401 titles (see Figure 3). After applying the selection criteria to titles and abstracts and removing duplicates, two articles were identified from citation tracking, resulting in 27 being included for a closer inspection. Reasons for exclusion at this stage were predominantly not recruiting breast cancer patients only, or not being related to an exercise programme or physical activity that did not target older cancer survivors. After retrieving and reading the full papers, a further 16 articles were excluded. These papers were excluded because they did not recruit older breast cancer survivors (5), did not target only breast cancer survivors (3), were not a journal article (1) were not an exercise or physical activity intervention (6), or involved one-off exercise testing and did not involve exercise or physical activity (1). The search resulted in identifying 11 articles that were directly relevant to the aims of the review of older breast cancer survivors and exercise.

```
Identification

Records identified through          Additional records identified
database searching                   through other sources
AMED, CINAHL, MEDLINE,               citation tracking
EMBASE, COCHRANE LIBRARY             (n = 2)
(n = 1401)

        Records after duplicates removed (n = 1141)

Screening

Records screened (titles & abstracts)          Records excluded
(n = 1141)                                      (n = 1112)

Eligibility

Full-text articles assessed for          Full-text articles
eligibility (n = 27)                     excluded (n = 16),
                                         reasons:
                                         did not recruit older BCS
                                                 (n=5)
                                         not an exercise intervention
                                                 (n=6)
                                         not a journal article
                                                 (n=1)
                                         not breast cancer only
                                                 (n=3)
                                         One off exercise test
                                                 (n=1)
Included

Studies included in
quantitative synthesis
(n = 11)
```

Figure 2: Flow diagram of study selection process (adapted from Moher et al., 2009)

4.4.1. Study characteristics

Of the 11 studies selected six were RCTs but three of these(Dobek, Winters-Stone, Bennett, & Nail, 2014; Winters-Stone et al., 2012b; Winters-Stone, Leo, & Schwartz, 2012a) were further analyses of Winters-Stone et al. (2011) the other two RCTs were both pilot studies; (Crane-Okada, Kiger, Sugerman, et al., 2012; Payne et al., 2008), four were non-randomised trials; one of two parallel groups examining the effects of resistance training on difference ages of BCS (Benton, Schlairet, & Gibson, 2014), and

three were single group pre-post design (Damush, Perkins, & Miller, 2006; Nyrop et al., 2014; Tunay, Akbayrak, & Kaya, 2012), two of which classed themselves as feasibility studies (Damush et al. 2006; Nyrop et al. 2014). One study was a cross-sectional design (Boyle, Vallance, Ransom, & Lynch, 2016).

All the RCTs were undertaken in North America. Two of these compared exercise groups against usual care (Payne et al., 2008; Crane-Okada et al., 2012) whilst one compared a progressive, resistance and impact training programme against a stretching only group (Winters-Stone et al., 2011). The only intervention study that did not come from North America was Tunay et al. (2012) which was from Turkey. The cross-sectional study (Boyle et al. 2016) originated in Australia.

4.4.2. Programme length

The length of interventions varied; one intervention was for seven days (Boyle et al., 2016); two were of six weeks' duration, (Tunay et al., 2012; Nyrop et al., 2014); one of eight weeks' duration (Benton et al., 2014); one of 12 weeks's duration (Crane-Okada et al., 2012); one of 14 weeks' duration (Payne et al., 2008); one of six months' duration (Damush et al., 2006;) and one of 12 months' duration (Winters-Stone et al., 2011).

4.4.3. Age of participants

Age was reported as a mean or range. Mean ages ranged from 51.7 years (Benton et al., 2014), although this was a comparison study of younger BCS to older BCS (mean = 68.3 years) to 71 years old (Nyrop et al., 2014) with an average age of 63.4 years across eight intervention studies. The only study not to report mean ages was Tunay et al. (2012)

who reported that all participants (n=40) were over 65 years of age. The range of ages of the participants in the intervention studies included in this review was between 50-90 years.

4.4.4. Time since diagnosis

Most studies reported the mean time since cancer diagnosis; ranging from 3-years (Damush et al., 2006; Boyle et al. 2016); five years (Winters-Stone et al., 2011); 6.3 years for Benton et al. (2014); with Crane-Okada et al. (2012) being on average 9.8 years since cancer diagnosis. Two studies did not report a mean time since diagnosis (Payne et al., 2008; Nyrop et al., 2014) and Tunay et al. (2012) only mentioned the time since surgery (8-44 months) with no indication whether participants had completed adjuvant therapy or not.

4.4.5. Exercise intervention characteristics

The setting for the exercise interventions was varied. Four studies reported home based interventions (Damush et al., 2006; Payne et al., 2008; Nyrop et al., 2014; Boyle et al., 2016;), three reported on a mixed supervised and home-based intervention (Winters-Stone et al., 2011; Crane-Okada et al., 2012; Tunay et al., 2012). Of these interventions Crane-Okada et al. (2012) encouraged participants to do further exercise at home daily throughout the duration of the 12 week intervention, recorded in a diary. Winters-Stone et al. (2011) prescribed two supervised classes and one home-based class per week for 12 months, although the home-based session did not begin until one month after the start of the supervised sessions to allow time for the participants to be properly

instructed in the exercise techniques. Tunay et al. (2012) supervised twice weekly physiotherapy and exercise sessions with participants instructed to do the given exercises daily. Benton et al. (2014) was the only study that was a supervised intervention and did not include any home-based exercise or additional physical activity.

4.4.6. Exercise prescription

Exercise prescription was generally described sufficiently to report the exercise programme (See Table 4), although there was a lack of information reported on exercise intensity. Exercise modes were split between aerobic and resistance training or a combination of both. Four interventions prescribed aerobic only exercises (Payne et al., 2008; Crane-Okada et al., 2012; Nyrop et al., 2014; Boyle et al., 2016). Three prescribed resistance only exercise (Winters-Stone et al., 2011; Tunay et al., 2012; Benton et al., 2014), with one intervention considering both aerobic and resistance exercises (Damush et al., 2006). Walking was the most popular choice of aerobic exercise reported by four interventions (Damush et al., 2006; Payne et al., 2008; Nyrop et al., 2014; Boyle et al., 2016). All used pedometers to encourage increases in aerobic activity but participants were not asked to record distance walked or report their usage. Crane-Okada et al. (2012) used movement and dance therapy as their exercise programme. Resistance exercise was performed using a variety of free weights (Winters-Stone et al., 2011) and machine weights (Benton et al., 2014) and therabands for home-based programmes (Damush et al., 2006; Winters-Stone et al., 2011; Tunay et al., 2012).

The general intensity of the exercise programmes was either not described or inadequately described. Three interventions did report the exercise intensity that was

followed. Payne et al. (2008) described their walking programme as "moderate" with only two interventions adequately describing the intensity of the exercise programme; Winters-Stone et al. (2011) used ACSM recommendations for resistance training and Benton et al. (2014) used a percentage of 1-repetition maximum.

The duration of prescribed exercise sessions within the exercise studies was varied. Two interventions were interested in increasing PA levels and therefore did not specifically prescribe a set exercise programme (Damush et al., 2006; Boyle et al., 2016). Aerobic exercise interventions ranged from walking 20 minutes per day on four days each week (Payne et al., 2008) 30 minutes a day on five days a week (Nyrop et al., 2013). In Crane-Okada et als'. (2012) study dance and mindful movement intervention was instructor-led once per week for 12 weeks, although participants were invited to practise at home for a minimum of five minutes daily for the first four weeks and gradually increasing to 15 minutes per day for the final four weeks. The resistance and impact training programme was described in detail by Winters-Stone et al. (2011) including frequency (2 x week supervised) and home-based (1 x week), intensity 60-70% of 1-repitition maximum (1-RM) for 1-3 sets with 8-12 repetitions with 3-4 sets for the upper body and 3-4 sets for the lower body. Each exercise session lasted between 45-60 minutes. Benton et al. (2014) also described the resistance training programme that was followed in detail. This eight-week programme, twice a week (16 sessions in total) consisted of three sets of 8-12 exercises to utilise all of the major muscles of the body. Exercise intensity was set for each exercise and the progression of load was increased 5-10% when participants could complete three sets of 10-12 repetitions.

4.4.7. Quality Assessment

The median score for methodological quality of all included trials was 2, with a range of 0-3 (Table 4.1). Using a score or 4 or more out of 8 was to be considered of a high methodological quality. No studies included in this review achieved enough of these criteria to be considered of high methodological quality. The most common methodological shortcomings in the included trials were: inadequate concealment of allocation (all eight studies scored unclear); where withdrawals and drop-outs were less than 10% (6/8 studies scored "no" or ? = unclear); was the outcome assessment described as blind? (7/8 studies scored "no"); and was the method of blinding of the assessment of outcomes well described and appropriate? (all studies scored "no").

Table 3: Methodological quality assessment of exercise interventions with older BCS

Author (year)	1	2	3	4	5	6	7	8	Total/8
Benton et al. (2014)	?	N	N	N	?	N	Y	Y	2
Boyle et al. (2016)	?	N	N	N	N	N	N	?	0
Crane-Okada et al. (2012)	?	Y	N	N	Y	Y	N	N	3
Damush et al. (2006)	?	N	N	N	Y	Y	N	?	2
Nyrop et al. (2014)	?	N	N	N	Y	?	Y	?	2
Tunay et al. (2012)	?	N	N	N	N	?	?	?	0
Payne et al. (2008)	?	Y	N	N	Y	N	N	?	2
Winters-Stone et al. (2011)	?	N	Y	N	Y	Y	N	N	3

Key: Y= Yes, N= No, ? = unclear/not reported

1) Adequate allocation concealment, 2) adequate method of randomisation reported, 3) blinded outcome assessments, 4) adequate method of blinding, 5) description of withdrawals or drop-outs, 6) intention-to-treat analysis, 7) withdrawals and drop-outs < 10%, 8) adherence (attendance or completion of exercise sessions) >70% (taken from McNeely et al. (2006)

4.4.8. The feasibility of exercise interventions with women over 60-years old

4.4.8.1 Recruitment

Recruitment rates differed for all studies and the reporting of the numbers of participants approached, those screened to be eligible to be recruited and those actually recruited to start the programme or intervention appeared to be very different. Benton et al. (2014) recruited 29 participants but gave no figures for how many participants had actually been approached or screened for eligibility. Of the 29 recruited, seven did not start the intervention due to: not returning forms (4), Medical Doctor (MD) refusal to allow participation, new medical condition diagnosed (1) and scheduling conflict (1). Boyle et al. (2016) reported a recruitment rate of 61.6% after approaching 552 eligible participants with 340 agreeing to take part. Crane-Okada et al. (2012) reported recruitment of 51.6% of the 95 eligible participants, with 49 enrolled on the programme. They further reported reasons for not enrolling on the interventions as: scheduling conflicts (25), distance to the classes (11), late enquiry (7) and having no interest (3). Damush et al. (2006) screened 509 older BCS with 101 being eligible for the study. Of these, 43 agreed to take part (42.6% recruitment rate); however, only 34 completed

baseline assessments (33.7%), although no reasons were given for the difference in numbers between agreeing to take part and actually completing the initial assessments. Reason were, however, reported for those not willing to take part; 24 were unreachable and 33 were not interested. Winters-Stone et al. (2011) assessed 359 BCS for eligibility, with 246 being deemed eligible and from these eligible participants, 106 of these recruited on to the study resulting in a 43.1% recruitment rate. Nyrop et al. (2014) had the highest recruitment rate of the intervention studies with 64.5% with 31 eligible participants and 20 starting the programme, although they did report 24 participants consenting to the study but gave no reasons for four not starting. Payne et al. (2008) recruited 20 participants from 58 eligible BCS, demonstrating the lowest (35%) recruitment rate of the studies in this review. Reasons given for not participating were: transport, time commitment to the study and the randomisation process, but no further details were given.

4.4.8.2 Sample size

For this review, study sample sizes were based on the numbers initially recruited for the study and not the final number that were used for the statistical analysis. Of the eight intervention studies, sample sizes ranged from 20-340 participants, although for six studies the average sample size was 30. In the RCTs, the number of participants randomised to the exercise intervention ranged from 10 – 52.

4.4.8.3 Retention

Home-based interventions and those attempting to increase PA reported better retention rates and lower attrition than supervised interventions, where participants were required to commit significantly more time in meeting supervised exercise schedules. Damush et al. (2006), Payne et al. (2008), Nyrop et al. (2014), and Boyle et al. (2016) reported an 88%, 90%, 95% and 80.6% retention rate, respectively, for their home-based interventions. Of the supervised exercise programmes, the drop-out rate was noticeably higher with Crane-Okada et al. (2012) reporting 21% in their 12-week interventions but Winters-Stone et al. (2011), a much higher drop out of 38%; however, this was for longer, 12-month, intervention. Benton et al. (2014) reported contrary findings, with an excellent retention rate of 91% for an 8-week resistance training programme.

4.4.8.4. Adherence

Adherence rates to the supervised or home-based exercise interventions were not routinely reported. Those that did not report adherence rates were: Damush et al. (2006); Payne et al. (2008); Tunay et al. (2012); Nyrop et al. (2014) and Boyle et al. (2016). Of those that reported adherence rates, Benton reported excellent adherence of 98% to the eight-week, twice a week, resistance training programme, whereas Crane-Okada reported a more modest 64.1% adherence and Winter-Stone et al. (2011) 67% for both groups for the supervised exercise intervention and much lower for the home-based programme, 23% for the resistance group and 44% for the stretching only group.

4.4.8.5. Reporting of adverse events

Only two intervention studies reported on adverse events (Winters-Stone et al., 2011; Benton et al., 2014). Winters-Stone et al. (2011) reported no injuries or adverse events in the weight lifting and impact group (intervention) and the stretching only group (control) after 12 months. Also, there were no changes in upper-arm circumference measures over time (as an indication of the development of lymphoedema). Benton et al. (2014) reported no injuries or changes in arm volume and participants denied any exercise-related discomfort, exacerbation or new onset of lymphoedema.

4.4.9 Health benefits of exercise interventions for older women with breast cancer

4.4.9.1 Endpoints and health outcome assessments

Two studies examined fatigue as an outcome measure (Damush et al., 2006; Payne et al., 2008) and one considered body composition or weight loss (Winters-Stone et al., 2011). Two studies used PA levels as outcome measures to improve physical and mental health (Boyle et al., 2016) and joint pain (Nyrop et al., 2014). Three studies used PA levels as an endpoint, along with bone mineral density and bone turnover (Winters-Stone et al., 2011, Winters-Stone et al., 2012a) and one year follow up of bone mineral density assessments and maximal muscle strength tests (Dobek et al., 2014), functional measures such as sit to stand in 30 seconds and a 12 minute walk (Winters-Stone et al., 2008), maximum bench press and leg press, timed chair stands, handgrip strength, self-report physical function and fatigue (Winters-Stone et al., 2012b). Two studies used quality of life as a primary endpoint (Crane-Okada et al., 2012; Benton et al., 2014) and

Damush et al., (2006) included it as a secondary outcome. Further details of these studies can be found in Table 4.

4.4.9.2 Benefits of home-based exercise interventions

Damush et al. (2006) considered the benefits of an oncologist referring BCS to an exercise self-management programme to improve PA levels and HRQoL. Participants (n=34) received three weeks of structured educational sessions on increasing self-efficacy and social support to increase PA. Telephone support was also offered throughout the programme. They found that this intervention increased weekly moderate PA (p<0.04), increased caloric expenditure (p<0.02) and significantly improved HRQoL (p<0.001). Other outcomes of exercise barriers, aerobic endurance and lower body strength approached significance

Payne et al. (2008) examined the effects of a home-based walking programme on biomarkers, fatigue, sleep and depression in older BCS (mean 64.7 years). They reported improvements in sleep (less sleep disturbances) but no other noted improvements.

Boyle et al., (2016) used accelerometers to measure PA and sedentary time levels of older BCS to examine the influence of these parameters on physical and mental health. A total of 259 BCS (mean age = 61-years, mean time since diagnosis = three years) wore accelerometers for seven days during waking hours. The BCS in this study were sedentary for 8.2 hours, engaged in light-intensity PA for 5.8-hours and in moderate to vigorous intensity PA for 32-minutes per day, with only 16% meeting PA guidelines.

A home-based feasibility walking programme developed by Nyrop et al., (2014) investigated the effects of walking on joint pain with older BCS (mean age = 71 years).

The minimum goal for the participants was to walk for 30 minutes per day, five days per week, although, adherence to this target was not reported. Small but not significant improvements in joint pain, fatigue and joint stiffness were reported.

4.4.9.3. Benefits of supervised exercise interventions

Four studies targeting older cancer survivors with supervised exercise interventions were conducted by Winters-Stone et al. (2011); Crane-Okada et al. (2012); Tunay et al. (2012); and Benton et al. (2014).

Crane-Okada et al. (2012) used dance and movement therapy to observe the effects on QoL with older women with breast cancer (mean 65.6 years). After 12 weeks, the intervention group did not significantly differ in the QoL domains of physical, psychological, social or spiritual well-being when compared to the control group (no exercise), but fear of recurrence was decreased and this appeared to be retained six weeks after the intervention was completed.

In a resistance only intervention Winters-Stone et al. (2011) found that the resistance + impact group preserved bone mineral density (BMD) at the lumbar spine (p=0.001) compared to the control and increases in lean mass were greatest in women on aromatase inhibitors (AIs) compared to controls not on this therapy.

Tunay et al. (2012) evaluated the effects of a physiotherapy programme including exercise with elderly BCS (>65 years) on shoulder function, pain and lymphoedema. Participants reported significant decreases in pain and increases in function, range of movement (ROM), muscle strength and decreases in lymphoedema volume (p<0.05).

Benton et al. (2014) evaluated the effect of age on quality of life in BCS after an eight week, twice a week resistance training programme. To examine the effects of age, they split the participants into two groups based on age. One group was 40-59 years and the second group was 60-80 years old. Both groups improved in chest press ($p<0.001$), leg press ($p<0.001$), arm curls ($p<0.05$) and chair stands ($p<0.001$). Overall adherence to the training programme was 98% for both groups, with no adverse events reported, demonstrating that older women with breast cancer will attend a supervised exercise programme with adherence rates similar to younger women, with no injuries or exacerbation of treatment related effects noted between the older women and the younger women. Although older women did have significant improvements in strength and function, they perceived very little improvement in QoL compared to younger women. Limitations to the study were the relatively small sample size (n=20) and the non-randomisation of participants.

Table 4: Brief overview of studies included in the review

Author, date, country	Study Design	Participants	Intervention	Outcome Measures	Threats to validity/ comments	Results
1.Benton et al. (2014) N. America	Non-randomised comparison of younger BCS vs older BCS on effects of resistance training on QoL A supervised exercise intervention	N = 20 YRT: n=12 (mean age = 51.7 years) ORT: n=8 (mean age = 68.3 years) Mean 6.3 ± 1.5 years since diagnosis.	8-week, whole body resistance training programme 2 x week 3 sets of 8-12 reps of 8 exercises 1-2-1 training	Body Image & Relationship Scale (BIRS) Arm curl test in 30 secs Chair stand test in 30 secs	Non-randomised	98% attendance at resistance sessions. No injuries or lymphoedema reported 80% YRT & 99% ORT ($p<0.001$) ↑ upper body strength 34% ($p<0.001$) ↑ lower body strength
2.Boyle et al. (2016) Australia	Cross-sectional study	N = 340 Mean age = 61 years Mean time since diagnosis = 3 years	Accelerometer measurement of BCa survivors' physical activity levels	Minutes engaged in PA in 7-days	Non-randomised case controlled study	Sedentary 57% of waking hours Low PA 40% of waking hours 32 mins per day in MVPA >70 years old sedentary time 2 x high as active time

						16% of BCS met PA guidelines (150mins/week)
3.Crane-Okada et al. (2012) N. America	Pilot study Randomised controlled trial A supervised exercise programme	N=49 (29=I, 20=c) Mean age 65.6 years Range 50-90 yrs Mean 9.8 years since diagnosis Range 1-32 yrs	RCT 12-weeks x 1/week (2/hours) self-directed movement/dance therapy Aerobic	QoL Drop out – 21% for intervention 69% attendance for 9/12 sessions	Mean age since diagnosis was nearly 10 years Exercise intensity not described Adverse events not reported	Session attendance was 64.1% 46.6% recruitment rate Fear of recurrence was reduced (p=0.02) Mindfulness attitude improved (p=0.026) Con Group improved upper body symptoms (p=0.04) at 12-weeks
4.Damush et al. (2006) N. America	Feasibility study Oncologist referred self-management programme to increase PA & HRQoL. Home based	N=34 Mean age 59.6 years Av. 3.1 years since diagnosis	6-month intervention 3 x week for 3-weeks educational sessions to support increasing PA. Telephone support 4, 6 & 10-weeks	Confidence to perform PA PA levels Calories expended Senior Fitness Test HRQoL Fatigue (FACT-F) Drop-out (N=4)	Single group study – pre/post-test -no randomisation Small sample Unable to determine effects of exercise alone	43% recruitment rate Freq. of weekly PA ↑ (p<0.04), aerobic endurance ↑ (p,0/04) and lower body strength ↑ (p<0.03). HRQoL

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Study	Design	Sample	Intervention	Outcomes	Limitations	Results
	Not a supervised programme Single group design		Aerobic & resistance. Pedometers & Theraband		due to social support Adverse events not reported	sig. improved (p<0.001)
5. Dobek et al. (2014) N. America	1-year follow up of a controlled trial A supervised exercise intervention	N=106 (52=I, 54=C) 1-year post adjuvant therapy Mean age 62 years Postmenopausal Mean time since diagnosis 6 years	RCT 1-year (2 x supervised, 1 x home-based) Resistance training +impact group (POWIR) vs flexibility (FLEX) group (control) 45-60mins 60-70% 1-RM ACSM guidelines	Musculoskeletal changes after 1-year of exercise 1-year longitudinal follow-up	Lack of a true control group Women already aerobically active Modest retention (62%) Adverse events reported: no injuries or lymphoedema	P=0.001 for POWIR group maintaining spine BMD and FLEX losing spine BMD from baseline to follow up Sig interaction for POWIR group increased lower body strength p<0.05 during the intervention but decreased strength during the follow up
6.Nyrop et al. (2014) N. America	Feasibility study Walking to ↑ PA levels and ↓ joint pain	N=20 Mean age 71 (65-87)	Self-directed walking. 6-week programme Minimum walking 30 mins / day x 5/day per week	Feasibility of recruitment & timeframe Attrition levels Time spent walking Joint pain Fatigue Joint stiffness	Lack of control Small sample (n=20) Self-reported walking times	30% recruitment rate 95% study completion rate. No. Achieving 150mins/week ↑ from 21% to 50% at 6-weeks (p<0.001) Joint pain ↓ 10% Fatigue ↓ 19%

						Joint stiffness ↓ 32%
7.Payne et al. (2008) N. America	Home-based walking intervention to improve sleep, fatigue & depression RCT vs usual care Not a supervised programme	N=20 (I=10, con=10) Mean age 64.7 yrs Range 56-78 yrs Pilot study Post treatment Time since diagnosis not reported	14 weeks Walking intervention vs usual care 20 mins x 4/week Moderate walking	Fatigue Sleep disturbance Depression Biomarkers PA levels	Small sample (pilot) Self-reported PA levels Adverse events not reported	Drop-out (N=2) = 10% Sleep was improved in the exercise group p=0.007. No changes in quality of sleep for the control group
8. Tunay et al. (2012) Turkey	Physiotherapy and exercise programme on shoulder function A supervised and home-based exercise programme	N=40 >65 years No mean age reported Single group 8-44 months	6-weeks 3 x 10 reps / day Shoulder ROM & strengthening exercises	Body composition Pain Shoulder ROM and strength Arm circumference Function (DASH) QoL (SF-36)	Not a randomised controlled trial Recruitment of 40 women over 4 years	Sig. ↓ in pain and ↑ function, ROM and strength (p<0.05) Lymphoedema vol ↓ (p< 0.05). Physical functioning, role-physical, role-emotional and body pain subscales of SF-36 (p<0.05)
9.Winters-Stone et al. (2011) N. America	1-year Controlled trial	N=106 (52=I, 54=C) 1-year post adjuvant therapy	RCT	BMD of the hip and spine Body-composition	Lack of a true control group	Retention 62% Drop out 38%.

	A supervised exercise intervention	Mean age 62 years Postmenopausal Mean time since diagnosis 5 years	1-year (2 x supervised, 1 x home-based) Resistance training +impact group vs flexibility group (control) 45-60mins 60-70% 1-RM ACSM guidelines	Bone turnover Home based 23% (Int) 44% (Con)	Women already aerobically active Modest retention (62%) Adverse events reported: no injuries or lymphoedema	Attend at supervised sessions 67% Resist + Impact group preserved BMD at spine (p=0.001) compared to control ↑ in lean muscle highest in resist + impact (p=0.01) compared to control
10.Winters-Stone, Leo & Schwartz (2012a) N. America	1-year Controlled trial A supervised exercise intervention	N=106 (52=I, 54=C) 1-year post adjuvant therapy Mean age 62 years Postmenopausal Mean time since diagnosis 5 years	RCT 1-year (2 x supervised, 1 x home-based) Resistance training +impact group vs flexibility group (control) 45-60mins 60-70% 1-RM ACSM guidelines	Secondary data analysis of age and exercise on BMD of the hip	Lack of a true control group Women already aerobically active Modest retention (62%) Adverse events reported: no injuries or lymphoedema	Retention 62% Drop out 38%. Attend at supervised sessions 67% BMD ↑ at a younger age with resist. + impact (POWIR) but POWIR less effective in stopping bone loss as age ↑. No change in total hip BMD for FLEX

						group regardless of age Younger women obtained more benefit in total hip BMD in POWIR group compared to older women (p=0.02)
11.Winters-Stone et al. (2012b) N. America	1-year Controlled trial A supervised exercise intervention	N=106 (52=I, 54=C) 1-year post adjuvant therapy Mean age 62 years Postmenopausal Mean time since diagnosis 5 years	RCT 1-year (2 x supervised, 1 x home-based) Resistance training +impact group vs flexibility group (control) 45-60mins 60-70% 1-RM ACSM guidelines	Strength & physical function 1-RM bench press and leg press Timed chair stands, 4m walk speed, Timed stance tests, handgrip, self-report physical function & fatigue	Lack of a true control group Women already aerobically active Modest retention (62%) Adverse events reported: no injuries or lymphoedema	Attend at supervised sessions 67% POWIR group sig. ↑ max leg and bench press strength (p<0.02) compared to FLEX group Adherence to the programme reflects degree of improvement

Abbreviations: N=Numbers involved in the study; RCT = Randomised Controlled trial; YRT= Young resistance training group; ORT= Older resistance training group; BCS= Breast Cancer Survivors; I=Intervention group; C=control group; POWIR= Power & resistance group; FLEX=flexibility group; BMD= Bone mineral density.

4.5 Discussion of findings

The findings from the 11 articles included in this review were inconsistent due to the different nature of research questions, the outcomes and endpoints evaluated and the types of exercise programme or physical activity intervention prescribed. The implications of these inconsistencies are discussed in further detail below; however, they do all offer an insight and further understanding of delivering exercise and physical activity interventions with this under-researched population.

4.5.1. Feasibility of an exercise intervention with older breast cancer survivors

It appears that it is feasible to recruit older women with breast cancer onto a supervised or home-based exercise programme with differing success rates. From the studies examined the mean time since breast cancer diagnosis was 3.1-years. Therefore, it is still uncertain whether women newly diagnosed with breast cancer (< 1-year since diagnosis) could be recruited onto an exercise programme, due to a lack of evidence at this time. Recruitment rates for older women with breast cancer ranged between 35% (Payne et al., 2008) and 64.5% (Nyrop et al., 2014). Once recruited onto an exercise study, retention to the study was acceptable, although home-based interventions generally reported higher retention rates of 80-95% (Damush et al., 2006; Payne et al., 2008; Nyrop et al., 2014; Boyle et al., 2016). Benton et al. (2014) reported an attrition rate of only 9% for an 8-week supervised resistance training programme; however, supervised programmes appeared to report higher attrition rates then home-based interventions (21% [Crane-Okada et al., 2012] - 38% [Winters-Stone et al., 2011]). Although home-based interventions reported better retention rates, supervised

exercise interventions actually reported better adherence rates. However, an issue with adherence rates to exercise interventions with older women with breast cancer is that they were routinely not reported, therefore, evidence is limited. Benton et al. (2014) reported an adherence rate of 98% for a supervised, twice a week resistance programme with more modest levels reported by Winters-Stone et al. (2011) of 67% and 64% reported by Crane-Okada et al. (2012). Adherence to home-based programmes was much lower at 23% for the resistance groups and 44% for the stretching only group (Winters-Stone et al. 2011).

A very important part of assessing the feasibility of an exercise programme with older women with breast cancer is the safety of exercise for this population exercising during and after diagnosis and treatment. It could be suggested that it is safe and therefore feasible for women to take part in an exercise programme at this time, as no studies reported any adverse events experienced by the women during or after any exercise programme. However, this evidence does need to be considered cautiously, as only two studies reported on adverse events (Winters-Stone et al. 2011; Benton et al. 2014), with neither study reporting any adverse events, onset of lymphoedema or any injuries as a result of the exercise programme. No other studies included in this rapid evidence review reported on adverse events so it is unclear whether this indicates poor reporting by these studies or the absence of any adverse events to report.

A home-based feasibility walking programme developed by Nyrop et al., (2014) investigated the effects of walking on joint pain with older BCS (mean age = 71 years). The minimum goal for the participants was to walk for 30 minutes per day, five days per week; however, adherence to this target was not reported. They also investigated the feasibility of recruitment with this population and attrition rates throughout the study.

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As a feasibility study the authors do not clearly report all of the primary outcomes linked to the feasibility of the intervention. They recruited to target (20 participants) from a clinical setting but wanted to know if this was feasible in a five months' time-frame; however, they do not report whether this target was met. Secondary outcomes related to joint pain were clearly reported and resulted in small but not significant improvements in joint pain fatigue and joint stiffness.

4.5.2. Health benefits of exercise for older breast cancer survivors

A number of health benefits of exercise for older breast cancer survivors have been reported in the literature, although with the evidence being very limited, it is difficult to suggest with any conclusiveness, the benefits that an older woman with breast cancer can expect to gain from participating in an exercise intervention during or after treatment for breast cancer.

The health benefits reported were wide ranging; with reported increases in weekly moderate PA, increased caloric expenditure and improved HRQoL (Damush et al., 2006); improvements in sleep (less sleep disturbance) (Payne et al., 2008); reducing the fear of recurrence and improved upper body symptoms (Crane-Okada et al., 2012); maintenance of bone mineral density of the spine and improved lower body strength (Dobek et al., 2014); decreases in joint pain, fatigue and joint stiffness (Nyrop et al., 2014); reductions in pain, improved function and range of movement and improved QoL (Tunay et al., 2012) and improvements in maximal bench press and leg strength (Winters-Stone et al. 2012b).

However, a number of limitations could have affected the outcomes reported: with Damush et al. (2006), it was a small sample size of 34 BCS and was a single group of consecutive patients in pre-test, post-test design. Thus, because the patients were not randomised, the results cannot be compared against a control group of usual care. Also, they reported the group were all Caucasian and of high social economic status. Additionally, the intervention included both exercise and social support, and it was not possible to determine whether the effects of the study were due to the exercise or social support alone. Despite these limitations, this method of referral and exercise self-management could still be considered to increase PA levels in older BCS and the associated benefits they can gain from this.

Payne et al. (2008) examined the effects of a home-based walking programme on biomarkers, fatigue, sleep and depression in older BCS (mean 64.7 years). This was a pilot RCT, with an intervention vs usual care design. They reported on improvements in sleep but no improvements in the quality of sleep. This was a very small sample (n=20) and therefore of limited power. Additionally, the authors did not record if the intervention group adhered to the walking programme, so therefore, it is not known whether the effects of the walking programme could be attributed to improving sleep.

Boyle et al. (2016) used accelerometers to measure PA and sedentary time levels of older breast cancer survivors to examine the influence of these parameters on physical and mental health. Objective measuring of PA levels accurately allows these levels to be recorded without relying on the very subjective reporting of these by the use of self-report. This was a large study recruiting 340 women with breast cancer. Although participants had to only wear the accelerometer on their waist band during waking hours for seven days, only 49.6% completed the study, which raises questions whether

the recruitment sample was representative of those eligible to participate. Also, the sedentary time was recorded whether the participant was standing or sitting whilst being still, which therefore may over-inflate the actual time a person was sitting sedentarily.

Four studies targeting older cancer survivors with supervised exercise interventions, were conducted by Winters-Stone et al. (2011); Crane-Okada et al. (2012); Tunay et al. (2012); and Benton et al. (2014).

Crane-Okada et al. (2012) used dance and movement therapy to observe the effects on QoL with older women with breast cancer (mean 65.6 years). After 12 weeks the intervention group when compared to the control group (no exercise) did not significantly differ in the QoL domains of physical, psychological, social or spiritual well-being as hypothesized, but fear of recurrence decreased and this appeared to be retained six weeks after the intervention was completed. The relatively small sample size (n=49), limits the generalizability of the results.

In a resistance only intervention, Winters-Stone et al. (2011) randomised 106 BCS (mean 62 years) to a resistance + impact only programme and compared these results to a stretching only group. They found that the resistance + impact group preserved bone mineral density (BMD) at the lumbar spine compared to the control and increases in lean mass were greatest in women on aromatase inhibitors (AIs) compared to controls not on this therapy. This study would have benefitted from having a usual care control group rather than a control group involved in a stretching only intervention, but the authors felt it would be unethical to assign women to a non-exercise control group. Retention was 62% which was much lower than other interventions included in this

review although the length of the intervention (12-months) was much longer than that reported by Crane-Okada et al. (2012).

Tunay et al. (2012) evaluated the effects of a physiotherapy programme including exercise with elderly BCS (>65 years) on shoulder function, pain and lymphoedema. Participants reported significant decreases in pain and increases in function, range of movement (ROM), muscle strength and decreases in lymphoedema volume. This was a single group study design so the findings could not be compared against a usual care control group. The data from this study could be used to estimate an effect size for an RCT to further evaluate and test the effectiveness of the intervention. As this intervention was a multidimensional physiotherapy programme involving complex decongestive physiotherapy (CDP), manual therapy and exercise it could not be determined to what extent each component had an effect on the overall outcomes, thus limiting the generalizability of the results.

Benton et al. (2014) evaluated the effect of age on quality of life in BCS after an eight week, twice a week resistance training programme. To examine the effects of age, they split the participants into two groups based on age. One group was 40-59 years and the second group was 60-80 years old. Overall adherence to the training programme was 98% for both groups, with no adverse events reported, demonstrating that older women with breast cancer will attend a supervised exercise programme with adherence rates similar to younger women, with no injuries or exacerbation of treatment-related effects noted between the older women and the younger women. Limitations to the study were the relatively small sample size (n=20) and the non-randomisation of participants.

4.5.3. Strengths and limitations of this review

This rapid evidence review used a comprehensive and systematic approach to identify and evaluate the evidence relating to exercise intervention with older women with breast cancer, which was transparent and easily replicable. Limitations to the review were the search term dates from 2003-2018 and further limitations were added to the searches, such as English language only and the age groups targeted. Additionally, the review was limited because of the lack of a full research team to conduct the search and appraise the literature; however, an experienced researcher (SB) was involved in the checking of articles to be included in the final selection. The absence of multiple reviewers in every stage of the methods may have added a degree of selection and reporting bias to the process; however, this is allowed in rapid review methodology (Grant & Booth, 2009; Khangura et al., 2012). The search found only a small number of RCTs that specifically aimed to target and recruit older adults. All these studies were found to be of variable and poor methodological quality. This was due to variable study designs, which tested different exercise modes of varying durations and a lack of uniformity in outcome measures. This variability is probably not so surprising given the lack of consensus or guidelines on optimal exercise prescription for this unique patient population, but these results make it premature to reach conclusions about the benefits of exercise for older breast cancer survivors or to evaluate which physical activity programmes are most effective. Despite these limitations, the evidence from this review suggests some benefits of exercise interventions in older BCS and the types of interventions that may be most acceptable.

4.6 Conclusion

Exercise could be considered effective in improving physical functioning and in reducing the declines in functioning associated with increasing age and cancer diagnosis. Studies have demonstrated improvements in QoL, increased muscle size, strength and power, along with preserved BMD and increases in lean muscle. Small sample sizes resulted in limited study power but they could be used to estimate effect sizes for much larger RCTs. Home-based interventions had much better attrition rates (mean 11.25%) compared with supervised programmes (mean 25.8%), although all physical activity interventions reported in this review appeared to be reproducible and feasible. Benton et al. (2014) reported adherence to the exercise intervention of 98% for an 8-week, twice weekly resistance training programme and, whereas Crane-Okada et al. (2012) reported an attrition rate of only 21%, all suggesting that older BCS appear motivated and willing to attend structured and supervised physical activity and exercise programmes on a regular basis. Further progress must be made to improve the quality of intervention trials targeting older cancer survivors, focusing on adequate randomisation, concealment of allocation and better reporting of withdrawals, drop-outs and adherence rates to the trials.

It could be considered that the poor or non-existent reporting of adverse events in most of the PA studies with older cancer survivors limits any conclusions about the relative safety of exercise with this patient population. Further, the small sample sizes do not provide sufficient power to detect differences in rates of adverse events, in particular, with the supervised exercise interventions.

A further limitation of these studies is with the timing of the exercise intervention in the cancer survivorship pathway. No trials have targeted older cancer patients during adjuvant therapy or immediately post treatment. The most recent older breast cancer survivors were recruited three years after diagnosis (Damush et al., 2006; Boyle et al., 2016), whilst Payne et al. (2008) and Tunay et al. (2012) did not report time since diagnosis. All other PA intervention trials that reported time since diagnosis were many years after a cancer diagnosis (mean 7 years post diagnosis). This limits any generalizability of findings to recently diagnosed older BCS.

To conclude this rapid evidence review, the adoption and maintenance of physical activity is a challenge for healthy adults and is likely to be even more difficult after a cancer diagnosis. With continually improving survival rates, the psychological and physiological well-being of cancer survivors is important from a public health standpoint (Irwin, 2009). However, long term adherence to exercise by older BCS is limited and the benefits they may gain from exercising during or recently after a diagnosis of breast cancer is still unknown for this older population of breast cancer survivors.

4.6.1. Gaps in the research evidence

What remains unclear from the research evidence to date is:

a) Can older women recently diagnosed with breast cancer be recruited into an exercise intervention trial?

b) Will older women recently diagnosed with breast cancer adhere to an exercise intervention trial at this time?

c) What benefits can women aged over 60 years recently diagnosed with breast cancer gain from participating in a supervised exercise programme?

d) Can older women with breast cancer derive the same benefits from exercise compared to the evidence on younger women with breast cancer?

e) Are older women with breast cancer more vulnerable to injury?

These gaps in the evidence will be addressed with this study by investigating the feasibility and acceptability of a supervised exercise intervention by specifically targeting recently diagnosed older breast cancer patients (aged over 60 years) during and post adjuvant treatment. The effects of the exercise intervention on functional capacity, QoL, body composition changes and long-term adherence to exercise will also be examined.

Aim of investigation:

To determine the feasibility and acceptability of a 12-week supervised aerobic and resistance training programme on women over the age of 60 who have recently been diagnosed with breast cancer.

Objectives:

➤ To assess the feasibility and acceptability of the trial and intervention (attrition and adherence);

➤ To assess the feasibility of recruitment of older women with breast cancer during and immediately after adjuvant therapy;

➤ To assess and monitor and changes in functional capacity before and after the exercise intervention (12-minute walk);

- To assess and monitor any changes in quality of life (QoL) outcomes before and after the exercise intervention;

- To estimate and monitor any changes in body composition between the exercise group and control during and after the trial;

- To assess and monitor and changes in PA levels before and after the exercise intervention;

- To record and report any adverse events to the exercise programme (injury, lymphoedema).

Chapter 5. Design, methodology and theoretical framework

5.1 Introduction

This chapter will outline the justification, application and critical evaluation of the researcher's epistemological and ontological position that informs the methodology, methods of enquiry and the research process in relation to this study. The Medical Research Council framework for the design, conduct and evaluation of complex health interventions was selected to be followed to ensure that the study followed a recognised and rigorous process (Craig et al., 2008). Following such a framework is in recognition of the challenges of understanding and promoting health behaviours (physical activity) in an under-researched population (older women with breast cancer) and that a pragmatic, step-wise approach was required.

The researcher's ontological and epistemological viewpoint is one of pragmatism. Pragmatism often avoids the contentious issues of "truth" and "reality" and from a philosophical viewpoint strives towards solving "practical" problems without strict adherence to only one paradigm, which can often impede progress in resolving these problems and finding solutions (Webb, 2007). Pragmatism offers an opportunity to mix research approaches to offer the best opportunities for answering the important research questions. It focuses on knowledge as the constantly changing and revising of experience and as such research design should include quantitative, qualitative and mixed methods depending on what method is considered be the most effective way of producing knowledge from the data generated or available (Biesta, 2010). By utilising the MRC framework that includes both quantitative and qualitative approaches, it is

considered the most appropriate way to develop a complex healthcare intervention with an under-researched population.

A pragmatic pilot RCT was selected as the means to assess the feasibility and acceptability of such an exercise intervention, as this is often considered the gold standard to assess the benefits and potential harm of new medicines and health interventions (Cartwright, 2007). Pilot and feasibility work is also extremely important to evaluate the viability of an intervention or trial and the feasibility and acceptability of the trial design and procedures to be subsequently used. It may prove very expensive to run a large-scale trial and little point if the intervention is unlikely to be implemented in practice. Also, if trial procedures prove to be unacceptable to participants or unfeasible then results may not be valid, therefore leaving policy makers, clinicians or commissioners without enough evidence to decide whether to adopt a trial or intervention. The MRC recommends pilot and feasibility trials using a process of steps in the hope that methodological differences and bias are resolved in advance of any efforts to conduct a larger-scale trial (Craig et al., 2008). If the research is novel, as is the population for this study, there are often uncertainties regarding recruitment, attrition, intervention adherence and whether outcome measures will be suitable. Thus, it is critical to understand these key parameters, which if found to be appropriate can be used to inform the future design and conduct of any large-scale trials with this population or to judge whether or not a large-scale trial is appropriate or ethical to even be conducted. Although not commonly reported in pilot studies, because of the novel population inferential statistics of the outcome measures will be reported as trends in the data, although no conclusions will be drawn from these statistics because of the degree of uncertainty with the inadequately powered sample size. Highlighting and

acknowledging any potential trends within or between groups in the data will further add to the evidence base lacking in this population and provide further information as to whether a full definitive RCT with this population should be carried out.

5.2. Pragmatism as a research paradigm

The popularity of pragmatism within mixed methods research can be somewhat explained by its ability as a philosophical vehicle for addressing many of the differences and often unhelpful dualisms of the "paradigm wars" (Biesta, 2010). These dualisms include assumptions regarding the subjective or objective nature of viewpoints of reality and the differences of quantitative and qualitative methods. Proponents of mixed methods research offer the integration of quantitative and qualitative research approaches. This does not sit comfortably within one or the other "worldviews" of positivism/post-positivism and constructivism for purists; however, it focuses on the problem to be researched and the consequences of the research (Feilzer, 2010).

Johnson and Onwuegbuzie (2004) consider pragmatism as an opportunity to mix research approaches fruitfully, in ways that offer the best opportunities for answering the important research questions. Ormerod (2006) suggests that scientists or researchers should turn away from *a priori* reasons and fixed principles in the quest for absolutes and consider only the facts as they exist to the problem encountered. He does not suggest logic or rigour should be discarded but that staunchly abiding by paradigmatic boundaries blocks the opportunities to move towards a common goal and is not in the interest of furthering research and the generation of new knowledge.

Pragmatic enquiry focuses on knowledge as the constantly changing and revising of experience and as such research design should include quantitative, qualitative and mixed methods depending on what researchers consider will be the most effective way in producing knowledge from the data generated or available (Biesta, 2010).

Pragmatism, when regarded as an alternative paradigm, avoids the often contentious issues of truth and reality, accepts, philosophically, that there are many realities that are open to research and strives towards solving practical problems in the "real world" (Creswell, Plano Clark, Gutmann, & Hanson, 2003). By avoiding these methodological constraints imposed by having to choose and side with post-positivism or constructivism researchers are free and not prisoners of a particular research method or approach (Robson, 2002). Webb (2007) considers classic pragmatism as having four salient features: pragmatists not believing the viewpoint that knowledge must begin with absolute certain truth and all else should be treated with scepticism, thus, scepticism is not required in the pursuit of the truth; every belief is subject to being fallible; neither knowledge through scientific enquiry nor common sense is privileged as both may be relevant to research, considering contexts of perspectives and purposes of inquiry, and a pragmatist believes that real things exist without perceiving them but follow regular laws of nature; however, theoretical entities do not exist except those that are created and used to generate empirical predictions.

At an epistemological level, pragmatism does pose some methodological concerns, as to how a phenomenon with different layers can be observed or measured. However, by using mixed methods research it can plug these gaps by using quantitative methods to measure some points of the phenomenon and qualitative methods to assess other aspects. So, by combining traditional research methods a more complete picture of

reality can be observed (Feilzer, 2010). However, all this may still not truly integrate the different research methodologies, as Bryman (2007) suggests that lots of mixed method researchers are looking at phenomena from different perspectives to gain an enriched understanding but then when it comes to the presentation of findings are displaying the data explored alongside each other but discussing the findings separately. Bryman (2007) continues arguing that good mixed methods research needs to be able to demonstrate the dichotomy of quantitative and qualitative methods and data and not present them as independent of each other.

An often unresolved issue within mixed methods research relates to research design and a major problem is the plethora of designs in existence. (Teddlie & Tashakkori, 2003) identified 35 mixed method research designs alone. In an attempt to simplify the mixed design choices, many researchers have developed typologies (Creswell et al., 2003). Unfortunately, these typologies appear to lack consistency or are too complicated or miss out important criteria for mixed methods.

Following the Medical Research Council (MRC) guidelines for developing and evaluating complex interventions (Craig et al., 2008) and considering a typology of mixed methods research designs suggested by Leech and Onwuegbuzie (2009) this study utilised a "partially mixed sequential dominant status design". This is because the research involved conducting a study with two phases that occurred sequentially. However greater emphasis is given to the quantitative phase by considering the feasibility of recruitment and the acceptability of the exercise intervention and the repeated time-points for follow up. The qualitative phase considers the population's motives, reasons for and barriers against being active during and after treatment for breast cancer.

5.3 A framework for designing and evaluating complex interventions to improve health

5.3.1. Medical Research Council (MRC) Framework for Complex Interventions

Complex interventions are widely used by health researchers and in areas of public and social policy that have important health outcomes, such as education, transport and housing and often may be described as interventions that contain several interacting components (Campbell et al., 2000). Designing and evaluating complex interventions is often made up of a number of different components that may act both independently and interdependently (Craig et al., 2008). In 2000, the Medical Research Council (MRC) published a framework to help researchers to recognise and adopt appropriate methods when designing and evaluating complex interventions. This guidance was updated and extended in 2008 in recognition that complex interventions in health policy involving individuals in education, obesity, physical activity, smoking or housing, in practice, may not follow the cyclic or linear sequence or a traditional drug trial (Craig et al., 2008). The 2008 guidance has more emphasis on the development and implementation phases of an intervention, as well as the evaluation. However, the MRC still suggests that although some aspects of good practice are clear there is still no consensus on exactly what is best practice (Craig et al., 2008).

RCTs are regarded as the "gold standard" for establishing the effectiveness of interventions if randomisation is feasible. However, effect sizes do not provide policy makers and researchers with information on how an intervention may work in practice

or be replicated in a specific context or whether outcome measures will be reproduced (Moore, Audrey, Barker, Bond, Bonell, Hardeman, Moore, O'Cathain, et al., 2015).

According to Craig et al. (2008) although all stages of developing, piloting, evaluating, reporting and implementing a complex intervention are very important and can not only be a lengthy process, more often than not researchers place too much emphasis and focus on the main evaluation of an intervention to the detriment of adequate development and piloting work. Also, insufficient emphasis may be placed on consideration of the practical issues of the actual implementation of the intervention. Without rigorous consideration of these underlying issues, weaker interventions that are harder to evaluate and are less likely to be implemented may result.

5.3.2. Developing a complex intervention

The process of developing a complex intervention should be considered following a number of steps or phases. The first step should be to identify what is already known in the literature about similar interventions as the one proposed and the methods that have been used to conduct and evaluate them (Craig et al., 2008). Reviewing the existing evidence ensures that the intervention can be developed to a point where it can reasonably be expected to have a worthwhile effect. By carefully and methodically reviewing the existing evidence and theory, a theoretical understanding of the likely processes of change that are expected and how they can be achieved will be clearer from the outset. This underpinning knowledge gained by reviewing the existing evidence and theory should be used to identify and develop theory, ensuring that the rationale for a complex intervention, changes expected and how these may be achieved is clear

from the outset. This step in the MRC framework (Phase 0 – Pre-clinical / theory) has been considered in the literature review in Chapters 2-4.

Modelling (piloting) a complex intervention before a full-scale trial can provide important further information about both the design of the intervention and the evaluation. An exploratory trial or series of small studies (which may be a mix of both quantitative and qualitative) is useful to consider all facets of the design and allow the researcher to progressively refine methods before embarking on a full-scale trial. This often involves testing the feasibility of delivering the intervention and the acceptability to providers and patients. The exploratory trial or series of studies may help to determine fidelity (whether the intervention was delivered as intended) and dose (the quantity of the intervention implemented) (Moore, Audrey, Barker, Bond, Bonell, Hardeman, Moore, O'Cathain, et al., 2015) and may identify weaknesses that can lead to cost-saving refinements or even show that a full scale evaluation is not warranted or feasible using the existing methods (Craig et al., 2008).

During this preparatory phase, the package of care or placebo can be decided for the control group and also consideration of how this may affect other variables within the intervention (e.g. recruitment). This exploratory phase should ideally be randomised, Craig et al. (2008) suggest that randomisation should always be considered because it is the most robust method of preventing selection bias and thus, a useful measure of assessing the effectiveness of the process. The initial pilot trial can provide a sound basis for estimating recruitment required in the main trial along with piloting outcome variables so investigators can ascertain which outcome measures are relevant to the patients and disease and which are important or required by the health care systems

(Campbell et al., 2000). Phase 1 and 2 (Modelling / exploratory phases) are referred to in Chapters 6 and 7 of this thesis.

5.3.3 Is a feasibility or pilot study necessary?

Current MRC framework guidance strongly recommends a feasibility and piloting phase after an intervention has been developed (Craig et al., 2008). The National Institute for Health Research (NIHR) defines feasibility studies as: "pieces of research done before a main study in order to answer the question: Can this study be done?" They are used to estimate important parameters that are needed to design the main study. These may include some or all of the following: willingness of participants to be randomised; willingness of clinicians to recruit; number of eligible participants; designing suitable outcome measures, response rates to questionnaires; adherence and compliance rates and the time and resource implications of data collection and analysis. (Moore, Carter, Nietert, & Stewart, 2011) define "pilot studies" as:

"preparatory studies designed to test the performance characteristics and capabilities of study designs, measures, procedures, recruitment criteria and operational strategies that are under consideration for use in a subsequent, often larger study".

They suggest that successful pilot studies are crucial in providing pertinent information in preparation for a larger study. NIHR (2011) supports this definition and describe pilot studies as a smaller version of the main study used to test whether the components of the main study can all work together. It considers that the pilot study should resemble the larger study in many aspects, including assessing outcome measures and should focus on the processes of the main study such as recruitment, randomisation, the

treatment (or intervention) and the follow-up assessments to ensure that they all work together so that no component could jeopardise the main study. (Arain, Campbell, Cooper, & Lancaster, 2010) suggest that feasibility studies do not need to evaluate the outcome of interest, as they believe that should be left to the main study. They suggest that if a feasibility is a small RCT, it may not have a primary outcome and that a power calculation does not need to be undertaken as the sample size of the feasibility study should be adequate to estimate recruitment rates to inform a larger study.

Thabane et al. (2010) consider that pilot trials can be comparative randomised trials designed to provide preliminary evidence on an intervention. They suggest that they are also commonly known as "feasibility studies" with the aim to assess the safety of treatment or interventions; to assess recruitment potential; to assess the feasibility of collaboration or the co-ordination of multi-centre trials and are the best way to assess the feasibility of a large, expensive full-scale study and consider them almost an essential pre-requisite. Thabane et al. (2010) stress the importance of conducting a feasibility or pilot study with the main goal of pilot studies to assess feasibility so as to avoid possible disastrous consequences of embarking on a large study – which could potentially "drown" the whole research effort. This is supported by Leon, Davis, and Kraemer (2011) who suggest that pilot studies are a fundamental phase of the research process and should be conducted to examine the feasibility of an approach that is intended to be used in a larger-scale study. They consider that a pilot trial should be used to evaluate the feasibility of recruitment, randomisation, retention and attrition, assessment methods and the implementation of a novel intervention.

Although the value and importance in the research process for conducting pilot or feasibility trials, terms that are used interchangeably, before embarking upon a full RCT

appear quite conclusive, Shanyinde, Pickering, and Weatherall (2011) found that when randomly selecting 50 articles from 3652 that used the terms pilot or feasibility in the title only 56% (95% CI, 41%-70%) actually reported and discussed methodological issues in substantial depth, only 18% (95% CI, 9%-30%) discussed future trials and only 12% of authors were actually conducting one. They suggest that many researchers when applying for funding or for publication in journals, having trials that are inadvertently underpowered to address clinically meaningful hypotheses may claim to have conducted a pilot or feasibility study in the hope of receiving a more favourable review.

For the purpose of this study, the approach will be to conduct a pilot study following the model for complex interventions advocated by the Medical Research Council, who explicitly recommends the use of feasibility studies before embarking on a phase III clinical trial (a randomised study comparing two or more drugs or intervention strategies to assess efficacy and safety), and the iterative nature of the processes of development, feasibility and piloting, evaluation and implementation (Craig et al., 2008).

5.4 Summary

This present study follows the guidance and framework suggested by the MRC (Craig et al., 2008). By considering and reporting on the implementation of the intervention, examining the quantity and quality of what was delivered and how it was implemented in practice, allows for critical consideration of these mechanisms using both quantitative assessments in Study 1 and qualitative investigation in Study 2. This pilot study assesses the feasibility of recruitment, randomisation, retention, attrition and the assessment methods used, along with the implementation of the intervention and long-term follow

up outcomes to determine whether any short-term changes persist in Study 1. Study 2 comprises a qualitative investigation examining motives and barriers to physical activity during and after breast cancer treatment. Taking this pragmatic mixed methods approach should help to further understand the context in which the complex intervention was delivered and any factors external to the intervention which may impede or strengthen the outcomes and effects of the intervention and ultimately whether a full scale, much larger RCT is warranted.

Chapter 6: Feasibility of the intervention procedures and outcome measures of a 12-week exercise intervention for women over 60 recently diagnosed with breast cancer

6.1 Introduction

This chapter reports on Study 1 - Feasibility and acceptability of procedures for a pragmatic pilot randomised controlled trial of a 12-week exercise intervention for women over 60 years old recently diagnosed with breast cancer. The study was considered to be a feasibility study as the population (women over 60 years, < 2-years after a diagnosis of breast cancer) had not been specifically targeted to be recruited at this time of diagnosis to an exercise intervention. Therefore, feasibility and acceptability data was first required to be collected to assess the design and implementation of an intervention with this unique population at this time and whether it would be viable to progress to a larger study in future.

6.2 Methods

6.2.1 Study Design

Study 1 was designed as a pragmatic pilot RCT of a supervised exercise intervention for women aged over 60 years with early stage breast cancer. There was a longitudinal 12-month follow up of study outcomes, assessed at 3 months, 6 months and 12 months. Participants were randomly allocated to either the intervention group (Ex) or the control group (Con). Participants in the Ex group completed a supervised exercise programme

once a week at the University of Huddersfield and were asked to complete an additional 30-minute home-based exercise programme twice a week. The control group did not access the supervised exercise sessions but were to continue with their normal everyday activities, which may or may not have included exercise. As this was a pilot study assessing the feasibility of whether such an intervention was possible, recruitment rates and timescales, randomisation, adverse events, acceptability of the intervention, retention and attrition rates and adherence rates were all collected. Outcome intervention measures of functional capacity (12-minute walk), body composition (fat mass and fat free mass), Quality of Life (European Organisation for Research and Treatment of Cancer EORTC - C30 and Breast Cancer specific questionnaire - BR23) and physical activity levels (Scottish Physical Activity Questionnaire - SPAQ) were assessed at baseline, 3 months, 6 months and 12 months. The study received ethical approval from the University of Huddersfield School of Human and Health Sciences Research Ethics Panel and the NHS Research Ethics Committee (Rec Ref: 12/YH/0258; IRAS No: 57057) (See Appendix 2).

Participants

Participants were recruited from either the Huddersfield Royal Infirmary (HRI) or Calderdale Hospital between October 2012 and July 2014 and through an outpatient educational programme delivered by the national cancer charity, Breast Cancer Care, between July 2013 and July 2014.

Eligibility

Inclusion

- Female

- > 60-years old

- No upper age limit

- Recently diagnosed with Breast Cancer (< 2 years)

- During or post adjuvant treatment

- Any ethnicity

- $\geq$ 3-months post-surgery

- Primary breast cancer

- No contra-indications to partaking in an exercise programme

- No mental disabilities that would prevent them from understanding what they are agreeing to do

- Able to fully understand written and verbal English (no translator service available)

Exclusion

- < 60-years old

- Not recently diagnosed with Breast Cancer (> 2 years)

- Males

- < 3-months post-surgery

- Secondary breast cancer (metastatic cancer)

- Any contra-indications to exercise

- Any metal disabilities that would stop them from fully understanding what they were signing up to

- Language barrier to understanding verbal and written English

Recruitment

Hospital sites

A consultant medical oncologist at HRI agreed to allow the recruitment of patients from the oncology clinics at Huddersfield and Calderdale and to be a clinical supervisor for the study. Breast care nurses at the participating hospitals considered the eligibility of the patients and gave out information sheets (see Appendix 3) to those who met the eligibility criteria following post-surgical review. Patients were asked verbally for their permission to allow their contact details to be passed on to the researcher, who would contact them, after they had had an opportunity to read through the participant information sheet. If the patient agreed, the breast care nurses passed their name and contact details to the researcher. The researcher then contacted potential participants to answer any questions, after allowing more than five days for the patient to read the information sheet. The researcher contacted these potential participants via telephone to discuss the study and if they were still willing to participate, a meeting was arranged to sign informed consent forms and take part in baseline assessments. This took place at the University of Huddersfield.

Breast Cancer Care - Moving Forward course

Participants were also recruited by the researcher during a four-week outpatient educational programme called Moving Forward, designed specifically for women recently diagnosed with breast cancer. It covered topics such as the management of breast cancer, breast re-construction, relaxation, exercise, lymphoedema and healthy eating. The researcher led the exercise session talk on week 3 where all potential participants were given information sheets about the study. This session enabled direct contact with potential study participants. If agreeable, eligible participants were then contacted by telephone to ask if they were interested in participating in the research and a date and time was arranged to sign consent forms (Appendix 4) and do baseline assessments. This took place at the University of Huddersfield. Randomisation took place once consent forms were signed, any questions about the study answered and baseline assessments done.

A cancer history and general health form (ACSM, 2012) was completed by all participants. This cancer-specific exercise questionnaire validated by the American College of Sports Medicine (ACSM) was completed to ensure clarity of cancer diagnosis, treatments and any ongoing side-effects that the participant may have been experiencing, along with any other conditions that may affect participation.

Sample Size

As this study was a pilot trial and the objective was not to prove the efficacy of a treatment, a formal power calculation was not undertaken (Lancaster, Dodd, & Williamson, 2004; Thabane et al., 2010). Therefore, the sample size formulae used for main treatment assessments are not usually applicable to pilot trials (Whitehead,

Julious, Cooper, & Campbell, 2016). However, according to Whitehead et al. (2016) current methods for setting pilot trial sample sizes are based on a set of rules, which they call "flat rules of thumb" and state five different sample sizes from the literature to use for a two armed trial. Within these rules, Brown and Marshall (1995) recommend at least 30 participants (15 in each arm) or more to estimate a parameter, whereas Julious (2005) considers only 12 participants per treatment arm is enough and Teare et al. (2014) suggest 35 per treatment arm, so 70 in total. Taking these current methods into consideration it was proposed that a sample size of 40 (20 per group) would be adequate to meet the primary objectives of the study and not to primarily power the trial to test for inferences found from the intervention. Inferential statistics only were used to consider any trends in the data.

Randomisation and concealment

Once a participant had agreed to participate in the research study and a consent form had been signed, participants were randomly allocated to either the intervention group or control group by a pre-determined block sequence randomisation schedule. Randomisation was carried once at least 3-4 participants had been recruited and subsequently when another 3-4 participants had agreed and signed consent forms, and so on.

Once consent forms were signed all participants were allocated a code for identity concealment only known to the researcher. These codes were passed on to an academic member of staff at the University of Huddersfield who was not involved in the research study, who then randomly allocated participants to groups using a block sequence allocation method. The allocation to groups was kept to no more than four extra in

anyone group at any time. Given the nature of the research and intervention it was not possible to conceal the treatment allocation from the participants or to blind the researcher from the treatments as it was the researcher who carried out the assessments and exercise intervention. No stratification of the participants was performed as the group was not considered large enough or significantly heterogeneous to provide any additional sub-groups of interest.

6.2.2. Exercise Intervention

To date, no formal exercise guidelines specific to cancer survivors have been published in the UK (Campbell, Stevinson, & Crank, 2012). However, exercise guidelines for cancer survivors have recently been published by the American College of Sports Medicine (Schmitz et al., 2010), and these were followed in the design of the study intervention. These guidelines suggest that cancer survivors should follow the 2008 Physical Activity Guidelines for Americans (US Department of Health & Services, 2008), but that specific exercise programmes may have to be adapted based on an individual's health status, disease trajectory and treatment-related adverse effects (ACSM, 2010). The US Department of Health and Services (2008) guidelines for aerobic activity are a weekly accumulation of 150 minutes of moderate intensity activity or 75 minutes of vigorous activity. Recommended resistance training comprises two to three sessions per week to include exercises for major muscles, with stretching of the major muscle groups on days that exercise is performed (Haskell et al., 2007; Nelson et al., 2007).

Exercise pre-screening assessment

A Physical Activity Readiness Questionnaire (PAR-Q) was completed by all exercise intervention participants as these participants would be taking part in the supervised exercise intervention. It is very important to undertake a professionally guided screening process to provide details regarding cardiovascular risk factors and signs/symptoms of a broader range of chronic diseases and /or conditions that require further information or explanation before engaging in an exercise programme (American College of Sports Medicine, 2013).

During the administration of the PAR-Q the participants may disclose a number of other co-morbidities such as a diagnosis of high blood pressure and/or high cholesterol and Type II diabetes (under control by medication) as an example. It was the role of the researcher (as the cancer exercise specialist) to consider these additional factors which may affect the patient's response or ability to participate in the exercise prescription (Woolf-May & Bird, 2006).

The supervised exercise intervention

The programme structure and content were based on guidelines developed by Palmer-McLean et al. (2009), Schmitz et al. (2010) American College of Sports Medicine (2013) and to ensure that the programme was evidence-based. Exercise intensity was set at 60-75% HRR and/or RPE 3-4. Participants in the exercise group took part in a 12-week supervised exercise programme, one session per week. Each session lasted approximately one hour and components of the sessions are summarised in Table 5.

Table 5: Pilot supervised exercise programme (RPE 3-4 or 60-75% HRR)

Warm-up (15 min)	5 min – walking on treadmill
	5 min – rowing or cycling
	5 min – mobility exercises/dynamic stretching
	Shoulder circles/shrugs, marching on the spot, squats, lunges, heel taps, side-ways and backwards stepping and calf raises
Exercise circuit (10 stations) 1.25 min-1.5 min per station x 2 circuits	1. Sit to stand
	2. Wall press Ups
	3. Step ups with knee lift
	4. Upper-body resistance exercises
	5. High knees/calf raises/side steps
	6. Lateral step ups
	7. Walking on treadmill
	8. Upper-body resistance exercises
	9. Step backs/lunges
	10. Step ups
	See figure 5.1 for circuit set up.
Resistance exercises (with dumbells) 1 x 10 repetitions At the end of the session	Shoulder press
	Squats
	Lateral raises
	Lunges
	Forward raises
	Calf raises
	Pectoral-flys
Floor work (core stability) At the end of the session	Drawing in
	Cycling the bike
	Back raises
	Supermans
Cool down (5-10 min) Mobility & static stretches	Walking on the spot, heel and toe taps, shoulder circles, head and neck mobility
	Static stretches (held for 20 secs)
	Upper-back, chest, inner thigh, hamstrings and calves

The exercises were adapted or amended depending on each participant's current levels of fitness, co-morbidities or joint/mobility issues.
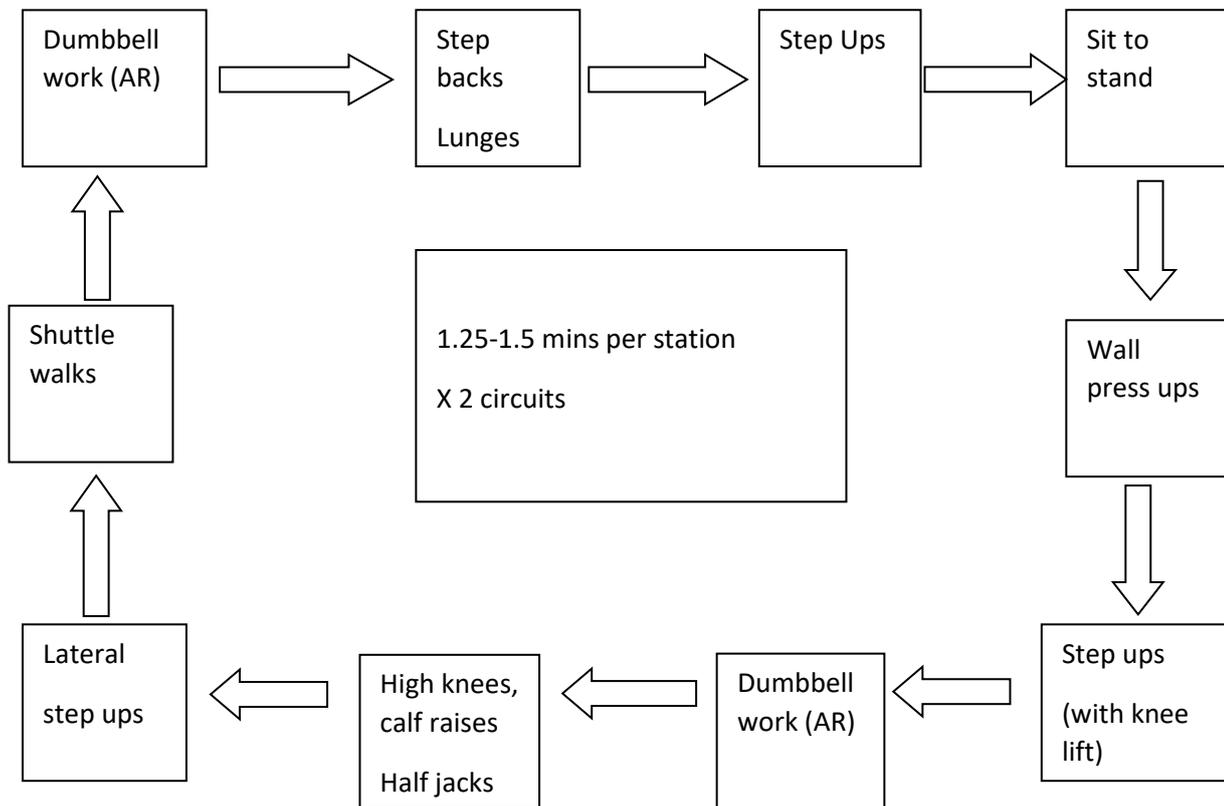
Figure 3: Circuit (RPE 3-4 or 60-75% Heart Rate Reserve)

Home-based exercise intervention

Participants were asked to follow a 30 min x 2-week home-based programme, which consisted of 15-20 minutes walking and the following circuit (10 min):

Table 6: Home-based exercise programme (RPE 3-4)

Warm up (10-15 min)	Walking/cycling/pulse raising movements
Circuit (10-min) 5 x stations 1 min per station 2 x circuit	1. Wall press-ups 2. Sit to stand 3. Step-ups 4. High knees 5. Calf raises
Cool down (5-min) Stretches x 2	Slow walking Static stretches (held for 20-sec each) Upper back, chest, inner thigh, hamstrings and calves

Home-based exercise prescription was based on the guidelines developed by Palmer-McLean et al. (2009), Schmitz et al. (2010), American College of Sport Medicine (2013). The exercises were all based on exercises from the supervised intervention so that the participants would be familiar with them and had been taught the correct technique for each exercise. From consulting with the population age range prior to the development of the intervention, it was considered that 20-30 minutes twice per week would be a manageable amount to do. Accelerometers would have been a very useful tool to measure objectively home-based physical activity compliance and also monitor additional PA levels from both the intervention and control groups. However, the University of Huddersfield did not have access to accelerometers so it was not possible to access this equipment. If they had been available, it would have helped greatly with the monitoring of home-based compliance and of objectively monitoring PA levels.

Table 7: Exercise prescription guidelines for cancer patients (adapted from (American College of Sports Medicine, 2013; Palmer-McLean et al., 2009).

Mode	Intensity/Frequency Duration	Progression	Goals	Special considerations
Aerobic Walking Stationary bike	60-75% HRR Should be able to talk during exercise 3-5/week Flexible to accommodate any scheduled cancer treatments 30-40 mins	30secs – 2mins/day	Increase peak VO_2 total work endurance	Patients unstable on their feet may benefit from a recumbent or stationary bike Begin intensity at 50% HRR and progress as long as RPE is 11-13 or 3-4 If needed divide exercise into two or three sessions per day and begin at 5-10mins
Resistance Machines Circuit Training	60-75% of one-repetition max or RPE 3-4 performed in an aerobic or circuit fashion 1-2 times/week 1 set of 12-15 reps		Increase muscle strength and endurance	Use machines instead of free weight to prevent injury from loss of control of the weights. No valsalva/breath holding No repeated overhead exercises
Flexibility Stretching Yoga	Before & after exercise 5-10 mins		Increase flexibility and range of motion (ROM)	

The content of the supervised exercise programme was based on the above guidelines ensuring that it complies with the most up to date evidence base of appropriate and suitable activities.

Monitoring exercise intensity (intervention participants only)

Exercise intensity was prescribed using HRR. The target HRR was 60-75%, which is equivalent to 3-4 RPE (see table 5 & 6). The participants' exercising heart rates were worked out using Heart Rate Reserve (HRR) a.k.a. the Karvonen formulae: 220 – age = max heart rate (MHR); MHR – resting heart rate = HRR; HRR x training intensity% + resting HR. Training intensities for the participants were selected based upon the guidelines of: Palmer-McLean et al. (2009); Schmitz et al. (2010), American College of Sports Medicine (2013) Ehrman, Gordon, Visich, and Keteyian (2018)

The Hosand heart rate monitoring system was used to monitor heart rate with the first two participants in the exercise intervention. This required participants to place a heart rate monitor strap across the sternum, just below the bra-line, fastened and held in place by an adjustable elastic strap. These monitors would transmit the participants' heart rates to a laptop computer in the room. The exercise instructor could monitor the participants' heart rates and the exercise intensity they were working at by observing the laptop screen.;

Ratings of perceived exertion (RPE) was selected in addition to heart rate monitoring. This was developed by Borg (1973). The RPE category ratio scale (0-10) was used for ease of understanding (Borg, 1998). Participants were asked to rate how hard they were working at varying times during each exercise circuit. Exercise intensity could then be adjusted depending on the number they indicated on the scale. Participants' exercise intensity was also monitored after each circuit using this scale, twice in total per exercise session. Participants were asked to record the level that they felt they had exercised during the circuit. Observations of participants' exercise levels and intensities were also closely monitored throughout the exercise sessions by the instructor using other

methods to ascertain exercise intensity level including observing breathing rates, sweating, redness and by utilising the talk test. This ensued that the participants were working at the correct and suitable intensity levels and utilising the RPE scale correctly and safely. Intervention acceptability was also measured using RPE as a surrogate marker considering common issues that needed to be evaluated in feasibility studies (Shanyinde et al., 2011).

6.2.3. Outcomes

Recruitment

Staff recruiting from the hospital recorded the number of patients they approached who met the inclusion criteria and those who declined to take part in the study. The reasons for declining were also recorded. The recruitment time-frame was noted to consider the length of time to recruit the numbers who participated. This was done at all sites.

Participant characteristics

Sample characteristics (age, stature, weight, ethnicity, marital status, employment status, stage of cancer, time since diagnosis, time post adjuvant therapy and surgery type, and treatment) were recorded at baseline to allow for comparisons with other breast cancer populations and other older adult groups (see table 8).

Acceptability of the exercise intervention intensity (experimental group only)

This was considered using the Ratings of Perceived Exertion Scale (RPE), which allows participants to subjectively rate on a scale 0-10 how strenuous they found the exercise during the exercise intervention. This subjective score was recorded twice per exercise session per participant.

Field notes of comments that were recorded verbatim from participants in the exercise intervention group were collected during the exercise programme sessions to consider the appropriateness and acceptability of the intervention and to further inform future exercise interventions with this population. Whilst they are not to be considered in-

depth qualitative evidence, they offer insight into the thoughts and feelings of the participants participating in the exercise programme at the time. Study 2 provides a more in-depth examination of the qualitative experiences of this population and examines barriers to and motivators for exercise and physical activity.

Adherence to the intervention (experimental group only)

Intervention adherence was defined as the total number of sessions available to each participant to attend compared to the actual number of sessions each participant attended. It was calculated by the sum of the total number of participants and the total number of sessions attended and compared to the total possible attendances. To monitor home-based activity and any additional activity outside of the structured exercise sessions participants were also asked to fill in a daily PA diary whilst taking part in the 12-weeks of structured activity.

Adverse Events

Adverse events were considered as anything that may jeopardise the health of a participant either temporarily or long-term as a direct consequence of the intervention.

Retention Rate

Retention rates were defined as the number of participants who remained in the trial at three different time-points: 3 months, 6 months and 12 months.

Trial Completion Rate

This was defined as the number of participants who completed all 12-months of the trial.

Intervention completion rate

This was defined as the number of participants who completed the 12-week exercise intervention.

Implementation fidelity

Implementation fidelity was defined using five elements: adherence to the intervention; exposure or dose; quality of delivery; participant responsiveness; and programme differentiation (Dusenbury, Brannigan, Falco, & Hansen, 2003; Mihalic, 2004). Adherence is defined as whether the intervention is actually being delivered as it was designed to be (Mihalic, 2004). Dosage refers to how much of the intervention is received by participants in terms of frequency and duration as described by the intervention protocol. Quality of delivery is defined as the manner in which the member of staff delivers the intervention. Is this in accordance with design intervention protocols or ensuring correct techniques are used or a consistent approach used for all participants? Participant responsiveness is measured by the participant's response to or engagement by the intervention and may include judgements by participants about the outcomes and relevance of the intervention. Programme differentiation is concerned with trying to determine which elements are essential for the success of the intervention and which outcomes are not required.

6.2.4. Intervention outcomes

To measure and assess the effectiveness of the intervention, outcome measures of functional capacity (12-minute walk), body composition, quality of life and physical activity levels were collected from all participants (intervention and control) at four time points of the study: baseline (week 1), between weeks 12 and 16 (3 months), during weeks 26 and 30 (6 months), and during weeks 50 to 52 (12 months). The range of time-points was due to the availability of participants at the nearest time to the follow-up time-periods.

Functional capacity – 12-minute walk

Participants were asked to walk at what they considered their comfortable walking speed. Timing was initiated once the participant indicated they were ready and began walking. The walking course was set out around a clinical laboratory at the University of Huddersfield in a rectangular pattern. Distance was measured using a linear trundle wheel with distances marked on the floor by plastic cones. Participants were advised that they could rest, by sitting or standing, at any point during the assessment. The researcher recorded the number of complete laps of the walking course the participant had managed and any additional distance. The total distance was then calculated and recorded.

Body composition - Air Plesythmography (BOD POD^{TM}).

Air Plesythmography (BOD POD^{TM}) measures the volume of air a person's body displaces while sitting inside a comfortable chamber. The Bod Pod system (Life Measurement, Inc,

Concord, CA) included the BOD POD plethysmograph, electronic weighing scales, calibration weights and cylinder, computer and software. This technology is fundamentally the same as Hydrostatic Weighing (under water weighing) but rather than using water it measures the displacement of air. The BOD POD first assesses the participant's mass and volume. From these measurements whole-body density is determined. Using these data, body fat and fat free mass are calculated. The BOD POD utilises the principles of whole body densitometry to estimate the amount of fat and lean tissue in the body. Whole body densitometry is based on the determination of body density by measuring body mass and body volume. Body mass is measured on the BOD POD electronic scale (outside of the chamber) and body volume is measured whilst sitting inside the BOD POD. Once body density is ascertained, the participant's percentage amount of fat and fat free mass are automatically calculated using these principles. Prior to completing the test all participants were advised not to eat or drink for at least two hours before testing and not to engage in any exercise. Participants were also asked to visit the bathroom (if necessary) before testing. All participants wore swimsuits for the test and were asked to remove any jewellery or spectacles. A swim cap was provided and the participant was instructed to ensure all hair was inside the swimming cap and any excess air was pushed out. After body mass had been assessed using the BOD POD electronic scale (wearing swimwear only) participants were asked to sit in the BOD POD chamber and remain very still, breathe normally and avoid talking during the test to ensure as accurate a result as possible. This lasted approximately 3-4 minutes depending on whether the machine took two or three measurements to ascertain body composition.

Quality of Life

The European Organisation for Research and Treatment of Cancer (EORTC) QLQ-C30 (See Appendix 7) has become the most widely used questionnaire for patients in clinical trials in Europe for cancer patients and is extensively used in America and around the world (Fayers, 2001). EORTC QLQ-C30 consists of 30 questions including five functional scales (physical, role, emotional, cognitive and social) and nine symptoms scales (fatigue, nausea and vomiting, pain, dyspnoea, insomnia, appetite loss, constipation, diarrhoea and financial difficulties) with one global health scale (GHS). The BR23 module (See Appendix 7) comprises 23 questions specifically designed for quantifying QoL for breast cancer. This includes five functional scales (body image, sexual functioning, sexual enjoyment, future perspective) and four symptoms scales (breast symptoms, arm symptoms, therapy side effects and upset by hair loss) (Saleha et al., 2010). After gathering the data from the participants, the raw score for each subscale was calculated in accordance with the EORTC Scoring Manual and transferred to 0-100 scales. Higher scores of any subscales were considered a higher level of functioning and QoL. Symptom scales were the opposite; higher scores indicated a higher level of the symptoms (symptoms were worse) and thus, indicated a poorer QoL (Fayers, 2001).

Physical Activity levels - Scottish Physical Activity Questionnaire (SPAQ)

All participants were asked to complete the Scottish Physical Activity Questionnaire (SPAQ) (Lowther, Mutrie, Loughlan, & McFarlane, 1999) for monitoring physical activity levels before and during the programme and to record any physical activity that was undertaken outside of the structured intervention (See Appendix 8). This questionnaire takes a 1 week snapshot of physical activity levels. Everyone completed this at baseline,

3, 6 and 12 months. Accurate measurement of PA in ways that reflect the multi-dimensional nature of people's lives and that validate their choices for activities is difficult. In particular, to accurately do this by physical activity questionnaires (PAQs) remain a challenge (Ainsworth et al., 2000). Although the majority of PAQs in use appear to have acceptable reliability, validity can only be considered moderate at best. However, despite more frequent use of objective assessments methods to measure physical activity, PAQs still provide a very practical method to use. More objective methods of measuring physical activity levels, such as accelerometers, were not available for use.

6.2.5 Data Analysis

Demographic characteristics of all participants were presented using descriptive statistics (means, standard deviations and range of scores). All data were tested for normal distribution using a Shapiro-Wilks test of normality. To analyse differences between the control group and intervention group, normally distributed data were analysed using independent samples t-tests and data found to not be normally distributed were assessed using Mann Whitney U. The QoL scores were assessed utilising the EORTC QLQ-C-30 and BR23 scoring system which is composed of both multi-item scales and single-item measures. These include a functional scale, and a symptom scale (both of which are specific to these study outcomes), a global health status / QoL score. Repeated measures ANOVAs were calculated and these results reported as trends in the data.

6.3. Results

Recruitment

Eighty-four women were approached during the time period October 2012 and July 2014 (22 months) who met the inclusion criteria, resulting in thirty-five agreeing to take part in the study (35/84, 41.6%). Figure 4 shows the flow of participants through the trial. Of the 35 women who agreed to take part in the study 19 were assigned to the control group and 16 to the intervention group through a block randomisation process. The majority of those who did not want to take part in the study reported travelling distance to the University as the main reason (n=16, 19%) or not interested (n=8, 9.5%). A number of other reasons were cited such as: caring duties (n=2) or holidays (n=2). A total of 12 (14%) could not be contacted after expressing interest in the study. All other reasons for not participating are reported in Figure 4. The time period for recruitment lasted a total of 22 months and was stopped because of PhD time-frames for completion. This meant the target of 40 participants (20 in each group) was not met. Recruitment was initially undertaken by Breast Care nurses at the hospital but with very limited numbers through this channel (over the 22 months, 33 were identified as eligible, 19 were interested, and 11 recruited, representing a 33% recruitment rate) Breast Cancer Care was approached and recruitment by the researcher began in July 2013 and lasted until July 2014 (over 12 months, 51 were identified as eligible, of whom 24 recruited, representing a 47% recruitment rate).
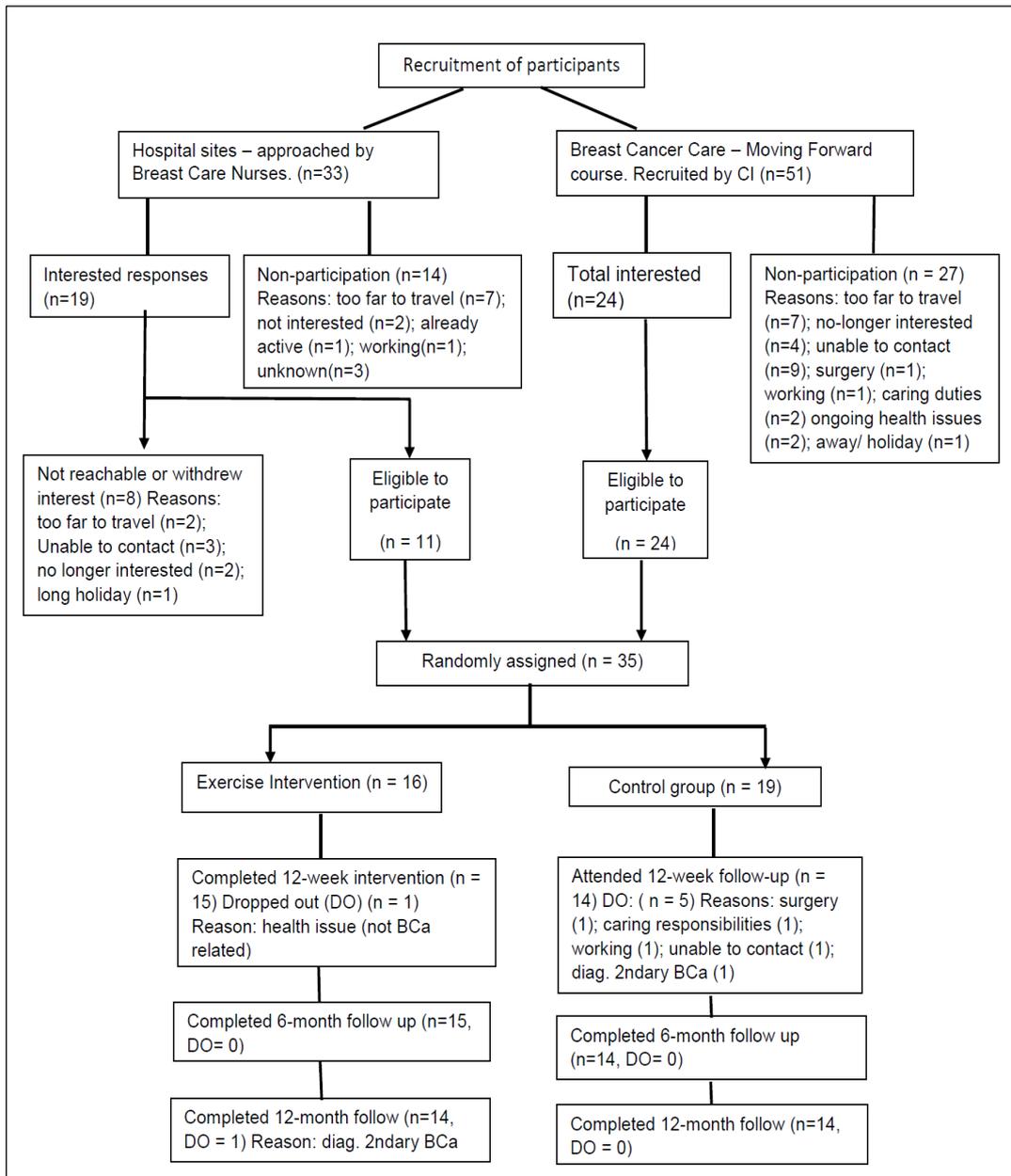
Figure 4: Flow chart of participant recruitment

Participant characteristics

Table 5: Study 1 Participant characteristics

Characteristic	All participants (n=35)	Treatment (n=16)	Control (n=19)
Age, (years)	67.14 $\pm$5.02	67.00 $\pm$3.50	67.26 (6.11)
Stature, (m)	1.62 (0.06)	1.61 0.08	1.63 0.05
Mass, (kg)	73.74 18.05	71.54 17.02	75.59 19.14
Body mass index kg/m^2	28.03 6.35	27.44 5.91	28.54 6.82
Race/ethnicity			
White (British)	White	White	White
Marital Status			
Single/ widowed / divorced	13	5	8
Married or co-habiting	22	11	11
Employment status			
Employed	3	0	3
Retired	32	16	16
Stage of cancer			
0	2	0	2
1	11	3	8
2	5	1	4
3	5	4	1
4	0	0	0
Don't know	6	4	2
Undetermined	1	0	1
Did not answer	5	4	1
Time since cancer diagnosis (months)	8.34 4.50	8.5 4.24	8.21 4.83
Months post-adjuvant Treatment (months)	5.17 4.59	4.75 4.01	5.33 5.11
Surgery Type			
Lumpectomy	19	6	13
Local wide excision	5	4	1
Mastectomy	8	3	5
Did not answer	3	2	1
Chemotherapy	1	1	0
Radiotherapy	26	13	13
Hormonal Therapy	27	13	14
Biological Therapy	1	1	0

Comparison of experimental and control group characteristics at baseline

Descriptive statistics of the data set at baseline are shown in Tables 11 and 12. All data were assessed to see if they were normally distributed. To check to see if the data were normally distributed a Shapiro-Wilks test of normality was used as the data set was less than 40 participants. Stature, % body fat, % fat free mass and PA levels were deemed to be normally distributed. Age, body mass, body mass index (BMI) and distance walked in 12 minutes were assessed as being not normally distributed.

Table 9: Baseline demographics of the study sample

Characteristic	Intervention (n=14)	Control (n=14)
Mean (SD) Age, years	66.36 (2.37)	67.00 (6.37)
Age range	62-71	60-81
Mean (SD) Stature (m)	161.5 (8.86)	162.5 (4.54)
Mean (SD) Mass (kg)	72.23 (18.16)	74.27 (18.87)
Mean (SD) Body mass index (kg/m^2)	27.69 (6.43)	28.09 (6.74)
Mean (SD) fat mass (%)	40.07(6.80)	39.46 (11.44)
Mean (SD) fat free mass (%)	59.93 (6.80)	60.27 (11.49)
Mean (SD) distance walked in 12 mins (m)	760.80 (105.20)	800.32 (124.26)
Mean (SD) PA levels (mins/week)	447.93(234.14)	545.36 (304.44)

Differences between control and intervention groups at baseline

To establish whether there were differences between the control group and intervention group at baseline (see Table 12), normally distributed data were analysed using independent samples t-test and non-parametric data (not normally distributed) was assessed using Mann Whitney U.

For stature, % body fat, % fat free mass and PA levels, there was found to be no statistically significant differences between groups at baseline, suggesting that both groups were well matched.

No significant differences ($p > 0.05$) were noted at baseline between groups for age, body mass, body mass index (BMI), 12 minute walk, stature, % body fat, % fat free mass and PA levels, suggesting that both groups were evenly matched and that any results from the study would not be due to any such differences.

Comparison between participants who dropped out and participants completing the trial

For all data that were normally distributed, to examine the differences between those participants who dropped out and those who completed the study (Table 12), independent samples t-tests were used. No difference between the groups for age ($p = 0.705$), % body fat ($p = 0.136$), % fat free mass ($p = 0.567$) and PA levels ($p = 0.056$) were found, which demonstrated the groups were evenly matched for these measures at baseline.

For data that were not normally distributed, a non-parametric test, Mann-Whitney U was used to examine whether there were any significant differences at baseline

between the participants who dropped out and all the participants who completed the 12-month trial.

There was a statistically significant difference between those who dropped out (Mean rank = 11.07) and those who completed all time points (Mean rank = 19.73) for the 12-minute walk distance. Mann-Whitney U-values was found to be statistically significant U = 49.500, (Z =2.000), p = 0.045, and the difference between the groups was moderate (r = .34), which may suggest that those who dropped out were of a lower level of fitness compared to those who did not drop out and those who went on to complete the full study.

Table 10: Baseline demographics of participants who dropped out during the study and those who completed all time-points

Characteristics	Dropped Out (n=7)	Completed (12-months) (n=28)
Age, years	68.71 (6.18)	66.68 (4.73)
Age Range	60-77	60-81
Stature (m)	1.61 (0.05)	1.62 (6.92)
Body mass (kg)	75.85 (18.88)	73.25 (18.20)
Body mass index (kg/m^2)	29.25 (6.22)	27.89 (6.47)
Fat mass (%)	45.96 (7.28)	39.92 (9.14)
Fat free mass (%)	54.04 (7.28)	60.09 (9.17)
Walk distance 12-mins (m)	619.25 (204.16)	782.13 (114.48)
PA levels (mins/week)	245.5 (82.61)	496.64 (271.07)

Note: Data are presented in mean and (standard deviation)

Acceptability of the intensity of the supervised intervention

Using the Hosand heart rate monitoring system was very time consuming (getting the heart rate monitors on, waiting for a signal), and beset with technological issues (heart rate signals "dropping out" and randomly spiking or not working). Therefore, using ratings of perceived exertion was selected as the sole method of monitoring exercise intensity.

RPE data were collected twice per participant per exercise session to consider how hard or easy they were finding the exercise intensity. Using the Borg category ratio scale (0-10) participants rated the exercise intensity of the sessions between 2 = very light and hard = 5

Table 11: Supervised intervention acceptability - Ratings of Perceived Exertion (RPE)

Week	N	RPE	SD
1	14	3.19	0.83
2	13	3.07	0.70
3	12	3.40	0.57
4	13	3.34	0.65
5	13	3.75	0.55
6	14	3.63	0.73
7	14	3.31	0.75
8	11	3.36	0.66
9	12	3.04	0.57
10	14	3.11	0.45
11	13	3.12	0.65
12	14	3.31	0.66

Note: Data are presented as mean and standard deviation

Narrative feedback and comments (participants' verbatim comments during the exercise intervention)

A number of comments and feedback recorded from the participants who took part in the exercise intervention have also been included to further consider the feasibility and acceptability of the exercise programme. Participant quotes have been integrated within this results chapter to provide further data in relation to the outcomes measured and the intervention itself. These have been integrated under common themes of group cohesion, improved functioning, improved arm functioning, less pain and feeling better. In-depth interviews of participants from both control and intervention groups, along with women from the study population are considered in detail in the next chapter.

Group cohesiveness

As discussed, participants provided comments about the usefulness of group exercise classes. These focused upon group cohesiveness as demonstrated in the excerpts below:

"You do more with others with you. I like the fact others are here". (Part 18 – week 1)

"Like the group environment – makes you focused and motivates you". (Part 14 – week 9)

"Sometimes it is getting here…but once here really enjoy it". (Part 14 – week 4)

"Found it hard coming to some sessions but knew that afterwards I would feel better and I did. I'd tell the new ladies…a lovely way of doing keep fit in moderation". (Part 14 week 12)

"Really working well. I'm enjoying it". (Part 29 week 2).

Feeling fitter and improved functioning

Participants in the study commented upon improved functioning and feeling fitter as can be seen in the excerpts below:

"I'm walking much faster. I feel much better. (Part 29 week 3).

"I can do more –I don't get out of breath as much". (Part 12 – week 5)

"Felt the exercises have really helped my legs. I find going up the stairs easier...think they are stronger". (Part 14 – week 5)

"I find I have more energy...more energetic". (Part 13 – week 6)

"I have found the exercise beneficial but I don't exactly know why but feel better". (Part 6 – week 11)

These excerpts show that exercise was found to be helpful at different stages in the programme.

Feeling better

Participants in the intervention group commented that:

"I don't know how you can't feel the benefits. It's really good... (Part 24 week 3)

"I feel like I'm getting back to myself". (Part 24 week 4)

"I'll feel better tomorrow...the exercise makes me feel better after. I went to the Maze at York and was walking lots and climbing with the grandchildren. My husband said you wouldn't have been doing that a few weeks ago. It is confidence...it gives you more confidence. (Part 32 week 6).

Improvements in arm and shoulder function

"Starting to feel the benefit of the exercises…paying off now. I found cleaning the bath so much easier…normally I struggle with the shoulders…reaching around". (Part 1 – week 11)

"This arm is much better from doing the home exercises…I don't know if you can remember but I couldn't straighten it above my head…now look! (Part 5 – week 4)

"What I find is that on a Thursday after the exercise class when I wake up my shoulders and arms feel much better and looser. On the other days they are stiff when I wake". (Part 6 – Week 3)

"Shoulder and arm functions is so much better. Really noticed dancing at a wedding how much better it was. Going to do more of a circuit in the gym and do some weights. Found it enjoyable and interesting". (Part 8 – week 11)

"Definitely feel without a doubt better for it. Now do more walking. Do my arm exercises all the time…really feel better, more loose". (Part 7 – week 11)

Less pain

"Getting a lot of joint pain before but think the exercises may have eased it…Definitely, joint pain is less (Part 13 – week 3)

"I really find the exercise beneficial for my back. I'm not in as much pain or it doesn't flare up as much (Part 14 week 10)

"I think the exercises has helped my Lymphoedema. It doesn't feel as lumpy or hard under my breast". (Part 1- week 4)

"I think the same…it is not as hard under my breast". (Part 3 – week 4)

"I wasn't aching so was really surprised! Really enjoyed it. (Part 7 – week 2)

Adherence to the supervised intervention (experimental group only)

Attendance at every supervised exercise session was recorded. Attendance was an average of 87.5% for all participants. Intervention adherence was calculated by summing the total possible number of attendances and the actual number of recorded attendances. The maximum number of supervised exercise classes available to all participants was 192 (16 participants x 12 weeks). Thus, the actual attendance was a total of 168 sessions = 87.5% attendances. Attendance rates were higher once the participant who dropped out during the intervention was excluded (161/180 = 89.4% attendance). Five participants completed all 12 sessions (31% = 100% attendance), five completed 11/12 sessions (31% = 92% attendance), one completed 10/12 sessions (6.25% = 83% attendance) and four completed 9/12 sessions (25% = 75% attendance). 10/15 who completed the 12-week intervention had an average attendance of 95.8%. Of the 15 participants who completed the 12-week intervention, 15/16 (93.75%) had an attendance of 90.5%. Mean attendance rate was 10.3 visits per 12. The reasons for non-attendance were: holidays; child-minding; family commitments; personal or family illness.

Adherence to the home-based intervention (experimental group only)

The monitoring of home-based PA and compliance to the home-based sessions was problematic. The compliance rate was very poor for the first seven participants with only

one fully completing the diary. The participants reported struggling to remember to fill it in at the time (daily) and found that they were repeating the same activities when filling it in at a later date. For this reason, the use of a daily PA diary was not continued and the SPAQ was used to record PA levels over a one-week period at all four time points with compliance at 100% for this. In hindsight, another method of monitoring the home-based programme should have been implemented, such as a simple yes or no for whether they had done the sessions or not. If available for use, PA monitors (accelerometers) would have been a very accurate measure of actual PA levels during this time-period. Although probably not appropriate to use for the full 12 weeks it may have provided useful data as to assess actual levels of physical activity versus perceived PA levels.

Adverse events

No adverse events were reported during or after the 12 week intervention by the exercise group or by any participants whilst doing the outcome assessments at any time-points.

Retention rate

Attrition in the control group (n=19) overall was 26% for the whole trial. Five participants dropped out during the trial and reasons for drop out included: re-diagnosis; too busy; poor health and full-time caring responsibilities; a knee replacement operation and severe arthritis and back pain. Control group drop-out to the trial was twice that of the intervention group. This resulted in an attrition rate of 20% overall for the study when

both groups were combined. The intervention group (n=16), with only one drop-out during the intervention (6.25%) and one before the 12-month assessments (6.25%) had an overall attrition rate of 12.5% for the whole study. At the 3-month stage 6/35 participants had dropped out (17.1%). At 6 months no more participants had dropped out only and a further one dropped out in the last few weeks at 12 months with a diagnosis of secondary breast cancer.

Table 12: Retention rate at each stage of the trial

Participants	Exercise group	Control Group	Total
Baseline	16	19	35
3-months	15 (1)	14 (5)	29
6-months	15 (0)	14 (0)	29
12-months	14 (1)	14 (0)	28

Trial completion rate

Overall seven participants dropped out of the trial over the 12 months with the majority (6/7; 85.7%) dropping out within the first 12 weeks. The trial completion rate was 28/35 (80%). However, more dropped out from the control group (5/19; 26%) compared to the intervention group (2/16; 12.5%).

Intervention completion rate

In the intervention group, 16 participants started the exercise intervention and 15 completed the 12-week exercise intervention (93.75%). One participant dropped out for health reasons during the exercise sessions (not related to the intervention) and one

participant dropped out just before the 12-month follow-up assessments due to a diagnosis of secondary breast cancer (although she completed the 12-week exercise intervention 11/12). As stated above compliance to the home-based sessions was not monitored, thus, an accurate account of the full intervention compliance is not available.

Implementation fidelity

Considering the five elements according to Dusenbury et al. (2003) the supervised exercise intervention was delivered according to protocol (see Table 5 & 6); however, the home-based programme was not monitored, therefore this element did not meet the protocol (see 6.4.3) so a true figure of overall intervention adherence is not available. Exposure or dose of the supervised intervention received by the participants, considering the frequency and duration according to the protocol was a total of 168 sessions = 87.5% attendances. Of the 15 participants who completed the 12-week intervention, 15/16 (93.75%) had an attendance of 90.5%. Mean attendance rate was 10.3 visits per 12. Again, because home-based sessions were not monitored an accurate account of the frequency and duration of home based activity and overall intervention adherence cannot be given (supervised and home-based combined). The quality of delivery was not independently or objectively assessed, therefore, this element of treatment fidelity cannot be assessed, however, the instructor was an experienced (20-years+) exercise instructor working with older adults with a range of health conditions and trained and qualified as a level 4 cancer and exercise specialist. In hindsight it would have been useful and appropriate to have an independent person monitor and observe a selection of sessions to verify the quality of delivery and of the exercise sessions being delivered as per the protocol. Participants appeared to respond well to the supervised

intervention with high adherence rates but found it difficult to monitor and adhere to the home-based intervention, resulting in this not being monitored. Comments and thoughts about the intervention were reported at the time using field notes (see 6.4.2). Programme differentiation was difficult to determine but recruitment via alternative channels than the hospital proved essential. The monitoring of adherence to the home-based programme is also important to give an accurate picture of adherence to the whole programme to consider the feasibility of additional unsupervised sessions. This would be important for any future trials.

6.3.1 Intervention outcomes

Comparison of body mass and body composition changes over 12 months between experimental and control groups

Table 6: Body mass and body composition changes over 12 months

Baseline:	Treatment (n=14)	Control (n=14)
Baseline		
Body mass (kg)	72.23 18.16	74.27 18.87
% body fat	40.07 6.80	39.76 (n=13) 11.44
% Fat free mass	59.93 6.80	60.27 11.49
3 months		
Body mass (kg)	71.47 17.82	74.45 (n=13) 18.69
% body fat	38.56 7.72	40.49 12.14
% fat free mass	61.44 7.72	59.52 12.16
6 months		
Body mass (kg)	71.11 17.44	74.42 (n=13) 18.61
% body fat	40.42 7.19	40.72 12.84
% fat free mass	59.58 7.19	59.31 12.85
12 months		
Body mass (kg)	70.63 18.24	74.22 (n=13) 17.57
% body fat	40.26 7.83	41.51 11.22
% fat free mass	59.74 7.83	58.49 11.22

Note: Data are presented as mean and (standard deviations)

This Table demonstrates that body mass decreased consistently for the experimental group over the four time periods; however, the control group's body mass did not change over the 12 month period. Body fat decreased for the experimental group during the 12 week intervention but then increased back to baseline levels by 12 months. However, in the control group, body fat increased consistently over the 12-month study. Fat free mass increased during the 12-week intervention for the experimental group but then returned to baseline levels by 12 months; however, the control group steadily lost fat free mass over the 12 months.

Comparison of distance walked in 12 minutes between the experimental and control groups over 12 months

Table 7: Comparison of changes in distance walked between groups over 12 months

Time	Treatment (n=14)	Control (n=14)
Baseline 12 min walk (m)	763.93 (105.20)	800.32 (124.26)
3 month 12 min walk	873.60 (112.63)	873.19 (150.04)
6 month 12 min walk	896.45 (120.66)	876.25 (135.03)
12 month 12 min walk	946.50 (116.65)	906.55 (138.63)

Note: Data are presented as mean and (standard deviations)

There was a significant increase in walk distance in 12 minutes by both groups ($p < 0.001$), although there was not a significant difference between groups in walk distance. However, the experimental group increased the distance they walked more than the control group (182.57m vs 106.23m – see Table 14).

Comparison of self-reported physical activity levels over 12 months between experimental and control groups

Table 8: Comparison of PA levels between groups over 12-months

Time	Treatment (n=14)	Control (n=14)
Baseline SPAQ (mins)	447.93 ± 234.14	545.36 ± 304.44
3-month SPAQ	575.86 206.20	579.14 319.52
6-month SPAQ	636.93 300.26	730.00 485.47
12-month SPAQ	574.86 199.86	501.79 291.79

Note: Data are presented as mean and (standard deviations)

Although there was no statistically significant change in PA levels between the groups, both groups significantly increased PA levels during the 12 months (p=0.040). As can be seen in table 15 both groups increased their PA levels up to 6-months but then both groups reduced PA levels between 6-12-months. However, the experimental group still maintained higher PA levels than at baseline, whereas the control group had reduced PA levels to below those at baseline.

Comparison of EORTC–C30 and BR-23 QOL variables between experimental and control groups over 12 months

Table 9: Quality of life changes over 12 months

Quality of Life Outcome	Group (n=14)	Baseline	12 months	Trend
Emotional functioning	Treatment	79.17 (17.53)	79.17 (17.53)	intervention
	Control	92.26 (12.43)	88.69 (14.47)	
Future perspective	Treatment	54.76 (16.57)	73.80 (23.31)	intervention
	Control	66.67 (32.03)	69.05 (33.24)	
Breast symptoms	Treatment	19.64 (11.61)	12.50 (9.67)	intervention
	Control	8.33 (9.81)	3.57 (4.28)	
Arm symptoms	Treatment	21.43 (17.14)	13.49 (17.53)	intervention
	Control	9.52 (8.56)	4.76 (8.40)	
Global health status /QoL	Treatment	66.67 (19.06)	72.02 (16.21)	intervention
	Control	78.57 (19.26)	77.98 (18.08)	
Physical functioning	Treatment	90.48 (11.31)	92.38 (10.41)	intervention
	Control	90.48 (11.31)	90.00 (9.70)	
Role functioning	Treatment	88.10 (20.07)	94.05 (12.42)	intervention
	Control	92.86 (10.77)	92.86 (12.60)	
Cognitive functioning	Treatment	83.33 (13.07)	85.71 (18.32)	intervention
	Control	91.67 (10.84)	92.86 (10.77)	
Social functioning	Treatment	90.48 (20.37)	97.62 (8.91)	intervention
	Control	94.05 (12.42)	95.23 (12.10)	
Pain	Treatment	16.67 (20.67)	14.29 (29.13)	intervention
	Control	14.29 (17.12)	14.29 (15.82)	
Body image	Treatment	80.95 (25.41)	84.52 (20.64)	intervention
	Control	87.50 (19.81)	89.88 (16.72)	
Systematic therapy SE	Treatment	13.61 (9.12)	11.90 (6.67)	intervention
	Control	10.54 (12.13)	12.93 (12.17)	
Fatigue	Treatment	18.25 (16.08)	17.46 (14.27)	control
	Control	15.08 (16.08)	11.90 (11.08)	
Dyspneoa	Treatment	14.29 (21.54)	14.29 (21.54)	control
	Control	14.29 (21.54)	9.52 (15.63)	
Insomnia	Treatment	23.81 (30.46)	30.95 (33.24)	control
	Control	23.81 (30.46)	28.57 (22.10)	

Note: Data presented as Mean and (standard deviation)

All scores have been converted into a score range of 1-100. For the functioning scales, a high score (nearer 100) indicated a high level of functioning. For the symptom scales, a low symptom score indicated fewer symptoms / problems. Emotional functioning, future perspective, breast symptoms and arm symptoms reached statistical significance for the experimental group. Trends have been used to demonstrate which scores favoured which group. As can been see from table 16, other than fatigue, dysneoa and insomnia, all trends were in favour of the experimental group.

6.4 Discussion

The primary purpose of this pragmatic pilot RCT was to examine the feasibility and acceptability of an exercise intervention for older women (> 60-years old) who have recently been diagnosed with breast cancer. The collection of this feasibility and acceptability data was to help address gaps in the evidence with this population and improve trial procedures to allow clinicians and researchers to replicate trial procedures or build on these research findings, so as to inform the design and conduct of any future large-scale trials with this population. Additional intervention outcomes of functional capacity, body composition, physical activity levels and quality of life outcomes were also assessed to consider what benefits may result from this intervention.

6.4.1 Recruitment

Recruitment was much more difficult and time-consuming than anticipated using only health care professionals. Breast care nurses recruited only 11/35 participants over a 22 month period revealing a feasibility issue that would need to be addressed if a future

larger trial is to be considered. Recruitment was considerably improved by the researcher approaching participants through a cancer charity, Breast Cancer Care, that had enrolled onto a 4-week educational programme "Moving Forward". This programme is not available throughout the country, so such a method of recruitment should be considered cautiously as a potential alternative or adjunct to using health care professionals; however, for this current pilot trial it was a successful method of recruitment (24/35 participants).

Recruitment difficulties appear to be a common problem in this research field (Campbell, Mutrie, White, McGuire, & Kearney, 2005a; Demark-Wahnefried et al., 2008; Demark-Wahnefried et al., 2006; Payne & Hendrix, 2010). In a pilot study of group exercise during breast cancer treatment, Campbell, Whyte, and Mutrie (2005b) highlighted some potential reasons for "recruitment not being as successful as predicted". These included a lack of time from nurses and nurses not viewing recruitment to the study a priority. Recruitment was also influenced by the nurses' "perception" of whether they considered the cancer patient to be "fit enough" to exercise. These may have been similar issues experienced in the present study; however, breast care nurses were not interviewed to ascertain if they experienced any issues or barriers to recruitment. This information would be useful for any future trials.

The above recruitment challenges suggest that the setting for the recruitment of participants and who actually does the recruitment are very important factors for consideration in future studies and the traditional method of recruiting via the healthcare professional may not always be the most effective method. Therefore, alternative methods of recruitment should be considered. Poor recruitment for physical activity interventions increases the chance of the trial being abandoned, with potential

important clinical effects of that trial either not being shared or reported (Oliver & Mossialos, 2004).

Although recruitment to the study was challenging, 41.6% of patients approached for this study agreed to take part. The biggest reason cited by the breast care nurses for potential participants not wanting to be involved in the study was that the University (where the intervention and outcome assessments took place) was too far away. It is not known whether this was a travel issue due to a lack of transport or a time issue to commit to the travelling. The delivery of the exercise intervention and the data collection of outcome assessments at only one site, which was a considerable distance from one of the hospitals involved in recruitment appeared to have hindered recruitment targets and took longer than anticipated. Understanding reasons for non-participation is therefore important because this information can be used to improve consent rates in future studies, and in turn, minimise one of the treats to precision of a trial (Hubbard et al., 2016). The ability for data to be collected and the exercise intervention to be delivered at multiple sites, making it more accessible and convenient, should be considered to improve recruitment in future studies.

Although the current study had a number of recruitment challenges, recruitment was high when compared to a number of other breast cancer and exercise research studies (Mutrie et al. (2007)= 18.2%; Daley et al., 2007 = 28.6%; Winter-Stone et al., 2011 = 29.5%; Courneya et al., 2007 = 33%). It appears that length of time since diagnosis may be an important factor in recruitment success. Crane-Okada et al. (2012) recruited 49 participants with a very favourable recruitment rate of 46.6%. However, the mean time since breast cancer diagnosis was approximately 10 years. LaStayo, Marcus, Dibble, Smith, and Beck (2011) recruited older cancer patients (but not breast cancer only) with

a mean age of 74 years to participate in a three times a week resistance programme. Those recruited were on average of 8.4 years post cancer diagnosis. Winters-Stone et al. (2011) recruited 102 older women with breast cancer with a mean age of 62 years. Recruitment rate was 29.5% with a mean time since diagnosis of 60.5 months, although they reported that all participants had to be at least 1 year-post treatment before commencing the study, thus, excluding potential participants who were during or immediately post-treatment. The reason for ensuring participants were at least 1-year post-treatment was not given. This time since diagnosis appears to be an important factor in recruitment, especially if participants are still undergoing active treatment and therefore may result in lower recruitment rates.

With no exercise studies specifically targeted older women with breast cancer during or immediately post adjuvant therapy it was unknown whether older women would be willing to participate during this time-frame and according to the literature it is more difficult to recruit during this time. However, this study has demonstrated that it is possible to recruit at this time-point, although challenging; older women should be encouraged to become more active during or post-treatment for breast cancer. Many exercise studies have recruited BCS onto an exercise study with varying degrees of success; however, the mean age for recruitment for most exercise and breast cancer studies was 51.6 years (Courneya et al., 2007; Daley et al., 2007; Ligibel et al., 2008; Milne, Wallman, Gordon, & Courneya, 2008; Mutrie et al., 2007; Penttinen, Nikander, Blomqvist, Luoto, & Saarto, 2009). This is an average age of 16 years younger than participants in the present study. With so few studies that have specifically targeted older women with breast cancer, it could be suggested that age may be a barrier to recruitment onto exercise trials.

When examining the recruitment rates of exercise trials specifically targeting older women with breast cancer, Crane-Okada et al. (2012) recruited 49 participants with a very favourable recruitment rate of 46.6%, with a mean age of 65.6 years to a 12-week intervention with follow-up after six weeks with questionnaire assessment. This demonstrates that it is possible to recruit older women to an exercise study; however, LaStayo et al. (2011) reported a very low recruitment rate of only 14% and Winters-Stone et al. (2011) had a recruitment rate of 29.5%. Demark-Wahnefried et al. (2006) managed to recruit older cancer survivors (mean age = 71.7 years) to a 6-month home-based diet and exercise intervention through a mailed recruitment drive (26% of responders). However, the authors did not meet their accrual target, and this was not a supervised exercise intervention so there was less involvement from the participants. All of these studies highlight the difficulties in recruiting this population of older BCS.

6.4.2 Adherence to the intervention

Adherence to the 12-week supervised exercise intervention in the present study was high (87.5%) in comparison to other breast cancer and exercise studies (Courneya et al., 2007; Crane-Okada, Kiger, Sugerman, et al., 2012; Daley et al., 2007; Dodd et al., 2010; Winters-Stone et al., 2011). However, the reported adherence rates in the above trials were considerably lower than reported by LaStayo et al. (2011) with a 95% adherence and (Courneya, Bell, Jones, Field, & Fairey, 2003) with a 98% adherence. Winters-Stone et al. (2011) recruited older women with breast cancer closer in time to their cancer diagnosis, recruiting women who were at least 1-year post-treatment onto a 12-month resistance + impact programme to examine the effects of this type of exercise on bone mineral density (BMD). Adherence to the supervised sessions was 66.5%, which may

suggest that the time elapsed since their breast cancer diagnosis may affect adherence. However, home-based intervention adherence was not monitored. Participants at the start of the intervention reported difficulties in remembering to fill in the daily activity diaries and remembering to do the home-based intervention. Therefore, without any home-based intervention adherence data we cannot draw any conclusions as to the success of the intervention and overall adherence rates could be significantly different if home-based intervention adherence would have been combined in these figures. The supervised intervention appeared to be acceptable given the high adherence rates but any future study must ensure that all intervention data is collected.

It could be suggested that older women with breast cancer are more willing to participate in exercise the longer they are from the time of diagnosis. However, what is not known is whether how many older women with breast cancer have been approached to participate in an exercise intervention during or immediately post-treatment as this has not been reported in the literature and it appears mainly younger women have been recruited to exercise interventions. Older women with breast cancer who have been involved in exercise trials have been many years post-diagnosis, suggesting that the period of time when an older breast cancer patient is undergoing or has just finished active treatment may be a difficult time to recruit to an exercise study, especially onto a supervised intervention. This view is supported by Young-McCaughan and Arzola (2007) who agree that the timing of the intervention in relation to diagnosis is important, as it is more difficult to participate in an exercise programme whilst still undergoing treatment.

In an early study, Young-McCaughan et al. (2003) found that 85% of those participants who had completed treatment completed an exercise programme, whilst only 40% of

those still in treatment completed the programme. Dodd et al. (2010) reported adherence rates of 74% to a 12-month home-based exercise intervention started during adjuvant treatment but the group that started exercising after completing all treatment had a higher adherence rate of 86%, which appears to concur with Young-McCaughan et al. (2003), in that it may be more difficult to exercise regularly during active treatment. It does appear that adherence rates are higher when participants have finished treatment. The reasons for this are often attributed to the cancer or treatment side-effects such as cancer-related fatigue, physical deconditioning, loss of range of movement or other side effect issues, such as a lack of self-confidence or self-image Courneya et al., 2008; Blaney et al., 2010; Blaney, Lowe-Strong, Rankin-Watt, Campbell & Gracey, 2013).

Thus, adherence rates of older adults (>60 years) in exercise interventions during or immediately post adjuvant treatment have not been reported in the literature before, which is not surprising given that there is a noted lack of studies that have specifically targeted this population. Another difficulty when comparing adherence levels between exercise interventions with breast cancer patients is the heterogeneity of studies. Exercise programmes ranged from eight weeks to 12 months and differed in the exercise prescription of frequency; 1 x week – 5 x week, intensity; low, moderate – using RPE, % of HR maximum or % of 1-RM loads, time; 20 minutes – 1 hour or progressive over time, and type; resistance, aerobic, stretching or combined. Studies were also a mixture of supervised or home-based exercise interventions. To add further heterogeneity to the studies, participants were recruited during treatment, post-treatment or many years after their initial cancer diagnosis, all of which may have affected adherence levels.

6.4.3. Adverse Events

No adverse events were reported during the trial from either the intervention group during the 12-week intervention or by any participants whilst participating in the outcome assessments. This is an important finding because although we are aware of the safety and efficacy of exercise during and after breast cancer treatment for younger women, it was not clear from the literature regarding this older population. The research literature on younger women with breast cancer clearly indicates that it is safe for participants to exercise during treatment(Courneya et al., 2007; Mutrie et al., 2007; Schwartz, Winters-Stone, & Gallucci, 2007), however, no studies with older women with breast cancer have recruited participants during this time period so the data from this pilot trial adds new evidence to the safety and efficacy of exercise with older women with breast cancer during or after adjuvant treatment.

6.4.4. Retention to the trial

Another trial parameter that indicates imprecision, is loss of participants to a study, which may include a combination of factors, such as, participants formally dropping out of the trial (retention) or failing to complete the outcome assessments (completion rate) or failing to provide data (missing data). Loss of participants during trial follow-up can introduce bias and reduce power, thereby affecting the generalisability, validity and reliability of results (Grimes & Schulz, 2002; Hubbard et al., 2016). Overall, the 12-month trial and 12-week exercise programme had an acceptable retention rate to the whole study (both groups combined) of 80%. This included a 12.5% drop-out from the intervention group (only one participant dropped out during the 12-week exercise

intervention and one at 12 months) and five participants dropping out from the control group (26%).

Possible explanations for this higher drop-out for the control group include: their exclusion from the intervention group and therefore being less willing to continue with the study; that the time and commitment required for the study was more than they initially imagined or that the physical assessment (12-minute walk) were more demanding than expected.

The attrition rate for this study was similar to that reported by Courneya et al. (2007) with 83.1% of participants providing data at 6-month follow up, although this follow-up data were obtained by a mailed questionnaire, thus did not require the participants to come into a centre, in person, as did the present study. At the primary end point follow-up assessment after the intervention, participant attrition was 7.9%, which is comparable to this study at the same time-point (6.5%). Mutrie et al. (2007) reported an overall attrition rate of 14% when following up at six months after a 12-week exercise intervention had taken place.

The home-based exercise groups had a better attrition rate of 17.5%, whilst the supervised exercise group had an attrition rate of 24%. A possible reason for this higher attrition by the supervised intervention group is that the intervention group was expected to attend the supervised exercise programme three times per week and also exercise at home on at least two other days per week. This is a substantial commitment and may have contributed to the higher attrition rates compared to the home-based sessions. Cadmus et al. (2009) also reported very low attrition rates of 11% for a

supervised exercise intervention lasting six months, which was started during adjuvant therapy.

(Stevinson & Fox, 2006) reported a much higher attrition rate of 25% for a 10-week intervention with participants attending a supervised exercise circuit once per week and 4 x week of home-based activity. With this study being a longitudinal study (12-months), with more time points for data collection and therefore, potentially more opportunities to drop out, the fact that attrition rates were comparable with other exercise and breast cancer studies recruiting younger participants further demonstrates the acceptability of the exercise intervention and the outcome measures selected for use in an exercise trial with older women with breast cancer.

6.4.5. Retention rates in exercise and breast cancer trials with older women

One of only a few studies that recruited older women with breast cancer to an exercise intervention, Crane-Okada et al. (2012) reported an attrition rate of 12%, and although this was a comparable 12-week intervention, follow up was only six weeks and by questionnaire. Winters-Stone et al. (2011) recruited 106 older women with breast cancer, (mean age of 62 years) and randomised them to a 12-month resistance and impact training programme or a control group of stretching only. The retention rate for the resistance and impact group at follow-up was 69.2%, and for the stretching only group 57.4% at 12 months, with a combined retention of 62%.

Although retention was lower than the present study (20% compared to 30.8%), their intervention was 12 months. Thus, considerable commitment and motivation was required of participants to continue with such a long intervention. Considering the

retention rates of this study and when compared to other similar breast cancer and exercise trials which have recruited both younger and older women with breast cancer, all with differing lengths of interventions and follow up, it could be suggested that the length of this present trial (with four time points), and the supervised exercise intervention was both suitable and acceptable by older women with breast cancer.

6.4.6 Outcome to measure the effectiveness of the intervention

Walking distance in 12 minutes was statistically significantly improved by both groups during the 12-month study. Although both groups significantly increased their 12 minute walk distance, there was more of an improvement by the intervention group than the control group. The intervention group also managed to maintain this improvement in walking distance in 12 minutes at 12 months when compared to the control group. There was a statistically significant change over time for PA levels for both groups.

Both groups increased their PA levels during the study from baselines until 6-months but then both groups reported a reduction in PA. The intervention group reported doing more than two hours' additional physical activity at the end of the study compared to the start of the study. The control group, however, at 12-months had reduced PA levels to below that reported at baseline.

No statistically significant findings were noted for body composition at any time points and between groups. However, an interesting observation was noted in the intervention group for body composition, with an observed loss of fat mass and an increase in fat free mass during the intervention period, although these changes could not be maintained over the 12 month trial. This positive body composition trend was noted in

favour of the intervention group throughout the 12 month trial, and may have statistical or clinical significance with a larger sample size.

Quality of Life domains of emotional functioning, future perspective, breast symptoms and arm symptoms reached statistical significance for the intervention group only. Positive trends in favour of the intervention group were observed for: global health status, physical, role, cognitive and social functioning, pain, body image, side effects, breast symptoms and arm symptoms. Positive trends noted in favour of the control group were noted for fatigue, dyspnoea and insomnia.

6.4.7 Physical activity levels

There was a statistically significant change in PA levels in both groups over the 12-month intervention. Both groups increased their PA levels over the first six months of the study, but were then reduced their PA levels between six and 12 months. The intervention group reported higher levels of PA at 12-months from baseline levels compared to the control group. The control group PA levels had returned to below baseline levels at the 12-month stage. The intervention group reported doing 127 minutes more PA at 12-months than reported at baseline, whereas the control group reported a reduction of 44 minutes less physical activity at 12 months then at baseline.

The mean time of PA for both control and intervention group at baseline was very high, 545 minutes and 447 minutes respectively, which suggests those recruited to the study group were already very physically active and highly motivated. It may also suggest that both groups could have over-estimated their actual PA levels, which could be due to self-reporting bias or social desirability or the actual questionnaire used may not have

been the most appropriate. Similarly, Mutrie et al. (2007) reported high levels of physical activity by their BCS at baseline (365 minutes and 367 minutes) for the control group and intervention group respectively, these figures are well above the national guidelines for physical activity (Haskell et al., 2007). In the same study both groups significantly increased their PA levels over the study duration but the exercise group maintained higher levels of physical activity at the 6-month follow up (Mutrie et al., 2007). In the follow-up at 18 months and five years, Mutrie et al. (2012) reported that the exercise intervention group was still more active than the control group at both follow-up time points.

These findings, albeit over a longer time period than the present study, appear to support the suggestion that starting an exercise programme may have positive long-term effects, not only on increasing PA levels but on other well-known health benefits associated with being more physically active. This increase in physical activity levels by both groups could have a very important clinical meaning, as indicated by Irwin et al. (2003), who reported that PA levels were significantly reduced after a diagnosis of breast cancer and they postulated that these lower PA levels had a greater potential for increases in weight gain.

Becoming overweight and/or obese has been associated with poorer overall survival and breast cancer survival (Chan et al., 2014). Bellizzi (2005) further alludes to the aforementioned points, stating that cancer survivors are less likely to meet the CDC/ACSM recommendations of PA (150mins/week) than those without a history of cancer. These figures continue to decline with increasing age with only 24.9% of cancer survivors over 65 years meeting the recommended levels of PA. M. D. Holmes, Chen, Feskanich, Kroenke, and Colditz (2005) in their prospective observation study of 2987

nurses concluded that 3-5 hours of PA after a breast cancer diagnosis may reduce the risk of breast cancer mortality.

These findings were supported in another observational study by Holick et al. (2008) who demonstrated that women with breast cancer who had greater levels of physical activity when compared to sedentary BCS had a significantly lower risk of dying from the disease. This dose-response relationship of physical activity and breast cancer mortality has been supported by the more recent research of Li et al. (2015) and Zhong et al. (2014) in their meta-analyses. Both analyses reported an inverse relationship between PA levels and breast cancer recurrence and breast mortality.

Li et al. (2015) suggested that breast cancer patients who are physically active up to 10 metabolic equivalent task (MET)-h/week may result in a risk reduction of breast cancer recurrence or mortality by 25%. Zhong et al. (2014), however, offered a slightly lower risk reduction of approximately 18%. Li et al. (2015) continued to suggest that being active over an equivalent of 15 MET-h/week may even offer a 30% risk reduction. These very recent meta-analyses of 69,011 cancer patients (Li et al., 2015) and 42,602 breast cancer patients (Zhong et al., 2014) both support the importance of BCS becoming physically active and at the very least trying to meet the ACSM recommended physical activity guidelines (Haskell et al., 2007). Therefore, it appears important for anyone with a diagnosis of cancer to increase their physical activity levels in order to reduce these poorer outcomes.

The data from this study demonstrate that older women with breast cancer can increase their physical activity levels during or immediately after a breast cancer diagnosis. Furthermore, it could be suggested that if breast cancer survivors start a supervised

exercise programme they may maintain higher PA levels than women who do not start a supervised programme, even if they do not continue with the supervised sessions after the intervention period. This interesting finding indicates that there is a need for further research in this area, as it would appear that by attending an exercising programme in the short term it may lead to longer lasting increases in PA compared to somebody who does not start a programme. This increase in PA, if maintained over time, could have important clinical meaning in terms of reducing breast cancer recurrence and breast cancer mortality.

6.4.8. Functional capacity (12-minute walk)

Both the intervention and control group significantly increased their 12 minute walk distance over the duration of the study. Although there were no statistically significant differences in walk distance between the groups, the intervention group increased their distance from 763.93 metres to 946.50 metres, a total increase of 182.57 metres, an improvement in walk distance of 23% over the 12-months. The control group managed an increase of 106.18 metres from 800.32 metres to 906.55 metres, an improvement of 13% over the 12 months. Thus, the intervention group had an improved walk distance of 58% compared to the control group, which may suggest that the exercise intervention did have some degree of benefit and success in improving functional capacity when compared to the control group.

Mutrie et al. (2007) reported very similar findings, both their intervention and control group improved their 12 minute walk distance over the duration of the study, with the intervention group having a more pronounced improvement, mirroring the findings of

this study. Their control group increased walk distance by 38 metres over six months, whereas, their intervention group increased by 130 metres. This was a 29% increase in walking distance compared to the control group. A possible explanation for this increase in 12-minute walk distance by both groups could be due to self-selection bias and the non-statistical differences between control and intervention group may be due, in part, to the small number of participants in this study and therefore further supports the need for a larger trial with greater numbers which may lead to significant findings.

With so many reported functional limitations with which BCS may have to deal as a consequence of cancer treatment and the association of increased fitness with improvements in mortality and morbidity, the importance of maintaining and improving cardiovascular fitness would appear to be essential. Sweeney et al. (2006) reported that women who were cancer survivors of less than two years reported more functional limitations than before diagnosis. Long-term cancer survivors when compared to non-cancer adults were much more likely to report that they were unable to perform heavy household duties (42% versus 31%), unable to walk half a mile (26% versus 19%) and unable to walk up or downstairs (9% versus 6%). Ness, Wall, Oakes, Robison, and Gurney (2006) study concurs with these findings, further demonstrating the functional limitations that cancer survivors experience. They reported that cancer survivors were 1.5-1.8 times (53% versus 21%) more likely to have physical performance restrictions and participation limitations than those with no history of cancer.

Thus, improving walking capacity after a diagnosis of breast cancer could have many important health implications for older women and may support older women with breast cancer to live a disease-free and functionally unlimited existence. The improved fitness of the participants in this study may also have a positive impact on the ability of

older adults to perform activities of daily living, such as walking up and downstairs, general household tasks, cleaning, preparing meals and shopping.

6.4.9. Body composition changes

Body composition was improved by the intervention group during the 12 weeks of the supervised exercise intervention, but this was not a statistically significant improvement. Also, the reduction in percentage body fat and increase in fat free mass was not maintained over the 12 months by the intervention group. However, the improvements observed in body composition during the 12 week intervention period appeared to have an important effect on the actual amount of body composition change over the subsequent nine months of the trial for the intervention group.

The interventions group's body composition was the same at 12 months as it was at baseline. This was in contrast to the control group whose percent body fat increased and fat free mass decreased consistently at all time-points over the 12month study period. If this trend of increasing fat gain and muscle loss continued for the participants in the control group, this could lead to sarcopenic obesity – increased fat and a subsequent loss of muscle and bone tissue - or other health conditions associated with increased weight. Again, despite non-statistical significance, this trend could have an important clinical meaning.

Excess or increased adiposity is linked to poorer prognosis through increases in circulating oestrogens, insulin and insulin growth factors (Sheean, Hoskins, & Stolley, 2012) and an increased risk of breast cancer recurrence and higher risk of breast cancer mortality compared to maintaining a normal weight after diagnosis (Chan et al., 2014;

Irwin et al., 2009). Garner and Erck (2008) in their small pilot study (n=11) used air plethysmography (BODPOD) to assess body composition, they also found no significant changes in percent body fat during an eight week aerobic and resistance training programme. However, a number of other studies have reported significant changes in body composition.

In a study comparing land-based exercise to water-based exercise, with a usual care control group exercising three times a week for eight weeks, Fernández-Lao et al. (2013) found that the land-based intervention group reported a statistically significant decrease in percent body fat when compared to the other groups. Burnham and Wilcox (2002) reported significant changes in body composition in their 10 week, 3 x week aerobic exercise intervention when compared to a no exercise control group, although this was a small number of participants (n=18) of both males and females. Similarly, Schmitz et al. (2005) reported significant increases in lean mass and significant decreases in percent body fat with a 12 month, twice weekly resistance training programme with recently diagnosed breast cancer survivors. If the effects of the exercise intervention on body composition could be maintained either by a more frequent intervention (3 x week), which the literature suggests, or by the continuation of the supervised sessions (longer duration), the differences between intervention group and control group in this present study may have been clinically meaningful.

It would appear that those studies with a supervised exercise intervention greater than 1x week reported significant changes on body composition. Schmitz et al. (2005) considered that if behaviour change could be maintained over time, the differences in body composition that they observed between BCS who continued to exercise and those who did not may have clinical significance. However, all the participants in the previously

mentioned articles that reported a significant improvement in body composition (n=201) had a mean age of 51 years, which may indicate that increasing age has an effect on the ability to significantly change body composition. This observation has direct implications for the participants in the present study. Therefore, we cannot ascertain from the results of this study or from the current literature what effect increasing age may have on the ability to change body composition for older BCS.

It is unknown from the literature with older breast cancer patients if an exercise programme can have significant effects on body composition or attenuate the negative side-effects of cancer treatment. However, from the present study, it was very promising and interesting to note the positive changes in body composition in the intervention group, during the 12 week intervention period. A larger trial, recruiting higher numbers of older women with breast cancer, would offer more statistically reliable results and would add more evidence to this important area of research with this under-researched population.

6.4.10. Quality of Life

The results of this study demonstrate that some QoL variables did change during and after the exercise intervention. However, only emotional functioning, future perspective, breast symptoms and arm symptoms were statistically significant in the intervention group compared to the control group (in a positive direction). No other QoL variables reached statistical significance; however, global health status/QoL, physical, role, cognitive and social functioning, pain, body image and side effects all demonstrated positive trends in favour of the exercise intervention group. Quality of Life variables of

fatigue, dyspnoea and insomnia appeared to have a positive trend in favour of the control group.

Similar to these findings, Courneya et al. (2007) offered both resistance and aerobic training with 242 breast cancer patients during chemotherapy for 17 weeks and found no significant improvements in cancer-specific QoL (assessed by the Functional Assessment of Cancer Therapy – Anaemia scale). In the UK, Mutrie et al. (2007) also conducted an aerobic and resistance training programme with two supervised and one home-based session per week for 12 weeks and followed up at six months and also did not report a significant effect of the 12 week intervention on QOL using the Functional Assessment of Cancer Therapy (FACT) questionnaire.

Courneya et al. (2003) reported a beneficial effect of exercise on QoL on postmenopausal BCS who took part in aerobic training 3 times per week for 15 weeks. Courneya et al. (2003) used the Functional Assessment of Cancer Therapy-Breast (FACT-B) to assess overall QoL. In this instance, it may suggest that increasing the frequency of the supervised sessions may lead to an improvement in QoL. However, Cadmus et al. (2009) found that exercise did not affect QoL after conducting two RCTs, one during adjuvant treatment and one post-treatment. These participants exercised five times per week at an exercise club. Three exercise sessions were supervised and two additional sessions were at the club or on their own. These findings suggest that the frequency of exercise does not affect QoL. Thus, the intensity of exercise may be a crucial factor in improving QoL.

Adamsen et al. (2009) used the EORTC-C30 to assess QoL and found significant effects on fatigue, vitality, physical functioning, role emotional, mental health, physical

component scale and mental component scale, but consistent with this study they found no improvements in global health status/QoL. This was a large exercise study recruiting 269 cancer patients (all types, mean age 47 years) onto a six week, four times a week multimodal intervention of high intensity exercise, relaxation, body awareness training and massage, totalling nine hours per week. The exercise activities consisted of high and low intensity equivalent to 43 metabolic equivalent of task (METs) hours per week. However, the applicability of this intervention is questionable. Forty-three METs is equivalent to moderate intensity walking for 14 hours per week. This appears to be a very unrealistic programme considering the challenges of encouraging cancer survivors to meet the government guidelines of 150 minutes of moderate exercise and the translation of this research into mainstream practice would be questionable (Belizzi et al., 2005).

These conflicting findings help demonstrate that it is still unknown as to what dose of PA can lead to an improvement in QoL; with no targeted research into older adults with breast cancer this is an area requiring much more research to try and establish the most effective dose relationship response for exercise to improve QoL. The present study did not significantly improve global health status/QoL, and this may be explained, in part, by a number of different reasons. The small numbers recruited into the study make findings difficult to generalise and do not have the power to ascertain if the results were not influenced by chance. This factor applies across the study and demonstrates that a much larger study is required. Nonetheless, the QoL trends found will be discussed and considered as to how they align with other research findings. The effects of the exercise intervention in this study may have been partly diluted by an insufficient amount or volume of exercise or an insufficient intensity of exercise.

Mischra et al. (2012) in a meta-analysis of 56 exercise studies during cancer treatment suggested that positive effects of exercise interventions are more pronounced with moderate or vigorous intensity versus mild intensity. In the current study, participants were guided to exercise within the category of moderate intensity (RPE 3-4), although the intensity would not have been considered vigorous. As the supervised intervention was only once per week and home-based exercise was not monitored, it could be suggested that the frequency of exercise may not have been optimal to improve QoL. However, other exercise studies of increased frequency did not elicit an optimal QoL response (Cadmus et al., 2009; Courneya et al., 2007; Mutrie et al., 2007) Another possible explanation could be that participants were simply functioning very well at baseline and thus, further improvements in QoL would be difficult to obtain. All participants reported very high functioning scores and low symptom scores when compared to reference values for the general population and cancer population (Zebrack, Yi, Petersen, & Ganz, 2008).

All participants reported high PA levels at baseline with both groups significantly exceeding the PA guidelines of 150 mins/week (Haskell et al., 2007). Both Chen et al. (2009) and Ferrer, Huedo-Medina, Johnson, Ryan, and Pescatello (2011) reported that those cancer patients reporting higher PA levels also reported higher QoL scores, suggesting a correlation between the two variables. Another reason why the group may have reported such high levels of QoL at baseline and throughout the study could have been attributed to the age of the participants in the present study. For example, Zebrack et al. (2008) stated that older cancer respondents reported better overall QoL and better mental health than younger cancer participants. With the age of the participants in this study all over 60 years old (mean = 67 years) this may have been another factor why QoL

was not affected. Zebrack et al. (2008) continued to suggest that QoL is often less interrupted for older people, possibly relating to greater life experiences in handling stressful events and better coping skills.

6.5. Study Limitations

6.5.1 Home-based intervention

One of the main study limitations was not being able to fully assess the feasibility of the intervention because home-based exercise adherence and additional PA outside of the supervised intervention was not fully monitored. Therefore, we do not know how effective the overall programme was. Therefore, the feasibility and acceptability of this part of the intervention is unknown. Although the supervised sessions of the intervention appear to have been successful on their own, it is not known whether a combined supervised and home-based intervention is effective, feasible or acceptable. In an attempt to address some of the shortcomings of not having home-based intervention data, study 2 was devised to consider barriers and motivators to exercise with this group. Additional physical activity outside of the intervention (during the 12-week supervised intervention) should also have be monitored for this reason and activity trackers or accelerometers would make an objective and accurate way of monitoring PA levels instead of daily PA diaries that participants in study 1 found to be tedious to fill in each day.

6.5.2 Selection bias

Those participating in health studies appear much more health conscious and motivated (Krishna, Maithreyi, & Surapaneni, 2010a), thereby willing to maintain, adopt and adhere to new health regimes causing a self-selection bias. There is always the possibility of selection bias within a study of this nature. The participants who volunteered to be in the study may have been of better health and may have been more physically active compared to the general older breast cancer population. Volunteers for health trials often tend to be more motivated and concerned about their health (Krishna et al., 2010a). Thus, it could be suggested that if the participants were more interested in health and motivated to be more active after their breast cancer diagnosis this may have attenuated the possible effects of the supervised exercise that the intervention group received. However, the nature of the randomisation process and assessing that both intervention and control groups were homogenous at baseline attempted to control for any potential bias in the outcomes and results. Both groups were socio-demographically homogenous and reported high levels of physical activity at baseline and therefore, may not be a representative sample of the overall population of older BCS. In future studies, alternative strategies in which to recruit under-represented populations must be considered.

6.5.3. Contamination of the control group

Contamination of the control group (Courneya et al., 2004), could also be a possibility in this research, whereby, the control group participants adopt, to some extent, the intervention and start exercising or increase their exercise levels. According to Courneya et al. (2004) contamination of the control group refers to the extent that the control

group actually adopts the exercise intervention, which can severely endanger the findings of well-constructed trials as much as poor adherence. It is possible in the present study that participants randomised to the control group may have started their own exercise programme or increased their physical activity levels in response to the study. Indeed, the majority of participants 27/35 (77%) were recruited after the researcher gave an educational talk to a breast cancer charity on the benefits of being physically active during and after treatment for breast cancer, before randomisation occurred.

This may have added to the "teachable moment" effect (Demark-Wahnefried, Aziz, Rowland, & Pinto, 2005), whereby women after breast cancer diagnosis evaluate their lifestyles and may make positives changes to increase their PA levels (Schwartz et al., 2001). Therefore, participants in both groups will have been aware of the importance of increasing physical activity levels to reduce potential breast cancer related side effects and the association with PA levels in reducing breast cancer recurrence and breast cancer mortality.

 Courneya et al. (2003) reported that 22% of mixed cancer survivors in the control group averaged at least 60 minutes of moderate-strenuous exercise over a 10 week period. Mock et al. (2001) highlighted a considerably higher number of 50% of BCS who adopted the study protocol of 90- minutes/week for three or more sessions over a six week to six month period, thus, potentially influencing the outcomes of the study. Courneya, Friedenreich, Sela, Quinney, and Rhodes (2002) also reported contamination in the control condition, with 22% of them averaging at least 60 minutes of moderate to vigorous exercise over a 10 week period.

Although maximising adherence rates is important to the success of any RCT, minimising contamination rates is equally important. It cannot be fully ascertained, in the present study, whether or not anyone in the control group who did not already exercise adopted an exercise programme or purposely started to exercise as a result of the study. However, the participants in the control group did significantly increase their physical activity levels from baseline over a six month period and significantly improved their 12 minute walk distance, which could be suggestive of a positive effect of either the educational talks on increasing exercise levels or the effect of enrolling onto an exercise study which may have attributed to this increase in physical activity.

6.5.4. Self-report questionnaires

PA levels were self-reported through the use of a questionnaire (SPAQ) and therefore can be viewed as being subjective. With both the intervention and control groups reporting such high levels of physical activity it could be considered that these reported figures were either over-estimated or the questionnaire misinterpreted. Participants sometimes reported any physical activity rather than just physical activity that was of a moderate to vigorous intensity. Self-reported PA questionnaires are frequently prone to measurement error and bias due to misreporting, by either deliberate (social desirability bias) or because of cognitive limitations due to recall or comprehension (Helmerhorst, Brage, Warren, Besson, & Ekelund, 2012). Participants have the capacity to over or underestimate true physical activity levels, which often may result in the inability to capture actual levels of physical activity.

Direct (objective) measures of physical activity are believed to offer more precise and accurate estimates of energy expenditure and remove the recall and response bias and consist of such measures as direct and indirect calorimetry (doubly labelled water), physiological markers such as measurement of cardiorespiratory fitness and motion sensors and monitors. Despite the potential advantages of using these direct methods, they also possess their own limitations of being time and cost intensive and intrusive, often require considerable researcher interaction, which can create a source of bias, require specialised training and physical proximity of the participant for data collection. In addition no single "gold standard" exists for measuring physical activity (Prince et al., 2008). Because of the limitations and feasibility of using any direct ways to measure PA levels it was considered that a self-reported PA questionnaire was an appropriate and valid method to assess PA in this population because of the practicality, convenience and low cost but it has also been demonstrated to be reliable and to hold strong validity and limited criterion validity (Lowther et al., 1999).

6.6. Study strengths

6.6.1. Trial Design

According to Altman (1996) randomised controlled designs are the best way to compare the effectiveness of different interventions, allowing valid inferences of cause and effect and have the potential to affect patient care directly through single trials with large numbers and to produce clinically meaningful outcomes. This may often be the result of combining a number of similar RCTs' findings by meta-analysis. RCTs are the most commonly used research designs in medical research. This study adopted this approach,

considering it not only an acceptable and traditional scientific method to use, but also the most appropriate way to assess the feasibility and acceptability of a trial of this nature to inform future larger intervention studies, whilst attempting to minimise the effects of bias and confounding variables, provide rigour, robustness, reliability and precision with the measurement equipment used. The study methods described are also transparent to ensure that the study could be replicated by others.

6.6.2. Age group

A strength of the study was the novel population recruited. It is the first ever study to recruit older women only (>60 years) very recently diagnosed with breast cancer onto a supervised exercise intervention and longitudinally follow them for 12 months. A small number of studies have specifically targeted older women with a supervised exercise intervention but these participants were recruited many years (mean 6.4 years) after their cancer diagnosis and treatment (Crane-Okada, Kiger, Sugerman, et al., 2012; LaStayo et al., 2011; Tunay et al., 2012; Winters-Stone et al., 2011). Although, many exercise and breast cancer trials have recruited some women in the age category selected by the present study, the mean age of breast cancer and exercise studies appears to be approximately 50 years. Thus, until now we were not aware of the acceptability and feasibility of such an intervention with older women recently diagnosed with breast cancer.

6.6.3. Novel measures

BODPOD, a novel measurement technology, was used to assess all participants' body composition using air plethysmography. This was the first study to use this measure with older women with breast cancer and to follow up participants for nine months after the intervention to assess any ongoing body composition changes. The assessment of body composition is very important in BCS as those who gain weight after breast cancer diagnosis may be at an increased risk of poorer prognosis and outcomes. Obese BCS have a 30% higher risk of breast cancer mortality, when compared to leaner women, regardless of when BMI is ascertained (Chan et al., 2014; Ligibel, 2011; Protani, Coory, & Martin, 2010). In the present study positive changes in percent fat and fat free mass were observed for the intervention group during the 12 week intervention but for the control group a worsening of body composition (increase in fat mass, decrease in fat free mass) was noted throughout the 12 months. These trends were interesting to observe. A larger sample size followed over a longer period may have resulted in a statistically significant meaning but more importantly be of clinical significance with the associations of increasing body fat and body mass with a poorer prognosis and increased breast cancer mortality (Chan et al., 2014).

6.7. Conclusion

Although aspects of the supervised intervention components went well and the outcome measures appeared to be acceptable, the success of the pilot trial can only be inferred because of the lack of home-based intervention adherence and retention data. A slight amendment to the original protocol was that heart rate data was not collected

because of issues with equipment, thus, no HRR or HR max data is available. This demonstrates the difficulties of using this method of monitoring exercise intensity. Using RPE was a more pragmatic approach. Heart rate data would have been useful to report for any future trials, although RPE data was still collected which does infer an equivalent heart rate intensity. Recruitment difficulties would need to be overcome to ensure appropriate recruitment timescales were adhered to, something that would need to be in place for a larger trial. Accordingly, "stop" and "go" procedures would need to be considered in accordance with the guidelines set down by (Eldridge et al., 2016) who suggest that criteria on which to decide whether or not to proceed to the next stage of research should be included. For future research it would be pertinent for investigators to have clear criteria on which to base decisions to carry on to the next stage of research (i.e. a larger trial) as to whether thresholds that may determine progression have not been met. This pilot study should have set some progression targets for recruitment (timescales) and also set thresholds linked to other feasibility outcomes such as retention and particularly relating to intervention adherence to the supervised and home-based exercise (Avery et al., 2016; Eldridge et al., 2016). This would have allowed for further consideration and discussion as to whether this pilot trial should proceed to a larger trial. These criteria could have been viewed as guidelines rather than strict thresholds as not meeting a target may not necessarily indicate that the trial is unfeasible but rather that an aspect of the design or protocol may need reviewing or changing (Hopewell et al., 2008). Although the strengths of a pilot RCT design are noted to collect feasibility and acceptability data to inform trial procedures for a larger RCT, this approach could not explore what is going on in a person's life and the relationships that influenced them to make some of their decisions (Broom & Willis,

2007). Therefore, utilising more of a qualitative approach to data collection would provide further data about how the selected population would feel about taking part in an exercise intervention, the potential barriers and possible motivators to becoming more active after a recent diagnosis of breast cancer. The next chapter explores the views of a selection of women over 60 years old with breast cancer; some were very recently diagnosed and still undergoing treatment; some had taken part in the feasibility trial either in the intervention group or control group and others were active exercisers. These views all add to the feasibility data collected and provide more evidence about exercise interventions with this population.

Chapter 7. A qualitative exploration of older Breast Cancer Survivors' views of the barriers and motivators to physical activity and exercise participation

7.1 Background

The rehabilitation needs of BCS have increased significantly over past decades in line with improved survival (Luoma et al., 2014). The important role regular physical activity can play in ameliorating the physical and psychological effects of the disease within this population is well documented (Brunet, Taran, Burke, & Sabiston, 2013b). Specifically, previous research has shown that regular physical activity produces improvements in fitness, strength, quality of life, fatigue, weight loss and psychological variables such as depression and anxiety (Fong et al., 2012; Schmitz & Speck, 2010). In addition, physical activity has been shown to reduce breast cancer recurrence, cancer-specific mortality and all-cause mortality (Li et al., 2015; Zhong et al., 2014). Thus, it is important that BCS initiate and maintain physical activity levels for beneficial health outcomes.

Physical activity guidelines and recommendations have been developed for cancer survivors (Schmitz et al., 2010) and BCS (J. Brunet, Sabiston, & Meterissian, 2012). These breast cancer specific guidelines suggest that women should engage in aerobic activity at least three times per week for 30 minutes, participate in strength training at least twice per week taking a whole body approach including all major muscles and do flexibility training three times per week for 50-60 minutes. Despite the known benefits of exercise, physical activity levels appear to fall significantly for many women after a

diagnosis of breast cancer and remain below the recommended levels following the cessation of treatment (Harrison, Hayes, & Newman, 2009). Other recent studies have also reported that cancer survivors are more sedentary than age-matched healthy individuals without cancer (Kim et al., 2013; Williams, Steptoe, & Wardle, 2013). Although structured exercise has emerged as an important factor in cancer survivorship (Luoma et al., 2014), physical activity advice and exercise rehabilitation programmes are not offered as part of standard clinical management following a cancer diagnosis in the UK (Lakoski, Eves, Douglas, & Jones, 2012).

To date, most of the research in this area carried out is quantitative in nature and thus, any interaction involving interviews and questioning to try and understand behaviours that cannot be controlled, measured or counted, appears to be lacking in the research literature (Midtgaard et al., 2015). Limited attention from researchers and clinicians has been given to understanding subjective experiences of older BCSs' views in taking part in an exercise programmes or their experiences and views of physical activity during and after treatment for breast cancer. Therefore, it is not yet well understood which factors are important in a BCSs' willingness to take part in physical activity and exercise and how taking part in exercise or physical activity may contribute beneficially to the enhancement of health and well-being during cancer rehabilitation (Luoma et al., 2014).

Furthermore, as stated in earlier chapters of this thesis, very few RCTs to date have specifically targeted the recruitment of older BCS and therefore, this population appears to be severely under-represented in the qualitative exercise literature as well. Qualitative research which explores the motivators for and barriers to exercise and physical activity in older women with breast cancer, may help to develop a broader and deeper understanding of physical activity participation. All of which may be important

in understanding any issues that older BCS may experience during and after treatment, to help improve the application and implementation of any structured exercise and physical activity programme targeting this population (Midtgaard et al., 2015).

7.2 Brief qualitative literature synthesis

In order to briefly review the qualitative literature on this topic a focused search was undertaken which identified six studies. A range of qualitative methods were used including individual interviews (Brunet, Taran, Burke, & Sabiston, 2013a; Bulmer, Howell, Ackerman, & Fedric, 2012) and focus groups (Crane-Okada et al., 2012; Luoma et al., 2014) with Whitehead and Lavelle (2009) utilising both interviews and focus groups as methods of data collection. Midtgaard et al. (2015) examined the qualitative literature in a meta-synthesis of 19 qualitative research studies. Studies included in this brief synthesis were conducted in a range of countries including: USA (Bulmer et al., 2012; Crane-Okada et al., 2012;), Canada (Brunet et al., 2013), the UK (Whitehead & Lavelle, 2009), Finland (Luoma et al., 2014) and Denmark (Midtgaard et al., 2015).

All of the primary studies included only BCS, whereas, Midtgaard et al's (2015) meta-synthesis included other cancer survivors. Whitehead and Lavelle, (2009) and (Crane-Okada, Kiger, Anderson, et al., 2012) were the only two studies that targeted older BCS (mean age 66.5 years). The other studies (Bulmer et al., 2012; Brunet et al., 2013; Luoma et al. 2015) reported a mean age of 54 years old of the participants. Whitehead and Lavelle, (2009) specifically targeted older BCS (mean age 66.5 years) to find out their views and preferences for physical activity and to consider their PA levels before diagnosis, during and immediately after treatment.

Crane-Okada et al. (2012) interviewed 48 older women with breast cancer (mean age 66.3 years), in focus groups to examine the women's perceptions of the effects of a Mindful Movement Programme (MMP). This programme consisted of dance and movement therapy and mindfulness. Participants attended 12 weekly 2-hour sessions. A typical session consisted of 15 minute walking/moving; 10 minute group dialog; 15 minute group circle discussion on mindfulness; 15 minute warm-up; 15 minute slow movements; 15 minute quicker and larger movements; 10 minute partner movement exercise; 5 minute verbal sharing with a partner; 10 minute active energetic moving; and 10 minute closing circle.

Bulmer et al. (2012) interviewed 45 women during and after the treatment for breast cancer to find out their experiences with exercise, particularly examining their perceptions of the benefits of taking part in an individualised programme. The individualised programme consisted of a weekly supervised aerobic exercise programme and participants were encouraged to do similar activity three times per week at home over a 12 month period. Brunet et al. (2013) interviewed nine BCS who had identified themselves as being "physically active", although no definition for this was given. Luoma et al. (2014) interviewed 25 BCS who had participated in a 12 month, once a week supervised aerobic exercise session and who were encouraged to do a further three aerobic exercise sessions at home per week although they did not report adherence to the exercise programme.

7.2.1. Barriers to physical activity with breast cancer survivors

When examining the barriers to physical activity from the identified articles, a number of common themes were reported. These themes and sub-themes were primarily related to physical, psychosocial and environmental or organisational barriers to becoming more physically active or staying active. Although the named titles of the themes and sub-themes differed in the individual studies and appeared to be different to the above-identified common barriers, on closer inspection the barrier had often been identified and included under the theme heading.

7.2.1.1 Physical barriers to physical activity

A number of physical limitations from cancer treatment were reported as factors which hindered the women in maintaining PA and consisted of mobility limitations due to the side-effects of treatment, shoulder range of movement problems, pain, strength losses, weight gain, fatigue and a lack of energy (Bulmer et al., 2012; Brunet et al., 2013; Midtgaard et al., 2015). Luoma et al. (2014) considered changes in appearance as a result of surgery as a barrier to joining an ordinary exercise group, whereas they felt that a tailored intervention for breast cancer survivors helped them to join an exercise because change in appearance was a common issue in the group. They also reported reduced fitness levels and fatigue contributed to reduced physical activity after treatment. Whitehead and Lavelle, (2009) reported that the main physical barrier to becoming more physically active or staying active was "getting older" and feeling stiff. Also, during and immediately after treatment their physical activity levels were greatly reduced due to soreness and pain after the operation, not feeling well after

chemotherapy or radiotherapy or generally just not feeling like doing anything. They also reported that a lack of muscle tissue following surgery or re-construction hindered their ability to return to physical activity.

7.2.1.2 Psychosocial barriers to physical activity

Brunet et al. (2013) identified a number of psychosocial factors that stopped or obstructed their breast cancer patients from being more active. These were: not having an exercise partner, a lack of motivation and low confidence in their ability to do the activity. Bulmer et al. (2012) concur with a lack of self-confidence to engage in activity as a barrier to starting exercising but also noted the stress of a breast cancer diagnosis ranging from mild anxiety to debilitating periods of depression. Another barrier they offered was the fear of dying and feeling fearful and vulnerable. According to Midtgaard et al. (2015) cancer survivors may not wish to only exercise with other cancer survivors although they appreciated the opportunity to exercise where their physical limitations or altered body appearance caused by the disease or treatment were accepted and sympathetically understood. Midtgaard et al. (2015) reported how the motivational aspects of exercising in a group was reported by most studies they included in their meta-synthesis and therefore would support the implementation of group-based exercise to help reduce this barrier. However, they did offer some caution, suggesting that post-intervention adherence is often modest or sub-optimal and that participants may become too dependent on the instructor or support from the health care professionals to continue with activity outside of the intervention period, thus, reducing their levels of activity when the intervention or supervised sessions finished. Whitehead

and Lavelle, (2009) cite lack of motivation by their older breast cancer women as a reason PA levels were reduced along with post-treatment depression and a number of other psychological barriers; of being self-conscious while actually exercising; fear of overexerting post-illness; fear of getting lymphoedema; fatigue and feeling low. What was interesting with this research specifically targeting only older women with breast cancer is that more barriers to physical activity were identified than the perceived benefits of physical activity.

7.2.1.3. Environment and organisational barriers to physical activity

Brunet et al. (2013) found weather to be the main environmental factor to affect outdoor activities such as walking. However, the women in Crane-Okada et al. (2012) considered the setting of the activity – outdoors or just it being in public could be distracting and off putting, along with the temperature, privacy and cleanliness of the facility - were important. Other reported barriers that could hinder physical activity compliance were the cost of exercise classes or equipment, inadequacy of facilities and the safety of the area. Organisational factors that the women felt compromised the time available to be as active as they would like included work and employment, caregiving and/or household responsibilities, a lack of time because of busy lives with family commitments and for some the side-effects from medications (Whitehead & Lavelle, 2009; Brunet et al. 2013).

7.2.2. Motivational factors for physical activity

From a motivation perspective, the studies identified a number of different factors that encouraged the starting, or maintenance, of a physical activity programme, these were included under two main themes of physical factors and psychosocial factors. The benefits of exercising in a group, particularly with other BCS and the importance of the instructor was also highlighted as a key factor in physical activity adherence and maintenance.

As an example, Midtgaard et al. (2015) reported on three main categories that they felt summarised and reflected the benefits of exercise rehabilitation according to cancer patients: emergence of continuity; preservation of health; and reclaiming the body. The findings suggested the potential for exercise to contribute to rebuilding structure in everyday life (organisational and environmental), creating a normal context (psychosocial) and re-establishing trust in their own body and physical potential (physical and psychosocial). These were important qualities recognised by participating in exercise or physical activity after a diagnosis of cancer and further add to the understanding of how meaningful exercise rehabilitation can be for a cancer patient. It highlighted that cancer survivors prioritise and benefit from exercise by considering exercising to be a "normalising" experience, an important point also supported by Luoma et al. (2014), "gaining a sense of normality", helping them to re-build or maintain their personal identify and re-gain a sense of control with their body or physical self.

7.2.2.1. Physical motivators of physical activity

A range of physical motivators to becoming or staying active were reported, which included the participants' perceptions of exercise improving their health and it helping to manage cancer symptoms and preventing further illness rehabilitation from surgery; improving confidence to go back to pre-cancer activities and the discovery of their physical capabilities. Exercise was considered by some as a way to get back in shape and return to pre-cancer energy levels; build and tone muscle and achieve a healthy body weight; for others it helped improve energy, strength, flexibility, sleep and clarity of thought were contributing factors for breast cancer survivors in maintaining PA (Bulmer et al., 2012; Brunet et al., 2013). Whitehead and Lavelle, (2009) and Luoma et al. (2014) considered increased well-being and energy levels as one of the most important motivators and benefits of exercising.

Another benefit of PA was the ability to reduce and manage weight and that being physically active had prevented them from gaining weight whilst on hormone therapy. They felt PA helped them to carry on with their normal daily activities; for some this related to fighting the ageing process and for others being fit for purpose, such as looking after the grandchildren. Crane-Okada et al's (2012) women spoke of "freedom" in the sense of the mindful movement programme giving them liberation, acceptance of their disease and current health status, permission to try new activities and movements without fear, safety of an experienced instructor and no judgement from other participants as all were in treatment or recovering from breast cancer. The theme "rediscovering" was described as how the programme allowed them to re-connect or re-capture the feelings and experiences of fun and enjoyment from past pleasures through the dance movements and music.

7.2.2.2. Psychosocial motivators of physical activity

Brunet et al. (2013) highlighted the importance for some BCS of having a positive attitude towards exercise before diagnosis that helped to motivate them to stay active and the enjoyment and fun of taking part in the activity. Social support and making friends or meeting others were central to activity maintenance. Body image and managing or improving appearance was also a strong motivator to routine exercise. Bulmer et al. (2012) reported the psychological benefits of activity as a motivator; relating to the exercise sessions as "empowering". This was considered in a number of different guises, feeling proud of having done something positive and proactive towards their health; adding structure to their lives, getting them out of the house; taking their mind off their focus on the disease; acting as a respite from anxiety, fear and depression. For some women exercise was considered essential in regaining self-confidence and moving forward after their breast cancer diagnosis with an exercise programme acting for some as a factor that might reduce their risk of the disease returning.

Luoma et al's. (2014) findings supported some of Bulmer et al's. (2013), suggesting that participating in exercise helped to gain a "sense of mastery" over their disease, gaining better psychological functioning and improved mood. Bulmer et al. (2012) also reported that socially, exercise also was positive for the women interviewed, who suggested the benefits of interactions with exercise programme staff and other women with cancer. They found the giving and receiving of social support from peers in a non-cancer environment was important. They valued the relationships with exercise trainers as a source of social support as well as providing a sense of safety and security and instilling confidence. Whitehead and Lavelle (2009) concurred with this as the social element of exercise gave their participants a reason to get out of the house and meet other people.

Crane-Okada et al. (2012) reported participants' descriptions of how they felt the movement, dance and mindfulness sessions allowed them to connect their physical bodies with their own perceptions of themselves, becoming more aware of their body and their feelings through exercise and activity. The focus group interviews resulted in four themes: freedom; rediscovering; body sense in moving; and in the moment. This final theme related to the women finding the programme as a source of stress relief and often as a way to lighten their mood, making them feel less fearful and happier by giving them the ability to slow down, concentrate on the present and focus on everyday tasks. All this helped them to worry less and decrease their fear of a breast cancer recurrence.

7.2.2.3 Group benefits and importance of the instructor

The benefits of exercising in a group environment and with an experienced, understanding and knowledgeable instructor were also highlight by the studies. Bulmer et al. (2012) described how interacting with exercise programme staff and other cancer survivors was a benefit of the exercise programme and how the giving and receiving of social support in this non-cancer environment was highly valued. They also noted how the exercise trainers were spoken of in high regard, whose expertise helped them to regain their fitness or range of movement and by having knowledge about their condition gave women the confidence that the prescribed exercise would enhance recovery.

Brunet et al. (2013) agreed with this point, suggesting in addition to these perceived barriers and motivators to activity, the women also considered the expertise and personality of the instructor as vitality important, along with the location and setting of

the exercise programme. They also considered that exercise and physical activity programmes should be offered in convenient, non-hospital settings. Whitehead and Lavelle (2009) reported that women emphasised the importance of having an instructor who understood the issues faced after a diagnosis of breast cancer and also understood the issues of being older which may bring its own health complications. They liked the idea of a tailored programme which could be suited to their needs and expressed a preference to the programme to be exclusive to their age range.

Crane-Okada et al's. (2012) participants enjoyed the benefits of a breast cancer only group, although they did report that they were grateful it was not a support group. They also expressed the importance of an instructor who had the ability to lead and create a welcoming and motivating environment. The importance of the group instructor was echoed by Luoma et al. (2014) whose participants recognised and appreciated that the instructor understood the crucial issues for recovery from breast cancer and this allowed them to feel safe in the knowledge that what was being asked of them was suitable for them.

7.2.3 Summary of the qualitative literature

It appears from the literature that a number of motivators and barriers to physical activity for BCS have been identified; however, very few studies have targeted older BCS and therefore this information is lacking. Worryingly, particularly, within these older adult studies, more barriers to being physically activity were identified than motivating factors to being active (Whitehead & Lavelle, 2009).

When considering and developing a research intervention with a population that is under-researched, such as older BCS, the Medical Research Council strongly suggests a piloting and feasibility phase first, in an attempt to establish recruitment, retention and attrition and outcomes measures, along with a qualitative assessment of the intervention, which may consider factors that influence the population's willingness to participate in a research intervention during or after treatment (Craig et al., 2008). Given the limitations to qualitative research with older women during and after breast cancer treatment, a qualitative approach is required to gain a further understanding of these potential obstructions to physical activity and motivators for older women with breast cancer to become more active and to examine any other potential issues (Brunet et al., 2013; Luoma et al., 2014). Thus, the objectives of this qualitative study were to explore the barriers to and enablers of the initiation and maintenance of physical activity during or after treatment in older women with breast cancer. The knowledge gained from this research may enable healthcare professionals, the fitness industry and researchers to extend their understanding of the barriers and motivators to exercise and physical activity for older women with breast cancer when developing interventions to increase exercise and physical activity in this population.

7.3 Methods

7.3.1. Design

This was a qualitative study design using semi-structured face-to face individual interviews, utilising the framework analysis method developed by Ritchie and Spencer (1994).

7.3.2. Participant recruitment

A purposive sampling strategy was used to recruit fifteen women aged over 60 years with breast cancer. Participants were recruited via a national breast cancer charity who had enrolled on a four-week breast cancer educational workshop or by attendance at a weekly exercise programme based at the University of Huddersfield. The exercise programme participants had all previously attended the breast cancer charity's education workshop. All participants were interviewed individually.

7.3.3. Inclusion and exclusion criteria

Participants were all women aged over 60 years who had been diagnosed with primary breast cancer stage I-III. All participants were either currently undergoing treatment or had finished initial adjuvant treatment other than ongoing hormone therapy. Women were recruited who were recently diagnosed with breast cancer (< 12-months) and also women who were already regular attenders at an exercise class who were mean 36 months since diagnosis. Women were excluded if they were not over 60 years of age and were more than 5-years post diagnosis and treatment.

7.3.4. Data collection

All interviews were recorded using a portable recording device (ALESIS Palm Track MP3).

The interviews took a semi-structured format and examined current and previous

physical activity levels, physical activity motivators and barriers to exercise after a breast

cancer diagnosis and support to be physically active. By using semi-structured interviews

and following a topic guide (Table 17) ensured the interviewed remained focused on

meeting the study objectives. The questions were open-ended to not limit the

interviewee's responses or choice of answers (J. Johnson, Gubrium, & Holstein, 2002).

Interviews were held at either a venue of the participant's choice, the University of

Huddersfield or the venue of the breast cancer charity's educational workshop. The

purpose was to provide the interviewer and interviewee a comfortable setting where

the topic could be discussed in detail without distraction. The interviewer made use of

cues and prompts to help direct the interviewee into the research topic area to enable

the gathering of in-depth or detailed data set (Creswell, 2003). At the end of the

interview participants were asked if there was anything further they would like to add

or discuss.

7.3.5. Development of the topic guide

A topic guide was developed to help inform the interview questions, from *a priori* issues

identified from Study 1 and by considering behaviour change models and frameworks

and other exercise and cancer interventions. An important issue for public health is to

try and understand why the majority of adults are insufficiently active to improve health

(Marshall & Biddle, 2001). According to (Miller, Trost, & Brown, 2002)) studying

"determinants" or correlates of physical activity is an important prerequisite for

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designing policy and effective intervention programmes. A well-recognised and popular behaviour change model, the Transtheoretical Model of Behaviour Change (TTM) postulates that people change behaviour in five stages that consider current behaviour with intention to maintain or change behaviour (DiClemente & Prochaska, 1998). Three factors are hypothesized to mediate change process. These are the individual's self-efficacy for change - one's confidence in one's ability to take steps necessary to be regularly active, the decisional balance of perceived advantages and disadvantages of changing behaviour and the strategies and techniques individuals use to modify their thought and feelings towards a behaviour (Marshall & Biddle, 2001). (Bandura & Wessels, 1997) cites self-regulatory self-efficacy – one's belief in one's ability to maintain physical activity in the face of challenges, as key to becoming a regular exerciser. He also considers environmental factors such as social support by family and friends, support from activity partners and feedback from exercise leaders as crucial to adherence to physical activity. Questions based around confidence to be active and any concerns and apprehensions about exercising were explored to consider self-efficacy. Reasons for participating in exercise and reasons for not being active were considered for the decisional balance aspect, which included side-effects of treatment and benefits of exercise and expectations of becoming physically active. Meeting public health guidelines for physical activity has been demonstrated to improve breast cancer outcomes and morbidities (Zhong et al., 2015); thus, questions were developed around activity levels, considering current physical activity levels and PA levels before diagnosis. Social support – the perceived support by others, such as family and friends - has been associated with increased physical activity (Courneya & McAuley, 1995), so a theme based on social support to be active was developed and questions relating to support

from family or friends and health care professionals were asked. More recently (Michie, Van Stralen, and West (2011) proposed a new framework to inform behaviour change interventions considering the existing literature and developing a "behaviour system" involving three essential conditions: capability, opportunity, and motivation – what they have termed COM-B. They define capability as the individual's psychological and physical capacity to engage with the activity concerned whether they have the necessary knowledge and skills to do the activity. Questions were developed around this construct which included side-effects of treatment, self-confidence to exercise, concerns and expected benefits of exercise and preferred types of exercise. Motivation is defined as all those brain processes, emotional responses and decision making; therefore, questions considered reasons, barriers and motivators to being active or not. Opportunity considers all the factors that lie outside the individual that make the behaviour successful or prompt it. Specific questions were considered about social support and the different opportunities that were offered to be active. This topic guide has been constructed from existing behaviour change frameworks in an attempt to overcome previous limitations of often only considering one behaviour change construct. It has the benefit of being derived from classifications and concepts already considered important and by considering the "behaviour change wheel" it is hoped to improve the translation of research into practice and to inform those designing interventions and planning policy (Michie et al., 2011).

Table 10: Interview topic guide

Theme: PA levels

Currently, how physical active / how much exercise do you do per week?

Active	Inactive
What do you do? How often?	Were you active before your BCa diagnosis?
Were you active before your BCa diagnosis?	What did you do? How often?
What did you do? How often? Did you do more before your diagnosis than now?	Reasons for not exercising since diagnosis?
Why did you decide to take part in an exercise programme?	Would you be willing to take part in a structured, supervised exercise session?
What did you expect may happen once you started exercising? Did it meet your expectations?	Do you have concerns about exercising? If not, why not? If so, what are these concerns?
Did you have any concerns before exercising? If so, what were these? If not, why did you think like this?	

Theme: Reasons for participating in PA	Reasons for not participating in PA
Why are you active?	Any reasons you are not active?
What are the reasons you are active / exercise regularly?	Have you any apprehensions to becoming more physically active?

Theme: side effects of BCa treatment

Have you or are you currently experiencing any side effects from your cancer treatment?
Did you have any during or after treatment?
If so, what were they?
How did they make you feel?

Theme: Benefits of exercise

Are you aware of any benefits of exercise in relation to your BCa diagnosis?
Do you consider exercise / PA an important part of your BCa treatment? How? Why?

Theme: Confidence to take part in PA / exercise

Active	Inactive
How confident did you feel in taking part in an exercise programme?	How confident would you be in going along and starting an exercise programme?

What would / may stop you from being a regular exerciser?	What would / may stop you from starting or maintaining an exercise routine?

Theme: Intervention assessments

Active (intervention participant)	**Inactive** (non-research participant)
How did you find the intervention assessments? 12-minute walk? Body Composition – BODPOD?	Would you take part in an exercise research intervention? How would you feel doing a 12- min walk assessment? How would you feel having your body composition assessed, in which you would have to wear a swimsuit in front of a female technician?

Theme: Supervised exercise

Active	**Inactive**
How do you find the supervised exercise programme? What do you like / dislike about it? Anything you can think of to improve it?	Would you prefer to exercise in a supervised programme or do your own exercise at home when you want? What are you reasons for this?
How did you find the intensity of the exercise programme? Did you feel it was suitable at the time after your diagnosis?	Would you prefer to exercise as part of a group or on your own? Reasons?
Do you prefer exercising in a group or on your own? Reasons?	

Theme: opportunities for exercise/PA

Do you feel there are enough opportunities for you to go along to exercise classes or be more physically active after a diagnosis of BCa? What stops you from going? What would encourage you to go?

Theme: Support for PA

Did you receive any support or advice to be more physically active after your BCa diagnosis?

Who was this from?

What did they advise / recommend?

Summary of topic guide themes

Reasons for participation; Reasons for apprehension to PA intervention; Benefits of physical activity; Side effects of breast cancer; Importance of PA in relation to health; Confidence in taking part in PA; Intervention assessments; Supervised exercise; Home-based exercise; Exercise intensity; Opportunities for PA; Activities of daily living; Support from family/friends; Health professional advice for PA

7.3.6. Ethical Considerations

All participants were fully briefed before they were interviewed and given participant information sheets to read before agreeing to the interviews. All participants had one week to read the information sheets and ask any further questions before the interview took place. Opportunity was given for participants to ask any further questions before consent forms were signed. All interviews were audio recorded at the time with the permission of the participants, who were informed that they were free to finish the interview when they so wished and that all recordings would be transcribed verbatim to help with remembering what was discussed and for analysis for the research. All transcriptions were made by the researcher or an experienced research administrative assistant and only the research team had access to the data. Transcribed data had any identities, venues or places removed to eliminate the possibility of identification through inference. All audio recordings were stored on a password-protected computer format for transportation, transcription and reviewing. Identities were protected using pseudonyms and information regarding the identity of the participant was stored separately and securely under password protection. Participants were informed that all data would be stored securely for a period of five years after PhD publication. Ethical approval for this part of the PhD study was granted by the University of Huddersfield Research Ethics Committee, School of Human and Health Sciences.

7.3.7. Data Analysis

All recordings were transcribed verbatim which enabled the researcher to understand and analyse each record. The data were analysed using Framework Analysis which was developed in the late 1980s by qualitative researchers working in social policy (Ritchie

& Spencer, 1994), as a pragmatic approach for real world investigations (Ward, Furber, Tierney, & Swallow, 2013). This approach identifies common themes and differences in the qualitative data, before focusing on the relationships between the different parts of the data gathered, whilst attempting to draw explanatory or descriptive conclusions from these themes (Gale, Heath, Cameron, Rashid, & Redwood, 2013). To ensure accuracy of transcriptions and to ensure familiarisation with the content of the interviews, all recordings were listened to again alongside the transcript. This process also allowed the researcher to consider any nuances within the interviews that the transcription may not have recorded (Seale, Gobo, Gubrium, & Silverman, 2004).

7.3.8. The process of carrying out Framework Analysis

Framework Analysis allowed for a structured and systematic approach to data analysis to be followed. Being flexible, systematic and rigorous, it offered a transparent audit trail of the research findings (Ward et al., 2013), and allows findings to be reviewed to understand how the final interpretation was developed (Ritchie & Spencer, 1994). There were a number of different stages that were followed, consisting of: familiarisation with interview transcripts, developing /identifying a working analytical framework, coding or indexing, charting and mapping the data into the framework matrix and interpretation / synthesis of the data.

7.3.8.1. Familiarisation

The analysis started with a familiarisation process of the data transcripts, which involved making notes of the main recurring themes and grouping these together to develop into an analytical framework. The researcher familiarised himself with all transcripts and

undertook all interviews which helped to speed up the time to become fully familiar with the data. After two interviews had been conducted, one of the researcher's supervisors listened to the interviews and provided useful guidance and direction to help improve interviewing skills. According to Srivastava and Thomson (2009) not every transcript needs to be reviewed at this stage, but the researcher felt that the sample size was small enough for all transcripts to be reviewed. This ensured that all the data from all the transcripts were reviewed and considered and nothing overlooked. This added time to the process but it was deemed extremely useful as the researcher was a novice in the use of Framework Analysis and it was thought that some of the data might be missed if not all of the data were reviewed. After nine interviews had been conducted a further meeting with supervisors was arranged. A sample of transcripts was given to the group. This allowed the researcher to learn from the more experienced supervisors. It was noted at this stage that with there being a noticeable difference between participants' length of time since diagnosis, the researcher should consider a question focused on physical activity levels during treatment and not just to consider current PA levels and PA before diagnosis. This would help to consider barriers to exercise during treatment.

7.3.8.2. Coding and Identifying / developing an analytical framework

Codes were identified utilising both a deductive and inductive approach. Utilising a deductive approach, a number of codes were identified utilising *a priori* themes, from the behaviour change literature, which helped to inform the topic guide, and from the research intervention. Others were identified in the familiarisation process and

subsequent interview analysis once the researcher was "immersed" in the transcripts. This inductive approach allowed emergent themes to be included as codes which both approaches then formed an analytical framework (Ritchie & Spencer, 1994). All transcripts were uploaded into NVivo, a computer software programme. This allowed the researcher to read each transcript line by line and apply a label or "code" that described the interpretation of the passage or something that they considered important for analysis. With this study being more deductive in nature (using *a priori* issues, specific area of interest to the intervention and the background literature) a number of these codes had been already considered and developed through the familiarisation process but it was still considered an important process not to miss out and subsequently many additional codes emerged from the data. Coding aims to classify all of the data so that they can be compared systematically with other parts of the data set (Gale et al., 2013). At this stage, one of the researcher's supervisors also independently coded two of the transcripts and these were compared and discussed with the researcher to obtain clarity of thinking, offering an alternative viewpoint and ensured that not only one perspective was taken or was to dominate. This led to an agreement of a set of codes to apply to subsequent transcripts. Table 18 shows the identification of codes using a deductive and inductive process.

Table 11: Coding Process

Deductive Approach – codes considered before interview analysis, utilising *a priori* themes / behaviour change evidence / research intervention	Inductive Approach – codes developed once "immersed" in the transcripts (emerging from the data)
Barriers to activity	Body image
Benefits of exercise	Healthy living
Confidence to exercise	Outlook of treatment & diagnosis
Consequences of treatment	Time to heal
Current amount of PA	Time to suggest PA
Exercise preferences	Group exercise benefits
Expectations of exercise	Intensity of exercise
Home based exercise / intervention	
Motivators to be active	
Opportunities to be active	
PA levels before diagnosis	
PA levels during treatment	
Research intervention / assessments	
Supervised vs unsupervised PA	
Support to be PA	
Type of activities	

7.3.8.3. Charting data into a framework matrix

Charting allowed for the identification of portions or sections of the data that corresponded to a particular theme. All the coded themes were arranged into charts that consisted of headings and sub-headings that were developed during the coding and analytical framework stage (see examples in Appendix 9). Utilising NVivo allowed for the interviews and framework headings to be combined to be generated into a spreadsheet or matrix. The data (responses from each participant) were then "charted" into the matrix by the researcher summarising the data by "code" from each transcript and placing under the relevant sub-heading in the matrix. This required an ability to reduce the volume of data, yet not miss out any important issues and to retain the "original" meaning of the interviews (Gale et al., 2013).

7.3.8.4. Interpreting the data

Mapping and interpretation of the data was the final stage and involved analysis of the key characteristics drawn up in the charts (Srivastava & Thomson, 2009), to define concepts and provide explanations for the findings. This was influenced by the original research objectives and the themes that emerged from the data. This stage highlights the transparency of Framework Analysis as each stage can be checked back to the original data (Ward et al., 2013).

7.3.9. Study rigour

Qualitative research has often been criticised for being too subjective to individual interpretation and is often considered anecdotal, with the absence of facts (Silverman,

2000). If these criticisms are to be accepted then it would appear that there is little place for qualitative research in the nursing, exercise or medical community. However, to counter these arguments and assumptions, guidelines, scientific standards, criteria and checklists have been developed to judge the quality of this qualitative research (Clissett, 2008; Guba & Lincoln, 1989; Lincoln & Guba, 1989). Applying the criteria suggested by Guba and Lincoln (1989) of: credibility, transferability, dependability and confirmability, also known as the trustworthiness criteria to this study allows for the scientific rigour to be judged. Reflexivity was an additional quality criteria suggested by Malterud (2001) and will also be discussed.

In an attempt to achieve credibility and ensure that the interviews were a true and accurate reflection, two participants were given access to their own verbatim interview transcripts and time to read the questions asked and their subsequent answers. Each participant considered her transcript to be an accurate representation of what she had said and meant. However, the further analysis of the transcripts, with codes, sub-themes and themes were not shared with the participants; thus, the extent to which the participants were happy with the final interpretation is unknown. Interpretation of these interview transcripts was done following the Framework Analysis approach developed by Ritchie and Spencer, (1994) and accordingly at the coding stage a member of the supervisory team independently coded two transcripts, with the subsequent codes compared and discussed with the researcher to ensure that no one perspective dominated or focussed on aspects peripheral to the research question (Clissett, 2008).

The transferability of the findings is somewhat limited due to the size of the population (n=15) and the nature of the older population (aged over 60-years) of BCS. Although numbers were relatively small, data saturation was reached with no new themes,

categories or explanations emerging after 15 participants. With all participants being white European, economically secure and diagnosed stage I-III breast cancer, this may further narrow down the transferability of the results; however, with very limited data from this population the reader will have to make a decision about the applicability of the findings to the population.

Dependability is very difficult to achieve in qualitative research as the interactive nature of interviews would make it impossible to replicate exactly in the future; however, detailed methods have been described as to the setting of the interviews, the interview questions and the participants.

Confirmability has been achieved by the transparency of allowing the original data and all the processes used to draw the interpretations and conclusions from the data to be viewed (Appendix 9). Although it is accepted that different researchers may deduce different assumptions and constructs from the same data (Glaser & Strauss, 1971) the process that has been followed in this study is available for review.

As a newcomer to qualitative data collection and interpretation, reflexivity rather than purely reflection played an integral role in data generation and in the subsequent interpretative analysis. Reflexivity has been defined in a variety of ways depending on the philosophical or pragmatic approach of the writer. To further understand reflexivity, the reflection to reflexivity continuum, described by (Woolgar, 1988) was particularly useful. It is important to understand the participants' experiences within the context in which they happen, thus allowing us to make sense of these experiences and ourselves, albeit bound by time and/ or place (Shaw, 2010).

As we all experience and interpret our world from a particular perspective and this perspective will always have an ingrained subjectivity, as Gadamer (1975) suggests, we have our own set of beliefs, preconceived ideas and these make up our own understanding and interpretation of events. By considering our views and feelings about the research and its relationship to us both personally and professionally we can appreciate the nature of the investigation and our relationship as a researcher and as someone experiencing the world of the participants from whom we wish to gather data.

The researcher did have to consider his own personal preconceptions before embarking on this qualitative research study and his background and experience, having worked with breast cancer patients for a number of years and having already delivered the exercise intervention for Study 1. The researcher had already worked with a number of the participants with whom he had already established an exercise instructor / researcher relationship and was very familiar with some of the participants who had been attending the exercise classes. However, the recently diagnosed women recruited via the breast cancer charity were unknown to the researcher so this may have affected their responses during the interviews and their willingness to be open.

In order to consider whether the interviews were accurate descriptions of events described and important contextual details were not missed, all interviews were recorded and transcribed verbatim. Two participants were involved in checking their transcripts to ensure accuracy and originality. These reflexive steps, participant and supervisory involvement in the coding process helped to minimise any biases or pre-conceived judgements that the researcher may have had that could have affected the data collection in a detrimental way.

7.4 Results

A total of 15 participants with breast cancer were interviewed individually for the study. Table 19 details participants' characteristics. All women were aged over 60 years, range 60 – 77 years (mean 67.3 years, SD 5.14 years). One participant was currently undergoing chemotherapy treatment, four were within 11 months of completing treatment and the others were all within five years of completing treatment (range 36-58 months). Seven participants had already been recruited onto the pilot RCT reported in Chapter 6 (2 = control group; 5 = intervention group). The other eight participants had not taken part in the previous study. All participants were white British, most were retired (87%) with one still working full time (6.5%) and one on long-term sick leave (6.5%). The duration of the interviews ranged from 13-38 minutes, with the mean length being 21 minutes. In terms of medical characteristics, all had been diagnosed with breast cancer stage I-III disease. All had undergone surgery, with the majority having radiotherapy (11/15, 73.3%). Only two underwent chemotherapy.

Table 12: Study Participant characteristics

Characteristic	All participants (n=15)
Age (years), mean, SD	67.33 years, SD +/- 5.14
Race/ethnicity	
White (British)	14
Irish	1
Education	
Did not complete high school	1
Nursery to High School	6
Attended college	1
Trade/vocational training	4
Bachelor's degree	2
Master's degree	-
Doctorate degree	1
Marital Status	
Single, never married	1
Married or domestic /civil partnership	13
Widowed	1
Divorced	-
Separated	-
Employment status	
Employed	2
Self-employed	(1)
Retired	12(1)
Stage of cancer	
0	-
1	3
2	5
3	4
4	-
Don't know	3
Time since cancer diagnosis	
Range (months)	4 – 60
Mean (months)	36
Surgery	
Lumpectomy	4
Local wide excision	4
Mastectomy	7
Chemotherapy	3
Radiotherapy	11
Hormonal Therapy	14
Biological Therapy	2

Three main themes and eight sub-themes were identified. Specifically, barriers affecting physical activity, factors enabling physical activity and the wider environmental context. These main themes and sub-themes are presented in Table 20. The main theme, Barriers affecting physical activity, included sub-themes of: accommodating other features of the life world; negative consequences of treatment and environmental influences. The main theme, Factors enabling physical activity consisted of the sub-themes of: perceived health and wellbeing impact; personal and inter-personal considerations and environmental influences. The main theme, Wider environmental context, cuts across both of the other main themes but included some of the codes that have / could be included in the sub-themes. These are: timing of exercise advice and family and friendship support.

Table 13: Main themes and sub-themes

Main Theme	Sub-themes
Barriers affecting physical activity	Accommodating other features of the life world
	Negative consequences of treatment
	Environmental influences
Factors enabling physical activity	Perceived health and well-being impact
	Personal and inter-personal considerations
	Environmental influences
The wider environmental context	Timing of exercise advice
	Family and friendship support

7.4.1. Barriers affecting physical activity

Factors that acted as a barrier or obstruction to being or becoming more physically active were: accommodating other features of the life world, negative consequences of treatment and environmental influences.

7.4.1.1. Negative consequences of treatment

The often debilitating side-effects of breast cancer treatment was the most limiting factor reported by the participants to starting or maintaining a physical activity or exercise routine. These included aching muscles and joints, joint pain, fatigue, hair loss, range of movement difficulties in the shoulder and other joints and the negative effects on self-confidence. Joint pain and range of movement difficulties were the major physical activity barriers that contributed to participants' reported reasons for struggling with physical activity and exercise:

"*I had quite a lot of physio to get my shoulder sorted, so I wasn't doing any, I think where I'm falling down is I'm not doing any sort of muscle building…[also], I had a lot of very aching legs, when I was having my treatment and after*" (SCS, 60-yrs, 22-months post diagnosis).

A participant described the effects of her chemotherapy treatment:

"*I had the first of my second chemo and that was the one that was really, really debilitating and I had the muscle pain, the joint pain*" (SES, 61-yrs, 10-months post diagnosis).

Another participant considered the effects of surgery on her whole body:

"*I was very, very stiff, as a body as a whole and I wanted that, I wanted some of the suppleness back, if I could, so yeah. I had a frozen shoulder at the left side, which was a problem, which I had quite a lot of physiotherapy for*" (FMF, 69 years, 48-months post diagnosis).

A number of participants expressed their thoughts about the effects of hormone treatment for breast cancer on energy levels and joint pain and thus, the negative effects it had on their ability to be physically active:

"*I did start to realise that the more I take Anastrozole and I realised that I was really affected by fatigue and that's made it more difficult as the time has gone on for me to continue to be as active as I would want*". (ADA, 64-years, 41-months post diagnosis).

Also, another expressed joint pain from the drugs and the possibility of the hormone treatment having caused osteoporosis:

"*Side effects from the drugs probably, errmm, a bit of pain at first, hip pain mainly… yeah, I think with the tablets. It does say with the side effects that you can have some pain. Also, I've now got Osteoporosis, and that's well we don't know really, probably from the drug or I don't know really, might have got it anyway I suppose, I don't really know*". (CJC, 68 years, 50-months post diagnosis).

The effects of hair loss after chemotherapy had a detrimental effect on decisions to be active:

"*Partly, I think I mentioned earlier, like doing Pilates, I had, I lost all my hair, so I had a wig or a hat and I was worried that when you're bending down and going upside down it would fall off and I didn't particularly want everybody to know…and still I think I'm still a bit, although my hair has grown back, there's not a lot of it and some people aren't always very tactful when they see you for the first time and then it's like do you explain or do you just ignore them and it can be tricky*". (HMH, 62-years, currently on-treatment).

7.4.1.2. Accommodating other features of the life world

For some of the participants the knowledge of what type of exercise or how much they should they be doing hampered their ability to engage with physical activity when they so wished and this lack of knowledge appeared to reduce their confidence to attend exercise classes or be more physically active because of the not knowing what was safe or suitable exercise. One participant described it as:

"*wondering what I should do and what I shouldn't do*", she continued, "*so I think I probably kind of toned it down…after the surgery, so I think I became less active*". (SCS, 60 years, 22-months post diagnosis)

Long-term conditions and previous illness or injuries separate to a cancer diagnosis limited some participants' activity levels and attendance at exercise classes:

"well the only thing that would stop me would be if my arthritis got worse". (MAM, 74 years, 36-months post diagnosis)

For one participant bereavement was a particular barrier to continuing with her activity because she attended the gym together with her husband as a couple:

"Well I mean dealing with bereavement isn't easy and I gave up going to the group that we were going to, because we weren't a couple anymore and I didn't want, I just didn't want to go really…I've just become less active, there's less motivation to do it, I think that's part of the problem, you know". (SJS, 70 years, 58-months post diagnosis)

7.4.1.3. Environmental Influences

The environmental influences that negatively affected performance were as follows: inclement weather, no friend to go with, unclear about what activity they could or should do in the form of information or health care professional advice, a protective (or over-protective partner) who may discourage activity. As one described the effect of inclement weather on going out walking:

"So really, I push myself to go out actually and if it's pouring down with rain and I'm gonna get wet through and it's windy I'll give it a miss". (BJB, 70 years, 57-months post diagnosis).

Another participant also found that it was important for her to have a friend to attend with – even if the other person stopped coming but to have that support at the start:

"…but then you're thinking but I don't know anybody, so I says right, I'll meet you and I started coming…even though she stopped coming…it was just that very first coming on your own". I knew I wouldn't go myself, on my own". (MAM, 74 years, 36-months post diagnosis).

This barrier was further alluded to by a number of other participants demonstrating the importance of social support to start or maintain PA.

Not knowing what exercise or physical activity to do acted as an obstruction to some women:

"wondering what I should do and what I shouldn't do…but it was the booklet really, rather than physically advising. I was reading the booklet and that was saying things that cause lymphoedema, sort of repetition if you like, things like you wouldn't want to do, like cleaning your windows, ironing, made me concerned". (SCS, 60 years, 22-months post diagnosis).

A protective partner may unintentionally discourage or actively stop physical activity and exercise participation because they considered it not to be safe to be active during or immediately after treatment:

"since he retired and cos I don't drive I'd use to have to and I mean it's three quarters…what 20 minutes to the bus, you know downhill or uphill but now he'd say "no you're not going for the bus" You know, he's sort of partly stopped me". (MSM, 72 years, 57-months post diagnosis)

Another reported her own concerns as to what activity to do and her husband's involvement:

"wondering what I should do and what I shouldn't do and then husband sort of, don't do that, when you're doing that" (SCS, 60-years, 22-months post diagnosis).

Health care professionals also appeared to play a vital role in potentially affecting physical activity levels as when one participant was asked: "Could you expand on who were the people who were saying about resting or not to do too much?

"staff on the Chemotherapy Unit, Radiotherapist people". (MRM, age 66, 45-months post diagnosis)

Another participant stated:

"You know the surgeon said don't ever get out of breath, you know, don't be silly just be a bit sensible about it". (BJB, 70-years, 57-months post diagnosis)

This lack of knowledge about the safety of physical activity and exercise during or after treatment for breast cancer from friends, family and health care professionals was responsible for a number of women not being physically active or reducing their physical activity levels.

7.4.2. Factors enabling physical activity

Factors which were considered to motivate or encourage exercise or physical activity consisted of the following sub-themes: perceived health and wellbeing impact; personal and inter-personal considerations and environmental influences. The most influential motivating factors were those aimed at improving the negative consequences experiences by the treatment for breast cancer.

7.4.2.1. Perceived health and well-being impact

Those reported consisted of losing weight, improving fatigue and having more energy, improving joint pain, recovering from breast cancer treatment, strengthening the body and regaining or improving shoulder range of movement. One participant described the tiredness and her reasons for starting exercise:

"think because I was so tired and I felt so out of sorts in myself, I got really lethargic, …I knew that the exercise would make me feel better, in every way…it was the fatigue and I knew that I needed to do something to stop it getting worse…". (ADA, 64-years, 41-months post diagnosis).

Another considered the additional energy she felt exercising gave her was motivational to continue:

"*You know, when I first started I was really tired when I left but I found now I've got used to doing these things that I feel more energised, I do really feel more energised*". (BJB, 70 years, 57-months post diagnosis).

Joint pain and range of movement difficulties affected a number of participants and exercising or doing physical activity to try and combat this pain was a reason reported by a number of women:

"*The joint pain, I just, I kind of manage that…and I do find that exercise helps me with my joint pain*".(ADA, 64 years, 41 months post diagnosis).

One considered exercise as a way to help recover from the breast cancer treatment:

"*Well I'd heard about how it was really important in the recovery from breast cancer, to do exercise and I thought well, you know, this is something really simple that I can try and what amazed me really was how much better I felt quickly after starting the exercise*". (RBR, 69 years, 60-months post diagnosis).

7.4.2.2. Personal and inter-personal considerations

The following were all considered as ways in which they helped with activity maintenance or the reason for starting to exercise and consisted of: having grandchildren to look after, enjoyment, the social side of exercise and physical activity and previous activity levels:

"*having my grandson to look after and so I'm out walking with him and because that's a lot of joy around that, so I needed a bit of a motivator and he was probably the motivator*". (ADA, 64 years, 41-months post diagnosis).

A number of women reported the actual enjoyment they found from being active and was important for motivation to continue:

"*Because I enjoy it and I have friends who I meet there, you know, we all play Badminton together, four of us, five of us and just to get back to normality really*". (MJM, 77 years, 11-months post diagnosis).

"*The main thing is that I really enjoy it. I've found something that I really enjoy so it's not a really a…don't think it a…oh no it's Wednesday and I've got to go and do this. I just love it. I just enjoy exercise. Yeah*". (RMR, 66 years, 45-months post diagnosis).

The social side of being active in a group was really important for a number of participants and the benefits that they considered with other people to meet and talk to:

"Well I've always been better off in a group, rather than a solo player. I need motivation and I find that in a group". (FMF, 69 years, 48-months post diagnosis).

"I feel, I don't want to be doing this on my own, or something on your own, particularly if you live on your own, which I do. Just being with others and seeing what we're all doing and seeing that we're doing pretty much the same things and it's taking it at your own pace, I mean it's not a race is it?". (BJB, 70 years, 57-months post diagnosis)

A consistent reason for being active and staying active after a diagnosis of breast cancer for some women was the fact that they had always been active previously and that exercise and being physical active was a way of life for them:

"Well it's kind of my, like it's always been my lifestyle, so you know, most of my friends have always been involved in sport. I played hockey, you know, from being a child up until I was in my thirties. I then sort of started playing golf". (DCD, 60 years, 4-months post diagnosis)

"Because I just, I've always been sort of active but since my breast cancer I just want to make sure that I'm just keeping myself as physically fit as I can because I don't know if it's going to come back so I want to be as strong to fight it if it does". (RMR, 66-years, 45-months post diagnosis)

"it's just the way I've been brought up I suppose to be active I think and because I've never driven I've had to make my own way to various places and things". (MSM, 72 years, 57-months post diagnosis)

7.4.2.3. Environmental influences

The environmental influences that worked positively to encourage physical activity and that acted as an enabler to starting or doing more exercise was as follows: the positive support from friends and family and the feeling of normality that being physically active produced.

"She dragged me here, yeah, I wouldn't have come on my own accord, I know I wouldn't, although I was interested, I wouldn't have made the effort to come on my own". (SSJSS, 68 –years, 36-months post diagnosis).

One participant pointed out how physical activity and in particular sport had always been part of her life:

"Well it's kind of my, like it's always been my lifestyle, so you know, most of my friends have always been involved in sport". (DCD, 60-years, 4-months post diagnosis).

"I have friends who I meet there, you know, we all play Badminton together, four of us, five of us and just to get back to normality really". (MJM, 77-years, 11-months post diagnosis).

7.4.3. Wider environmental context

A number of codes were considered which could act either positively as enabling or negatively as obstructing physical activity and exercise, depending on the participant's viewpoint. These were related to the timing of when exercise and physical activity education or advice was given and the role of family or friends in physical activity support.

7.4.3.1 Timing of exercise advice

The timing of being given exercise advice or encouraged to be active in relation to diagnosis and treatment may have encouraged some to become more active earlier whereas some thought it would not have made a difference, although a number of participants felt they did not know what type of exercise or how much physical activity they could do, so this acted as a barrier to being more active.

One reported on the timing of the exercise information and the leaflet format and it not being the right time to consider it:

"every time you see anybody, they give you another leaflet and another leaflet and another bit of information. To be honest, I shoved most of them in a bag and I didn't look

at them. So there might well have been something about exercise, but if there was, I don't, I didn't want to know at the time". (HMH, 62-years, 8-months post diagnosis).

Another participant felt that when recovery was complete would be a good time to give exercise advice:

"*I think you've got to get people, give people time to physically heal from where they are, because they do the exercises that they've given in the hospital, we all do those, because you want to get better and then I think maybe a couple of months after the end of their treatment, when they're beginning to try and start to think about how to get back to a normal, whatever that normal is, so give them time to recover from the surgery, then maybe a couple of months and then maybe is a good time, because that's when you start to readjust and think*". (ADA, 64-years, 41-months post diagnosis).

For some the education and knowing what exercise was safe or appropriate was important and because that was missing it stopped them from being more active, as one participant described:

"*So I think it would be the confidence to, if I'd have gone to that gym that day and if somebody there had said oh yeah, we can do, you know, with the treatment you've had, etc and this is the right programme, I probably would have done it...*" (SCS, 60 years, 22-months post diagnosis)

No consensus of when would be the best time or the "correct" time to give exercise advice or encouragement to be more active was noted. For some, they may have benefited from exercise advice straight away during diagnosis and treatment but others felt they would not have considered exercise at this time then but would have benefited a few months after treatment had finished.

7.4.3.2. Supportive or over-protective partner

A supportive or over-protective partner could again act as a barrier to or enabler of physical activity, depending on the family or partner's views on the benefits of being active during treatment or after and their subsequent encouragement or discouragement to be active. A supportive partner was noted as being helpful to being more active, although some also felt that some over-protective partners / family may have discouraged them from doing more activity:

"*Yeah, my husband nags! Yes, it's much easier, if he didn't want to go out, then it would be that much harder for me*". (RBR, 69 years, 60-months post diagnosis).

"*I mean my husband was just really protective and so you know, but he knows, in some respects, pull me back, because you know, he was always where's your mother, oh she's, you know, she's in the garden or brushing up*". (SES, 61 years, 10-months post diagnosis).

"*I didn't want to go on the Moving Forward class…I didn't want to do that. It was [husband] that made me go, 'oh yeah, I think you should go, I think you should go', but it's not something that, group activities are not really me. So, did you feel your husband*

helped with that motivation [researcher]. Yeah, yeah, it's just totally different lifestyle now, yeah". (SJS, 70-years, 58-months post diagnosis)
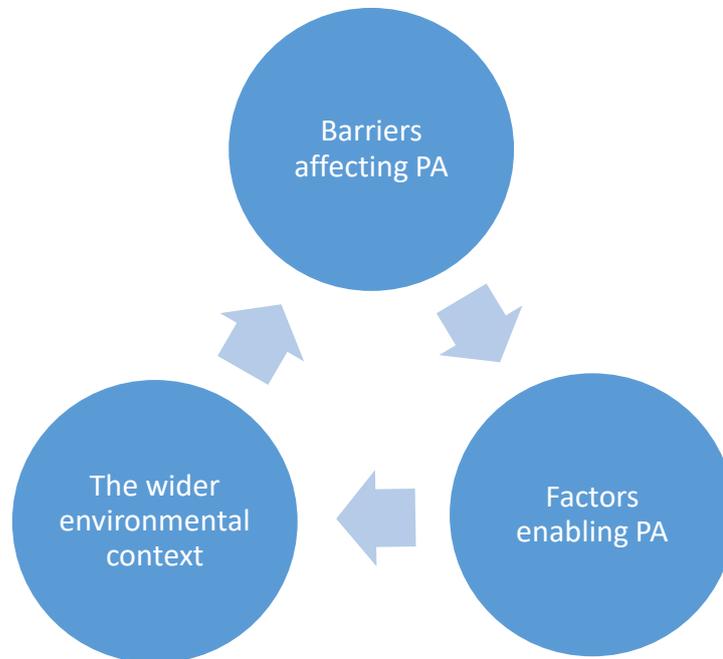
Figure 5: Conceptual framework - barriers to and motivators of PA.

7.5 Discussion

This qualitative study gives a unique insight into the barriers to and enablers of exercise and physical activity for older women with breast cancer. The perspectives of older women with breast cancer, recently diagnosed (< 12-months) and older women mean 36-months since diagnosis, who had taken part in an exercise research study and were currently active were examined. Research to understand factors that may support or obstruct the maintenance of physical activity and exercise is crucial. To date, very few studies have examined the factors that influence the initiation or maintenance of PA and exercise in older women after a diagnosis of breast cancer.

Therefore, the aim of this study was to find out what are the barriers and obstructions that may halt or hinder women aged over 60-years with breast cancer from starting or continuing an exercise programme and the factors which help to motivate and enable this population to start or continue being physical active during and after treatment for breast cancer. The findings from this study confirm there are multiple factors which can aid or obstruct older women with breast cancer from starting or continuing with a physical activity programme during or after treatment.

7.5.1. Barriers to physical activity

The main barriers to exercise and physical activity evident from this study can be attributed to the consequences of breast cancer treatment, a unique set of barriers experienced by breast and cancer survivors, which supports previous literature (Whitehead & Lavelle, 2009; Blaney et al., 2010; Crane-Okada et al., 2012). Participants in the study reported the main barriers to starting PA or maintaining a physical activity programme were perceived obstructions that ranged from the negative consequences of breast cancer treatment (shoulder problems, pain, joint pain, stiffness, fatigue, hair loss), to a lack of knowledge surrounding exercise (what type of exercise was safe, how much exercise and knowing what to do), to environmental and inter-personal issues (poor weather, no partner/friend to accompany them or over-protective partner).

These findings recognise multiple perceived barriers which can inhibit the ability to start an exercise programme or hinder the maintenance of regular physical activity. Furthermore, they appear to be consistent with previous research with breast cancer survivors (Courneya et al., 2008; Ottenbacher et al., 2011; Whitehead & Lavelle, 2009),

highlighting the unique barriers to physical activity relevant to BCS during and after treatment.

With many physical symptoms, such as pain, aching and stiffness and range of movement difficulties as a result of treatment being reported as an obstacle to starting or maintaining physical activity, researchers and health care professionals should seek to develop or improve symptom management, along with other strategies to reduce cancer specific obstructions to support women in maintaining a physically active lifestyle after a breast cancer diagnosis.

Given the findings that a barrier to exercise was not having a friend or partner to go to an exercise class or take part in physical activity alongside, it may be helpful if health care professionals discussed with their patients enlisting social support from individuals who are reliable and willing to provide support in establishing or maintaining their exercise behaviour. They could also identify different ways that this support could be provided, e.g. through social media, telephone support and local cancer support groups.

A lack of drive, motivation or will power to be active was reported by a number of participants in the present study. This was one of the most commonly-reported barriers to exercise in a number of other studies (Courneya et al., 2008; Ottenbacher et al., 2011; Brunet et al. 2013), suggesting this is an important barrier to be address in any future research. Milne, Guilfoyle, Gordon, Wallman, and Courneya (2007) noted a lack of motivation as one of their most frequently reported barriers to activity. However, having a "lack of willpower" or motivation is a difficult construct to understand and measure, therefore it may be more productive to consider this alongside other barriers that are more tangible such as "unsure or what type of exercise to do" or "how much exercise is

safe?". These barriers could be addressed by educating participants on exercise prescription and exercise efficacy.

A lack of motivation or drive to be physically active or engage in regular exercise could also be related to cancer related fatigue (CRF), something a number of women in this study reported as a barrier. Fatigue was at the centre of the majority of barriers that Blaney et al's. (2010) participants experienced, but it was the combination of fatigue and physical deconditioning that they felt contributed the most to declines in physical activity. They postulated that the experience of CRF, physical de-conditioning and this subsequent decline in physical activity, can lead to a cyclic reduction in PA levels, which may be further exacerbated by advice to rest and take things easy (Lucía, Earnest, & Pérez, 2003). Milne et al. (2007) considered fatigue as a recurrent theme that had a significant impact on physical activity levels as well as it interfering and affecting everyday tasks.

Bulmer et al. (2012) reported that participating in a cardiovascular and resistance training programme provided many psychological and physical benefits, with some women considering "feeling better" being synonymous with having more energy and exercise helping to "re-vitalise" and return to pre-cancer energy levels. Whitehead and Lavelle, (2009) reported fatigue as a key influence on physical activity levels, that also acted as a barrier to returning to exercise and physical activity. However, a number of participants perceived reduced fatigue as a benefit of already being physically active as opposed to a motivator to become active. This positive effect of exercise on fatigue levels and vitality should be used as a tool to motivate breast cancer patients to start becoming more active or to return to exercising and taking part in physical activity. Cancer-related fatigue was reported as one of the top exercise barriers (Courneya et al.,

2008) for breast cancer patients during chemotherapy treatment. They also demonstrated that over 50% of all reported barriers to missing exercise sessions were disease and treatment related and that addressing the side-effects of chemotherapy and cancer treatment is a crucial issue in improving exercise adherence during treatment.

Another barrier to exercise reported by participants in this study was a lack of knowledge about safe and effective exercise and "knowing what to do". This was also supported by Sander, Wilson, Izzo, Mountford, and Hayes (2012)who reported in their study that participants believed the information provided from the health care team about safe and effective exercise was insufficient and advice regarding resistance training was inconsistent depending on which member of the care team they had spoken to. Thus, ensuring more education for patients and health care professionals regarding exercise may be beneficial in reducing this barrier.

7.5.2. Factors enabling physical activity

The perceived motivators for becoming more physically active or exercising noted from this present study were mainly related to helping to counteract the side-effects of treatment consequences (joint pain, fatigue and recovering from treatment) and weight gain. Brunet et al. (2013) reported improving health and symptom management as contributory factors to physical activity maintenance and motivation to stay active, along with weight management being a key motivator to routine physical activity. Increases in body weight and in particular body fat is a frequent side effect of breast cancer treatment either due to chemotherapy, hormone therapy or treatment-related menopause (Holmes & Kroenke, 2004)) or related to reductions in physical activity

(Demark-Wahnefried et al., 2001). Nock et al. (2015) reported breast cancer patients citing body composition and improvements in strength and function as motiving factors in becoming more active.

The social aspect of exercising in a group where all others had a shared experience was a motivational aspect for a number of women in this present study. The group benefits were reported in a number of ways by the participants; "…meeting friends…the social side…not doing it on your own…then you go and have a coffee and a chat". The benefits of exercising in a group environment are supported by a number of other studies (Luoma et al., 2014; Martin et al., 2015; Midtgaard et al., 2015). Martin et al. (2015) reported that the group bonding developed during the exercise sessions allowed for more open discussions and sharing and that the group became the main source of enjoyment and motivation for the patients to continue exercising. Luoma et al's. (2015) participants reported that because the tailored exercise programme was only for breast cancer patients they felt it was much easier to join and any anxieties over their altered appearance and poor fitness after treatment was not so important. They experienced the exercise group as a source of practical and psychological support and beneficial for sharing experiences and gaining a sense of normality. Midtgaard et al. (2015) supported the implementation of group-based exercise because of the motivational aspect of a group environment.

However, they offer a caveat to the benefits of group exercise, and suggest that the time-limitedness of many structured programmes may explain the often sub-optimal levels of post-intervention adherence once the programme is finished. They suggest that research into cancer patients becoming too dependent on their exercise instructor is required and whether this dependence on the instructor has a negative effect on

becoming autonomous and independent exercisers outside the group setting. However, they further suggest that more research is required to demonstrate whether unsupervised and less structured programmes offer the same physical and psychological benefits as group instructor supervised programmes.

Enjoyment of being active and exercising was another factor that was a key motivator to women interviewed in this study. As one described it "The main thing is that I really enjoy it. I've found something I really enjoy!". Brunet et al's. (2013) breast cancer patients described how they were motivated to engage in physical activity because of the enjoyment and fun they experienced from participating. Nock et al. (2015) reported that for a number of breast cancer patients simply "liking the exercise" and having "fun" were motivating factors to continue and maintain an exercise routine. Whitehead and Lavelle (2009) identified four main motivators for physical activity with enjoyment being one. For women who found an activity they particularly enjoyed this was their main reason for taking part. The older women interviewed in Whitehead and Lavelle's study also acknowledged that forcing oneself to participate in exercise or an activity that was unenjoyable would not lead to prolonged adherence.

Instructor support was also considered an enabler to becoming active and engaging with an exercise class, as a number of participants noted how knowing that the instructor was supervising the activity made them feel safe and gave them confidence to undertake the activity and exercises. This instructor support was a key motivating factor reported by a number of other studies (Whitehead & Lavelle, 2009; Bulmer et al., 2012; Luoma et al., 2014), who described the benefits of having an instructor who understood the issues faced by those who have had breast cancer. Sander et al's. (2012) participants wanted safe and effective exercise guidelines from exercise providers who understood

the risk of developing lymphoedema and Blaney et al's. (2010) participants described the need for an exercise programme to be supervised by trained health care providers with the knowledge that they would not prescribe exercise that would prove detrimental to them. Bulmer et al. (2012) reported that the women found working with personal trainers knowledgeable about their condition gave them confidence that the prescribed exercises would enhance their recovery and not complicate it.

7.5.3. Limitations

Although the use of in-depth interviews provided a great deal of rich data on older women recently diagnosed with breast cancer and on women having participated in an exercise research study it was not without its limitations. Although the sample size allowed for a wide range of opinions to be expressed, it was a small sample size (n=15), with all of the participants being white European, economically secure women over 60 years old. Therefore, this limits the results of the study as we cannot be sure whether the views expressed in this study would be a true representation of other ethnicities with breast cancer. All the participants were patients with stage I-III breast cancer with no other diagnoses or further staging.

Future qualitative studies targeting older women with breast cancer should aim to include a wider range of stages, including secondary breast cancer, and aim to recruit participants from varying backgrounds and ethnicities. Selection bias may have occurred in that those recruited through the breast cancer charity who were recently diagnosed may have had an interest in a study about physical activity and therefore more likely to volunteer to take part than those who were not.

7.6. Conclusions

The findings of this study highlight the barriers to and motivators for starting or maintaining physical activity or an exercise routine in both older women (>60-years old) recently diagnosed with breast cancer and active older women who had taken part in an exercise research pilot study. BCS have high rates of physical inactivity, which can lead to increased risk of chronic conditions (Irwin et al., 2003). Additionally, some treatments can increase a women's risk of osteoporosis (Bulmer et al., 2012).

As breast cancer survivorship increases so will the cost of treating inactivity-related diseases in this population if healthy lifestyles including regular physical activity are not adopted. Therefore, encouraging women diagnosed with breast cancer to start or stay physically active is an important public health priority given the known physical and psychosocial health benefits of regular activity (Furmaniak et al., 2016; Lahart, Metsios, Nevill, & Carmichael, 2018).

The main barriers found in this study were related to the cancer and treatment side-effects in particular joint pain, range of movement difficulties as a consequence of surgery and fatigue but also appearance issues of hair loss and how they may look whilst exercising. On a positive note, many reasons for starting and maintaining physical activity were offered, notably the benefits that they experienced in helping to reduce treatment related issues, benefits, such as weight loss, less fatigue and more energy and improved recovery from treatment. The social side of group activity was identified as a reason for continuing to be active and attend an exercise programme, along with the benefits of an exercise professional knowledgeable about safe exercise programming

with their disease and treatment gave participants the confidence that the exercise would enhance and not complicate their recovery.

A further positive of this study is that the majority of barriers identified by older women with breast cancer can be alleviated by exercise (fatigue, weight gain, range of movement difficulties) or reduced through education (not sure what to do, how much exercise, partner fears). Although a vast amount of both quantitative and qualitative research has identified the benefits of exercise and physical activity during and after treatment for breast cancer, very little research has targeted older BCS. Even with the publication of the ACSM roundtable of exercise guidelines for cancer survivors (Schmitz et al., 2010), motivating and finding suitable exercise programmes for breast cancer survivors and particularly older breast cancer survivors remains a challenge.

An interesting observation from this study is that the barriers and enablers to physical activity identified by this older population of BCS was similar to those reported in other studies that targeted younger BCS, such as more energy and less fatigue (Bulmer et al., 2012); more education and advice about the type of exercises that were suitable (Sander et al., 2012); improving health and improving side-effects (Brunet et al., 2013); changes in body composition, often by losing weight but also by improving strength (Nock et al., 2015) and the social benefits of exercise (Martin et al., 2015). This demonstrates that this older population of BCS still experiences often the same barriers and enablers to becoming more active as younger BCS and therefore, ensuring that these barriers are considered when designing any exercise interventions for breast BCS will benefit all ages during and after treatment.

A routine lack of regular exercise, medical co-morbidities and concerns about efficacy of exercising and a lack of knowledge about the safety of activity can all interfere with an older person's willingness to start or maintain a regular exercise programme (Crane-Okada et al., 2012). The evidence presented in this study should contribute to the further development of exercise and physical activity programmes for older women with breast cancer, whether newly-diagnosed or many years after-diagnosis. For these programmes to be successful, careful consideration of these barriers and enablers to exercise should support with the development of successful programmes. Ensuring better education for patients and health care professionals at all stages of diagnosis, treatment and recovery will allow for more opportunities to engage with physical activity and the promotion of locally, supervised, cancer specialist instructor-led, group exercise sessions will give more options for the support to become active may assist older BCS to lead a more physically active lifestyle.

Chapter 8   General Discussion

8.1 Overview of thesis rationale and purpose

The effects of exercising during and after treatment for breast cancer has been extensively researched over the last 20-years suggesting the importance of being active during and after a diagnosis of breast cancer on physical and psychosocial health (Fong et al., 2012). Although older women are diagnosed with breast cancer more often and have poorer outcomes than younger women, the exercise research has predominantly been conducted on younger women with breast cancer (circa. mean age 50-years). Therefore, there is very limited evidence of the benefits that older women with breast cancer may experience from taking part in exercise. In recognition of this, this PhD research examined the feasibility and acceptability of an exercise programme during or after treatment for breast cancer for older women (> 60-years old). To do this the Medical Research Council framework for designing complex health care interventions was used as a guide (Craig et al., 2008).

8.2 Summary of key findings and contribution to knowledge

Study 1 was designed to examine the feasibility and acceptability of a 12-week exercise intervention targeting women over the age of 60 years who had recently been diagnosed with breast cancer with a longitudinal follow-up over 12 months. As this study was the first to target this population, considering the age and time since diagnosis, the Medical Research Council suggests feasibility testing before a full RCT should be

considered. As very little is known about this population, from an exercise perspective, a pragmatic pilot RCT was designed in order to find out important information as to recruitment, randomisation, adherence and acceptability of an exercise intervention with this population.

A recruitment rate of 41.6% (35 participants out of 84 approached) appeared to be good when compared to other breast cancer and exercise studies (Courneya et al., 2007; Daley et al., 2007). However, the length of time taken to recruit the participants (22 months) and the low numbers recruited by the breast care nurses (11 participants) may bring into question the viability of a large-scale RCT using only this method of recruitment from local general hospitals.

What served as a useful method of recruitment was approaching a national breast cancer charity that was offering a 4-week education programme to women newly-diagnosed with breast cancer from the two local hospitals. This method of recruitment resulted in 24 participants (69% recruitment rate) over a shorter time period (12 months). The Medical Research Council guidelines advocate using stop-go targets for recruitment to studies (Craig et al., 2008). This ensures that numbers and timescales can be accounted for and that if these targets are not being met either weekly or monthly, then alternative plans or procedures could be offered. If these targets continue to not be met, then it would put the study in jeopardy of continuing as it may not be financially or ethically feasible. These targets and stop/go indicators were not put in place for the current study; however, for future studies it would be pertinent to consider setting targets for timescales for recruitment, acceptable retention and adherence rates based on previous research, which will better inform the time taken to recruit the number of participants required and whether retention and adherence rates are acceptable. Given

the level of difficulty in recruitment through the breast care nurses and the lack of home-based exercise intervention data then these are important learning points from this study.

These barriers to recruitment would need to be carefully considered and overcome if a larger study was to be considered and a recruitment target would be required. In order to try and improve recruitment the researcher offered to lead an education session on exercise and physical activity; however, because the researcher delivered an educational session on the benefits of exercise and physical activity, this may have added an element of selection bias to the recruitment process.

Although recruitment was difficult and time consuming, once the participants were recruited to the study attrition rates were acceptable (20% to the whole study; 26% for the control; 6.25% for the experimental group) when compared to similar breast cancer and exercise intervention studies (Stevinson & Fox., 2006; Courneya et al., 2007; Cadmus et al. 2009). Intervention completion rate (93.75%) and adherence rates to the 12-week supervised intervention were very favourable with an overall attendance rate of 87.5%, although 15/16 participants had an attendance rate of 90.5%.

The supervised exercise programme could be considered acceptable by the participants by the use of Ratings of Perceived Exertion (RPE) used to monitor exercise intensity levels. The range for all sessions was between 2 (very light) and 5 (hard) with the mean of 3 (somewhat hard) for each session, suggesting that the exercise intensity was suitable and appropriate and that each session was delivered at an intensity meeting exercise guidelines for older people and for cancer survivors (Schmidt et al., 2013).

Unfortunately, home-based attendance was not monitored after the first seven participants complained of poor compliance and commitment to filling in the 7-day physical activity recall diaries. In hindsight, another method of monitoring the home-based intervention should have been utilised. Although, PA levels were monitored via the SPAQ, compliance to the 2 x week home-based intervention was not; therefore, the total acceptance of the exercise intervention and overall adherence was not known.

An important and valuable finding from the study was that no adverse events were reported by any participant during or after the 12-week exercise intervention or by any participant whilst doing the physical outcome assessments. This demonstrates the safety of a supervised exercise programme during or immediately after treatment for breast cancer, supporting the findings from exercise studies with younger BCS (Mutrie et al., 2007; Schwartz et al., 2007; Cadmus et al., 2009).

Although the testing of outcome measures and the use of inferential statistics to demonstrate the efficacy of an intervention is not the main priority of a pilot study, but rather to assess the design and implementation of study procedures, a number of outcomes were analysed. The comparison of body mass and body composition between groups demonstrated a consistent loss of body mass (-1.6kg) over the 12 months for the experimental group, whereas, the control group did not change body mass (-0.05kg) over the 12 month period.

An interesting observation was the changes in body composition between the groups over the 12-week intervention and the 12-month study period. Body fat decreased (-1.51%) for the experimental group during the supervised 12-week intervention but then returned to near baseline levels at 12 months (+0.19%). In comparison the control group

increased body fat over the 12 months (+1.75%). The opposite effect was observed for fat free mass, with the experimental group increasing fat free mass (beneficial) whereas, the control group lost fat free mass (negative).

Sarcopenic obesity has deleterious effects and after breast cancer treatment women face challenges relating to the loss of bone and muscle tissue and the corresponding increase in fat mass (Harvie et al., 2004; Demark-Wahnefried et al., 2005). However, optimal frequency, duration and intensity of exercise sessions that may be required to elicit body composition changes, remain unknown, and given the importance of body composition after a breast cancer diagnosis on QoL, recurrence and mortality, exercise studies focusing on body composition warrant further investigation.

Walk distance over 12 minutes was significantly increased by both groups. A number of reasons could explain this. For some it could be due to the learned effect of repeating assessments (Roediger III & Karpicke, 2006), for others, an increased confidence to be more active and exert themselves more physically as time from diagnosis increased, or it may be the characteristics of the participants who volunteered to come on the study, as those who volunteer for health interventions are usually more motivated and interested in improving their own health (Krishna, Maithreyi, & Surapaneni, 2010b).

Both groups also significantly increased their PA levels over six months. However, both groups then reduced PA levels up to 12 months, although the experimental group still maintained higher PA levels than at baseline, whereas the control group PA levels dropped to below baseline levels.

Quality of Life scores demonstrated some significant differences in favour of the experimental group for emotional functioning, future perspective, breast symptoms and

arm symptoms, although, the majority did not reach significance, most were in favour of the experimental group (see table 16). The fact that QoL was not really altered significantly over the study period may be because the participants demonstrated good functioning and low symptom scores at baseline and thus, the exercise intervention did not have enough of an effect to change these significantly.

Study 2 examined the barriers to physical activity for older women with breast cancer and the reasons that motivated some to start being active or to maintain their PA levels during and after treatment. Limited evidence was available of research that had targeted older breast cancer patients, considering barriers to and motivators of PA with this population (Whitehead & Lavelle, 2009; Crane-Okada, 2012). Given that adherence data to the home-based exercise intervention was not collected after the intial participants struggled with commitment and motivation to do the exercise and/or fill in the log book, study 2 was important to consider any barriers like this that the nature of study 1 would not examine.

This qualitative study examined the views and opinions about starting or continuing exercise and physical activity from women who were still undergoing treatment or had recently been diagnosed but may have finished adjuvant treatment and women who were currently active exercisers and attending an exercise class.

The main barrier to physical activity reported was the negative, debilitating, physical consequences of treatment, such as, shoulder mobility problems, aching muscles and joints, joint pain, fatigue and the effects of hair-loss. Other obstructions that had a negative effect on physical activity were not knowing what exercises to do, inclement weather and not having a friend or partner to go and exercise with.

A number of factors that were described as a motivation to start exercising or to continue to be active were related to trying to improve or overcome the negative physical barriers from treatment. These were: improving fatigue and having more energy, improving joint pain, strengthening the body and improving shoulder mobility and losing weight. The psychosocial benefits and motivators reported were: enjoyment, the social side of exercising with others and the routine of always having been active before diagnosis.

Some factors were considered as an obstruction to physical activity, whilst others found that they could be positive to becoming active, so acted as a motivator. These were the timing of exercise advice and a partner who was supportive or may be over-protective. For some, knowing what exercise to do and getting exercise advice early in the treatment process would have been useful to encourage them to start exercising earlier after diagnosis; however, others felt that advice needed to be given later when treatment had finished. For some a partner / friend was instrumental in encouraging them to be active, whereas others reported that their partner may have been over-protective and may have discouraged them from being more active.

The barriers to and motivators of becoming more physically active during or after treatment for breast cancer in older women were supported by the literature (Whitehead & Lavelle, 2009); however, if appears that the majority of barriers reported were unique to breast cancer patients as they were related to their cancer diagnosis and particularly the negative consequences of treatment.

8.3 Implications for clinical practise

Clinicians need to be made aware of the benefits that taking part in physical activity can have on breast cancer patients from both a physical and a psychosocial perspective, especially in relation to the negative consequences that the treatment itself may cause and how exercise may alleviate these. Older women diagnosed with breast cancer have poorer clinical outcomes than younger women; however, to date, less research has been undertaken with this population.

The recruitment of this population was difficult and unfortunately the nature of the difficulties that breast care nurses or health care professionals may face around discussing or encouraging PA with older newly diagnosed patients remain largely unknown. Future research should consider the difficulties that HCPs may face when asked to recruit to an exercise study or daily clinical barriers to giving routine exercise and physical activity advice to patients.

This PhD study demonstrates that once recruited onto an exercise intervention, older women are willing to attend and have high adherence levels similar to younger women with breast cancer (Courneya et al., 2007). However, advocacy from clinicians is required to ensure enough older women are encouraged to be active to give them the opportunity to gain the possible benefits associated with being active and alleviate treatment-related side-effects.

Additional education of health care professionals regarding exercise would be beneficial to ensure they are knowledgeable and confident to advocate PA during and after treatment. Also, exercise professionals need to work more closely with oncology professionals to ensure pathways are available for breast cancer patients to start or to

continue to exercise after a diagnosis of breast cancer. Limited opportunities to access safe and structured exercise will only act as a barrier to PA, as this study demonstrated, as the main reason for not participating in study 1 was reported as the distance to the exercise programme.

Older breast cancer patients reportedly enjoyed the group social side of exercise with people of a similar age and condition so did not feel "different" because of treatment-related appearance changes (hair-loss, weight gain). They also appreciated a knowledgeable instructor in whom they felt confident who understood their treatment and condition and could prescribe appropriate and safe exercise. Exercise and recreation professionals need to ensure that a similar environment can be replicated with an appropriately trained and experienced exercise professional leading the classes. With increasing evidence of the relationship of exercise on reducing breast cancer recurrence and related cancer mortality, along with improving survival rates, there is never a more important time for health care professionals to be promoting exercise and PA and for exercise professionals to be offer more opportunities for breast cancer patients to become more active.

8.4 Limitations and future research

One of the main study limitations was not being able to fully assess the feasibility of the intervention because home-based exercise adherence was not monitored. Therefore, we do not know how effective the overall programme was and whether the supervised sessions of the intervention were successful on its own or whether it needs to be combined with a home-based programme for more beneficial outcomes. However,

although home-based intervention adherence was not monitored, the qualitative study, which considered barriers to and motivators of exercise, attempted to address some of the shortcomings of not having home-based intervention data. Future interventions should collect both supervised intervention data and home-based PA data to ensure that any benefits of an exercise intervention programme can be attributed to the actual intervention. Additional activity outside of the intervention should also be monitored for this reason and activity trackers or accelerometers would make this more accurate and probably less of a burden than the daily PA diaries that participants in study 1 stopped using.

Another limitation of this study was not recruiting enough participants in study 1; therefore, it was not possible to draw any firm conclusions as to the benefits of the supervised exercise intervention. Stop/go indicators should be set for any future complex intervention research with unfamiliar populations. This would ensure that additional data is available as to the feasibility of recruiting to timescales and attrition within a study. Furthermore, it is still unclear as to the range of benefits an older woman with breast cancer can gain from being active during and after treatment due to the lack of research with this population.

However, as a feasibility study, it provided evidence and information as to the design and implementation of an RCT with this population and the difficulties that need to be overcome before a full trial can be implemented. Other limitations to the study are the generalisability of any results, as only white European women, who were economically stable and reported high levels of physical activity participated, so self-selection bias may have been evident and because of this it may not have been a representative sample of older women with breast cancer.

Although a valuable way to recruit participants was through the educational programme of a national breast cancer charity, because the researcher delivered an educational session on exercise and physical activity, this may have caused some contamination of the control group. It is not known in the present study whether anybody in the control group did start an exercise programme or increase PA levels as a result of being recruited onto the study; however, participants in the control group did significantly increase PA levels over six months and improved their 12-minute walk distance.

Study 2 was again limited by a small sample size, although it appeared data saturation was reached when no new themes or information emerged from the later interviews. Also, this study only recruited white European women who were stage I-III so again, this limits the generalisability of any findings.

Future work should aim to improve recruitment strategies to ensure that sufficient numbers can be recruited within appropriate time-scales. Future targets for recruitment, retention and adherence to either the supervised intervention or the home-based intervention should be considered according to Avery et al. (2017), who suggest a traffic light system, whereby a trial can proceed with modifications rather than just a stop/go basis.

The supervised exercise intervention must be available at multiple venues to ensure that distance to the supervised exercise programme is not a barrier. Interviews with oncology professionals would be useful to examine their opinions as to the difficulties of recruitment of newly-diagnosed older women with breast cancer to find alternative ways to support this method of recruitment.

An interesting observation related to the increase in fat free mass and decrease in fat mass for the experimental group during the 12-week supervised intervention. As weight gain and sarcopenic obesity in particular are negative side-effects and increase risk of breast cancer recurrence and mortality, future work targeting older women and examining the effects of exercise on body composition are warranted.

8.5 Conclusion

To summarise, the main purpose of this PhD research was to establish whether it was feasible and acceptable to offer an exercise intervention to women aged over 60 years during or immediately after treatment for breast cancer. This study was the first in the UK to specifically try and recruit women over the age of 60 after a very recent diagnosis of breast cancer on to an exercise trial.

This study demonstrated that it was feasible to deliver a supervised exercise intervention during this time, although recruitment of this population via clinical channels was very difficult and time-consuming. Therefore, in order to recruit a larger number of participants for a full-intervention trial, satisfactory methods of recruitment need to be established. This may be by having designated clinical recruiters across multiple hospital sites.

The intervention must also be offered at multiple sites to ensure that travel or distance to the exercise site is not a barrier. The study found that once recruited the older participants adhered to the supervised intervention well and with no adverse events reported, which suggested that a supervised exercise programme at this time was safe. Retention to the full study from both groups was also acceptable.

Barriers and obstructions to being physically active at this time were generally unique to a breast cancer diagnosis and treatment; however, the majority of barriers to activity could be overcome with regular physical activity. Therefore, it further demonstrated the importance of promoting and advocating exercise and physical activity for older women during or after treatment. Although, to do this, better education of the patients, health care professionals, friends and family regarding exercise is required to ensure a lack of knowledge of safe exercise is not a barrier to becoming active.

However, much research with this population is still required. Only white European, economically stable women, diagnosed with breast cancer stage I-III were recruited to studies 1 and 2, therefore generalisability to the whole older breast cancer population is limited. Secondly, home-based exercise was not monitored, therefore the effectiveness of the whole intervention cannot be determined, only the effect of the supervised exercise programme. Finally, because heart rate monitoring was unable to be carried out, these data would have been useful, alongside the RPE monitoring to further understand the acceptability of the supervised exercise intervention.

With limited evidence as to the effectiveness of exercise on physical and psychosocial factors with this population and not knowing if there is an optimum type or intensity of exercise, duration or frequency of intervention on beneficial outcomes with this population, additional studies are therefore still required with this increasing population of older breast cancer survivors.

8.6 Dissemination of findings from this thesis

Publications

Kipling, K.N., McCluskey, S., Kirshbaum, M.N., Garbutt, G. and Boduszek, D. (2014). *Supervised exercise for older women treated for breast cancer. Preliminary results from a pilot randomised controlled trial.* Psycho-Oncology 24 (Suppl. 1).

Kipling, K.N., McCluskey, S., Kirshbaum, M.N., Garbutt, G. and Boduszek, D. (2015). *Supervised exercise for older women treated for breast cancer. Results from a pilot randomised controlled trial*, Journal of Sports Sciences, 33:sup1, s85-s93, DOI: 10.1080/02640414.2015.1110333

Oral Presentations

Supportive and Palliative Care Research Group, University of Nottingham, May 2010.

Does exercise training during chemotherapy treatment for breast cancer protect

against cardiotoxicity?

University of Huddersfield, Post-graduate research festival, September, 2012.

Exercise during treatment for breast cancer: a Randomised Controlled Trial. Poster

Presentation

Invited Oral Presentations

Breast Cancer **Care.** Young Women's Forum. Holiday Inn, Manchester, January 2014.

Invited speaker. Exercise and Physical Activity during and post treatment for Breast

Cancer

Breast Cancer Care. Living with secondary breast cancer. Novotel, Leeds, June 2014. Invited speaker. Exercise, Physical Activity and Breast Cancer.

North of England Oncology Association. 8ᵗʰ North of England Breast Cancer Symposium, April 2016. University of Hull. Invited speaker. The role of exercise in reducing morbidity and mortality in Breast Cancer.

Poster Presentations

British Psychosocial Oncology Society, annual conference, March 2015. Leeds Beckett University. Supervised exercise for older women treated for breast cancer. Preliminary results from a pilot randomised controlled trial. Poster presentation. Psycho-Oncology 24 (Suppl. 1).

British Association of Sport and Exercise Science, annual conference, December 2015. Poster presentation. Supervised exercise for older women treated for breast cancer. Results from a pilot randomised controlled trial. Day 2. Posters – Physical Activity for Health, Journal of Sports Sciences, 33:sup1, s85-s93, DOI: 10.1080/02640414.2015.1110333

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Appendices

Appendix 1: Search terms for rapid review

AMED

(Breast AND cancer).ti,ab OR (Breast AND neoplasms).ti,ab OR
(Breast AND carcinoma).ti,ab OR (Breast AND ductal).ti,ab) AND
((aerobic AND training).ti,ab OR (cardiorespiratory AND
training).ti,ab OR (physical AND fitness).ti,ab OR (endurance AND
training).ti,ab OR (resistance training OR weight training OR
weight lifting OR strength training).ti,ab OR (strength AND
training).ti,ab OR (resistance AND training).ti,ab OR (weight AND
training).ti,ab OR (weight AND lifting).ti,ab OR (exercise OR
physical activity OR physical therapy OR physical fitness).ti,ab))
AND ((Older breast cancer survivors OR breast cancer
survivors).ti,ab OR (older AND elderly).ti,ab OR ((post AND
menopausal) AND cancer).ti,ab OR (older AND cancer).ti,ab OR
((older AND breast) AND cancer).ti,ab)) [DT 2003-2018]
[Languages English]

Appendix 2. Ethical approval letter for the study

NHS
Health Research Authority

NRES Committee Yorkshire & The Humber - South Yorkshire
Millside
Mill Pond Lane
Meanwood
Leeds
LS6 4RA

Telephone: 0113 30 50128
Facsimile: 0113 85 56191

16 July 2012

Mr Kevin Kipling
Senior Lecturer
University of Huddersfield
Queensgate
Harold Wilson Building HW3/13
Huddersfield
HD1 3DH

Dear Mr Kipling

Study title:	Exercise for women over 60 years old during adjuvant endocrine treatment for breast cancer with or without radiotherapy
REC reference:	12/YH/0258
IRAS project number	57057
Protocol number:	KNK_Uni_Hudd_April_12

Thank you for your letter of 13 July 2012, responding to the Committee's request for further information on the above research and submitting revised documentation.

The further information has been considered on behalf of the Committee by the Chair.

Confirmation of ethical opinion

On behalf of the Committee, I am pleased to confirm a favourable ethical opinion for the above research on the basis described in the application form, protocol and supporting documentation as revised, subject to the conditions specified below.

Ethical review of research sites

NHS sites

The favourable opinion applies to all NHS sites taking part in the study, subject to management permission being obtained from the NHS/HSC R&D office prior to the start of the study (see "Conditions of the favourable opinion" below).

Non-NHS sites

The Committee has not yet been notified of the outcome of any site-specific assessment (SSA) for the non-NHS research site(s) taking part in this study.   The favourable opinion

A Research Ethics Committee established by the Health Research Authority

Calderdale and Huddersfield **NHS**

NHS Foundation Trust

Research & Development Department
3rd floor, Learning Centre
Huddersfield Royal Infirmary
Lindley
Huddersfield
West Yorkshire
HD3 3EA

Telephone: 01484 347007
Email: r&d@cht.nhs.uk

24 July 2012

Mr Kevin Kipling
School of Human and Health Sciences
University of Huddersfield,
Queensgate,
Huddersfield
West Yorkshire.
HD1 3DH

Dear Mr Kipling

1007   **Exercise for women over 60 years old during adjuvant endocrine
treatment for breast cancer with or without radiotherapy**

The Research and Development department has considered the following documents in
support of the application for approval to undertake the study on the premises of
Calderdale and Huddersfield NHS Foundation Trust:

Document	Version	dated
Evidence of Insurance or Indemnity		
Investigator CV		
GP letter	1	02-Apr-12
Academic supervisor CV		
Participant Consent Form	3	13-Jul-12
Participant Information Sheet	4	13-Jul-12
Protocol		02-Apr-12
Questionnaire: EORTC QLQ-BR23		
Questionnaire: EORTC QLQ-C30		
Questionnaire: 6 and 12 month questionnaire	1	11-May-12
Questionnaire: Questionnaire for participants who drop out	1	11-May-12
REC application		03-May-12
Response to Request for Further Information		13 Jul-12
Summary/Synopsis	1	02 Apr 12

Your study now has R&D approval on the understanding and provision that you will
adhere to the following conditions:

Chairman: Andrew Haigh
Chief Executive: Owen Williams   **INVESTORS IN PEOPLE**   POSITIVE ABOUT DISABLED PEOPLE   **Your Care Our Concern**

Appendix 3. Participant Information Sheet

Participant Information Sheet

Study Title:

Exercise for women over 60 treated for breast cancer.

You are being invited to take part in a research study which is being completed as part of a PhD degree. Before you decide to take participate in the study it is important that you understand why the research is being done and what it will involve.

You have been considered suitable to participate in this study by your medical Oncologist and breast care nurses at the Huddersfield Royal Infirmary. You are considered suitable because you meet the criteria for selection, which are: female, over sixty years old, recently diagnosed with breast cancer and undergoing treatment and you have no disabilities that will prevent you from taking part in an exercise programme.

Please take time to read the following information carefully. Feel free to ask any questions if you do not understand anything or if you would like more information.

What is the purpose of the study?

The purpose of this study is to investigate the effects of a 12 week exercise programme during treatment for Breast Cancer in women over 60 years old.

The study will look at the effects the exercise programme may have on your physical and psychological health – heart rates during exercise, distance walked in 12 minutes (before and after the programme), body composition and your Quality of Life (QoL) will all be measured. These assessments will be compared with a control group of women who will not participate in the supervised exercise to see what effects the exercise programme may have.

What will I have to do?

The researcher would like you to agree to participate in the research study. This may involve you participating once a week in an exercise programme (1 hour per session) for 12 weeks to take place at the University of Huddersfield and to do two other additional sessions for 30 minutes once per week at home in your own time.

The exercise programme will be fully supervised and you will be closely monitored to ensure that it is safe and appropriate for your current level of fitness and medical condition. You will also be asked to fill in a Quality of Life

Appendix 4. Informed consent form

UNIVERSITY OF HUDDERSFIELD

Exercise for women over 60 treated for breast cancer

Exercise Programme Consent Form

Tick

Box

I have been fully informed of the nature of this research by reading the Participant Information Sheet version 4 June 12 and by asking the researcher any questions ☐

I understand that I have the right to withdraw from the research study at any time without giving any reason and I have a right to withdraw my data if I wish ☐

☐

I give permission to be quoted (by use of a pseudonym)

I understand that my identity will be protected by the use of a pseudonym and that n☐ information will be included in any research report or publication that could reveal my identity

I understand that information about me will be retained and used in the research eve☐ if I am no longer able to continue participation due to worsening health

I understand that relevant sections of medical records/data collected during the stud☐ may be looked at by individuals from the University of Huddersfield, from regulatory authorities or from the NHS Trust, where it is relevant to my taking part in this research. I give permission for these individuals to have access to my records. ☐

I agree to my GP being informed of my participation in my study

Name of participant:

Signature :

Date:

Name of researcher

Signature

Date

Researcher contact details:

Kevin Kipling, Senior Lecturer, Division of Health and Wellbeing, University of

Huddersfield, Harold Wilson Building HW3/13, Queensgate, HD1 3DH. Tel: 01484

473834. Email: kevin.kipling@hud.ac.uk

Appendix 5. PAR-Q

Figure 4.1 Exercise Center Intake Form

Name: _____   Date (DD/MM/YR): _____

Date of birth (DD/MM/YR): _____   Age: _____

Emergency Contact

Name: _____   Relationship: _____

Home phone number: _____   Cell phone number: _____

Medical History—Cancer

1. What was the date of your cancer diagnosis (MM/YR)? _____

2. What type of cancer were you diagnosed with (e.g., breast, lung)? _____

3. What stage was your cancer? ☐ 0 ☐ I ☐ II ☐ III ☐ IV ☐ Undetermined ☐ Don't know

4. If applicable, which side of the body was your cancer on? ☐ Left ☐ Right ☐ Both ☐ N/A

5. What types of cancer treatments have you received or will you receive in the future?

   Surgery   ☐ No ☐ Current ☐ Completed: date (MM/YR):___/___
   ☐ Future/planned: date (MM/YR):___/___

   Chemotherapy   ☐ No ☐ Current ☐ Completed: date (MM/YR):___/___
   ☐ Future/planned: date (MM/YR):___/___

   Radiation   ☐ No ☐ Current ☐ Completed: date (MM/YR):___/___
   ☐ Future/planned: date (MM/YR):___/___

   Type of surgery (if known): _____

6. Please provide any other comments you have about your cancer or cancer treatment (if applicable):

   _____

   _____

Medical History—General

7. Do you have any other current medical conditions? (Please check all that apply.)

   ☐ Hypertension (high blood pressure)
   ☐ Diabetes
   ☐ High cholesterol
   ☐ Arthritis or joint pain
   ☐ Other (specify): _____

8. Please list your current medications and supplements, including any medications that are part of your cancer treatment, such as hormone therapy. (Please provide the names as best as you can remember them and what they are for.) _____

   _____

   _____

Appendix 6: Borg Ratings of Perceived Exertion Scale

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

Appendix 7. EORTC C30 and BR23

EORTC QLQ-C30 (version 3)

We are interested in some things about you and your health. Please answer all of the questions yourself by circling the number that best applies to you. There are no "right" or "wrong" answers. The information that you provide will remain strictly confidential.

Please fill in your initials: ⌶⌶⌶⌶
Your birthdate (Day, Month, Year): ⌶⌶⌶⌶⌶⌶⌶⌶
Today's date (Day, Month, Year): 31 ⌶⌶⌶⌶⌶⌶⌶⌶

		Not at All	A Little	Quite a Bit	Very Much
1.	Do you have any trouble doing strenuous activities, like carrying a heavy shopping bag or a suitcase?	1	2	3	4
2.	Do you have any trouble taking a <u>long</u> walk?	1	2	3	4
3.	Do you have any trouble taking a <u>short</u> walk outside of the house?	1	2	3	4
4.	Do you need to stay in bed or a chair during the day?	1	2	3	4
5.	Do you need help with eating, dressing, washing yourself or using the toilet?	1	2	3	4

During the past week:		Not at All	A Little	Quite a Bit	Very Much
6.	Were you limited in doing either your work or other daily activities?	1	2	3	4
7.	Were you limited in pursuing your hobbies or other leisure time activities?	1	2	3	4
8.	Were you short of breath?	1	2	3	4
9.	Have you had pain?	1	2	3	4
10.	Did you need to rest?	1	2	3	4
11.	Have you had trouble sleeping?	1	2	3	4
12.	Have you felt weak?	1	2	3	4
13.	Have you lacked appetite?	1	2	3	4
14.	Have you felt nauseated?	1	2	3	4
15.	Have you vomited?	1	2	3	4
16.	Have you been constipated?	1	2	3	4

Please go on to the next page

EORTC QLQ - BR23

Patients sometimes report that they have the following symptoms or problems. Please indicate the extent to which you have experienced these symptoms or problems during the past week.

During the past week:	Not at All	A Little	Quite a Bit	Very Much
31. Did you have a dry mouth?	1	2	3	4
32. Did food and drink taste different than usual?	1	2	3	4
33. Were your eyes painful, irritated or watery?	1	2	3	4
34. Have you lost any hair?	1	2	3	4
35. Answer this question only if you had any hair loss: Were you upset by the loss of your hair?	1	2	3	4
36. Did you feel ill or unwell?	1	2	3	4
37. Did you have hot flushes?	1	2	3	4
38. Did you have headaches?	1	2	3	4
39. Have you felt physically less attractive as a result of your disease or treatment?	1	2	3	4
40. Have you been feeling less feminine as a result of your disease or treatment?	1	2	3	4
41. Did you find it difficult to look at yourself naked?	1	2	3	4
42. Have you been dissatisfied with your body?	1	2	3	4
43. Were you worried about your health in the future?	1	2	3	4

During the past four weeks:	Not at All	A Little	Quite a Bit	Very Much
44. To what extent were you interested in sex?	1	2	3	4
45. To what extent were you sexually active? (with or without intercourse)	1	2	3	4
46. Answer this question only if you have been sexually active: To what extent was sex enjoyable for you?	1	2	3	4

Please go on to the next page

Appendix 8. Scottish Physical Activity Questionnaire (SPAQ)

Physical Activity: Scottish Physical Activity Questionnaire (SPAQ)

Scottish Physical Activity Questionnaire (with minor amends agreed with the authors, for use with the Cancer and Physical Activity Standard Evaluation Framework)

The following questions relate to your physical activity over the previous week. Please mark in the appropriate box the number of minutes spent doing a particular activity. Please try and think carefully and be as accurate as possible with your answers and only include activities of either moderate or vigorous intensity. Examples are given of what should and should not be included.

LIGHT INTENSITY - Your heart rate and breathing rate are no different from what they are when you are standing, sitting etc

MODERATE INTENSITY - Your heart rate and breathing rate are faster than normal. You may also sweat a little. Brisk walking or sweeping and mopping are good examples of how you might feel

VIGOROUS INTENSITY - Your heart rate is much faster and you have to breathe deeper and faster than normal. You will probably sweat. Playing football or squash are good examples of how you might feel

LEISURE TIME PHYSICAL ACTIVITY - Remember, do not include light intensity activities

In the past week how many minutes did you spend each day:

	MON	TUES	WED	THUR	FRI	SAT	SUN	TOTAL
Walking outside of work? DO include — e.g. walking to the shops, walking to work, walking the dog, stairwalking; DO NOT include — e.g. standing, sitting, driving, walking whilst at work								
Manual labour outside of work? DO include — e.g. cutting grass, decorating, washing car, DIY, digging; DO NOT include — e.g. weeding, planting, pruning								
Active housework? DO include — e.g. vacuuming, scrubbing floors, bed making, hanging out washing; DO NOT include — e.g. sewing, dusting, washing dishes, preparing food								
Dancing? DO include — e.g. only include time actually spent dancing; disco, line, country; DO NOT include — e.g. time spent not actually dancing								
Participating in a sport, leisure activity or training? DO include — e.g. exercise classes, cycling, football, swimming, golf, jogging, athletics; DO NOT include — e.g. darts, snooker / pool, fishing, playing a musical instrument								
Other Physical Activity if not already covered (please write in)								

PHYSICAL ACTIVITY AT WORK (Please complete this section if you are in regular employment, remember not to include light intensity activities)   TOTAL

In the past week how many minutes did you spend each day:

	MON	TUES	WED	THUR	FRI	SAT	SUN	TOTAL
Walking whilst at work? DO include — e.g. walking up or down stairs, to and from your desk, "doing the rounds"; DO NOT include — e.g. standing, sitting at desk etc; i.e. time spent not actually walking								
Manual labour whilst at work? DO include — e.g. lifting, stacking shelves, climbing ladders, building work, cleaning; DO NOT include — e.g. sitting at desk, answering telephone, driving, check-out operation								

Was last week typical of the amount of physical activity you usually do?   TOTAL

YES				
NO - I usually do more		Normally, how much more?		Of which activity?
NO - I usually do less		Normally, how much less?		Of which activity?
Additional comments/reasons?				

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Appendix 9. Analytical framework charting stage of framework analysis from NVivo

Benefits of Exercise

	A : benefits of exercise	B : Expectations of PA activity	C : Group exercise benefits	D : Healthy living
1 : AM_100417	doing your, your arm exercises, maybe that's, you know, that's helped, So I think the exercises, especially your arm exercises are important, to make it that you've got your full movement of your arms afterwards. AM: I think its just the social part as well, because as you're doing your exercises, you're chatting as well, unless you tell us we've to shut up, keep quiet and get on with it, but you know, you can have a little chat as well, you see, as you, especially when you're on the treadmill. When you're on, you know, on the weights and that, you're just saying then, you know, have	Well just that I would feel a bit better, but also it was like the meeting people and you know, like if you've any little problems, you chat with them to see whether they've had it and it were, so you could interact with them,		

Motivators to physical activity

11 : JSun_190417	**1. A friend to attend with 2. Health benefit (weight loss, feel fitter)** JSun: She dragged me here, yeah, I wouldn't have come on although I was interested, I wouldn't have made the effort to come on my own. But after the Moving Forward class, we left our emai touch and after a week or two, Paula emailed me and said do you want to meet for a coffee and I said yeah, so we did and she was she'd lost quite a lot of weight and I thought oh that sounds alright. So I came along with Paula and so that's, that's how I came. KK: Right, so it was that support with [JSun: yeah] a friend [JSun: that's right, yeah, yeah]. So you, so once you started coming [JS out of the class and did you maybe find? JSun: I don't know what I hoped to get out of it really, perhaps to lose some weight, which I haven't, but just generally just general e yeah, yeah, nothing in particular. KK: So would you say you're trying to be active [JSun: yeah] for health benefit or [definitely, yeah, yeah, definitely]
12 : MF_100417	**1. Group element / dynamics 2. Improving cancer treatment outcomes** MF: Well I've always been better off in a group, rather th and I find that in a group and the fact that I'd had my lymph nodes removed and my immune system was fairly well shot, I thought th a whole, it may help to keep infection at bay, whether that's of any consequence, I don't know.
13 : MH_150517	**1. Not letting down a friend 2. Commitment through having already paid**. Probably its, perhaps not groups, but its easier to do used to run every week, I ran with a friend and if I'd been going on my own, a lot of the time, I'd think oh I can't be bothered, but bed else, you make the effort and same with like group Pilates. If I paid for a course up front, we used to, you'd pay half a term at a time paying on the day in some ways, because you're sort of committed to it.
14 : MR_190417	**1. Fit to fight cancer recurrence 2. Enjoyment 3. To be as fit as possible for health** MR - Because I just, I've always been sort of active but since sure that I'm just keeping myself as physically fit as I can because I don't know if it's going to come back so I want to be as strong to fight it if it MR - The main thing is that I really enjoy it. I've found something that I really enjoy so it's not a really a…don't think it a…oh no it's Wednesday it. I just enjoy exercise. Yeah. MR - Well, I think exercise is a benefit is beneficial to general health anyway so I just presumed that, you know, just get myself generally fit you MR - Just like I've said, you know, to be fit and get my body fit, errrr, because, I think having a fit body will only be beneficial really, you know to

Supervised exercise for older women treated for breast cancer. Preliminary results from a pilot randomised controlled trial. Kipling, K.N., McCluskey, S., Kirshbaum, M.N., Garbutt, G. and Boduszek, D. (2015).

Title: Supervised exercise for older women treated for breast cancer. Preliminary results from a pilot randomised controlled trial.

Kipling, K.N., McCluskey, S., Kirshbaum, M.N., Garbutt, G. and Boduszek, D. (2014)

Background: There is compelling evidence of the benefits of exercise in cancers survivors and older populations but very limited research on exercise interventions conducted with older breast cancer survivors. **Aims:** The study investigated whether a supervised exercise intervention (1 x week) and home based (2 x week) lasting 12-weeks with older women treated for breast cancer (>60 years) during and post-adjuvant therapy improved functional capacity (walking ability), body composition, quality of life (QoL) and levels of physical activity over 12 months. **Methods:** A pilot randomised controlled trial assigned 35 recently diagnosed female breast cancer patients (mean = 67 years; SD = 5.02) to either a supervised exercise intervention (n = 17) or a control group (n = 18). Outcome measures were assessed at baseline, 3, 6 and 12 months. **Results:** Preliminary analyses of walking distance, body composition and physical activity for the first 3-months of the study were conducted. The intervention group significantly increased their walking distance ($p < 0.001$) and their physical activity levels ($p < 0.05$) but there were no significant differences in body composition between groups. The control group also significantly increased their walking distance ($p < 0.01$). **Conclusion:** The intervention group significantly improved walking distance and daily levels of physical activity over 3-months with no adverse events reported. It will be interesting to observe whether these changes can be maintained to have a positive effect on health, functional capacity and QoL and whether this increase in daily physical activity levels will have any effect on body composition.
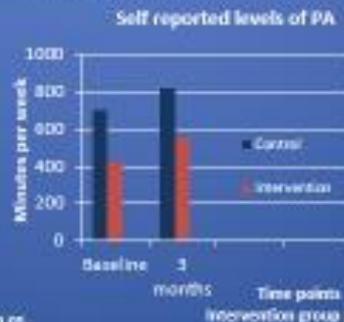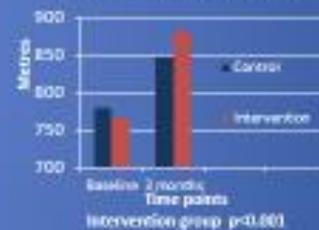
Appendix 11. British Association for Sport and Exercise Sciences (BASES) Poster and Abstract publication

Supervised exercise for older women treated for breast cancer. Results from a pilot randomised controlled trial.

KEVIN N. KIPLING[1*], SERENA McCLUSKEY[1], MARILYNNE. N. KIRSHBAUM[2], GED

GARBUTT[1,3] & DANIEL BODUSZEK[1]

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North Manchester General Hospital.

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There is compelling evidence as to the range of benefits that breast cancer survivors (BCS) can experience by participating in physical activity during or post cancer treatment (Campbell et al., 2012, a concise evidence review, Macmillan Cancer Support). Research involving younger cancer survivors and older "cancer free" adults has demonstrated that exercise can play an important part in ameliorating some of the effects of cancer treatment and of the ageing process (Courneya et al., 2004, Critical Reviews in Oncology/Hematology, 51, 249-261). However, evidence from older BCS is extremely limited, despite the higher incidence of diagnosis and lower survival rates in this population. Therefore, the aim of this study was to investigate whether a supervised (1 x week) and home based (2 x week) exercise intervention, lasting 12-weeks with older women (>60 years) being treated for breast cancer, improved functional capacity (12-min walk), body composition, quality of life (QoL) and levels of physical activity (PA) and could be sustained over a 12-month period. The feasibility of recruitment, adherence and acceptability with this population was also assessed. Ethical approval was obtained from the local university and NHS panels. Thirty-five participants (mean age = 67 years; SD = 5.02) were assigned to either a supervised exercise intervention group (n = 17) or a usual care control group (n = 18). Outcome measures were assessed at baseline, 3, 6 and 12-months. Statistical analyses of walk distance, body composition, physical activity,

and QoL for the four time points of the study were conducted using descriptive statistics and mixed between-within subjects ANOVA. No significant interaction terms were detected. Both intervention and control groups significantly increased their walk distance and physical activity levels over 6 months ($P<0.05$) but there was a decrease at 12 months. Participant's global health status/QoL improved over 6 months but decreased slightly at 12 months in both groups. There were no significant differences between control and treatment groups on any of the measures at any time point. Attrition rates to the study were good (80%) with no adverse events reported by the intervention group and adherence to the supervised exercise sessions was high (>85%). Recruitment onto a supervised exercise intervention with older BCS was feasible with high adherence levels without any adverse events. Future studies should incorporate larger sample sizes to evaluate whether PA can improve and maintain physical function and QoL and how this can be sustained in this under researched population.

References

Campbell, A., Forster, J., Stevinson, C. and Cavill, N. (2012) The importance of physical activity for people living with and beyond cancer. A concise evidence review. Macmillan Cancer Support.

Courneya, K.S., Vallance, J. K.H., McNeely, M.L., Karvinen, K.H., Peddle, C.J. and Mackey, J.R. (2004) Exercise issues in older cancer survivors. Critical Reviews in Oncology/Hematology, 51, 249-261.

Appendix 12. North of England Oncology Association 8th Breast Cancer Symposium – agenda

NORTH OF ENGLAND ONCOLOGY ASSOCIATION
www.neonc.org.uk   Charity registration no. 1140666

RCR Category 1 CPD
6 credits awarded

8th North of England Breast Cancer Symposium
Saturday 23 April 2016 held at the University of Hull, Cottingham Road, Hull HU6 7RX
Registration and Refreshments in Staff House Foyer from 08:30. All lectures will be held in the Lindsay Suite, Staff House

0910-0915 Welcome by Dr Sunil Upadhyay, Chairman NEONC

0915-0955 Hormonal Receptors and Their Interpretation in the Management of Breast Cancer
Prof Jonas Bergh, Professor of Oncology, Oncology (Mimi Althainz' donation), Karolinska Institutet and University Hospital 171 76 Stockholm, Sweden
0955-1000 Q&A: Chair: Dr Sunil Upadhyay

1000-1040 Hormonal Agents and Bisphosphonates and the Level of Their Benefits in Breast Cancer
Prof Richard Gray, Professor of Medical Statistics, Clinical Trial Service Unit, Oxford
1040-1045 Q&A: Chair: Dr Joji Joseph

1045-1125 De-escalating treatment in early Breast Cancer – Less is More
Dr Andreas Makris, Consultant Clinical Oncologist Mount Vernon Cancer Centre, Northwood, Middlesex, London
1125 -1130 Q&A: Chair: Dr Mohammad Butt

1130-1145 *Refreshment break (Myton Room)*

1145-1220 Contrast Enhanced Spectral Mammography in the Imaging of Early Stage Breast Cancer
Dr Eleanor Cornford, Consultant Radiologist, Nottingham University Hospital
1220-1235 Q&A: Chair: Dr Penny O'Neill

1235-1310 Surgical Techniques to Achieve Normality following Breast Cancer Reconstructive Surgery
Mr Niri Nirangan, Consultant Plastic & Reconstruction Surgeon, Chelmsford & Colchester Hospitals
1310-1315 Q&A: Chair: Mr Phil Turton

1315-1400 *Buffet Lunch & Sponsored Exhibition (Myton Room)*

1400-1435 Micro-metastasis in Brain and its Optimum Management
Prof Michael Brada, University of Liverpool
1435-1440 Q&A: Chair: Dr Sunil Upadhyay

1440-1510 The Role of Exercise in Reducing Morbidity and Mortality in Breast Cancer
Mr Kevin Kipling, Senior Lecturer, Sport and Exercise Science, University of Huddersfield
1510-1515 Q&A: Chair: Mr Tapan Mahapatra

1515-1550 Current Challenges in Management of pain & Supportive Care in Oncology
Prof Sam Ahmadzai, Professor Palliative Medicine, University of Sheffield
Q&A: Chair: Dr Mohammad Butt

1555-1630 Neo-adjuvant/adjuvant Management of Early Stage HER2 Positive Breast Cancer
Dr Mark Verrill, Consultant Medical Oncology, Freeman Hospital, Newcastle
Q&A Chair: Dr Joji Joseph

1630-1635 Closing Remarks – Dr Joji Joseph, Vice Chair, NEONC

1635-1645 *Coffee and Sponsored Exhibition (Myton Room)*

The 2016 Symposium is being sponsored by the following companies via provision of an exhibition stand and will be present on the day.
AstraZeneca • Chugal Pharma UK Ltd • GeneHealthUK • Novartis Oncology • Roche Products Limited

The sponsors have provided funding to enable this meeting to take place, and have a stand at the meeting but have had no input into the programme, selection of speakers, topics or awards, unless expressly stated.

Chairman: Dr Sunil Upadhyay Vice chairman: Dr Joji Joseph Secretary: Dr Mohammad Butt Treasurer: Mr Tapan Mahapatra
Scientific Committee:
Chairman: Mr Philip Turton Medical Oncology: Dr Penny O'Neill Clinical Oncology: Dr Amandeep Dhadda
Steering Committee: Dr Omar Din, Dr Rajeev Chitnis, Dr Shazza Rehman and Dr Narottam Thanvi

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