Motivational interviewing in female breast cancer survivors and its influence on step count and quality of life: A randomised crossover pilot study

Master of Research degree thesis

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Table of Abbreviations

Abbreviation	Definition
ACSM	American College of Sport and Medicine
AIMSS	Aromatase Inhibitor-Induced Musculoskeletal Symptoms
ANZCTR	Australian and New Zealand Clinical Trials Registry
BCS	Breast Cancer Specific Subscale
BMI	Body Mass Index
BREQ2	Behavioural Regulation In Exercise Questionnaire 2
CI	Confidence Interval
CINAHL	Cumulative Index to Nursing and Allied Health Literature
DALY	Disability Adjusted Life Years
DCIS	Ductal Carcinoma In Situ
DIG	Delayed Intervention Group
EB&TSE	Exercise Barrier and Task Self-Efficacy
EORTC QLQ-BR23	European Organisation for Research and Treatment of Cancer Breast Cancer-Specific Quality of Life Questionnaire 23
EWB	Emotional Well Being
FACIT-F	Functional Assessment of Chronic Illness Therapy-Fatigue
FACT-B	Functional Assessment of Cancer Therapy-Breast
FACT-G	Functional Assessment of Cancer Therapy-General
fBCS	Female Breast Cancer Survivors
FWB	Functional Well Being
GRADE	Grading of Recommendations, Assessment, Development and Evaluations
HADS	Hospital Anxiety and Depression Scale
HIV	Human Immunodeficiency Virus
HREC	Human Ethics Research Committee
IIG	Immediate Intervention Group
LGA	Local Government Area
MD	Mean Difference
MHHREC	Melbourne Health Human Research Ethics Committee
MI	Motivational Interview

MIAPA	Moderate Intensity Aerobic Physical Activity
Mins	Minutes
MVIAPA	Moderate to Vigorous Intensity Aerobic Physical Activity
NAC	Neo-Adjuvant Chemotherapy
NCCS	National Coalition for Cancer Survivors
NCI	National Cancer Institute
OCS	Office of Cancer Survivorship
PA	Physical Activity
PAPHIO	Physical Activity, Psychological Health and Immunological Outcomes
PICF	Patient Informed Consent Form
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
PWB	Physical Well Being
QLACS	Quality of Life in Adult Cancer Survivors
QoL	Quality of Life
RCT	Randomised Controlled Trial
RevMan	Review Manager
SCT	Social Cognitive Theory
SDT	Self Determination Theory
SES	Socio-Economic Status
SF-36	Short Form - 36
SMD	Standarised Mean Difference
SSA	Site Specific Assessment
SWB	Social/Family Well Being
TOI	Trial Outcome Index
TPB	Theory of Planned Behaviour
TTM	Trans-Theoretical Model
VIAPA	Vigorous Intensity Aerobic Physical Activity
WHO	World Health Organisation
yoa	Years Of Age

Abstract

Up to 70% of female breast cancer survivors (fBCS) fail to achieve recommended physical activity (PA) levels due to unique geographical, financial, emotional, aspirational and physical barriers that commonly as a result of diagnosis and treatment. This is problematic as it can lead to a poor health prognosis long-term. Therefore, research into motivational strategies to improve adherence to PA is pivotal. However, studies commonly incorporate complex interventions that are not always feasible nor founded in established behavioural change theories. The overall aim of this cross-over randomised pilot study was to investigate the effect of a psychological tool, motivational interviewing (MI), on levels of self-directed PA (as measured by step count), quality of life (QoL), self-efficacy and self-regulatory types. The behavioural change theory used to inform the design of the intervention, the self-determination theory (SDT), focuses on enhancing an individual's intrinsic motivators to change and developing a strong sense of autonomy over their behaviour. This pilot study is a component of a larger trial that will investigate the outcomes mentioned before in addition to immune function and psychological health. The results of this pilot study showed there was no effect of MI on any of the outcomes except for the breast cancer subscale within the QoL measure. There is great variation in these findings in comparison to other research, however, understanding the sources of the large heterogeneity found between studies is vital to finding the key moderators and help to inform future research. Limitations included the global COVID19 pandemic which impacted recruitment, health status and ability of the participants to engage in self-directed PA as well as the small sample size which means results should be interpreted with caution. Additional limitations were possible under-reporting of step count data from the FitBit monitor. Suggestions for future research are inclusion of other tools such as tailored print materials, additional self-reporting PA measures, a change of QoL measure, online support and group walking sessions. Additionally, increasing the number of MI sessions including an initial in-person session as well as other objective measures to ensure the fidelity of the MI. Finally, incorporating another behavioural framework to enhance social aspects of the self-directed PA components and intentional aspects of the intervention to facilitate greater changes as well as a two-armed RCT design rather than cross-over is recommended. This study has been invaluable in identifying key aspects of MI and study design to help inform future research that may produce evidence to ultimately improve the well-being of fBCS long-term.

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Student Declaration

I, Katherine Harkin, declare that the Master of Research thesis titled "Motivational interviewing in female breast cancer survivors and its influence on step count and quality of life: A randomised crossover pilot study" is no more than 50,000 words in length, including quotes and exclusive of figures, tables, appendices, references and footnotes. The thesis contains no material that has been submitted previously, in whole or in part, for the award of any other academic degree or diploma. Except where otherwise indicated, this thesis is my own work.

I have conducted this research in alignment with the Australian Code for the Responsible Conduct of Research and Victoria University's Higher Degree by Research Policy and Procedures.

[redacted] 20.10.22

Signature Date

Ethics Declaration

All research procedures reported in the thesis were approved by The Royal Melbourne Hospital Melbourne Health Human Research Ethics Committee (MHHREC), Reference Number: HREC/45268/MH-2018 (Appendix 1). The Western Health Office for Research (Appendix 2) and Victoria University Human Research Ethics Committee (Appendix 3) reviewed and approved amendments made to the originating MHHREC.

[redacted] 20.10.22

Signature Date

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Chapter 1.

Literature Review

Literature Review

Introduction

A significant proportion of female breast cancer survivors (fBCS) lack the motivation and self-efficacy to increase physical activity (PA) levels due to unique challenges and barriers that commonly occur as a result of diagnosis and treatment. Increasing levels of PA can help to improve long-term well-being in these cohorts of women. Therefore, finding strategies that can improve adherence to PA are important otherwise any other health benefits can be lost. Motivational interviewing (MI) is a psychological tool that is used to resolve an individual's state of ambivalence to change and has been shown in the literature to be effective in producing a change in behaviour. Additionally, MI is feasible given its: adaptability to many types of behavioural change models, acceptability by participants and ability to be applied in a remote setting. However, few studies have implemented this tool as an intervention with the aim of improving PA behaviour in fBCS and investigating if there is an influence on quality of life (QoL), self-efficacy and self-regulatory types. This study aims to investigate the effect of a MI intervention, designed using a framework (the self-determination theory) that enhances one's intrinsic motivation and autonomous control, on self-directed PA levels (as measured by step count), QoL, self-efficacy and self-regulatory types.

1.1. Epidemiology

1.1.1. Global trends of breast cancer

The International Agency for Research on Cancer (the specialised cancer agency of the World Health Organisation (WHO) reported that, in 2020, breast cancer was the most commonly diagnosed cancer and the fifth most common cause of death from all cancers [1]. The number of new cases diagnosed worldwide is predicted to increase from 2.26 million, diagnosed in 2020, to 3.19 million, estimated by 2040, which is an increase of 41% [1]. Incidence, mortality and survival rates can vary between countries and commonly reflect the healthcare disparities between nations. For example the five-year survival rates of breast cancer in lower-income countries can be as low as 35% [2] (Western sub-Saharan Africa) compared to 90% in higher-income countries such as the United States [3].

Breast cancer is one of the most burdensome cancers globally, with a total disease burden of 20.6 million Disability Adjusted Life Years (DALY)[1] in 2019 [4].
Combining the large disease burden and high prevalence worldwide, it is easy to see why this disease has a vast impact on individuals, communities and health systems.

1.1.2. Australian trends of breast cancer

In Australia, breast cancer is the most commonly diagnosed cancer nationwide –an estimated 19,866 in 2021 - and was projected to be the second most common cause of death in female cancers in 2021 – an estimated 3,102 deaths [5]. In addition, global research has revealed that more developed countries generally experience higher incidence rates, yet lower mortality rates related to breast cancer, as illustrated in Figure 1. This trend is evident in Australia and New Zealand which have one of the highest incidence rates of breast cancer worldwide (age-standardised rate of 95.5 per 100,000), yet one of the lowest mortality rates (age-standardised rate of 12.1 per 100,000) [6].

[1] DALY is a metric that is used to quantify and thus compare the burden of various diseases and is comprised of fatal (years of life lost) and non-fatal (years lived with disability). One DALY is equal to one year of a normal 'healthy' life lost due to impact of living with effects of disease or premature death.

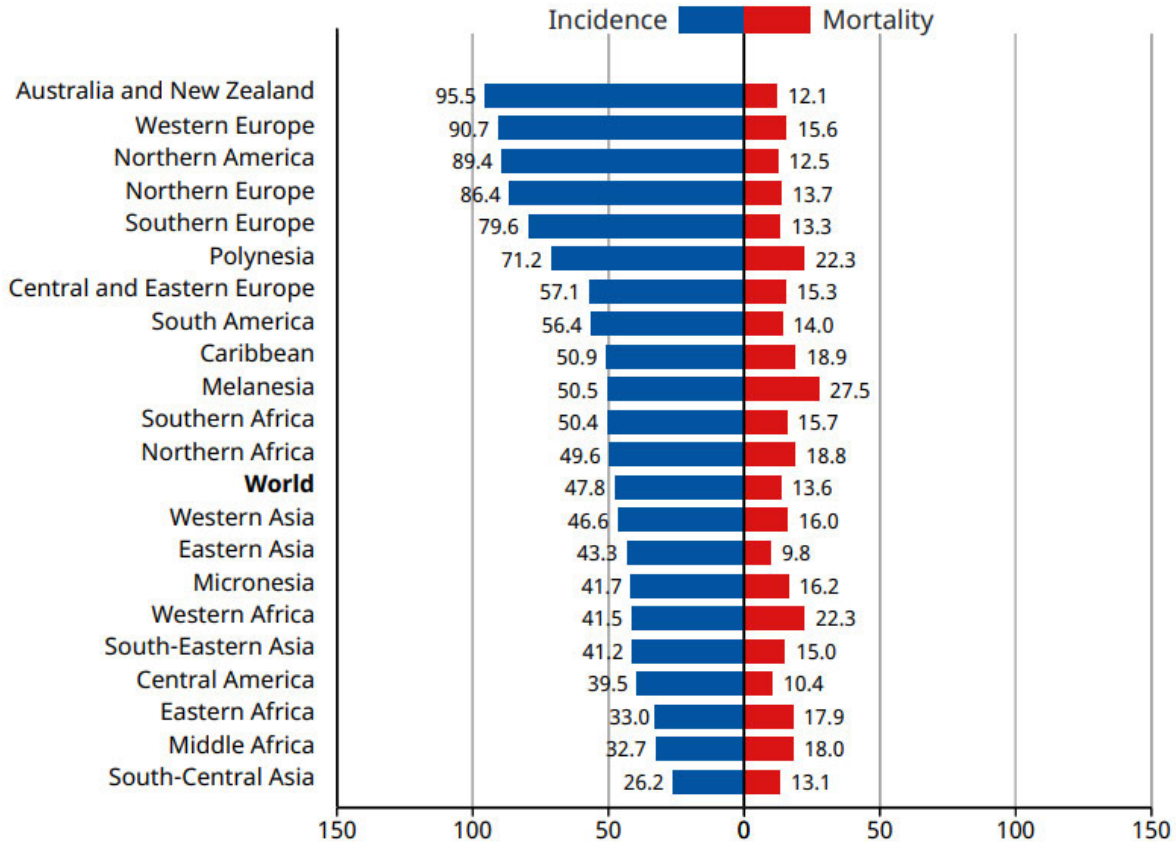

Figure 1. Incidence and Mortality Age-Standardised Rates (rate per 100,000) according to global regions for Female Breast Cancer in 2020.[2]

Literature suggests there are three categories of contributing factors that can help explain these discrepancies between nations [2, 3, 6]:

1) Hormonal risk factors – such as later menopausal age, earlier menarche age, older age at first birth, smaller numbers of children, decreased rates of breastfeeding, higher oral contraceptive medication usage and hormone replacement therapy usage rates;
2) Lifestyle risk factors such as higher alcohol intake, increased body mass index (BMI) and decreased PA levels; and
3) Health services - more extensive mammography screening resulting in higher detection rates and higher quality treatment options

[2] Reprinted with permission from; 'Breast – Fact Sheet, Source Globocan 2020'. Global Cancer Observatory, International Agency for Research on Cancer, World Health Organisation. Webpage: https://gco.iarc.fr/. Accessed Feb, 2022.

According to the most recent reporting of breast cancer data in Australia[3], 91.5% of females diagnosed with breast cancer, survived five years or more from the date of diagnosis, and 86% survived more than 10 years. [7].

Using the most recent data available, in 2019, 3,212 women died from breast cancer in Australia, the mean age was 71.2 years of age (yoa), and the average age of diagnosis was 62 yoa [7]. Similar to the previously mentioned global burden levels, breast cancer was the highest cause of cancer burden in Australia, in 2019, reporting a DALY of 69,690 (p50) [8]. Therefore, research that addresses issues within the survivorship stage of fBCS is particularly pertinent within the Australian population given its prevalence and burden. QoL is a valuable outcome measure used in many studies as it quantifies the subjective wellbeing of a patient which can greatly influence patient-centred care decisions by health professionals.

1.2. Quality of life

1.2.1. Evolution of the 'Quality of Life' concept

Historically, an individual's health status was primarily determined using objective biological measurements such as blood insulin levels, height and weight. In contrast, population health was defined by mortality and morbidity statistics, without any consideration of the 'quality' of one's health status.

However, in 1948 the WHO defined health in a different context: *"a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity"* (p.3) [9]. This definition recognises an individual's health status is influenced by more than just their biological makeup or disease status. Thus, researchers sought to design an appropriate measuring tool to assess one's health status, reflecting the aspects stated in the 1948 definition. Hence the QoL construct was developed.

QoL is the commonly used term that encapsulates the subjective nature of one's own perceived health status. Additionally, it recognises the multifactorial framework of biological, social and psychological aspects that underpin that perception. The WHO more recently define QoL as: *"an individual's perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns. It is a broad ranging concept affected in a complex way by the*

[3] Based on data between 2013-2017

person's physical health, psychological state, personal beliefs, social relationships and their relationship to salient features of their environment." (pg.4) [9].

1.2.2. Methods of measuring Quality of Life

In research, subjective data is traditionally gathered via qualitative methods such as interviews. However, questionnaires are useful when quantifying and analysing subjective data from large sample sizes [10]. In 1995, the WHO developed a QoL questionnaire (WHOQOL-100) that encompassed the three domains of QoL as outlined in both definitions above. Additionally, questions were generic enough to be transferrable to various cultures worldwide, enabling researchers to quantify an individual's QoL and, more broadly, larger communities globally [11].

Since its inception, there have been many versions of the original WHOQOL-100. The shortened version (WHOQOL-BREF) and language-specific versions, enable the questionnaire to be suitable for different nationalities and cultures. Additionally there are disease-specific versions such as the WHOQOL-HIV, which was developed to measure the QoL in Human Immunodeficiency Virus (HIV) patients by including questions that are specifically common to this cohort, such as: HIV status, treatment history and route of infection [12].

In cancer research, using disease-specific questionnaires is imperative to accurately quantify an individual's wellbeing. This becomes an important factor for clinicians when deciding upon treatment plans for individuals to ensure patient-centred care. Given the prevalence and longevity of this disease, investigating QoL outcomes in response to a specific intervention has become a particular focus for breast cancer researchers, particularly in the last decade. Two researchers from Iran recently reviewed the literature for QoL in breast cancer patients (survivors and active) in the decade from 2008-2018 [13] compared to 1974-2007 [14]. They found three times more literature in the form of systematic reviews (82 reviews) published in the last decade than there were in the preceding three decades (29 reviews). However, all of the reviews were in either patients receiving active care or in a cohort of fBCS and active patients but none contained fBCS only thus highlighting a gap in the literature for QoL in fBCS.

Such demand for quantitative measures to assess QoL has led to the development of more specific, reliable and accessible questionnaires. Moreover, many of these questionnaires have

progressed through various updates to become more specific to certain demographics of particular cohorts. An American observational study by Sohl et al, identified that some questionnaires such as the Short Form 36-item[4] (SF-36), were too generic and non-disease specific. However, whilst other measures such as the European Organisation for Research and Treatment of Cancer Breast Cancer-Specific Quality of Life Questionnaire (EORTC QLQ-BR23) and the Functional Assessment of Cancer Therapy-Breast (FACT-B) are breast cancer specific, they still contain questions that are relevant to effects of primary treatment (e.g. nausea and loss of appetite), which may not be applicable in the survivor cohort. The authors suggested that topics more relevant to the survivorship period, such as financial challenges, fear of recurrence and cognitive decline, were not covered thus rendering results from such questionnaires as not truly reflective of the QoL status during survivorship phases [15]. A literature review by Van Leeuwen et al [16], examined quantitative and qualitative studies for health-related QoL issues in cancer survivor cohorts. The results concurred with the study by Sohl et al [15] of the non-survivor-specific nature of the EORTC QLQ-BR23 and the FACT-B, however also highlighted that certain items that covered topics such as insomnia and fatigue can be relevant in both the active and survivor cohort groups, as they can often be latent adverse side effects from treatment. Van Leeuwen et al [16] also claim that the change-over point at which the common short term effects from treatment have worn off and the long term effects are more prominent is around one-year post-primary treatment. Sohl et al [15] also highlighted the importance of the 'survivorship transition period' from 1-5 year post-diagnosis as patients leave regular health care and reintegrate into a new 'life-normal'. They suggest the Quality of Life in Adult Cancer Survivors (QLACS) scale is similar to the FACT-B cancer-specific questions, covering all physical, psychological and social aspects. At the same time, the QLACS also investigated topics such as fear of recurrence and appearance concerns, which might be pertinent to this transition to the survivorship period.

Many studies that measure health-related outcomes include individual surveys that assess a number of components within the QoL construct and the use of an overall QoL survey. For example, a cross-sectional study of 356 fBCS (and a control group of 252 non-cancer women) used the QLACS survey to measure QoL and the Hospital Anxiety and Depression Scale (HADS) to measure mental health status. From the QoL survey, they found that most

[4] The term 'item' (when used within reference to questionnaires) is interchangeable with the term 'question' from this point onwards within this thesis.

domains were significantly worse (compared to controls) including; cognitive function, sexual function, fatigue, negative feelings and anxiety [17]. However, the mental health survey showed there was only minor higher probability of anxiety (yet not significantly) but not depression when compared to controls. Thus the question may arise as to why use two surveys to measure similar domains and which is more accurate? An earlier review paper on the use of QoL measures suggests that whilst specific adverse health outcomes can be present for a person such as feelings of anxiety, it may not impact on their ability to socially interact or be physically functional. Conversely (as seen in the previously mentioned study), health outcomes may not be affected but the overall QoL can be [18]. Therefore, studies need to incorporate QoL surveys to help contextualise the impact interventions may have on the overall health and well-being of cancer survivors.

1.2.3. Quality of life in female breast cancer survivors

Despite having lower disease-related mortality than other cancers, fBCS report many long-term adverse health effects resulting from the disease or treatment which affects their QoL [19]. These adverse effects commonly include: insomnia, infertility, fatigue, nausea, pain, weight gain, fear of cancer recurrence, relationship problems, financial challenges, depression, sexual dysfunction and cancer-related cognitive impairments [16, 20, 21]. Furthermore, many of these adverse long-term effects or symptoms, can have causal relationships between one another and are not always a direct result of diagnosis and treatment [22]. Symptoms such as fatigue, insomnia, pain and depression can be physiologically and psychologically interrelated and are therefore defined as a ‘symptom cluster’ [23].

Many reviews have highlighted the importance of having QoL as outcome measures within cancer studies which can be translated into clinical settings [24, 25]. The United States has been the leader in initiating institutional change at a national level for awareness of cancer survivor issues. In 1986, the National Coalition for Cancer Survivorship (NCCS) was established, which advocated for more dedicated care for survivors and their communities in all stages during the cancer continuum from diagnosis to death and beyond [26]. A decade later, the Office of Cancer Survivorship (OCS) at the National Cancer Institute (NCI) was created with a primary focus to facilitate and promote research and awareness around cancer survivorship issues for academics, clinicians, patients and their wider communities [26].

These institutions were fundamental in informing the landmark report published in 2006 by the Institute of Medicine, and National Research Council titled: *'From Cancer Patient to Cancer Survivor – Lost in Translation'.* The report detailed 10 recommendations that highlighted the importance of cancer survivorship care immediately following the completion of active treatment [27]. Many nations worldwide implement survivorship care programs, including the United States, Australia, United Kingdom, Canada, Netherlands and New Zealand [28]. However, in 2019, a National Cancer Institute Cancer Survivorship workshop of researchers, survivors, institutions and clinicians identified six significant gaps in evidence that underpin many of these survivorship care plan policies that needed to be addressed. Two of the six areas identified were gaps in evidence relating to the management of chronic adverse QoL issues (physical, psychological and social) in cancer survivors, specifically those from diverse cohorts [29]. To bridge this gap in evidence, it is important to understand the factors influencing baseline QoL levels in these cohorts.

1.2.4. Demographic factors that influence the quality of life in female breast cancer survivors

There are many demographic factors that can influence the baseline QoL in fBCS. It is important to understand these factors as they may influence outcomes in studies and help contextualise the true efficacy of interventions. These factors can also form many barriers to behavioural change which will be discussed later within this chapter.

1.2.4.1. Type of cancer treatment received

Breast cancer treatment plans consider biological components such as type and stage as well as the patient's needs and preferences. According to the principle of 'patient-centred care', treating oncologists must weigh up the effectiveness of any given treatment with the impact that it might potentially have on the patient's long-term QoL. For example, the decision-making process in considering fertility conserving treatment for a 20 yoa patient compared to a 75 yoa post-menopausal patient, would be very different [30].

Treatment options for breast cancer have changed due to advancements in surgical techniques, radiological technology, chemotherapy and hormonal therapies [31]. In addition, more recent changes in combinations and sequencing of these treatments, early detection and

genetic profiling techniques allow for a more targeted approach resulting in improved prognosis and QoL outcomes [32]. An example of this is using neo-adjuvant chemotherapy (NAC), which is the use of chemotherapy prior to primary treatment such as surgery. Traditionally, NAC was reserved for more advanced and aggressive tumours; however, more recently, it has become the preferred universal protocol for certain types of early operable breast cancers [32]. Long-term survival rates for having NAC versus adjuvant chemotherapy (following surgery) for early operable breast cancer are not dissimilar [33]. However, advantages for NAC are seen in more positive, longer-term, QoL outcomes due to the reduced need for radical mastectomy or axillary lymph node dissection - thus lowering the chance of lymphedema occurrence and allowing more options for reconstructive surgery [34].

Surgery:

A recent systematic review and meta-analysis [35] compared the health-related QoL in groups of women who had received either breast-conserving surgery (lumpectomy), mastectomy or breast reconstructive surgery. The authors found that although there was a high level of heterogeneity in the studies, breast-conserving surgery and breast-reconstructive surgery produced similar improvements in health-related QoL outcomes compared to mastectomy alone. The main domains of QoL which showed improvement were body image, sexual, social and physical health, however, this greatly varied between age groups of patients [35]. The authors reported that some studies found younger survivors place more concern over sexual health and body image components. In contrast, older survivors who underwent reconstructive surgery had a higher incidence of post-surgical complications, impacting their QoL long term. A systematic review on factors impacting QoL in women who had undergone post-mastectomy breast reconstruction surgery found that patient involvement in the treatment decisions reduces the incidence of decisional regret post-surgery, thus positively influencing QoL [36].

Radiation:

Radiotherapy treatment is commonly used as an adjunct to other modalities such as surgery [37], however, its impact on patients' QoL is not well reported. For example, a systematic review that investigated the reporting of health-related QoL outcomes in trials of breast cancer patients receiving radiotherapy found that only 20.8% of randomised controlled trials (RCT) involving breast cancer patients who received radiotherapy had health-related QoL outcomes as endpoints [38].

Other studies report that long-term adverse effects of radiotherapy treatment including pneumonitis, cardiotoxicity and recurring malignancy (radiotherapy induced); while the most common types of secondary malignancies for primary breast cancer are lung, leukemia and the opposite breast [39].

Acute effects of radiation therapy commonly destroy the stem cell layer of many protective linings of the body, including oral mucosa, intestinal lining and the integumentary system, which generally will recover. However, in the presence of other cytotoxic treatments such as chemotherapy, these cellular breakdowns can become permanent and lead to organ failure, which further impacts health and QoL such as fatigue, reduced respiratory function and reduced immune capacity [39].

Chemotherapy:

Certain chemotherapy treatments have gonadotoxic effects that can cause infertility issues in younger pre-menopausal patients [40]. Alternative medical procedures such as ovarian tissue preservation [41] and ovarian suppression medications [42] have shown to be feasible in increasing fertility post-treatment. However, younger survivors facing potential chemotherapy-induced menopause (and thus potential fertility challenges) report higher emotional and psychological distress [21]. Fatigue is one of the most common and ongoing adverse effects of chemotherapy treatment. It is reported as occurring well into the survivorship period by longitudinal studies [43], qualitative studies [44] and systematic reviews [45].

'Chemo brain' refers to the cognitive decline known to occur due to chemotherapy treatment [13, 20, 46]. This effect is described in qualitative studies by patients as: "fogginess, forgetfulness and the tendency to go blank" (E30) [47]. Participants within this same study reported how this decline impacted their overall QoL, including feelings of being stigmatised. Studies using functional technology have identified brain changes in breast cancer patients - that have been exposed to chemotherapy, which potentially explain this cognitive decline [48]. A recent observational study found that older (≥60yoa) fBCS who had received chemotherapy experienced more burdensome long-term (36 months post-treatment) adverse effects impacting QoL compared to those who had received hormonal therapy [49].

Hormonal therapy

Hormonal therapy within the fBCS cohort mainly consists of either Tamoxifen or Aromatase Inhibitors (AI) which are used to block oestrogen production. These medications are commonly prescribed for long-term use (up to 10 years post-primary treatment) to help prevent breast cancer recurrence [50]. Multiple joint pain and stiffness, referred to as Aromatase Inhibitor-Induced Musculoskeletal Symptoms (AIMSS), is one of the commonly reported adverse effects of patients receiving AI [51]. The presence of AIMSS is responsible for high levels of non-compliance (between 25% and 50% of patients) thus leading to a high risk of cancer recurrence [52]. Although these hormonal treatments are associated with better prognostic outcomes, they have significant side effects that negatively impact QoL [52]. Other adverse effects reported by fBCS receiving Tamoxifen and AI are hot flushes, increased weight, drop in libido, mood swings, vaginal dryness and insomnia [53].

1.2.4.2. Point within the cancer continuum

The term 'cancer continuum' refers to the time period from cancer diagnosis through active treatment phase into either the terminal or survivorship phase. Just as an individual's QoL status can change during various stages of their life, a cancer patients' QoL status may vary depending on where they are within the cancer continuum (diagnosis, active treatment, survivorship period). In addition, as outlined previously, common effects of treatment that impact QoL can vary according to the mode of treatment. However, it is important to consider which effects persist or change into the survivorship period.

A 10-year longitudinal population-based study [54] looking at QoL (as measured by the EORTC QLQ/B23) in fBCS showed impairments of other aspects of QoL exacerbated during the 5-10 year survivorship stage, including; social and physical functioning, pain and financial difficulties. The researchers postulated that this was possibly due to the normal aging process or lesser health support during the five+ year stage of survivorship [54]. A study that measured the QoL of fBCS at various time-points from diagnosis to five-years post-diagnosis stated whilst most aspects of QoL were worse during the active treatment phase (both compared to baseline and age-matched non-cancer controls), most of these QoL factors improved by the five year time-point and were equal to, or sometimes better than, non-cancer controls. The authors proposed that this could be due to a 'recalibration' of their perception of QoL components [46]. Sleep and cognitive issues were the two symptoms found to be significantly worse at the five year time-point compared to baseline [46].

Interestingly, fatigue was the most common adverse symptom reported within the global QoL score. During linear regression analysis, fatigue alone accounted for 29% of the variance in QoL scores [46]. This suggests that fatigue is perhaps a key factor in perpetuating long-term complaints via the 'symptom cluster' concept described earlier. However, all of the women within the non-control group had participated in a 12-week exercise intervention either during or immediately following active treatment, suggesting these women were more health literate or proactive in combatting adverse effects of treatment and may not be representative of the overall fBCS cohort [46].

This literature highlights the importance of ongoing adverse issues that can continue through into the longer-term survivorship period, and thus the importance of research into interventions that can alleviate them.

1.2.4.3. Age at time of cancer diagnosis

The age of the cancer patient at the point of diagnosis has significant influence on QoL during the survivorship period [16, 55]. A systematic review in 2012 reviewed cross-sectional, longitudinal follow-up and intervention studies [21]. The authors found that younger fBCS (defined as <55 years of age) suffered from depression, fertility concerns, menopausal symptoms and fear of recurrence of cancer compared to both older fBCS and non-cancer age-matched women [21]. These findings were mirrored in another systematic review [16]. The reasoning postulated by the authors was that, generally, younger survivors face different psychosocial challenges such as family planning, future capacity to work and commencing new romantic relationships, whereas older cancer survivors have more life experience, enabling them to be more resilient to adverse effects [16]. Contrary to these findings, a large cohort study (n=303) in Austria found that younger age in fBCS was a predictor of improved physical and psychological QoL outcomes. However, the authors acknowledged a potential selection bias given the cohort was generally healthy with an average BMI within normal limits (24.2kg/m^2), within a partnership (83%), educated (62.6 % completed high school) and physically active (79% exercised regularly) [56] – all predictors of improved QoL [57].

In a study that investigated the QoL in older fBCS (≥60yoa), it was reported that cognitive decline, sleep issues, anxiety and neuropathy were significantly worse compared to age-matched controls over the 36month period following diagnosis [49]. These longer-term complaints of cognitive decline and sleep issues are consistent with another study that

measured QoL outcomes in fBCS at a five-year follow-up time-point, with comparisons to age-matched controls, where the average age of the cohort was 54 yoa [46]. It has been argued that these issues are perhaps more related to menopausal changes or incidence of co-morbidities that are normal age-related [58]. However, using healthy age-matched controls in these studies and other literature, provide evidence of a higher incidence of co-morbidities in older cancer survivors [58] compared to healthy controls. The evidence thus far would suggest that, overall, both younger and older cancer survivors face impacts to long term QoL, albeit in different domains.

Understanding the influence of demographic factors on QoL can help to contextualise outcomes in research and help to identify which subgroups of fBCS are most at-risk for poorer QoL. This will also help to justify the need for more focused research and help inform the study design of future research.

1.3. Physical activity effect on quality of life in female breast cancer survivors

Demographic factors influence QoL in fBCS, as outlined previously, which correlate with potential mediating factors such as the success or limitation of exercise interventions. If a baseline measurement of QoL is already low, there is a greater ability for the magnitude of improvement compared to a higher baseline QoL where there is limited improvement capability - known as the 'ceiling effect' [59].

1.3.1 Physical activity recommendations

The WHO 2020 PA Guidelines for adults [60] are outlined in Figure 2. These recommendations are based upon high-quality evidence reported, by the *PA Guidelines Advisory Committee* in their 2018 report [61] shows the positive influence PA levels have on the various impacts of a healthy adult's QoL. High-quality evidence indicates that regular Moderate-to-Vigorous Intensity Aerobic PA (MVIAPA) reduces the risk of breast cancer. In addition, there is evidence that regular Moderate-Intensity Aerobic PA (MIAPA) following breast cancer diagnosis, reduces the risk of breast-cancer specific and all-cause mortality, in fBCS. Interestingly, within these 2020 guidelines, additional recommendations for reducing

sedentary behaviour has been underpinned by further evidence produced by the same committee since their previous recommendations to the WHO in 2008 (which is the foundation for the 2010 WHO Guidelines) [62]. The 2020 recommendations for reduction in sedentary behaviour is best described in Part A of the executive summary: *"For any given increase in moderate-to-vigorous physical activity, the relative gain in benefits is greater for individuals who are below the current public health target range than for individuals already within the physical activity target range. For individuals below the target range, substantial reductions in risk are available with relatively small increases in moderate-intensity physical activity."* (pg. A-5) [61].

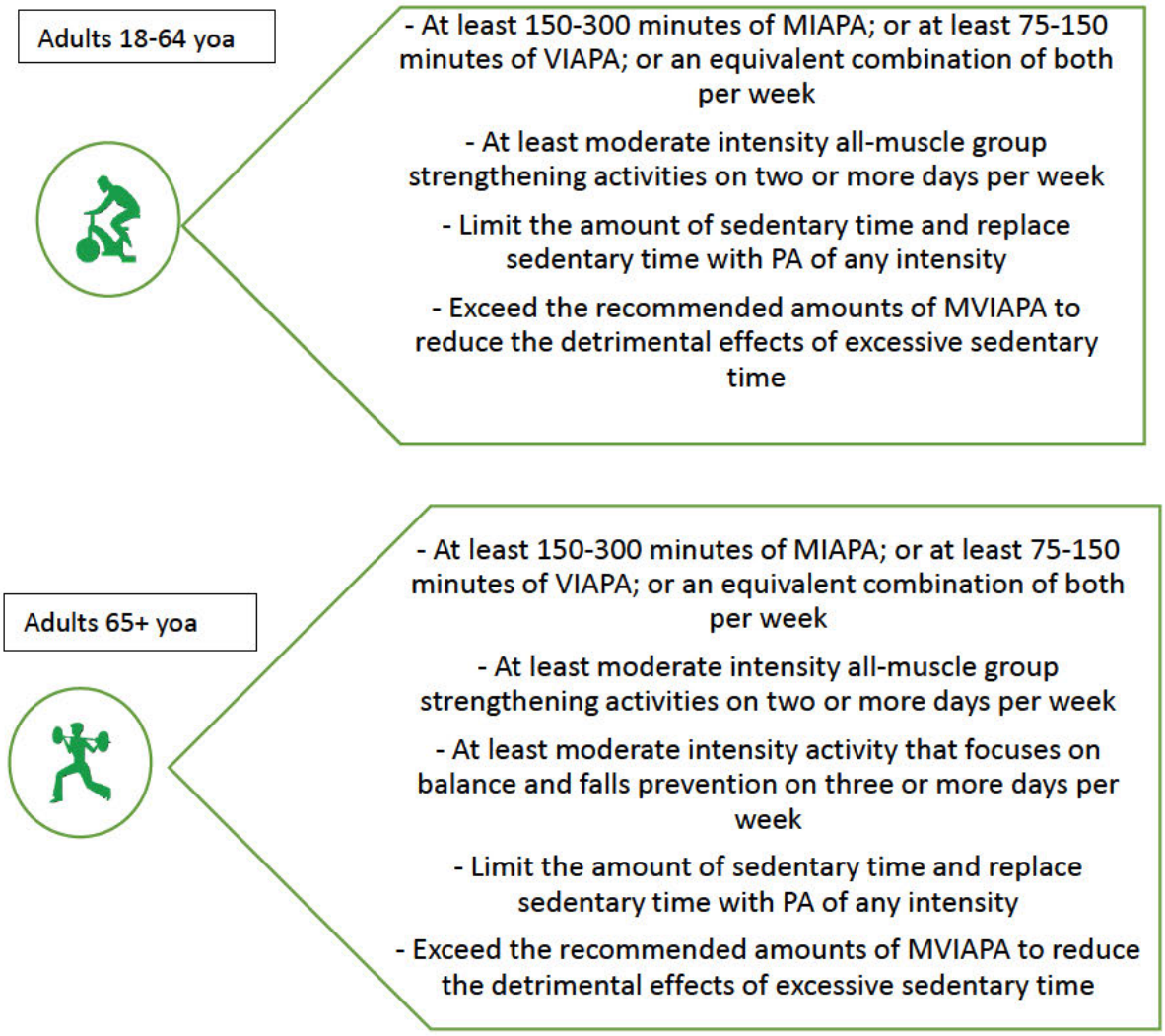

Figure 2. Physical Activity Recommendations. The 2020 World Health Organisation (WHO) recommendations for sedentary time and physical activity, intensity and duration for adults 18-64 years and older adults 65 yoa and above[5].
MIAPA: Moderate Intensity Aerobic Physical Activity, VIAPA: Vigorous Intensity Aerobic Physical Activity, PA: Physical Activity

Furthermore, a 2018 roundtable amalgamated evidence from various academics, researchers and clinicians to update the previous 2010 PA guidelines specifically for cancer survivors [63]. The cancer survivor guidelines indicated 'strong evidence' to support that a combined moderate-intensity aerobic and resistance exercise program performed at least 2-3 times per week for at least 12 weeks resulted in significant improvements on health-related QoL in

[5] Translated version from; WHO Guidelines on Physical Activity and Sedentary Behaviour. Geneva: World Health Organization; 2020. Licence: CC BY-NC-SA 3.0 IGO. This translation was not created by the World Health Organization (WHO). WHO is not responsible for the content or accuracy of this translation. The original English edition shall be the binding and authentic edition.

cancer patients during both active and survivorship stages [63]. However, within these guidelines, the magnitude of improvement was dependent upon certain aspects such as: the baseline demographics of the cohort and the characteristics of the PA intervention.

This literature highlights that in order to achieve a significant improvement in QoL, it is important to consider the previous PA levels of the individual before setting goals. By separating these variables within studies and seeing which components have more significant impacts on QoL (and, later in this chapter, impacts on PA adherence), future study designs can be tailored to enhance optimal outcomes.

1.3.2. Factors that influence quality of life outcomes in physical activity intervention studies

Many systematic reviews and meta-analyses have shown that PA interventions mostly produce a small to moderate significant improvement in QoL in fBCS [64-67]. Many of the variables that have been used to explain these results include baseline demographics such as type of cancer treatment received, point within the cancer continuum and age at time of cancer diagnosis (as explained previously). However, there are also variables within the exercise intervention that have been identified to influence QoL outcomes in cancer cohorts [67]. These intervention variables include Frequency (and duration) of exercise sessions, Intensity of exercise, Type of exercise session and Timing of exercise intervention i.e. point within the cancer continuum – commonly referred to as the FITT components, and will be expanded upon here.

1.3.2.1. Frequency and duration of physical activity intervention

A meta-analysis investigated all the different exercise intervention characteristics to determine which had the most significant impact on QoL in fBCS. It was noted that the 'time in session' was the most impactful component of the exercise intervention with the greatest effect size seen in those studies that involved >60-90 minutes (mins) duration per session [68]. This finding was from a total of 18 studies, of which did not contain a high risk of selection, adherence, attrition or reporting bias which suggests a higher quality of evidence.

1.3.2.2. Intensity of physical activity intervention

Various studies, reviews and meta-analyses show that both moderate-intensity and moderate to vigorous-intensity exercise have significant improvements in QoL in cancer survivors compared to control groups [67, 69, 70]. When comparing these levels of intensity, there is no substantial or consistent evidence to show one is more impactful than the other [68]. However, a meta-analysis of exercise characteristics that positively impacts QoL in mixed cancer survivors showed that moderate-intensity aerobic over a longer duration (26 weeks) had a greater effect rather than high intensity aerobic over a shorter duration (8 weeks) [71]. However, contrary to this, evidence shows that higher intensity exercise has a greater impact on individual QoL components such as anxiety, depression and fatigue in mixed cancer survivors [63].

1.3.2.3. Type of physical activity intervention

A randomised controlled trial by Odynets et al. [72] compared three groups: yoga, Pilates and water-based exercise interventions over 12 months on QoL (as measured by FACT-B) in breast cancer patients following surgery. All three groups showed a significant improvement in QoL, with the yoga intervention having a greater improvement in the social/family well-being aspects and the water-based having a greater improvement in emotional well-being and breast cancer-specific symptoms. One could postulate that the social aspect of group exercise could have explained the more significant results in the yoga and water-based exercises however all groups were conducted in a supervised group setting. Therefore the explanation of the difference in QoL outcomes in the Odynets et al study is more likely to be due to the type rather than the mode (group, supervised, in-person) of the exercise intervention. However, a systematic review and meta-analysis concluded that yoga is as effective as other interventions for improving QoL, however not any more effective than others [73].

Group-based exercise interventions have shown to be pivotal in producing significant improvements in QoL outcomes in fBCS [67, 68]. A qualitative study showed that the social environment produced via group-based exercises classes influenced fBCS reported improvement in the social domains of QoL [74].

Supervision of exercise interventions are preferred aspects of exercise interventions to help facilitate adherence and QoL outcomes within recommendations [63] and clinical practice

guidelines [75]. However, more specific meta-analyses outline that supervised interventions is not necessarily more impactful on QoL of cancer survivors than unsupervised [71], especially when the unsupervised (or self-directed) exercise intervention is supplemented with social support (such as with friends or family) or motivational tools [76]. In contrast, a large meta-analysis of 66 RCTs involving 6509 cancer survivors, found that supervised exercise interventions were responsible for the most significant beneficial improvements in QoL compared to unsupervised [67]. But when this meta-analysis did a sensitivity analysis on fBCS, only they found the effect sizes of supervised versus unsupervised exercise interventions on QoL were comparable. The authors rationalized this finding due to the larger heterogeneity of the intervention types in the breast cancer RCT's, which may explain the variation in outcomes.

A meta-analysis of RCT showed minor, but not significant, improvements of health-related QoL in breast cancer patients (post-primary treatment of surgery) following a resistance exercise intervention [77]. The authors stated that these improvements were still clinically important and not necessarily a reflection of the intervention. Rather, the majority of studies showed higher baseline health-related QoL scores, hence the presence of a 'ceiling effect' [77]. Additionally the authors noticed that there was almost a halving of odds of breast cancer-related lymphedema incidence or exacerbation if patients undertook a resistance exercise program following surgery. Similarly, a RCT used a resistance exercise intervention over 16 weeks in a group of obese and overweight fBCS (n=100) and found not only was there a statistically significant improvement in QoL, but it was sustained at 3 months post intervention [78]. This large magnitude of improvement was reported to be, in part, due to lower baseline QoL levels (hence a 'floor effect' which is opposite to a 'ceiling effect') in the obese and overweight fBCS participants. More recently, an extensive systematic review, in 2020, of all literature regarding resistance training in fBCS made an interesting point that of the initial 133 publications sourced (of which 47 were reviews and meta-analysis), more than half of these were derived from only 16 trials of which only two had large sample sizes over 240 participants (most had less than 80 participants) [79]. Nonetheless, the review produced quality evidence that resistance training produces a significant improvement on QoL in fBCS but there was no comparison to forms of exercise hence it could not be concluded that resistance type exercise is superior to others.

1.3.2.4. Timing of physical activity intervention

There is much discussion within the literature as to when is the most opportune time to introduce an exercise intervention for maximum health outcomes and sustainable PA levels to be established. As highlighted previously, prior levels of PA can be strong predictors of continued PA during and after treatment [80]. However, it has been suggested that immediately following a cancer diagnosis can be a pivotal time where patients are potentially highly motivated to engage in PA (irrespective of previous PA levels) to maximize their health outcomes of treatment and ongoing prognosis [81]. A pilot study investigated whether the timing of an exercise intervention in relation to the cessation of primary treatment had any bearing on QoL outcomes. The study consisted of a 12-week supervised combined aerobic and resistance exercise intervention implemented in groups of fBCS who had received their primary treatment either less than one year or more than one year prior to the exercise intervention. Whilst there were significant (moderate) improvements for both groups between baseline and post-intervention, the earlier stage of survivorship group (less than one year) had a greater improvement in the emotional well-being domain post-intervention [82]. However, there was no control group nor randomization of participants, hence no causative links or significance can be deducted from these results.

This literature shows that the efficacy of an exercise intervention is not necessarily dependent upon FITT factors. Rather, exercise interventions should be tailored to the needs and capabilities of the cancer cohort to produce significant change in QoL outcomes. These sentiments are mirrored in a systematic review of home-based PA programs for fBCS which found that they are just as effective at producing significant improvements in QoL as more structured and supervised programs [83]. Furthermore, certain cohorts of women, such as African Americans, found home-based programs more convenient and affordable and thus more achievable than other more complex exercise programs [83]. Therefore, awareness of the barriers and facilitators relevant to PA in certain cancer cohorts means tailored interventions can be designed to maximize adherence otherwise improvements to QoL can be lost.

1.4. Physical activity adherence levels in female breast cancer survivors

Thus far, the literature has indicated the beneficial impact that PA has on various health outcomes in fBCS. However, up to 70% of fBCS are not meeting the minimum guidelines for PA [56, 84, 85], which are 150minutes of MVIAPA per week, as recommended by the American College of Sport Medicine (ACSM) for cancer survivors [63] and the Breast Cancer Network of Australia [86]. These figures are concerning, particularly given the literature stating the potential consequences of not meeting these PA recommendations. A recent large prospective study of 1340 American breast cancer patients revealed that patients that are physically active for at least 150 minutes per week at moderate intensity at two years post-treatment (survivorship phase) have a 55% lower risk for cancer recurrence and 68% lower risk of all-cause mortality [87]. However, contrary to this claim for lowering the risk of cancer recurrence, the 2018 *Physical Activity Guidelines Advisory Committee* report stated that: *"Insufficient evidence is available to determine whether physical activity after diagnosis is associated with risk of breast cancer recurrence or second primary breast cancer."* (pg. F10-12) [61].

In a WHO study of over 1.9 million participants from 168 countries worldwide, an average of 32% of adult women do not meet the recommended guidelines for PA [88]. Hence, fBCS are considered 'at-risk' of several modifiable health concerns, given they are, generally, twice as physically inactive as their healthy counterparts.

Researchers generally engage in either subjective or objective methods of reporting PA levels within a particular cohort. It is important to understand the inherent bias that can occur during reporting of PA levels as they can lead to inaccurate results and thus misinterpretation of results. Subjective methods include self-reporting logs by participants, can be prone to reporting bias and can lead to either over or under-reporting. Over estimation of PA levels can occur due to the 'Hawthorne effect' phenomenon. This effect occurs when participants exaggerate their answers due to being observed (both in real-time such as supervised exercise sessions or asynchronously such as responses within a written survey) to impress the researcher or person of contact [89]. On the other hand, under-reporting can occur as participants may not know the definition of PA and may not include incidental activity such as domestic duties within their calculations [90]. Objective measures such as reporting from supervising persons, digital trackers and mobile devices are less prone to error [91, 92].

However, these latter methods have limitations, including digital illiteracy and reduced or intermittent wear time, particularly prevalent in older or intellectually challenged cohorts [92]. The placement of the monitor is also a factor in inaccurate reporting of actual PA levels, as in the case of arm wrist bands that don't record step count unless there is sufficient movement of the arms [93, 94].

Furthermore, digital trackers can be a motivational tool in studies by giving real-time feedback to individuals about their progress [91, 95]. Interestingly, a meta-analysis of 138 RCTs into the characteristics of successful promotion (as measured by adherence) of exercise interventions reported no difference in study results that reported PA by objective or self-reported measures [96]. This analysis was conducted on studies involving survivors of many cancer types; however, within this same report, the authors state that cancer type was also not an influential factor in the magnitude of intervention effectiveness.

A RCT (n=100) used an entirely supervised combined aerobic and resistance training intervention over 16 weeks in obese and overweight postmenopausal fBCS with higher than normally expected improvements in QoL and session attendance (96%) [78]. The authors postulated that it may have been due to the supervised component that ensured participants' safety, encouragement and feedback. Interestingly, the supervised sessions were one-on-one; hence the social aspect of training with others was not present, but one could argue the social aspect between the individual and the health professional could have had a motivational influence on attendance. Additionally, the flexible timing of sessions (5am-8pm on seven days per week) and financial reimbursement for transportation options to and from the sessions may have been contributing factors. Several meta-analyses [67, 70, 96] concur with the finding that a supervised exercise intervention is more effective in improving adherence to PA than unsupervised exercise interventions. Mediators of the beneficial influence of supervised interventions are believed to be associated with socialization, whether related to supervisors' feedback and encouragement or the social aspect of group exercise programs. Both are found to increase health outcomes, such as QoL [97].

Improving adherence to PA levels in fBCS requires understanding of the unique barriers and facilitators that these at-risk women face.

1.4.1. Barriers to physical activity for female breast cancer survivors

When considering how to categorise the barriers to PA in fBCS, it can be helpful to consider the 'ecological model', which recognizes the factors that interact with an individual in their surroundings that can influence their behaviour [98]. These have been grouped by the NIH as; individual, intrapersonal, organisational, community and policy [99]. See Table 1 for a summary of barriers to PA according to the 'ecological model' components.

Table 1. Barriers to physical activity in female breast cancer survivors

Categories	Factors
Individual	Lack of time [100-102] Pain, obesity and depression [101-105] Lack of energy [44, 100, 102, 104, 106] Ageing process [101] Bra discomfort [107] Fear of injury [44, 101] Lack of discipline/motivation [44, 100, 101, 104] Lack of self-efficacy [102, 108] Lack of previous experience of physical activity [84, 109] Less-educated [101] Higher Body Mass Index [104] Diverse ethnic backgrounds [100, 103] Younger survivors (lack of time and energy) [104] Older survivors (accessibility and physical limitations) [101] Poor physical health [104] Received lumpectomy treatment [106]
Interpersonal	Lack of social support [102, 106] Lack of trust in advising health professionals [102]
Organisational	Poor weather [101] Air pollution [102]

Community and Policy	Less accessibility to facilities [101, 104] Lack of personal security [102] Traditionalist cultural beliefs [102] Lower-income [110]

As shown in Table 1, there are many reported barriers to PA in fBCS. This list is not exhaustive nor are all the barriers applicable to each survivor. Many factors influence adherences, such as lower socioeconomic status (SES) who may have poorer health literacy [111] and not have an awareness of the importance of PA on their morbidity or the financial means to attend supervised PA sessions [100, 104, 110]. This link between lower SES and poorer health literacy is supported by statistics from the Australian Institute of Health and Welfare whereby, adjusting for age in 2019, 1 in 2 women in high SES areas achieved PA recommendations compared with 1 in 3 women in lower SES areas [112]. The participants within our pilot study were fBCS who were recruited through a public hospital (Sunshine Hospital) which services areas that are deemed by the Australian Government to be one of the ten most socioeconomically disadvantaged regions within the country [113]. Therefore, the women within our study were more likely to be faced with lower baseline PA levels and more barriers to PA. However, as highlighted before, whilst evidence shows improvements in QoL are more likely to occur if certain thresholds of PA are achieved [63], a reduction in sedentary behaviour can be just as key in improving QoL outcomes especially for inactive cohorts [61]. It is for these reasons that a self-directed program of incrementally increasing step count per week, thus reduction of sedentary behaviour, was set for the goal for participants within our study which will be expanded upon later in Chapter 3. Study Design.

The factors outlined in Table 1 highlight the focus of the large bulk of research focused on the personal barriers to PA. However, many of these personal factors are interrelated and are underpinned by intrinsic components such as motivation and self-efficacy (amongst many others) and were well articulated by a participant in the qualitative study of fBCS in a running intervention study by Avancini et al. [102] *"Even if I cannot go, I say to myself: no, someone is waiting for me, I cannot skip, I need to go and workout with them."*

Most of the literature identifying the factors mentioned in Table 1 is from studies conducted at a particular time without any longer-term follow-up. One of the references in the table, Emery et al. [106], was a prospective study that investigated the biopsychosocial factors that

predicted PA levels in a cohort of breast cancer patients five years following a psychosocial intervention immediately post-diagnosis. The researchers looked at PA levels at various time-points throughout the five years. They reported that levels returned to lower than baseline (immediately post-diagnosis) soon after the intervention ceased, highlighting that interventions should be aimed toward sustainable behavioural change. Another two large RCTs investigated the long-term impact of a combined aerobic and resistance training exercise intervention on QoL outcomes in fBCS. The results highlighted how lower baseline PA levels negatively influence long-term motivation to PA behaviour. One study, Penttinen et al, used a 12-month exercise intervention [114] and the other, Mutrie et al, used a 12-week exercise intervention [115]. Both studies measured QoL outcomes using the same measure at various time-points over a five-year period post baseline. Whilst there was an increase in QoL over the five year period for both studies, there was no significant difference between intervention and control groups. Interestingly, the authors in the Mutrie et al study reported a dropout rate of 58% at the five-year follow-up time-point compared to 17% in the Penttinen et al study. This difference in attrition rate between studies was proposed, by Penttinen et al, to be related to baseline activity levels of participants where 80-85% of participants within the Penttinen et al study were regularly physically active at baseline whereas those in the Mutrie et al study were sedentary at baseline. This correlates with other literature that identifies baseline sedentary lifestyle as a predictor of poor exercise adherence in fBCS [109]. However, a recent Cochrane review reported that baseline PA levels are commonly poorly reported in the literature [116]. This comparison suggests that higher baseline activity levels can be a predictor of longer-term motivation and adherence to exercise irrespective of exercise intervention duration.

1.4.2. Facilitators to physical activity for female breast cancer survivors

A recent systematic review found the predictors of adherence to exercise in cancer cohorts [117] were similar, albeit in an inverse direction, to those outlined in Table 1. The authors report that the literature supports the idea that maximal adherence is gained by increasing motivation and addressing socio-demographic factors such as accessibility and social facilitation. A systematic review and meta-analysis found the three most common features of successful PA interventions to facilitate change in fBCS specifically were [76]:

1. A component of supplementary tools, e.g. pedometers, logs or social support that act as motivators.
2. An in-person group component including one-to-one attention that produce a social environment which further enhanced motivation.
3. A home-based component (or progression to) for sustainable change and to help encourage intrinsic motivators.

In an updated review two years later by the same authors [118], the effect of in-person interventions was not necessarily more significant than other methods such as phone or email. The authors warned of inferring these findings to all cohorts as they mainly consisted of white, healthy women living in metropolitan cities. However, the study highlighted that more remote ways of supervising interventions are just as effective and, thus, more feasible for long-term implementation in facilitating sustainable behavioural changes [118]. However, one consistent recommendation that was made as a result of the two meta-analyses was that using interventions founded in established behavioural change models, has a higher likelihood of sustainable improvements in PA outcomes in fBCS [76, 118].

1.5 Behavioural change models

Achieving sustainable behavioural change, and understanding the mechanism underpinning it, has been the focus of many studies over many decades. In 2018, the WHO reported that 70% of the total global mortality (41 million deaths) was attributed to four main non-communicable diseases (NCD): cardiovascular disease, cancer, chronic respiratory disease and diabetes [119]. There are four common modifiable risk factors associated with these NCD: tobacco use, unhealthy diet, alcohol use and physical inactivity [120]. Notably, each of these risk factors requires a behaviour change (either cessation of an old one or adoption of a new one) for change to occur. Therefore any study using an intervention to increase PA levels - requires a behavioural change theory underpinning it. This is a sentiment strongly expressed by the United Kingdom Medical Research Council in their recommendations on developing a complex intervention within research studies [121] and the 2018 PA Guidelines Advisory Committee Scientific Report from the United States which states: *"Strong evidence demonstrates that individual-level interventions can increase the volume of physical activity performed by youth and by adults, especially when the interventions are based on behavioural change theories and techniques."* (pg. A-5) [61]. Furthermore, according to a

recent Cochrane review, there is still poor use and reporting of behavioural change theories underpinning exercise adherence interventions within studies [116].
There are four main established theories (models) that are used to explain the behavioural change in the context of engaging in PA. These are; the Theory of Planned Behaviour (TPB), The Social Cognitive Theory (SCT), The Trans-Theoretical Model (TTM) and the Self-Determination Theory (SDT).

1.5.1 Theory of Planned Behaviour

The TPB assumes that the individual's intention to perform a specific behaviour is the primary predictor of change. Furthermore, one's intention is primarily moderated by one's own ability to exert self-control over performing that behaviour (whether that involves overcoming barriers or behavioural capability). According to Ajzen (2020), there are three determinants of an individual's intention [122]:

1. *Attitude:* the individual's attitudes and beliefs towards the behaviour and the probability of its potential outcomes
2. *Subjective norms:* the individual's perception of the attitudes and beliefs of those around them towards the behaviour
3. *Perceived behavioural control:* the individual's perceived own capacity (including confidence and intention) to engage in the behaviour which involves overcoming any associated barriers

A large randomized controlled trial (n=337) investigated the effects of PA behaviour change based on the TPB (in the form of print materials or pedometer) in fBCS and found there was a statistically significant increase in PA levels at post-intervention (12 weeks) [123]. In a subsequent article, the 12-week intervention study results were analysed to investigate if the TPB constructs mediated the effects seen within their previous study. The researchers found that the constructs and beliefs improved compared to the control group and were more significant in the areas of attitude, intention, planning, control and behavioural beliefs [124]. It was postulated that this was due to the 'response shift theory', which relates to the recalibration of one's internal perception that occurs as a response to the increase in the desired behaviour.

A meta-analysis in 2020 [125] showed that the interplay between intention and self-efficacy factors in predicting improved PA behaviours in cancer survivors most closely aligned with the TPB.

Limitations to this theory include:

- No consideration of the value of autonomy in the motivation for behavioural change.
- No acknowledgement of other intentional factors such as past experience, negative emotion (fear or threat) or environment/accessibility.
- An assumption that the individual has been exposed to the resources to achieve the desired behaviour.
- No account for a change in decision making choices over time regarding the desired behaviour nor any associated time-frames between intention and execution of behaviour.

1.5.2. Social Cognitive Theory

The SCT model emphasises the social determinants of health and how they influence an individual's change in behaviour. Within this theory three constructs are believed to interact dynamically: personal, behavioural and environmental factors, as outlined in Figure 3.

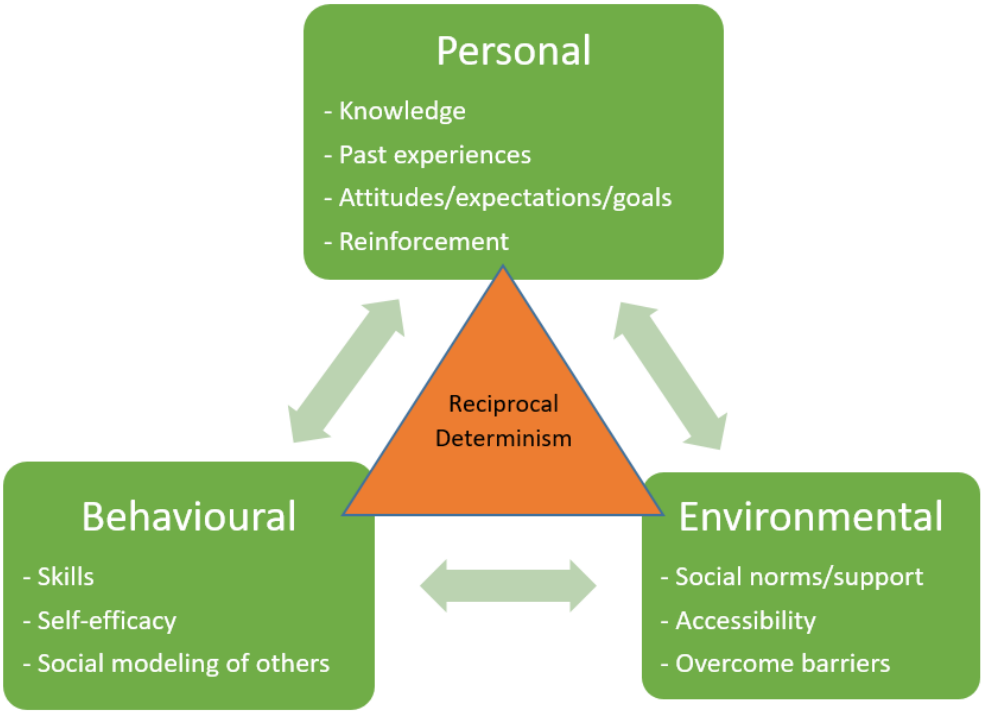

Figure 3. Social Cognitive Theory

Reciprocal Determinism is the central construct of this model. Not one factor alone is responsible for enacting behavioural change, rather, a constant interaction of any, or all, of the factors mentioned above is outlined in Figure 3 [126]. This model is unique because it caters for reinforcement from self/others/environmental factors that can contribute to a sustainable behavioural change [127], which is particularly important in PA behaviour [128]. Whilst the weighting of factors varies depending on the individual, the cohort and the behaviour in question, self-efficacy seems to be the most pivotal factor in enacting change [129]. More specifically, self-efficacy has both a direct (behavioural capability, attitudes, goals) and indirect (overcoming barriers) role, which is particularly pertinent in the breast cancer survivor cohort [129].

There are limitations to this model, such as:

- The framework's complexity caters to many factors. However, it can be hard to identify which or how many factors are responsible for the outcome.
- There is an assumption that other social or environmental factors always influence the individual's behaviour which is not always the case.
- There is no consideration of the individual's biological, genetic or hormonal factors of the individual that can influence behaviour.

A systematic review and meta-analysis conducted in 2015 examined the efficacy of SCT-based interventions in RCT to enact behavioural change in either the diet or PA domains for cancer (mixed type) survivors [127]. The researchers found a significant improvement for SCT-based PA interventions in cancer survivors. However, an analysis (using cross-lagged panel correlations) of longitudinal data from 1,009 cancer survivors demonstrated evidence against some of the SCT assertions, of reciprocal determinism, mostly that outcome expectations can influence self-efficacy but not necessarily affect PA levels [130].

1.5.3. Trans-Theoretical Model

The Trans-Theoretical Model, also termed the 'Stages-of-Change' model, this framework was described by two prominent psychologists, James Prochaska and Carlo DiClemente, in 1982 and originated in the context of quitting smoking [131]. It involves five distinct phases that an individual goes through when making healthy behavioural changes and is schematically depicted in Figure 4:

- Pre-contemplation: where change has not entered the awareness of the individual
- Contemplation: consideration of the idea of change, albeit with a degree of ambivalence
- Preparation: planning and commitment to the change are commencing
- Action: execution of desired behaviour
- Maintenance: using effort to sustain the desired behaviour long-term

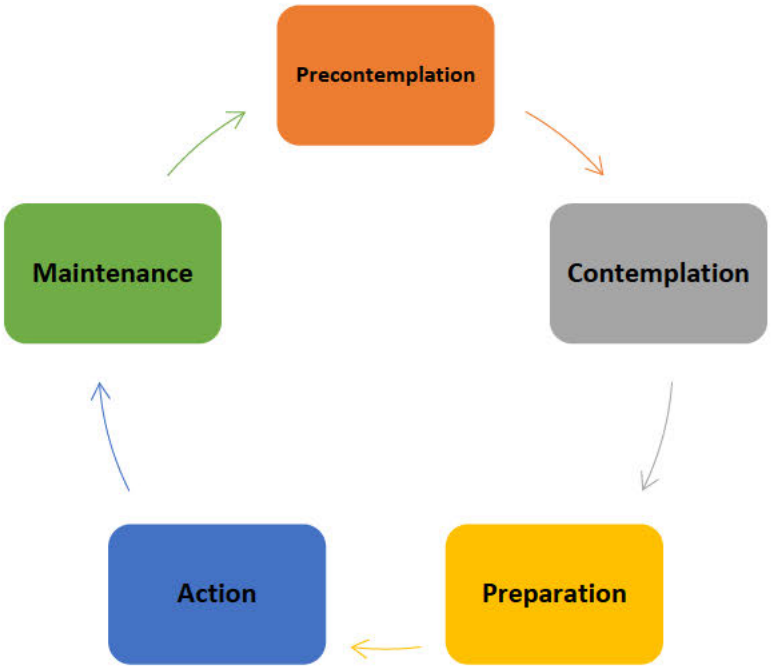

Figure 4. 'Stages-of-Change' Model

An individual can enter the cycle at various stages and either stay stagnant, relapse or progress depending on various cognitive, affective and reflective processes [132]. Key predictors or facilitators of progression through this cycle are self-efficacy and decisional balance (weighing up the negative and positive consequences of selecting the new behaviour). This model has been useful as it allows researchers to tailor interventions depending on which stage the individual is at which has been shown to be more effective than non-tailored interventions [133]. In addition, it caters for 'second chances'.

A recent cohort study investigated the TTM constructs within the dietary and PA behaviours of 700 Hawaiian residents over two years [134]. The authors found that the 'stages of change' cycle becomes more of a continuum whereby 'processes of change' and 'self-efficacy' are secondary outcomes rather than determinants of progression. This would mean that the behaviour change (PA) would be the determining factor for progression through the later stages and thus causing a change in decision making and self-efficacy [134].

A study measured the exercise behaviours and key constructs of the TTM six months following cessation of a 12-month supervised exercise (combined aerobic and resistance) intervention in a group of older (<65 years of age) fBCS. The researchers found that 57% of

participants were considered to be sufficiently active six months following cessation of the 12-month exercise program [135]. Furthermore, higher levels of both constructs (self-efficacy and decisional balance) of the TTM at a post-intervention stage were significantly associated with higher levels of PA measured at the six months follow up time-point.

Some limitations for this model are:

- It doesn't account for social influences or contexts such as cultural norms and expectations
- There is no clear definition of thresholds for each stage progression nor any validation or standardization of questionnaires that evaluate this model.
- There are no set time-frames for within or progression between stages.
- There is an assumption that logical planning processes occur during the progression from one stage to another, which is inaccurate.

1.5.4. Self-Determination Theory

The Self-Determination Theory, developed in 1985 by Ryan and Deci, encompasses a framework that posits that an individual's capacity to change and develop is dependent upon the facilitation of three essential psychological needs of autonomy (a sense of one's control over their behaviour), relatedness (a sense of belonging and connectedness) and competency (one's sense of capability to perform a behaviour) [136]. This theory emphasises that autonomous intrinsic motivators are stronger and more sustainable drivers of behavioural change than extrinsic motivators. However, motivation (and their associated methods of self-regulation) to engage in change moves along a continuum [136] (outlined in Figure 5). As Figure 5 illustrates, levels of autonomy incrementally increase as types of motivation (underpinned by self-regulatory types) move from left to right with the highest levels of self-determination and autonomy within intrinsic motivation. *Amotivation* relates to the state of non-intention to change, *external regulation* is where an individual is motivated through either fear of punishment or a desire for external praise or reward, *introjection regulation* is motivation to protect one's ego or avoid guilt, *identification regulation* is motivation is through gaining benefits that result from the desired behaviour, *integration regulation* is motivation through how the behaviour aligns with one's values, *intrinsic motivation* is motivation to perform a behaviour purely for the enjoyment of it [136].

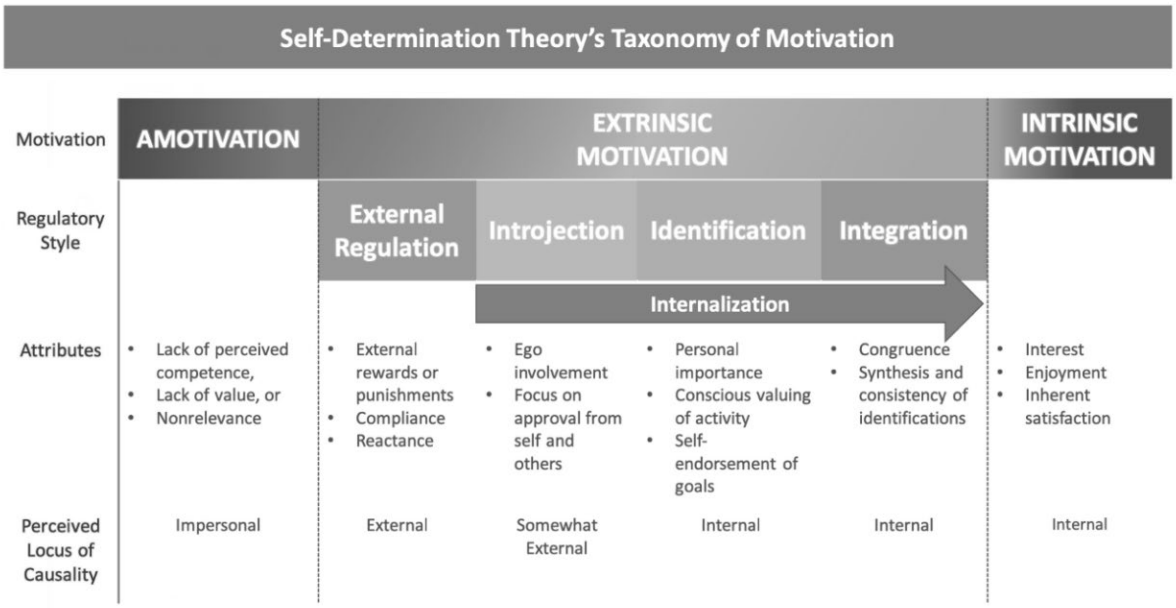

Figure 5. Self-Determination Theory's Taxonomy of Motivation[6]

In contrast to other models that rely heavily on external factors such as social approval or professional recommendations, the SDT targets the internal satisfaction constructs that an individual experiences. Therefore, by aligning a behavioural change with one's beliefs, values and life goals, there is no need for external validation or encouragement, which is believed to be the rationale for its success in producing a strong driver for change and a lasting change [137, 138]. However, this could become a limitation in some instances such as an individual valuing the enjoyment they may get from substance abuse despite external health encouragement to stop because of potential adverse health effects.

A cohort study showed that 31% of a sample of Australian 558 fBCS were meeting recommended levels of PA at the average time-point of 25 months post-diagnosis [139]. In the subgroup of women meeting PA recommendations, there were significantly higher reported levels of autonomy support, competence, identified self-regulatory types and intrinsic motivation (all key constructs of the SDT) than those not meeting the PA

[6] Reprinted with permission from Ryan, R.M. and E.L. Deci, *Intrinsic and extrinsic motivation from a self-determination theory perspective: Definitions, theory, practices, and future directions.* Contemporary Educational Psychology, 2020. **61** 136. Ryan, R.M. and E.L. Deci, *Intrinsic and extrinsic motivation from a self-determination theory perspective: Definitions, theory, practices, and future directions.* Contemporary Educational Psychology, 2020. **61**.

recommendations. Upon further regression analysis, the authors found that the constructs within the SDT were responsible for 20.2% of the variance in the PA levels showing that the SDT gives a plausible framework to help understand PA behaviour in fBCS.
A recent meta-analysis of 73 studies investigated the effect of SDT-based interventions on changes in health behaviour, health outcomes and constructs of the SDT at both post-intervention (mean duration of intervention 133.4 days) and follow up (ranging from one week to 30 months) time-points [140]. There were positive changes in health behaviours (of medium effect size) and physical and psychological health outcomes (of small effect size) at the post-intervention time-point. However, only small positive changes were seen at follow-up in the health behaviour outcome. There was also a small to medium effect of positive change in SDT constructs associated with autonomous motivation at the post-intervention period [140].

The four behavioural change models outlined above have advantages and disadvantages which make them adaptable to suit most study designs to best facilitate a desired outcome. However, one of the aims of this pilot study is to investigate an effective method of motivating fBCS to engage in self-directed PA. As outlined previously, fBCS face unique barriers to PA which require increased levels of confidence in their own capability to overcome. Furthermore, developing motivators that more closely align with one's values and goals is important for sustainable change to occur. Furthermore, a meta-analysis which included a regression analysis provided evidence that counselling styles which were patient-centered and promoted volitional control over one's behaviour were strong predictors for effective and sustainable positive change in PA and dietary intake [141]. It is for these reasons that the SDT was selected to inform the design of the intervention in this pilot study given its focus on developing more intrinsic motivators and autonomous control over one's behaviour. Additionally, two outcome measures were able to be used to assess change in two of the working constructs within the SDT (self-efficacy and self-regulatory types), as a result of the intervention, to help give feedback on the applicability of the SDT in this study.

1.6. Predictors of behaviour change

In a recent meta-analysis of the predictors of PA behaviour in fBCS using data from longitudinal studies, the authors found six main predictors were identified that commonly

formed many of the constructs within the afore-mentioned behavioural change models [125]. These predictors included attitudes, norms, social support, past behaviour, self-efficacy and intentions.

Attitudes

Attitudes are defined as an individual's judgement of the expected outcomes of behaviour and have two aspects – 'affective' and 'instrumental' [125]. 'Affective' pertains to the individual's feelings about behaviour performance such as running because of the enjoyment of it. In contrast, 'instrumental' pertains to the practical consequence of performing the behaviour such as running because one understands that it is good for their health.

Norms

Norms are defined as common beliefs around the performance of behaviour [125]. The consensus is there are two types – 'injunctive' and 'descriptive'. 'Injunctive' norms relates to the beliefs of those close to the individual such as running because their doctor told them to do it and 'descriptive' norms relates to the individual's observation of others behaviours such as an individuals' awareness that other people engage in exercise for health benefits whereas they may not.

Social support

Social support is defined as an individual's perception of how others facilitate and encourage their attempt to perform a behaviour goal [125] for example, *"My husband is really supportive as he stays home with the kids rather than going early to work whilst I go to the gym".*

Past behaviour

Past behaviour is someone's history of a particular behaviour which can help understand the motivational and capability components of performing the said behaviour [125].

Self-efficacy

It is defined as an individual's confidence in their capabilities to perform a behaviour [125]. There are two subtypes: i) Barrier self-efficacy, which is one's confidence to overcome barriers to an exercise behaviour and ii) Task self-efficacy, which is one's confidence in their ability to perform an exercise behaviour [125].

Intentions

Defined as an individual's decision and determination to perform a behaviour [125].

Hirschey et al (2020) [125] used a meta-analytic approach using structural equation modelling of the PA data from studies involving cancer survivors. The authors found that intention and self-efficacy were the greatest predictors (of a medium magnitude) for higher PA levels. However, attitudes, norms and self-efficacy must be established for intentions to be strengthened. The analysis also showed a larger discrepancy between intention and performance of a behaviour in cohorts of cancer survivors than in healthy adults i.e. a larger, more significant gap between survivors knowing they should be exercising but don't. This behaviour gap is proposed to be greater in cancer survivors because of unique barriers to diagnosis and treatment such as fatigue, fear of aggravation of adverse symptoms and no feeling of control over their behaviour or body (which can be a belief adopted as a result of cancer treatment) [125].

Self-efficacy is a commonly investigated predictor within these models and interventions. Self-efficacy has consistently been associated with increased PA levels in studies on fBCS [80, 100, 102, 135]. A meta-analysis of the influence of PA interventions on the two subtypes of self-efficacy in healthy adult cohorts revealed that exercise task self-efficacy was more involved with the adoption of new exercise behaviour. In contrast, exercise barrier self-efficacy was more involved with maintaining exercise behaviour [142]. However in healthy cohorts, a previous meta-analysis indicated that prompting barrier identification reduces self-efficacy [143]. However, this may not necessarily be applicable as survivors face unique barriers compared to healthy cohorts. Therefore interventions that focus on enhancing self-efficacy as well measuring self-efficacy as an outcome are vital [144].

1.7. Tools to increase adherence to physical activity

It was identified previously that complex interventions should be designed and underpinned by established behavioural change theories [61] to ensure optimal outcomes. Methods commonly adopted within studies to satisfy this recommendation are the utilisation of tools to improve any of the key constructs or predictors that ultimately impact motivation and adherence to behavioural recommendations or interventions.

1.7.1. Motivational Interviewing

Motivational Interviewing (MI) is a counselling technique developed in the early 1980s by William R. Miller, a Clinical Psychologist specialising in addiction (specifically alcoholism). Miller observed that the stagnant stage for most alcoholics was when they continued with the consumption of alcohol whilst experiencing the conflicting awareness of its adverse health effects, thus being in a state of cognitive dissonance [145, 146].

MI is primarily a patient-centered process that includes posing open-ended questions designed to help reveal reasons or barriers responsible for the state of ambivalence to change. Furthermore, goals are set by the individual in addition to strategies on how to overcome any potential barriers that may arise, and the practitioner can pose suggestions if the individual fails to provide any. It is vital to the success of the intervention that the practitioner expresses empathy and validation of the individual's challenges to foster an environment whereby a sense of autonomy is maintained. It is also important that any resistance is not met with a negative attitude or judgement by the practitioner, as the trusted relationship with the practitioner may be compromised. Instead, a gentle reminder of the desired behaviour and associated goals would be a more effective alternative [147]. This process helps to facilitate and strengthen feelings of self-efficacy and competency on the patient's behalf.

The structure of the motivational interview centers around four main processes [148] outlined in Figure 6.

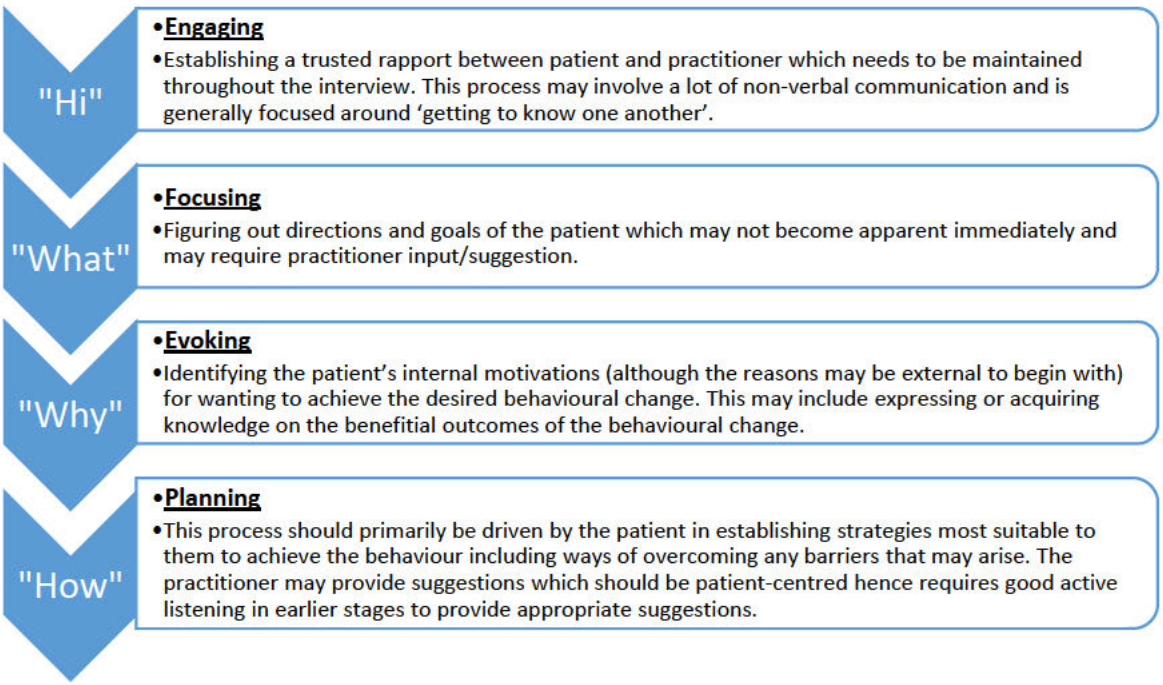

Figure 6. Four processes of Motivational Interviewing

Within these processes, four core interviewing skills are suggested to obtain optimal results and facilitate the three psychological needs of the patient detailed earlier. These four skills as described by Miller and Rollnick [148]:

1. Open questioning: Enables the patient to give longer answers with more detail, allowing them to 'tell their story'.
2. Affirming: Being genuine in acknowledging and supporting the patient's views without sounding contemptuous.
3. Reflecting listening: This requires active attention to what the patient is saying so that further exploration of topics can be safely done. Additionally, asking questions that follow on from previous answers allows the practitioner the chance to show empathy towards the patient.
4. Summarising: Using the patient's words, repeating back the information gained. This clarifies the correct interpretation of what has been said for the practitioner and allows clarification from the patient. This skill also demonstrates genuine respect and interest on the practitioner's part, proving that their full attention is on the patient. This further helps to develop rapport in later interactions.

Once this process is repeated, the patient will hopefully become familiar with the type of questions and process involved in each interview. Thus, developing 'training wheels' as such for a process of self-reflection that the individual may use to help increase motivation during a period of ambivalence or stagnation which facilitates the chance for ongoing sustainable change.

A 2010 meta-analysis investigated the effect of MI on the change in behaviour in various domains compared to other treatments and control groups [149]. The authors found overall that there was a small yet significant effect of MI on enacting positive behavioural change with the largest impact seen in groups that involved cessation of behaviour (alcohol, tobacco, cannabis and miscellaneous drugs) when compared to no treatment. However, there was no significant difference when compared to 'treatment as usual' groups (such as those that received standard withdrawal medication but without MI). There was a minimal effect when looking at adoption of healthy behaviours such as diet, exercise and adherence to medical recommendations [149].

A more recent systematic review into the effect of MI interventions on various health behaviours in cancer survivors showed great variation in effects [150], because there was significant heterogeneity amongst studies such as cancer type, interview specifics (duration, timing, online/in-person) and type of health behaviour. Regarding PA behaviours, the research found that MI was mostly successful except in studies that conducted the intervention during active phases of treatment where there were high dropout levels [150]. Interventions that were supplemented by print materials such as information booklets and diaries also showed more statistically significant improvements.

Other features of the MI interventions associated with more improved outcomes were; MI delivered by trained health professionals which whom participants already had a rapport and also studies that contained measures that were taken to ensure the fidelity of the MI delivery such as regular reviews of an external MI supervisor [150]. Interestingly a RCT that used an MI intervention, on a group of fBCS, that was delivered by a combination of health professionals and other fBCS was effective in producing significant improvements in adherence to recommended PA levels, BMI, cardiovascular function and dietary intake and reported high levels of satisfaction of the MI by participants [151].

More recently three other RCTs used MI as an intervention in fBCS cohorts. One study used it as the sole intervention on patients with invasive breast cancer, albeit post-adjuvant treatment measured both health-related QoL and home-based self-directed PA levels, and found significant yet small to moderate improvements [152]. The other two RCTs used MI in

conjunction with pedometers. Both showed a small but statistically significant improvement in self-directed PA levels [153], with one of them also reporting a significant reduction in sedentary behaviour [154]. These small to moderate positive effects on PA levels resulting from MI in fBCS have been seen in other studies, including those with chronic conditions such as obesity, hypercholesterolemia, cardiovascular conditions or multiple sclerosis [155]. A qualitative study showed that the framework of the SDT aligns well with the principles of MI as they are both patient-centered processes and because of their goal of enhancing the individual's intrinsic aspects of self-control and motivation [156]. Furthermore, MI has been shown to be feasible due to its effectiveness in diverse cohorts [149], reproducible with minimal training [157] and ability to be delivered remotely [155, 158]. It is for these reasons that MI (using the SDT as the underpinning framework) was chosen to be the intervention used within this study.

1.7.2. Digital Trackers

Digital trackers such as accelerometers and smart phones, are commonly used within PA studies primarily for objective reporting of PA levels however they have also been shown to have a powerful motivational influence by providing interactive feedback on steps completed, time spent in-session or other self-regulation methods such as reminders of goals, and the importance of overcoming barriers [85, 91, 159]. Two RCTs that used a combination of MI and a pedometer to record and enhance PA levels in cohorts of fBCS found significant improvements in PA outcomes post intervention [153, 154]. The authors from both studies indicated the feasibility of the use of the digital trackers reporting that they were scalable, inexpensive and user-friendly. A qualitative study of 96 fBCS utilizing an online PA intervention using a digital tracker showed that participants felt a sense of accomplishment, encouragement and motivation when they achieved their goals. However, the individual would feel a reduction in motivation and desire to disengage if these goals weren't met [85].

The associations between digital trackers and motivation are outlined in a recent study conducted in America, which surveyed a large number (n=608) of cancer survivors (of mixed type) [160]. The authors assessed associations between the levels of digital tracker usage and motivational and self-regulatory types identified within the SDT via regression analysis. The authors also measured the associations between digital tracker usage and meeting the 2010 cancer survivor PA recommendations of at least 150 minutes of MIAPA per week [63]. The

results showed that cancer survivors were 1.6 times more likely to achieve recommended PA goals if they used a digital tracker. Additionally, there was a higher association between individuals who utilized a digital tracker and their motivation to participate in PA being driven by feelings of internal guilt and exercise enjoyment and a desire for an improved physical appearance [160].

1.7.3. Print materials

In this section 'print materials' encompass materials used for informative purposes or diarising behaviour performance or goal achievement.

In a three-arm RCT the effect of two types of PA promotional print materials on PA outcomes in a cohort of fBCS were investigated [161]. One group was given a bespoke combined aerobic and resistance exercise regime (at three time-points over the 12-week intervention period) with information on benefits, exercise description and goal setting established with the individual at the baseline assessment. Another group was given a one-off 54-page booklet with information on PA recommendations (including aerobic and resistance exercises) specifically for fBCS. The last group (considered the control group) was given a standard one-off brochure describing the national PA recommendations for healthy adults. The results showed that although there was a higher likelihood of achieving aerobic exercise recommendations for fBCS within the two intervention groups compared to the control, the effect size was not statistically significant. However, in the context of the resistance exercise component, there was a statistically significant effect size of meeting recommendations in the bespoke group compared to the control group [161]. When comparing their results to those of other studies, the authors found that higher baseline PA levels, higher intensity and duration of PA recommendations and the use of supplementary pedometers and Therabands® were contributing factors to more significant positive PA outcomes [161].

The literature shows that the use of a supplementary tool, such as counselling, digital trackers and print materials, to PA interventions or as a way to increase adherence to PA is largely successful in cancer cohorts. Furthermore, using a combination of such tools has been shown by meta-analyses to produce an even higher effect on PA outcomes in cohorts of fBCS [76, 162]. This background literature forms the rationale for the use of a digital tracker in combination with MI in our study on a cohort of fBCS.

Gap in the literature

This chapter has highlighted many issues on the topic of female breast cancer. While there is no shortage of literature into breast cancer, there still remains a gap in research for practical and effective strategies for improving PA behaviour and QoL in at-risk fBCS cohorts. Australia (and New Zealand) have the highest ratio of incidence to mortality rates of breast cancer in the world which translates to a higher amount of women within the 'survivorship' stage currently and in the coming years. Yet, much of the research conducted is focussed on treatment modalities and during the active stages of treatment.

The beneficial impact of PA on various aspects of QoL are well known in the fBCS cohort. However, what also is known is the poor adherence rates to PA recommendations that exist within this cohort of women. Many of the barriers that are responsible for such low adherence rates greatly affect motivation to engage in PA. Therefore conducting research to assess strategies to improve adherence are essential otherwise benefits to QoL outcomes in fBCS can be lost. Unfortunately, the majority of research into this area have been in cohorts of fBCS that are from privileged, educated, higher SES backgrounds with higher baseline levels of PA and QoL. Furthermore, most interventions are supervised, frequent, and delivered within an equipped facility which is costly (financially and timely) and thus unachievable for many fBCs from more disadvantaged backgrounds.

This review has indicated that there is no one 'ideal' intervention that will definitively increase PA behaviour in fBCS, rather finding one that produces the highest adherence rate is more likely to produce significant and sustainable change in QoL in fBCS.

Therefore, this study aims to fill the literature gap by investigating if the use of MI (designed using the SDT framework) produces changes in self-directed PA (as measured by step count), self-efficacy, self-regulatory types and levels of QoL in a cohort of fBCS.. Given the tool of MI will form the intervention used to affect change within this study, the next chapter will provide information on the effectiveness of MI on health behaviours and outcomes in cancer cohorts specifically which will help further justify the specific design of this pilot study.

Chapter 2

The Impact of Motivational Interviewing on Behavioural Change and Health Outcomes in Cancer Patients and Survivors: A Systematic Review and Meta-Analysis

The Impact of Motivational Interviewing on Behavioural Change and Health Outcomes in Cancer Patients and Survivors: A Systematic Review and Meta-Analysis

2.1. Background

The prevalence of cancer is steadily increasing every year, with an estimated 151,000 new cancer diagnoses in Australia in 2021 [7]. Whilst there is great variation in prognosis between cancer types, overall survival rates have improved, with 70% of all diagnoses surviving more than five years [7]. Despite this improved mortality rate, many patients suffer from adverse effects of cancer diagnosis or treatment including fatigue [163], depression [164], pain [13], financial challenges and social isolation [54] both during active treatment and well into longer-term survivorship periods. Consequently, an individual's motivation and ability [102, 165] to engage in recommended levels of healthy behaviours can become limited. A review showed that only 10% of fBCS achieve recommended PA levels [76], and an American surveillance study found 15% of cancer survivors are cigarette smokers [166]. Unhealthy behaviours such as these are disadvantageous because maintaining healthy behaviours can help to ameliorate many adverse effects of treatment [63], improve cancer prognosis and reduce further cancer risk [166, 167]. The challenge then becomes how to facilitate behavioural change in cancer cohorts. The time of initial diagnosis and treatment is proposed to be a 'teachable moment' which presents a unique opportunity for health professionals to advise and motivate cancer patients to engage in behavioural change. Paradoxically, this is also the time whereby adverse effects can maximally impact one's capacity to change [81]. The importance of behavioural change strategies in boosting adherence to desired behaviour in cancer cohorts has been recognised within the research literature. A recent meta-analysis found that using of a combination of motivational tools such as pedometers and print materials or counselling produced greater improvements to self-directed PA outcomes in fBCS compared to those who didn't receive any motivational strategies [162]. Similarly, another meta-analysis showed that the use of motivational tools designed to enhance adherence to the PA or nutritional interventions in cancer survivor populations consistently produced significant improvement effects in desired behaviour change compared to controls

[127]. One commonality found in the conclusions of the studies described above is that all of the interventions analysed were founded on one or more behavioural change theories.

The United Kingdom Medical Research Council guidelines on the design of complex interventions within research studies [121] recommend the inclusion of motivational strategies to enhance adherence to research studies. Additionally, the WHO recommends that established behavioural change theories underpin these strategies to gain maximal benefit [61]. Four main behavioural change theories that are commonly used within the research literature are the; TTM [118], SCT [118], TPB [168] and the SDT [139]. Examples of the two more common theories used include a group-based PA intervention class for fBCS [169] or a nutritional workshop in a social group setting for mixed cancer survivors [170] using SCT as an underpinning framework. Other studies use motivational tools as the primary intervention to facilitate changes in self-directed behaviour. An example is an intervention based on TTM principles using weekly telephone counselling sessions plus a pedometer to enhance adherence to PA recommendations in breast cancer patients [171].

MI is a motivational tool primarily designed to resolve an individual's ambivalence to behavioural change [147]. Whilst MI is a generic tool, it has specific hallmarks that ensure its effectiveness. These include collaboration between practitioner and patient, showing empathy, identifying reasons for ambivalence, being flexible with resistance to change and reinforcing a patient's confidence in their capacity for change. The principles of MI have been shown to closely correlate with the SDT whereby developing one's sense of autonomy over their behaviour and awareness of benefits and attitudes around the desired behaviour can drive more intrinsic motivators to enable change to occur [156]. Therefore, MI can be useful in the design of: a) particular goals such as eating a healthy diet (behavioural change) or managing pain (perception and attitudes to symptoms) and b) using an underpinning theory to suit the cohort or context. A meta-analysis of MI effects in non-cancer cohorts showed significant improvements in desired outcomes with a small effect size [149]. However, previously mentioned, cancer patients and survivors face unique challenges when adopting behavioural change: thus these meta-analysis results may not be transferable. A systematic review conducted in 2016 examined MI in cancer cohorts to achieve behavioural change. The authors found that common features of MI associated with improved outcomes included conducting the interview over the phone with a trained nurse, the use of worksheets or diaries and targeting improving PA behaviour [150]. Additionally, a more recent quasi-experimental study used weekly phone-based MI as an adherence tool to supplement a combined home-

based exercise and dietary intervention in fBCS during the recent lockdown during the COVID pandemic in Italy. They found a statistically significant improvement in PA levels and adherence to a recommended Mediterranean diet over 12-week intervention period [172].

There has not been a meta-analysis conducted on the effect of MI on health behaviour change and health outcomes in cancer cohorts. Hence, this systematic review and meta-analysis will investigate what aspects of MI effectively enacting behavioural change and other health outcomes in people diagnosed with cancer. Findings from this review will help to inform future research in methods that can improve the well-being of cancer patients and survivors.

2.2. Objective

The objective of this systematic review and meta-analysis is to review the literature and analyse if there is an effect of MI on health behaviour (PA) and health outcomes (QoL, anxiety and depression, functional tasks, self-efficacy, BMI and fatigue) in cancer patients and survivors. Findings from this review will help to inform future research in methods that can improve the well-being of cancer patients and survivors

2.3. Methods

2.3.1. Eligibility criteria

2.3.1.1. Participants

Studies were included if participants were: 1) 18 years or older and 2) had a previous or current diagnosis of cancer.
Studies were excluded if participants were: 1) younger than 18 years of age, 2) Animal and 3) had no diagnosis of cancer (these include studies that include individuals who are ‘at risk’ of developing cancer).

2.3.1.2. Intervention

The review included studies that used MI as the solitary intervention or in combination with other components such as primary exercise or diet interventions. In addition, studies using

interventions termed ‘counselling’ or ‘coaching’ were included as long as it was stated that they were using MI principles and were interactive, i.e. not print materials.
Studies were excluded if they used a motivational/adherence tool or strategy within their intervention but didn’t explicitly state that it utilised MI principles. Additionally, studies that articulated that MI, or tools using MI principles, were optional in addition to the primary intervention were excluded.

2.3.1.3. Comparator

Studies included in this review were RCT and quasi-experimental studies which involved using one or more comparators or a control group within the design. Pilot RCTs and quasi-experimental studies were also included, provided they included a comparator or control group. Those with a mixed-methods design were included if the relevant quantitative data could be extracted. In three-arm studies involving two interventions (one with and one without MI) and one control group, two comparisons conducted within the analysis. One comparison was between the two intervention groups and the other was between the intervention group containing the MI and the control group. Studies were considered eligible if the control group received either no intervention or ‘usual care’ so long as it did not involve any components of MI.

2.3.1.4. Outcome

The primary outcomes of this systematic review and meta-analysis are health behaviours and health outcomes. Therefore, studies that measured either or both of these were included. Examples of health behaviours included: PA, diet, smoking cessation, safe sex, medication and medical screening adherence, self-efficacy and adverse symptom management. Examples of health outcomes included: QoL, fatigue, anthropometric measures, cardiovascular fitness and functional tasks.
Studies that used qualitative measures only to assess health and behavioural outcomes were not included. Feasibility studies that assessed participants’ or investigators’ satisfaction of the MI intervention were not included as they did not align with the primary aims of this review.

2.3.1.5. Report characteristics

This review included articles that were peer-reviewed with full-text availability. Additionally, only articles published and available in English were included.

Systematic reviews, literature reviews, meta-analyses, theses, opinion pieces, editorials, study protocols, cross-sectional studies, observational studies, case studies or those with only a qualitative methodology such as focus groups and interviews were excluded from the review.

2.3.2. Information sources and search strategy

The lead reviewer (Katherine Harkin (KH)) designed the search strategy in collaboration with experienced university librarians from the College of Health and Biomedicine, Victoria University, Australia. A pilot search strategy was conducted jointly by two reviewers (KH and Nicholas Tripodi (NT)) for the investigation of the volume and availability of relevant articles. The final search was conducted in January 2022 by KH and NT. The following electronic databases were searched with articles published between January 1980[7] to January 2022 and limited to human research; PubMed, PsychINFO (EBSCOhost), SPORTDiscus with full text (EBSCOhost) and Cumulative Index to Nursing and Allied Health Literature (CINAHL) with full text (EBSCOhost). The terms used within each database during the final search are presented within Table 2.

[7] This publication date was decided upon as MI was developed in the early 1980's. Additionally, another meta-analysis had reported the earliest literature pertaining to MI was published in the early 1980's 149.
Lundahl, B.W., et al., *A meta-analysis of motivational interviewing: twenty-five years of empirical studies.* Research on Social Work Practice, 2010. **20**(2): p. 137-160.

Table 2. Database search strategy

Database	Search Strategy
Pubmed	(neoplasms (MesH) OR neoplasm (MesH) OR malignancy (MesH) OR cancer (MesH) OR oncology (MesH)) AND (motivational interviewing (All fields) OR motivational interview (All fields))
CINAHL	(neoplasms (AB) OR neoplasm (AB) OR oncology (AB) OR cancer (AB) OR malignancy (AB)) AND (motivational interview (TX) OR motivational interviewing (TX))
APA PyschInfo	(neoplasms (AB) OR neoplasm (AB) OR oncology (AB) OR cancer (AB) OR malignancy (AB)) AND (motivational interview (TX) OR motivational interviewing (TX))
SPORTDiscus	(neoplasms (AB) OR neoplasm (AB) OR oncology (AB) OR cancer (AB) OR malignancy (AB)) AND (motivational interview (TX) OR motivational interviewing (TX))

Search results from each of the four databases were imported into EndNote X9 and manually checked for duplicates. The resultant articles were kept within the EndNote X9 library for future reference and reporting. All articles were then exported into the Covidence platform, where there was an additional check for duplicates. Two reviewers (KH and NT) independently conducted the title and abstract screening and full-text review of the articles according to the eligibility criteria. Any inconsistencies or disagreements were resolved by a third reviewer (JF). A summary of article inclusion and exclusion at each stage was conducted using the Preferred Reporting of Items for Systematic Reviews and Meta-Analyses flow diagram of identification, screening, eligibility and inclusion of studies template [173].

2.3.3. Data extraction

Data from the final included studies were extracted and manually entered into a Microsoft Excel spreadsheet by a reviewer (KH). Authors of studies where data was inconsistent or not reported were contacted via email, however, if no response was received, then the study was excluded. This process was independently reviewed by another reviewer (NT). Any discrepancies were resolved by a third reviewer (JF).

The following data were extracted from each study: publication details (author and year), type of study design (RCT, quasi-experimental), sample size, demographic details of participants (mean age, cancer type, patient stage such as active or survivorship and mean time since treatment if stated), intervention characteristics (the aim of MI, duration/frequency/number of MI sessions, delivery mode of MI: combined, in-person or phone and other components such as diet or exercise), outcome details (outcomes measured and measurement follow-up time-points) and additional comments such as financial reimbursement and if intervention fidelity measures were undertaken.

2.3.4. Assessment of risk of bias

The two independent reviewers (KH and NT) assessed the risk of bias in the included studies using a modified version of the Cochrane Collaboration's tool assessing the risk of bias Version 5.1.0. [174]. The assessment tool usually includes seven domains: 1. Selection bias (random sequence generation), 2. Selection bias (allocation concealment), 3. Performance bias (blinding of participants and personnel), 4. Detection bias (blinding of outcome assessment), 5. Attrition bias (incomplete outcome data), 6. Reporting bias (selective reporting) and 7. Other bias. However, blinding participants to motivational interviewing and any other components to the intervention was impossible, therefore, the third domain of performance bias was modified to be defined as blinding of personnel only. This was deemed appropriate as other meta-analyses that use PA interventions in cancer cohorts have deleted this domain using the same rationale [67]. Furthermore, the reporting bias domain was defined as being specific to the reporting of outcomes by the authors and researchers and not reporting bias of self-reporting of outcomes by participants such as medication adherence and PA levels. If there was a suspected reporting bias due to participant self-reporting measures, it was included as a high risk within the 7th domain.

Each of the domains were then be assigned either 'low risk', 'high risk' or 'unclear risk' according to the description within Table 8.5.d: Criteria for judging the risk of bias in the Cochrane handbook [174]. Any disagreements were resolved by a third reviewer (JF).

2.3.5. Synthesis of results

Two reviewers (KH and NT) conducted the meta-analysis using Review Manager (RevMan) Version 5.4.1 (The Cochrane Collaboration, Denmark).

For continuous outcome data, mean change from baseline or post-intervention and standard deviation was calculated for each study. Functional task data were analysed using the Mean Difference (MD) statistic as all included studies utilising the same outcome measuring tool. QoL, anxiety, depression, BMI, PA, self-efficacy and fatigue were analysed using the Standardised Mean Difference (SMD) statistic given the heterogeneity between outcome measuring tools. The effect score of SMD or MD was considered as either; small (<0.20), moderate (0.20-0.80) or large (>0.80).

The I^2 statistical measure was used to identify heterogeneity between studies and assigned one of the following categories: no relevant heterogeneity (0-40%), moderate heterogeneity (30-60%), substantial heterogeneity (50-90%) and considerable heterogeneity (75-100%).

The Grading of Recommendations, Assessment, Development and Evaluations (GRADE) framework was used to assess the quality of evidence across five criteria [175]. The five criteria were modified and based upon those in other similar meta-analyses of MI [155]:

1. Risk of Bias: Assigned 'Yes' if >25% of studies included within the outcome analysis were classified as high risk
2. Inconsistency (unexplained heterogeneity): Assigned 'Yes' if I^2 value was >50%
3. Indirectness: Assigned 'Yes' if there were any of the following: a) Indirect comparison between MI and the comparator group or b) Specifics of the MI mode delivery was difficult to ascertain
4. Imprecision (wide CIs): Assigned 'Yes' if The CI for the SMD was $\geq$ 0.8 (a large effect according to Cohen [176].
5. Publication Bias: Assigned 'Yes' if funnel plot was used to evaluate when >10 studies within the same outcome

For every 'Yes' assigned to each criteria there was one point deduction (downgrading of quality of evidence) from a starting total figure of five. Reporting bias was evaluated by visual analysis of the funnel plot, if there were adequate studies. Overall quality criteria were assigned a classification of: High if 0 'Yes' responses, Moderate if 1 'Yes' response, Low if 2 'Yes' responses, Very Low if 3 or more 'Yes' responses. See Table 4 for results.

2.4. Results

2.4.1. Study selection

The four databases yielded a resultant total of 683 articles: Pubmed (125), CINAHL (345), APA PsychInfo (101) and SPORTDiscus (112). This number was reduced to 492 after duplicates were removed within endnote and covidence. Of these, 429 studies were excluded after the title, and abstract screening revealed irrelevance to the topic or non-eligibility. There were 3 of the remaining 63 studies which could not be retrieved. Full-text screening was conducted on the remaining 60 studies with a final 21 studies included for data extraction. This process is illustrated in Figure 7 in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses [177].

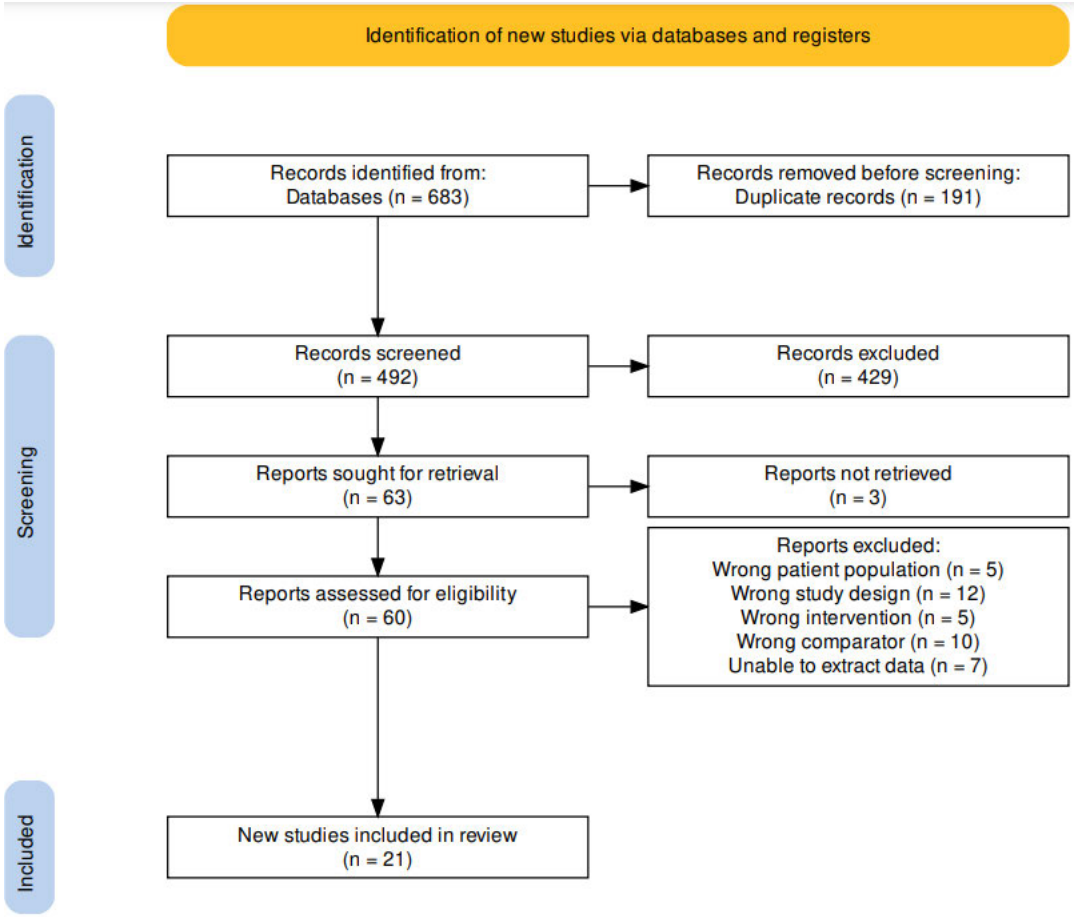

Figure 7. Literature search flow diagram according to the PRISMA guidelines

2.4.2. Study characteristics

Study characteristics are summarised in Table 3.

2.4.2.1. Study details

There were a total of 17 two-arm [151, 153, 178-192] and 2 three-arm RCT [192, 193], one quasi-experimental [194] and one non-randomised controlled study [195]. The 21 included studies had 4154 participants (1752 intervention and 2402 control or non-MI intervention) with a mean age range from 43.7 to 67.1 years of age.

2.4.2.2. Demographic characteristics of participants

There were several cancer types that constituted the participant cohort with eight studies in mixed cancer [178-180, 186-188, 193, 194], nine in breast cancer [151, 153, 181, 182, 184, 185, 189-191], one study in each of abdomino-pelvic [195], head and neck [192], lung [183] and colorectal cancer [196] cohorts. The point within the cancer continuum that participants were at varied with the mean-time since the end of treatment or diagnosis being; one year or more in eight studies, between ten weeks and one year in five studies, between hospital discharge and one month in four studies, during the active phase of treatment in three studies and during pre-treatment phase in one study.

2.4.2.3. Intervention characteristics

The focus of the MI differed across the 21 included studies. Five studies were aimed at increasing or achievement of recommended PA levels [153, 178, 180, 188, 189]. Four studies focused at improving general healthy behaviour (diet and PA) and symptom management [151, 184, 195, 196] and three studies used MI targeting general health behaviour (diet and PA), symptom management and self-efficacy [183, 192, 194]. Only one study aimed at improving general behaviour (diet and PA) [185]. Two studies focused on management of symptoms only; one primarily aimed at improving fatigue [187] and one aimed at pain [193]. Adherence to dietary goals was the focus in three studies [181, 182, 191] and adherence to oral medication was the focus in one study [179]. One study aimed their MI at improving smoking cessation and pain management [186] and one study used MI that was targeting improving sexual behaviour and body image [190].

Five studies delivered the MI in-person [184, 188, 190, 192, 196], six were over the phone [180, 181, 186, 187, 191, 193] and ten were a combination of both in-person and over the phone [151, 153, 178, 179, 182, 183, 185, 189, 194, 195]. There was great heterogeneity between the number, duration and frequency of MI sessions ranging from one to 32 sessions, 10 to 75 minutes in duration and between a few days to 6 months apart.
Many studies utilised other components within their intervention such as; pedometers [151, 153, 178, 181, 188, 189, 195], supervised PA sessions [151, 180], group education sessions [151, 180, 191], workbook or diary [151, 180, 185-187, 191, 195] and information booklets [151, 153, 179, 181-183, 185-188, 190, 193-196]. Nine studies contained methods that were taken to ensure fidelity of the MI intervention [180-184, 187, 188, 193, 194].

2.4.2.4. Outcomes

All studies measured at least one outcome with a mixture of both health behaviour and health outcomes. Nine studies measured PA behaviour [151, 153, 178, 180, 181, 185, 188, 189, 195], four assessed dietary behaviour [151, 181, 182, 191], one measured adherence to oral medication [179] and one measured smoking cessation [186]. Many studies measured specific health outcomes such as; QoL [178, 180, 181, 183, 184, 186, 189, 192, 193, 195, 196], fatigue [178, 180, 187-189], anthropometric measures [151, 153, 181, 185], functional and fitness measures [153, 178, 180, 183, 185, 193, 195, 196] and mental health [180, 183, 184, 186-188, 192, 195, 196]. Self-efficacy was the most investigated outcome (equally with QoL) being measured in eleven studies [151, 178-180, 183, 184, 187, 188, 192, 194, 195].

Study details		Demographic characteristics		Intervention			Outcome		Additional comments
Author (year), study design	**Sample size**	**Mean age (years)**	**Cancer type**	**Aim**	**Duration, number, frequency and mode**	**Other components**	**Outcomes, measurement tools**	**FU (wks)**	
Bennett (2007) [178] RCT	IG = 28 , CG = 28 , Total = 56	IG = 55.5, CG = 60.1	Mixed Ca, Survivor (mean 42M since completion of tmt)	^PA Behaviour	3 x 30min sessions at T0, 2M and 4.5M, C	Pedometer (IG only), 2 x social phone calls (CG)	1) PA 2) Self-efficacy 3) Aerobic fitness 4) QoL 5) Fatigue	12, 24	Received $10 at each of the three measurement time-points (IG & CG
Çakmak (2021) [179] RCT	IG = 40 , CG = 40 , Total = 80	IG = 57, CG = 62	Mixed Ca, During active oral chemo tmt	^Adherence to oral medication	5 x 15-20min sessions at T0, Wk1, Wk3, Wk 6 and Wk 9, C	Print materials (IG and CG), 2 x interviews on understanding of booklet info (CG)	1) Self-efficacy: 2) Medication adherence	12	
Coolbrandt (2018) [194] Quasi-	IG = 72 , CG = 70 , Total = 142	IG = 62 (median), CG = 65	Mixed Ca, During active chemo tmt	^Self-efficacy, healthy behaviours and	Minimum of 2 x 10-60mins sessions	Print materials (IG and CG)	1) Overall Symptom Distress & Severity	3, 6, 12	Using TTM to inform the MI design.

experi-mental		(median)		symptom management	(more if requested) at T0 and few days later, C		2) Self-efficacy		Measures taken for MI fidelity
Dennett (2018) [180] RCT	IG = 22 , CG = 24 , Total = 46	IG = 57, CG = 60	Mixed cancer, Combined during and post active tmt (mean 4.4M since tmt)	^PA Behaviour	7 x 20min sessions wkly, P	Oncology rehabilitation (CG and IG): twice wkly (2hrs combined IP exercise and group education on cancer management strategies) + home-based exercise sessions + print materials	1) PA 2) Physical function 3) Self-efficacy 4) Fatigue 5) QoL 6) Mental Health 7) Blood analysis	8	Measures taken for MI fidelity
Djuric (2011) [181] RCT	IG = 20 , CG = 20, Total = 40	Combined 52.3	Breast Ca, About to start chemo tmt	^Adherence to dietary goals	19 x sessions (2x wkly, 11 x fortnightly, 6 x monthly), P	Print materials + pedometer (IG and CG)	1) Anthro-pometrics 2) PA 3) QoL 4) Dietary intake 5) Blood analysis	24, 52	Measures taken for MI fidelity. Received $25 for each measurement

									visit (IG & CG).
Frawley (2020) [195] Non-randomised, controlled before and after study	IG = 84, CG = 104, Total = 188	IG = 66.1, CG = 67.1	Abdomino-pelvic Ca, Completed surgical tmt (70.5 mean days since surgery)	^ Adherence to PA and dietary recommendations + emotional management	16 x 1 hr group education sessions (twice wkly for first 8wks) + 6 x individual sessions (1-2 calls per month for last 16wks), C	Combined IP and home-based ex program + print materials and pedometer (IG)	1) Feasibility 2) Physical Function (IG only) 3) PA 4) Mental Health 5) QoL 6) Self-efficacy 7) Pelvic floor symptoms	8, 24	
Hartman (2018) [153] RCT	IG = 43, CG = 44, Total = 87	IG = 58.2, CG = 56.2	Breast Ca, Survivor (mean time since surgery 30.1M)	^PA Behaviour	3 x sessions (1 x T0, 1 x wk2 and 1 x wk6), C	Individualised PA recommendations + accelerometer (IG), General Health behaviour advice +	1) PA 2) Objective neurocognitive functioning 3) Self-reported cognition 4) Anthro-pometrics	12	

						accelerometer (CG)			
Hoy (2009) [182] RCT	IG = 975, CG = 1462, Total = 2437	IG = 58.6, CG = 58.5	Breast Ca, Survivor (within 365 days of active tmt)	^ Adherence to dietary goals	34 x 60min (16 x fortnight, 18 x every 3M, + optional monthly group sessions), C	Individual diet plan + print materials (IG), print materials (CG)	1) Dietary intake 2) Anthro-pometrics	12, 24, 36, 48, 60, 72	Measures taken for MI fidelity. SCT informing the low fat eating program and TTM informing MI
Huang (2018) [183] RCT	IG = 15, CG = 15, Total = 30	IG = 57, CG = 61.1	Lung Ca, Immediately post-surgery	^Self-efficacy, healthy behaviours and symptom management	6 x 15-40min: 1 x T0 (post-operation), 1 x discharge from hospital, 1 x 2wks, 1 x 1M, 2 x 2-3M), C	Print materials (IG and CG)	1) Feasibility 2) Acceptability 3) Self-efficacy 4) QoL 5) Mental Health 6) Social Support 7) Subjective Wellbeing 8) Coping Styles 9) Post-traumatic Growth	12	Measures taken for MI fidelity.

							10) Pulmonary rehabilitation effect		
Kvale (2016) [184] RCT	IG = 40 , CG = 39 , Total = 79	IG = 57 CG = 59	Breast Ca, Survivors (mean time since tmt 115 days)	^Healthy behaviour + symptom management	1 x 75min session at T0, IP		1) QoL 2) Self-reported health 3) Depression 4) Limitations in Social roles and activities 5) Self-Management 6) Self-efficacy 7) Care co-ordination	12	Measures taken for MI fidelity.
Lahart (2018) [185] RCT	IG = 16, CG = 16, Total = 32	IG = 52.5, CG = 52	Breast cancer, Survivors (mean time since tmt 10.9 wks)	^Healthy Behaviour	4: 1 x 30-45min at T0, 3 x 15-20min monthly, C	Last 2 months (4 and 5) received individualised print materials (IG only). PA recommendations only (CG)	1) Cardio-vascular fitness 2) Exercise tolerance 3) PA 4) Anthro-pometrics	24	

Pollak (2018) [186] RCT	IG = 14, CG = 16, Total = 30	IG = 60, CG = 54	Mixed Ca, Survivors (within 5 years of diagnosis)	^Smoking cessation + pain management	4 x 60min wkly (first 4 wks), P	NRT + print materials (IG only)	1) Feasibility 2) Acceptability 3) Abstinence 4) Mental Health 5) Coping 6) QoL	8	
Ream (2015) [187] RCT	IG = 23, CG = 21, Total = 44	IG = 52, CG = 55	Mixed Ca, Undergoing active chemo tmt	Symptom management (mostly fatigue)	3 x at start of each treatment cycle T0 was 3rd treatment cycle (time between not stipulated) (1 x 40min T0, 2 x 20min), P	Print materials (IG only)	1) Global Fatigue 2) Fatigue distress 3) Self-efficacy 4) Mental Health	3 treatment cycles (length of treatment not stipulated)	Measures taken for MI fidelity.
Sheppard (2016) [151] RCT	IG = 15, CG = 16, Total = 31	Combined 54.7	Breast Ca, Survivors (mean time since tmt 1.7 years)	^ Adherence to PA and dietary recommendations + emotional management	6 x 60min fortnightly (during IP group education	Print materials + 6 x 30min supervised exercise sessions + pedometers	1) PA 2) Anthro-pometrics 3) Cardio-vascular fitness	12	Some interviewers were fBCS. MI informed by the TPB and

					sessions) + 6 x 15min on alternating fortnightly sessions (individual P), C	(IG). Print materials (CG)	4) Self-efficacy 5) Dietary intake 6) Intervention satisfaction		SCT. $25 gift cards received at T0 and completion (IG & CG).
Thomas (2012) [193] 3 arm RCT : 2 x IG (1 x MI coaching + education, 1 x education only) + 1 x CG	IG (MI) = 105, IG (non-MI) = 103, CG = 109, Total = 317	IG (MI) = 61.8, IG (non-MI) = 62.5, CG = 58.7	Mixed Ca, Survivor (mean time since diagnosis: IG (MI) = 30M, IG (non-MI) = 37.5M, CG = 31.9M)	Symptom management (pain)	4 x 30min (every 1-2 wks), P	Video + print materials (both IG groups)	1) Pain 2) Physical Function 3) Attitudinal barriers 4) QoL	12	Measures taken for MI fidelity.
Tsianakas (2017) [188] RCT (mixed methods)	IG = 21, CG = 21, Total = 42	IG: Male = 65, female = 60,	Mixed Ca, Advanced (mean time since diagnosis:	^ PA behaviour	1 x 15min at T0, IP	<30mins walking on alternate days + print material + pedometers	1) QoL 2) Health status 3) PA 4) Fatigue 5) Mental Health	6, 12, 24	Measures taken for MI fidelity.

		CG: Male = 66.2, female = 58	25% less than 1 year, 35%1-2 years, 10% 3-4 years, 20% 5-9 years, 10% 10 years+)			(50% of participants in each IG and CG) for feasibility reasons - not outcomes	6) Self-efficacy 7) Feasibility		
Turner (2019) [192] 3 arm RCT: 2 x IG (1 x MI intervention, 1 x information intervention) + 1 x CG	IG (MI) = 36, IG (non-MI) =36, CG = 37, Total = 109	Combined IG and CG: <60 years = 49.1%, >60 years = 50.9%	Head and Neck Ca, Completed tmt within 1M prior	^Self-efficacy, healthy behaviours and symptom management	1 x 60 min at T0, IP	MI + print material + usual care (routine clinical hospital care) (MI IG group), print material + usual care (non-MI IG), usual care (CG)	1) QoL 2) Mental Health 3) Self-efficacy	12, 24	
Vallance (2020) [189] (Lynch, 2019 for PA	IG = 43, CG = 40, Total = 83	IG = 61.3, CG = 61.9	Breast Ca, Survivor (completion of primary	^PA Behaviour	6 x sessions (1 x T0, 2 x wkly, 2 x fortnightly,	Goal setting + pedometer (IG), pedometer only (CG)	1) Fatigue 2) QoL 3) PA	12, 24	

outcomes) [154] RCT			tmt - no values given)		1 x month), C				
Yang (2020) [196] RCT	IG = 34, CG = 34, Total = 68	IG = 59.97, CG = 63.62	Colorectal Ca, Survivors (post-surgical but pre-discharge)	^Healthy behaviour + symptom management	3 x (1 x 30min at T0, 1 x 15-20min at 1M, 1 x 15-20min at 2M), IP	Print materials (IG & CG)	1) QoL 2) Mental health 3) Functional status 4) Healthy lifestyle	4, 12	
Zangeneh (2019) [190] RCT	IG = 30, CG = 30, Total = 60	IG = 43.7, CG = 45.9	Breast Ca, Survivor (Completion of mastectomy-no values given)	^Sexual behaviour and body image	5 x 45min wkly individual sessions (post-group educational sessions), IP	Group educational sessions IP (IG and CG)	1) Sexual satisfaction 2) Body Image	5	
Zuniga (2018) [191] RCT	IG = 76, CG = 77, Total = 153	IG = 55.3, CG = 58.4	Breast Ca, Survivor (mean time since last tmt: <6M: IG = 13.3%, CG = 12.3%,	^Adherence to dietary goals	6 x sessions (monthly), P	Monthly group education nutrition and cooking workshops + print materials (IG)	1) Adherence to diet 2) Spices and herbs intake 3) Nutrient analysis	24	

			>24M: IG = 65%, CG = 61.5%)			Monthly info brochures (CG)			

Table 3. Study characteristics

^ = Increase/improve, PA = Physical Activity, QoL = Quality of Life, M = Months, Wks = Weeks, Wkly = Weekly, BMI = Body Mass Index, FU = Follow up measurement time points (baseline time point assumed), C= combined, P = Phone, IP = In-person, min = minutes, T0 = baseline, IG = Intervention Group, CG = Control Group, RCT = Randomised Controlled Trial, TTM = Trans-theoretical model, TPB = Theory of Planned Behaviour, SCT = Social Cognitive Theory, Chemo = Chemotherapy, Info = Information, Tmt = treatment, Ca = Cancer, NRT = Nicotine Replacement Therapy

2.4.3. Risk of bias within the studies

The randomisation and concealment of allocation into groups was well reported by most studies thus enabling a clear risk of bias either way. Due to the inherent nature of the intervention, MI, being delivered by personnel, all studies were deemed 'high risk' in the criteria of performance bias. However, with regards to the reporting of blinding of assessors to the participant allocation, there were two that clearly stated the assessors were not blinded [190, 196] and 11 studies that didn't clearly report if the assessors were different personnel to those delivering the intervention therefore they were deemed 'unclear risk' for that criteria. The reporting on management of missing data was poor with more than half either not reporting [151, 181-184, 188-190, 192] or showing missing data in the outcomes but no description on how that as accommodated for within the analysis [179, 187, 195], thus deemed unclear risk by the reviewers. One study was deemed high risk as the authors made the assumption that non-responders to surveys were ongoing smokers (in a study assessing smoking cessation rates) [186]. There was one study that was deemed high risk for reporting bias where not all domains within the QoL outcome were reported [193]. Finally, seven studies were deemed high risk of 'other' bias which included: possible between group contamination during an outcome assessment [178, 188], contamination between groups during intervention delivery of the exercise component (which both groups received) [180], bias in reporting due to self-reported outcome measures that could otherwise be measured with objective methods such as PA and medication adherence or smoking cessation [151, 178, 179, 181, 185, 186, 188, 195], control groups which were 'wait-list' rather than pure controls as stated [186], non-assessment of components of physical and mental health [189] or subject expectancy [196]. The risk of bias is summarised in Figure 8.

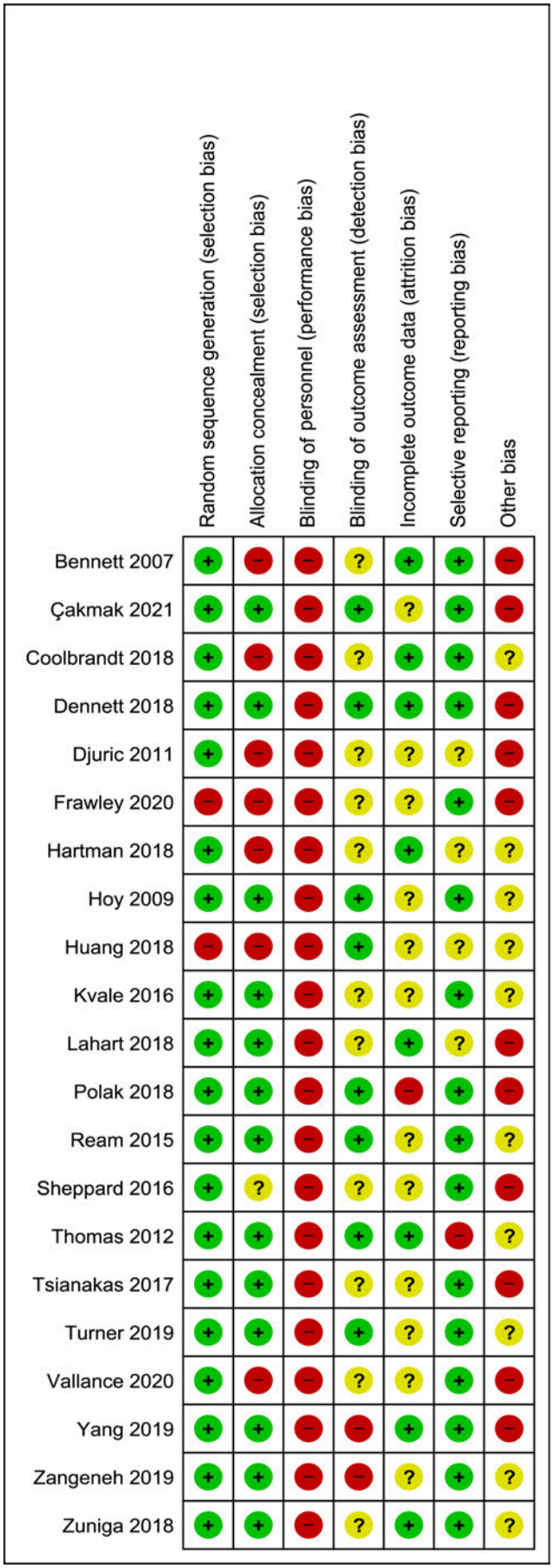

Figure 8. Risk of bias summary

Table 4. Quality of evidence classification

Outcome	Risk of Bias	Inconsistency	Indirectness	Imprecision	Publication Bias	Overall Quality
Quality of Life	Yes	Yes	No	No	No	Low
Anxiety	Yes	No	No	No	No	Moderate
Depression	Yes	Yes	Yes	No	No	Very Low
Functional Tasks	Yes	Yes	No	Yes	No	Very Low
Body Mass Index and body weight	Yes	No	No	No	No	Moderate
Physical Activity - Total	Yes	No	No	No	No	Moderate
Physical Activity - Step Count	Yes	No	No	No	No	Moderate
Physical Activity - overall	Yes	No	No	No	No	Moderate
Self-Efficacy	Yes	Yes	Yes	No	No	Very Low
Fatigue	Yes	Yes	Yes	No	No	Very Low

2.4.4. Synthesis of results

2.4.4.1. Quality of Life

When investigating the impact of MI on QoL outcomes, using the data from eight studies (with ten comparisons), there was no effect of MI on QoL compared to control groups (SMD 0.09; 95% Confidence Interval (CI) -0.05 to 0.23, $p = 0.22$, $I^2 = 69\%$, n = 789). The studies in this outcome were downgraded to low-quality due to risk of bias and inconsistency (Table 4).

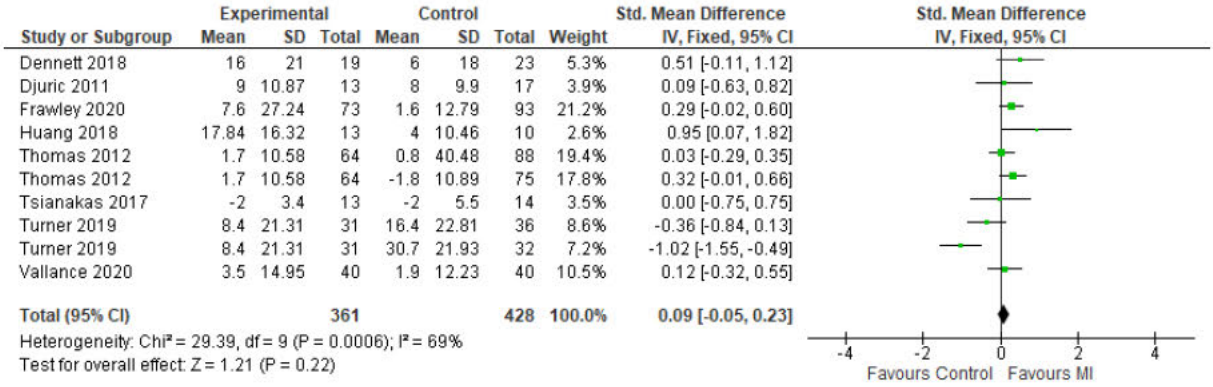

Figure 9. Forest plot of the effects of MI on Quality of life

2.4.4.2. Anxiety

There was no effect of MI on levels of anxiety, using the data from five studies (with six comparisons), compared to control groups (SMD 0.09; 95% CI -0.12 to 0.29, $p = 0.23$, $I^2 = 28\%$, n = 365). The studies in this outcome were downgraded to moderate-quality due to risk of bias

(Table 4). The five studies within this outcome were downgraded to a moderate quality of evidence due to risk of bias (Table 4).

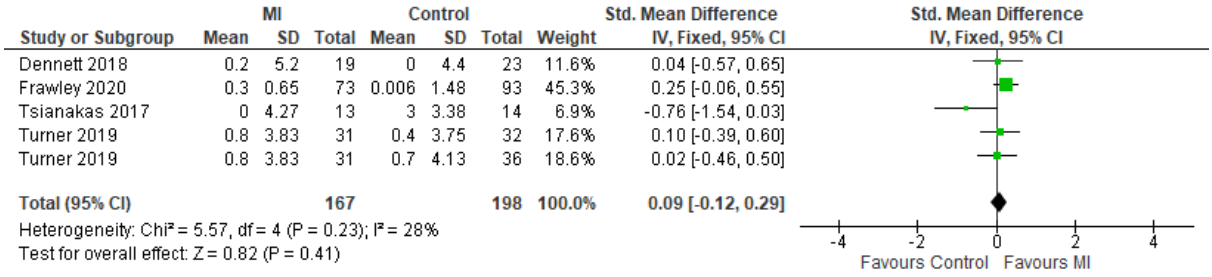

Figure 10. Forest plot of the effects of MI on anxiety

2.4.4.3. Depression

There was a moderate effect of MI on levels of depression compared to control groups using the data from seven studies (with eight comparisons) (SMD 0.38; 95% CI 0.20 to 0.56, $p < 0.0001$, $I^2 = 72\%$, n = 502). The studies in this outcome were downgraded to very low-quality due to risk of bias, inconsistency and indirectness (Table 4).

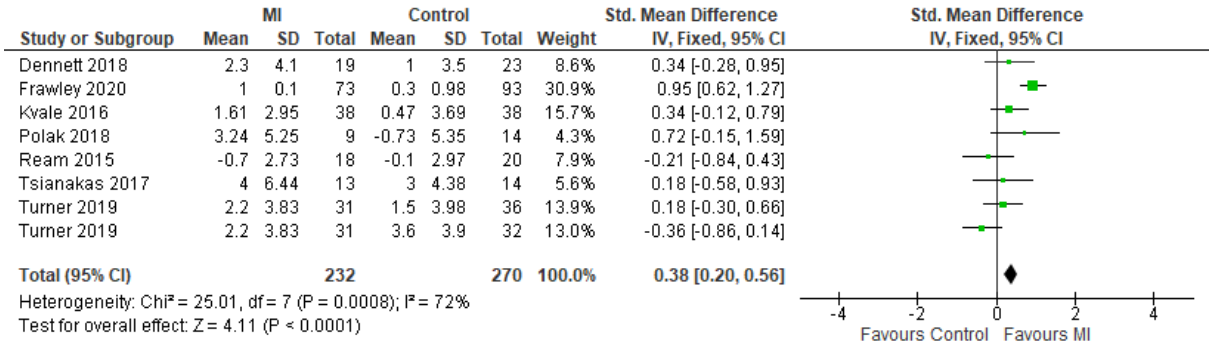

Figure 11. Forest plot of the effects of MI on depression

2.4.4.4. Functional tasks

There was a large effect of MI on functional task outcomes compared to control groups using the data from three studies (MD 50.24; 95% CI 22.04 to 78.44, $p = 0.0005$, $I^2 = 83\%$, n = 111). The studies in this outcome were downgraded to very low-quality due to risk of bias, inconsistency and imprecision (Table 4).

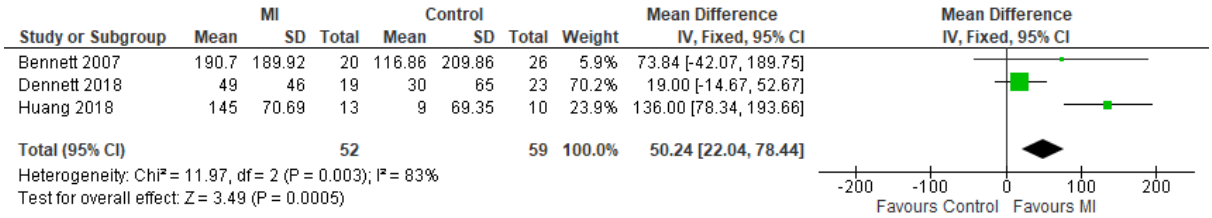

Figure 12. Forest plot of the effects of MI on functional tasks

2.4.4.5. Body Mass Index and body weight

MI had a moderate effect on BMI and body weight outcomes compared to control groups using the data from six studies (with seven comparisons) (SMD 0.25; 95% CI 0.14 to 0.37, $p < 0.0001$, n = 1241). There was no heterogeneity between the studies ($I^2 = 0\%$). The studies in this outcome were downgraded to moderate-quality due to risk of bias (Table 4).

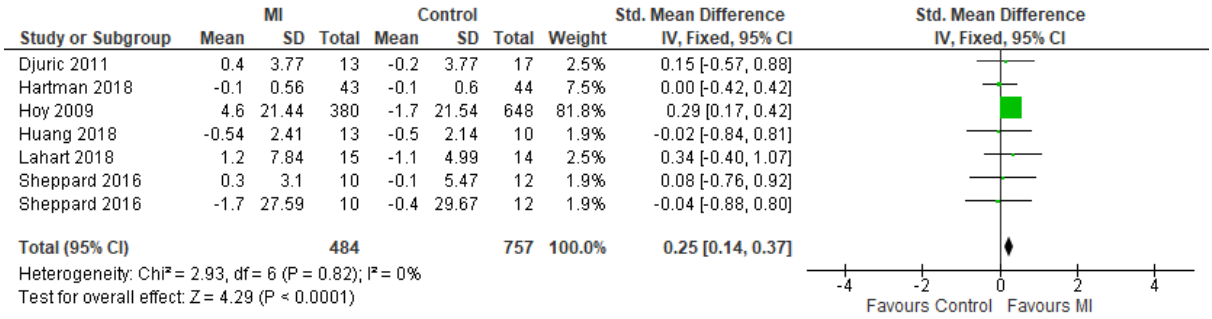

Figure 13. Forest plot of the effects of MI on Body Mass Index and body weight

2.4.4.6. Physical Activity

There was a moderate effect of MI on total PA outcomes compared to control groups (SMD 0.35; 95% CI 0.12 to 0.58, $p = 0.003$, $I^2 = 42\%$, n = 304). There was a moderate effect of MI on step count compared to control groups (SMD 0.62, 95% CI 0.25 to 0.99, $p = 0.001$, $I^2 = 0\%$, n = 119).

Combined, there was a moderate effect of MI on overall PA compared to control groups (SMD 0.42; 95% CI 0.23 to 0.62, $p < 0.0001$, $I^2 = 32\%$, n = 423). The studies in this outcome (both sub-categories and overall) were downgraded to moderate-quality due to risk of bias (Table 4).

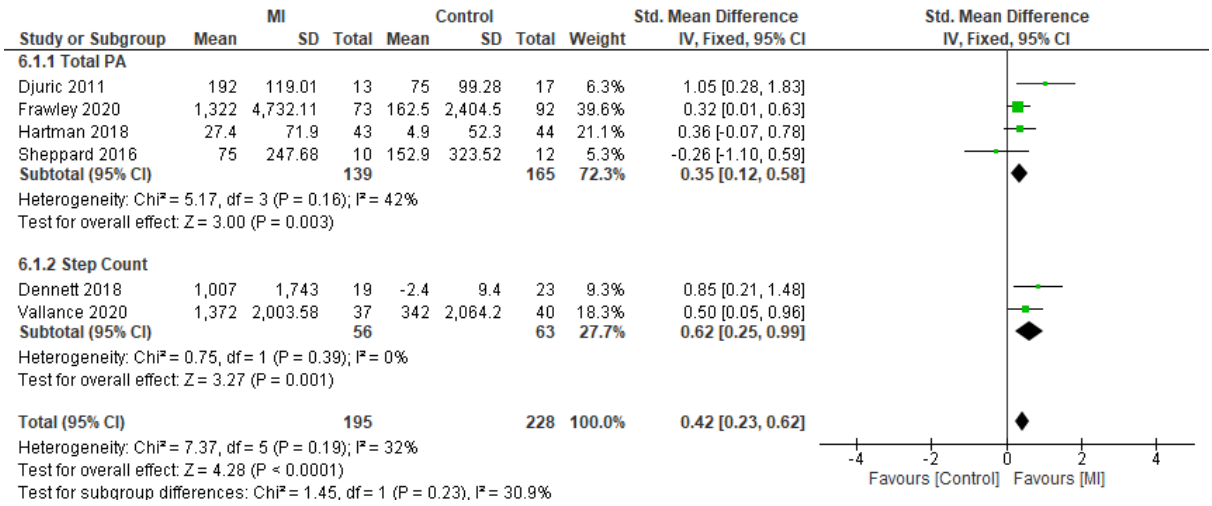

Figure 14. Forest plot of the effects of MI on physical activity

2.4.4.7. Self-efficacy

MI had a moderate effect on self-efficacy outcomes compared to control groups from a total of eight studies (ten comparisons) (SMD 0.33; 95% CI 0.19 to 0.48, $p < 0.0001$, $I^2 = 78\%$, n = 746). The studies in this outcome were downgraded to very low-quality due to risk of bias, inconsistency and indirectness (Table 4).

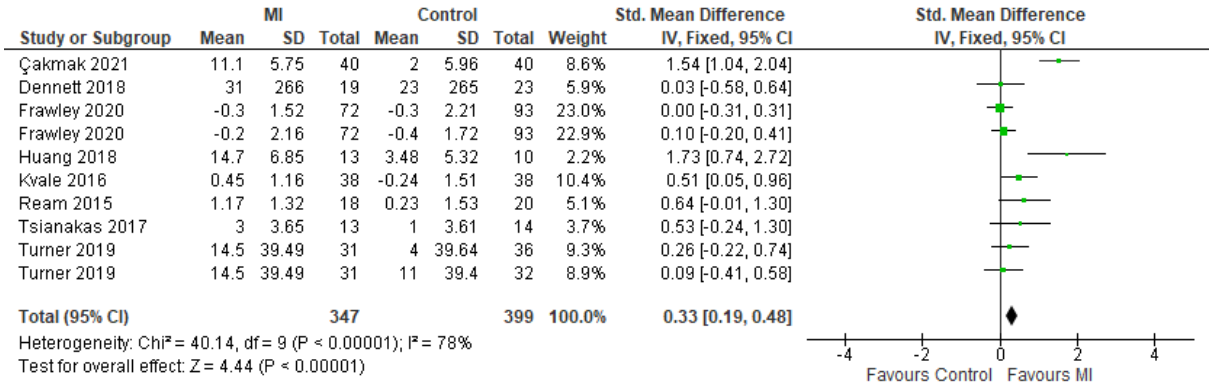

Figure 15. Forest plot of the effects of MI on self-efficacy

2.4.4.8. Fatigue

There was no effect of MI on fatigue outcomes compared to control groups from a total of five studies (SMD 0.25; 95% CI -0.01 to 0.52, $p = 0.06$, $I^2 = 66\%$, n = 233). The studies in this outcome were downgraded to very low-quality due to risk of bias, inconsistency and indirectness (Table 4).

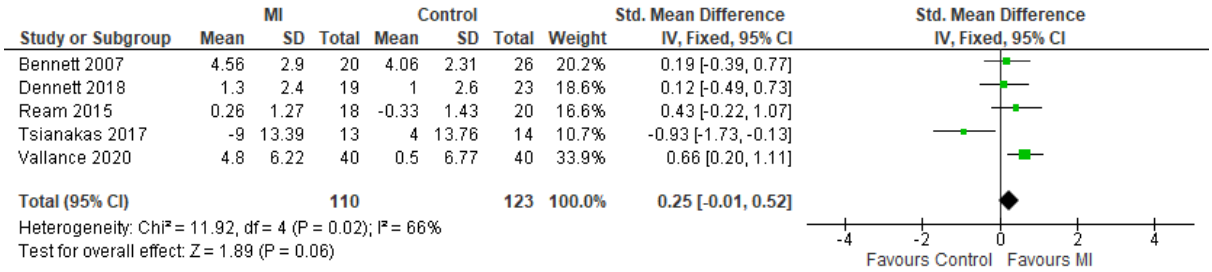

Figure 16. Forest plot of the effects of MI on fatigue

2.5. Discussion

2.5.1. Summary of evidence

This review and meta-analysis provides new evidence that demonstrates a positive effect of MI on PA, depression, functional tasks, BMI and self-efficacy in cohorts of cancer patients and survivors. These findings are important as cancer patients and survivors face unique challenges that can result in poor health behaviours and health outcomes. Understanding what tools are feasible and effective at improving these outcomes can inform future study designs, and also health professionals to working with cancer patients.

The moderate positive effect that MI has on PA and BMI outcomes found in this analysis is similar, however, to a slightly larger magnitude than found in other meta-analyses. Three meta-analyses reported a statistically significant, yet small effect, of MI on PA levels in non-cancer cohorts [149, 158] or in those with a chronic disease such as obesity, cardiovascular disease, multiple sclerosis and fibromyalgia [155]. A fourth meta-analysis also reported a small significant increase in adherence to medical recommendations with increasing PA levels following a MI intervention [157]. Interestingly three of these analyses also found significant decreases in BMI [149, 157, 158] as a result of significant changes in PA levels [149]. This finding, that improvement in PA levels influence secondary objectively measured health outcomes, could help explain the improvement in functional task outcomes found in our analysis. However, another meta-analysis which found no effect of MI on functional tasks (using the same outcome measure as our analysis) postulated that the increase in PA levels may not have been enough to produce changes in functional tasks [155]. This was perhaps more due to the participants within this analysis were diagnosed with either fibromyalgia [197] or multiple sclerosis [198] which are conditions that primarily affect functional capacity therefore their ability for improvement of functional task outcomes are limited. Furthermore, these studies did not contain specific added exercise components to the intervention whereas in the analyses that did report improvements, there were [149, 158]. This may suggest that whilst MI is effective in

increasing motivations to engage in PA, incorporating an exercise component may be pivotal in increasing PA to a level high enough to produce changes in other objectively measured health outcomes particularly in people with chronic health conditions.

The purpose of changing one's behaviour, most commonly, is to effect a change in health outcomes [120] . In objectively measured health outcomes, such as BMI and functional tasks, that can mostly be affected by a change in behaviour i.e. exercise and diet, the link is relatively clear. However, when considering the impact of MI on subjectively measured health outcomes such as QoL, mental health and fatigue, the link is not as clearly defined [63, 150]. A meta-analysis found significant improvements in worry, anxiety, depression, pain and global QoL measures using studies that utilised MI in addition to a lifestyle program component such as dietary and exercise regimes and print materials in a mixed cohort of adults with diagnoses of diabetes, stroke and chronic heart failure [157]. A more recent systematic review of the effect of MI on cancer cohorts found that there were improvements in certain health outcomes such as fatigue, symptom distress and pain in studies where the MI was focused on management of that outcome [150]. However, the results within this current analysis demonstrated the particular focus of the MI did not seem to have a bearing on the effect on any of the outcomes analysed. For example, the only study within the current fatigue subgroup analysis that had an MI targeting fatigue symptom management produced a significant improvement in fatigue outcomes [187] but was only surpassed in effect size by a study (which also carried the greatest weighting) that used an MI focused on improving PA behaviour alone [189]. This was also true for the study that produced the greatest positive effect on depression outcomes which included an MI intervention targeting a combination of health behaviours and symptom management [195].

Research has shown that, in cancer cohorts, improving an individual's level of self-efficacy is key in predicting successful PA behavioural change in cancer survivors [125] and a major factor in being able to manage adverse symptoms [199]. This may suggest that significant improvements in subjectively measured health outcomes, as a result of an MI intervention, are more likely to occur if: 1) there is an element of self-efficacy to symptom management within the MI or 2) PA levels achieve a minimum threshold enough to produce changes in said health outcome.

One common point made within the meta-analyses mentioned thus far, was the high level of heterogeneity between their included studies which prompt many of them to perform regression analysis to identify possible moderating factors. Meta-regression analysis has shown that people from ethnic minorities show a larger effect size in health behaviour change and health outcomes as a result of MI [200]. This has been proposed to be due to the empathic and self-empowering processes involved in MI which are particularly impactful for people within ethnic minority

groups who are subjected to more social rejection and societal pressures [149]. The one study, within our analysis, that included participants from an ethnic minority group did not produce statistically significant improvements in PA levels when compared to controls [151]. However, this study had a small sample number (n = 22) and baseline PA levels of the intervention group were significantly higher than the control group hence a possible ceiling effect of maximal PA improvements that could be achieved.

Three meta-analyses reported that measures that are taken within studies to ensure fidelity of the delivery of the MI intervention was a moderator of improved outcomes [155, 157, 158]. However, this was not shown to be a moderator within our results as the nine studies included within our analysis, that incorporated methods to ensure fidelity of the MI intervention, [180-184, 187, 188, 193, 194] showed varying effects in a range of outcomes. Similarly, other proposed moderating factors shown to increase the MI effect are: higher number of sessions [149], higher qualification of the interviewer [158], self-reporting outcome measures [157] and use of other additional motivational strategies, such as pedometers and print materials [162]. However, a regression analysis was not performed in our analysis due to time limitations, so it is inconclusive as to whether the aforementioned factors are moderators of MI efficacy on outcome, within cancer cohorts.

The quality of evidence for four of the eight outcomes within this analysis was from very low quality studies, which would suggest the results should be interpreted with care. One component that downgraded every outcome was the high risk of bias which was present in every included study. Figure 8 shows that each study was deemed high risk of performance bias in the 'blinding of personnel' criteria. This is an inherent, yet unavoidable, bias for studies that incorporate behavioural and psychological interventions. A similar meta-analysis that investigated the components of exercise interventions that produce significant clinical outcomes in fBCS claimed that a study deemed to be high risk in the performance bias criteria, did not necessarily indicate poor quality [68]. Therefore, in our analysis, when this criteria was hypothetically removed from the overall risk of bias assessment, five studies would have been upgraded to overall low risk of bias [182, 184, 187, 191, 192]. However, this would not have made a difference to the overall quality of evidence (via the GRADE tool) for any of the outcomes given at least one other study, within that outcome, would still be regarded as overall high risk of bias.

The large heterogeneity between studies included within this analysis and the absence of regression analysis limit any conclusive recommendations to be made with regard to effects of MI on behavioural and health outcomes within cancer cohorts. However, there are clear trends towards positive influences that MI has on increasing PA levels, BMI, depression, functional tasks and self-efficacy.

2.5.2. Limitations

A major limitation of this review is the small numbers of studies within each of the outcomes measured which can result in unreliable estimations of the mean weighted effect sizes. The small study numbers combined with lower methodological quality of some of the studies means that interpretation of findings should be done with caution. Additionally a large majority of these studies were feasibility studies or studies that did not contain a large sample size thus results may have not achieved power significance.

Publication bias was another limitation with the use of four databases and selecting studies that are only published in English. Furthermore several studies did not publish outcome data in the format that could be used within the meta-analysis and authors did not respond with requests for further information. Another limitation, which has found to be common within other meta-analyses [155, 201], is the few number of included studies that incorporated measures to ensure that the fidelity of MI was consistent between deliveries and aligned with the true principles as to which it was intended. This was circumvented through incorporating strict inclusion criteria that dictated the use of the term and principles of MI within the study article.

2.6. Conclusion

This review found that MI has positive effects on various health behaviours and health outcomes with more significant results in PA behaviour, BMI, depression, functional tasks and self-efficacy in cancer cohorts. This is an important finding given the unique barriers and health challenges these individuals face as a result of diagnosis and treatment. MI is a feasible intervention that can be used by various health professionals to optimise clinical outcomes in cancer patients and survivors. This review highlights the various factors that can influence the efficacy of MI interventions and future studies would benefit by using more definitive methods of identifying the moderating factors that facilitate this change.

This review also revealed that there was no study that could be located, which investigated the effect of MI on step count, QoL, self-efficacy and motivation types in a cohort of fBCS. Therefore, the next chapter will outline the design of this pilot study to achieve this aim.

Chapter 3

Study design

Study Design

3.1. Introduction

The Physical Activity, Psychological Health and Immunological Outcomes (PAPHIO) Study is a randomised trial, with a cross-over design, primarily investigating the effects of MI on self-directed PA (as measured by step count), psychological health, QoL, self-efficacy, self-regulatory types and immune function outcomes in fBCS [202]. This larger trial is a single site research trial conducted through Western Health at Sunshine Hospital in Melbourne, Australia, in collaboration with Victoria University.

This pilot study is aiming to investigate smaller components of the larger trial by investigating the effect of MI on the self-directed PA levels (as measured by step count), QoL, self-efficacy and self-regulatory types outcomes.

3.2. Overall research aim

To investigate if there is an effect of MI on levels of self-directed PA levels (as measured by step count), QoL, self-efficacy and self-regulatory types in fBCS?

3.2.1. Specific research questions

1. Is there an effect of MI on self-directed PA behaviour (measured in step count) in fBCS?
2. Is there an effect of MI on levels of self-efficacy and self-regulatory types in fBCS?
3. Is there an effect of MI on QoL outcomes in fBCS?

3.3. Methodology

3.3.1. Overall design

The pilot study design is a cross-over randomised trial involving two separate groups of fBCS. The benefits of a cross-over design are that smaller participant numbers are required, and each participant effectively acts as their own ‘control’ [203].

In summary, all participants completed 24 weeks of self-directed PA, which was monitored via a digital step tracker. The intervention of MI was conducted at four-time points (different for each

group). PA (as measured by average daily step count), QoL, self-efficacy and self-regulatory type outcomes were assessed at three-time points (week 1, 12 and 24) for both groups.

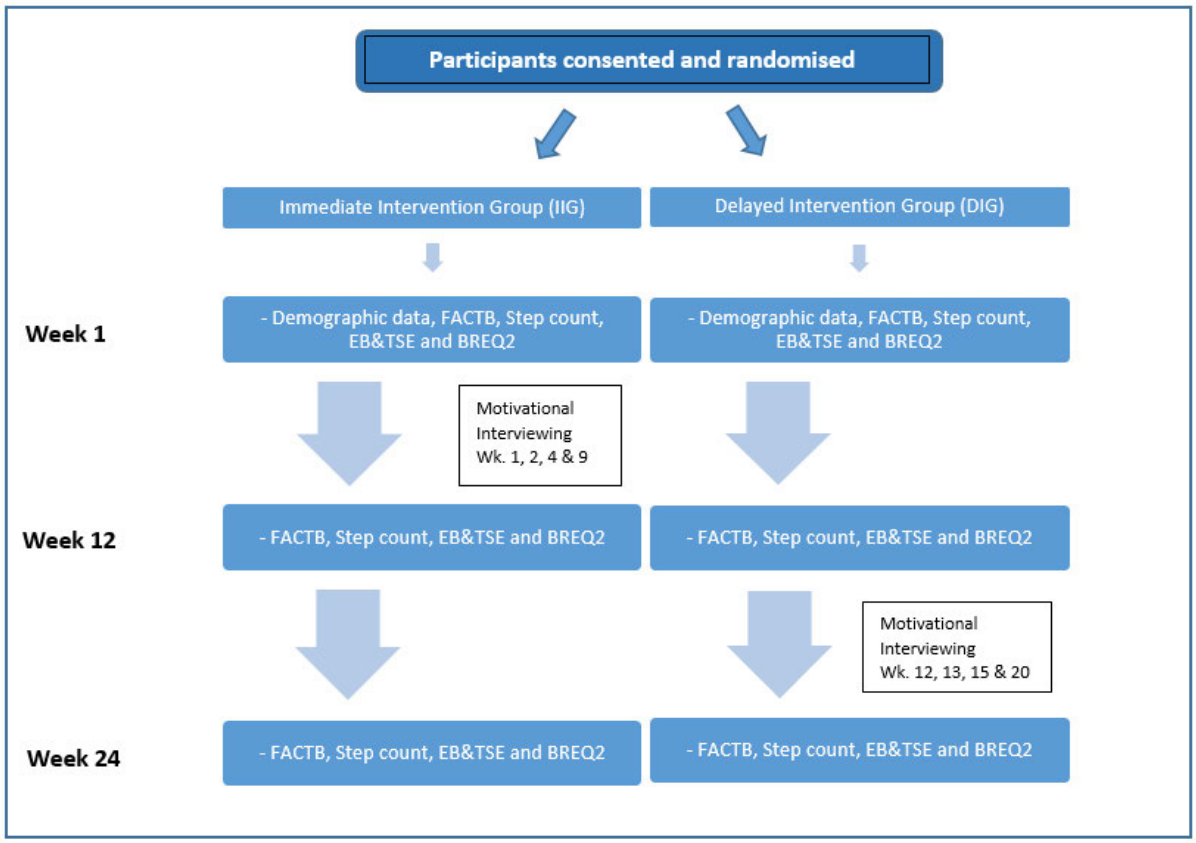

Figure 17. Pilot study design
FACTB = Functional Assessment of Cancer therapy – Breast, EB&TSE = Exercise Barrier and Task Self-Efficacy, BREQ2 = Behavioural Regulation in Exercise Questionnaire 2

3.3.2. Ethics

The larger PAPHIO study trial was registered with the Australian New Zealand Clinical Trials Registry (ANZCTR) ACTRN12619001271190 on 13th September 2019.

Human Ethics Research Committee (HREC) Approval

Initial ethics approval was gained on 29th April 2019 through the Melbourne Health Human Research Ethics Committee (MHHREC) (Appendix 1) with the following details:

- HREC Reference Number: HREC/45268/MH-2018
- Melbourne Health Site Reference Number: 2018.339

Governance authorisation Site Specific Assessment (SSA) approval to conduct a research project at Western Health was attained on 4th December 2019 (Appendix 2).

The initial ethics documents and subsequent approvals mentioned to this point were completed by the previous PhD student, Supa Pudkasam. However, this author (KH) commenced participation within this study from July 2020. During the period from July 2020 until December 2020, there was a transitional 'hand-over' of primary researcher roles from Supa to this author. This included; application of amendments to all study documents (including the online ethics portals) to remove Supa's name and replace with this authors name as the primary researcher and contact person. Various ethics amendment applications were made from inception to current and is listed in Appendix 4. Note that those dated prior to July 2020 were completed by Supa Pudkasam, those dated between July 2020 and December 20th 2020 were jointly completed between Supa Pudkasam and this author and those dated after December 20th 2020 were completed solely by this author.

The license for the use of the FACT-B questionnaire (Appendix 5) and approval for use of the EB&TSE questionnaire (Appendix 6), Good Clinical Practice training (Appendix 7) and a Western Health Office for Research Appointment as an Honorary Researcher (Appendix 8) were all obtained to achieve the standards required to enable this author's safe and effective research role.

3.3.3. Data collection

The following strategies were designed to maintain confidentiality. Furthermore, they were in accordance with the National Statement of Ethical Conduct in Human Research [204]:

- Questionnaires, signed informed consent forms and data from the Fitbit monitor were de-identified, upon collection, via linkage keys and UR hospital numbers according to the Australian Privacy and Data Protection Act 1988 [205]. Following de-identification, all data were scored and entered into the IBM® SPSS® Version 27.0.1 software platform stored within the secure R Drive of Victoria University. Hard or additional copies were kept in a locked cabinet in the Western Health Office of Research in Sunshine hospital, and access was restricted to pre-approved members of the research team.
- Data will be kept for 15 years. A decision will be made within the research team about its destruction, which will be done via shredding of hard copies and deletion or overwriting of digital data.
- Participants were informed as to these above-outlined strategies and their right to withdraw from the study at any point prior to obtaining written consent.

Note that all recruitment of participants and the collection of relevant data (and storage) was conducted by Supa Pudkasam between January 2020 and July 2020. During the period of July 2020 and December 20th 2020, these roles were completed jointly by Supa Pudkasam and this author and from December 20th 2020 these roles were completed solely by this author.

3.3.4. Informed consent

The researcher advised participants to take as much time as required to read through the Patient Informed Consent Form (PICF) (Appendix 9) and contact the researcher for any clarification or queries. Additionally, potential participants were made aware (both in writing and verbally) that their participation in the study was entirely voluntary and based upon information included in the PICF which is in accordance with the *National Statement on Ethical Conduct in Human Research* [204]. This section states, "Participation that is voluntary and based on sufficient information requires an adequate understanding of the purpose, methods, demands, risks and potential benefits of the research" (p16). These components of the study were included in the 12-page PICF with additional information on researcher contacts, confidentiality and privacy processes and dissemination and publication of results. Additionally, a 'Withdrawal of Participant' form was included, outlining the participant's right to withdraw at any point without any consequences, which again is following national standards in ethics [204].

A more recent amendment to the PCIF was approved on the 15th of March 2021 by the MHHERC to include information regarding COVID-19 risk within the *'What are the potential risks to participating in this project'* section (Appendix 10).

3.3.5. Recruitment

Participants were recruited primarily via breast care nurses, medical oncologists and breast surgeons in the Western Health Breast Care Services department at Sunshine Hospital in Melbourne, Australia. Western Health is a Victorian state government body that provides health services (in the public setting) to the western region of Melbourne, with a catchment population of close to 1 million people. This region of Melbourne is considered one of the ten most socioeconomically disadvantaged local government areas in Australia, containing people who are culturally and linguistically diverse, with an average of one in eleven people a recent migrant or refugee [113].

Additionally, other ethics-approved avenues of recruitment occurred through community health centres, advertising material and social media (Facebook).

Participants were screened for eligibility by either the health professionals at Western Health or relevant research team members. In addition, they required a health clearance by a medical physician prior to gaining consent. Recruitment commenced in January 2020 and is currently ongoing; however, the final data included in this pilot study were collected in December 2021.

3.3.6. Inclusion and Exclusion criteria

3.3.6.1. Inclusion criteria

- Minimum 18 years of age
- fBCS who have had a previous cancer diagnosis [stages 0-III including ductal carcinoma in situ (DCIS)] within the last three years and are a minimum of 6 months post active treatment; surgery, chemotherapy or radiotherapy
- Both premenopausal and postmenopausal fBCS
- Women currently undergoing hormonal therapy including tamoxifen, aromatase inhibitors and Herceptin
- Participants with non-English literacy (translators will be used during the informed consent process and validated versions of questionnaires in other languages such as Greek, Chinese, Vietnamese and Macedonian were available during the data collection stages).

3.3.6.2. Exclusion criteria

- fBCS who are currently or within six months of receiving active treatments; surgery, chemotherapy or radiotherapy or are more than three years post active treatment
- Male breast cancer survivors
- Cognitively impaired or illiterate
- Have a diagnosis of metastatic disease

Once the staff at the recruitment sites deemed individuals eligible, verbal consent was sought from the participants to pass on their personal details (UR hospital number, date of birth, name and phone number) to the primary researcher. The researcher then contacted the participant and requested their email for the PICF.

3.3.7. Sample size estimation and justification

Statistical power analysis, according to Cohen, was conducted to calculate the sample size required for the larger PAPHIO study using significance criteria (alpha), sample size and

estimated effect size [176]. A methodologically similar double cross over designed study, with a sample size of n=29 in each group, found there was an effect size of 2.23 and the between-group difference mean score was 27.9 [206]. Using a software calculator for crossover studies [207] using the values of 13 for within-group SD of the Total FACT-B summary score and with a minimum mean difference of 8 [208]. The sample size was calculated to be a total of 53 participants. However, to cater to a predicted 10-20% attrition rate reported within other similar studies [209, 210], the final total sample size was set at 64.

The sample size estimation and justification described above is that of the larger PAPHIO trial which was calculated and decided upon as part of the protocol that was the basis for original MHHREC approval. However, due to a slowing of recruitment soon after commencement of the study, as a result of the global pandemic restrictions, a power analysis was not conducted as it was predicted that the calculated required sample size would not be achieved.

3.3.8. Allocation and study schedule

The study design is illustrated in Figure 17. Once informed consent was gained, participants were randomly allocated to the immediate intervention group (IIG) or the delayed intervention group (DIG) in a 1:1 ratio. Randomisation was performed via the use of a random number table.

All participants were given the Fitbit Alta HR monitor at the time of the baseline data collection. Baseline data collected at the commencement of Week 1 were:

- Demographic data
- Completion of the Functional Assessment of Cancer Therapy-Breast (FACT-B + 4; version 4) Questionnaire (QoL) (Appendix 11)
- Exercise Barrier and Task Self-Efficacy (EB&TSE) questionnaire (Appendix 12)
- Behavioural Regulation in Exercise 2 (BREQ2) questionnaire (Appendix 13)

The baseline average daily step count was obtained at the end of week 1 (to allow for seven days-worth of data to be accumulated). Additionally, the number of hours per day and days per week of monitor usage was obtained at baseline. Participants were then advised to commence as much self-directed PA as is comfortable for the entirety of the 24 weeks with an aim to increase the step count volume each week. All of the data mentioned above (except demographic data) were repeatedly obtained at the T2 (week 12) and T3 (week 24) time-points, as demonstrated in Figure 17.

The first participant was recruited in February 2020 and the final participant (for this pilot study) in May 2021. Figure 18 is a flowchart demonstrating participant recruitment and allocation data, including the women who withdrew from the study.

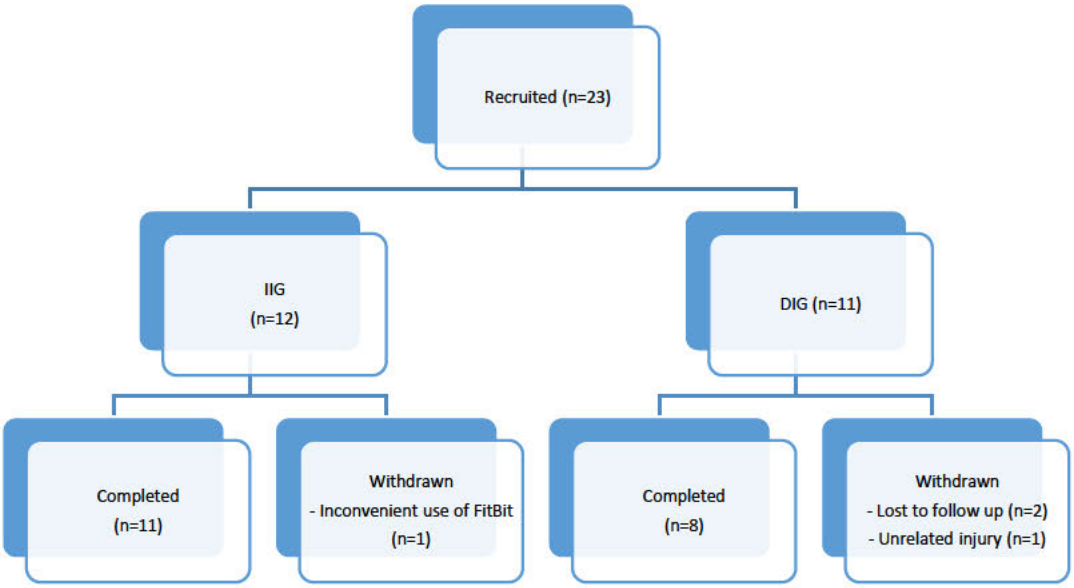

Figure 18. Participant recruitment flowchart

IIG = Immediate Intervention Group, DIG = Delayed Intervention Group

3.3.9. Intervention

Motivational Interviewing

MI is a technique founded on the self-determination theory and is designed to facilitate a change in health-related behaviours [148]. It focuses on fostering the three basic psychological needs of competence, autonomy and relatedness which is believed to successfully facilitate one's control over their behaviours, thus utilising more intrinsic motivators to drive effective and sustainable change [136, 137]. The technique is a collaborative yet primarily patient-centred approach to identifying barriers and facilitators to behavioural change and planning strategies to maximise change. Research has demonstrated that MI is preferred by patients [211] and is more time and cost-efficient than other forms of behavioural change intervention methods [149, 212].

To ensure fidelity of MI sessions, the counsellor consistently followed a script containing ten questions targeting improving PA behaviour (Appendix 14). In accordance with MI principles, there were four subcategories of questions; engage, focus, evoke and plan, which were designed to reflect on current PA behaviour, beliefs, motivations, goals and strategies to increase PA levels.

The MI were conducted at four intervals over 12 weeks (IIG: week 1, 2, 4 and 9, DIG: week 12, 13, 15 and 20) by a trained counsellor and were 15-20 minutes (the initial session was usually 20-30 minutes) in duration per interview. The first interview was face-to-face or online via zoom with the researcher present, and both counsellor and researcher took notes. The following three interviews were done via phone call by the counsellor only, who took notes and sent on to the researcher for confidential storage. The rationale for grouping interviews earlier in each of the intervention phases is to allow for a four-week 'wash-out' period [203] to minimise any latent effects of the intervention.

3.3.10. Data

3.3.10.1. Demographic data

All participants were required to complete a form outlining data such as date of birth, menstrual history and health history relating to breast cancer diagnosis and treatment (Appendix 15). Understanding the specific characteristics of participants is important as they may be influential when looking at the outcomes of this pilot study. In addition, the literature highlights that many of these demographic characteristics may be factors that impact health and behavioural outcomes in cancer patients [15, 16, 213, 214].

3.3.10.2. Average daily step count

Participants were advised of the global PA recommendations for cancer survivors of: "*moderate-intensity aerobic training at least three times per week, for at least 30 minutes"* (p2385) [63]. These recommendations have been endorsed as safe and beneficial for cancer survivors by governing bodies such as the American College of Sports Medicine [63] and the Breast Cancer Network of Australia [86].

The participants were advised to engage in as much PA as they could manage per week with the intention to increase the time-in-activity (increase in step count) each progressive week. Whilst intensity of activity was not the focus of this study, the recommendations mentioned in the previous paragraph contain an intensity parameter. Tudor-Locke et al. [215] reviewed the literature on what cadence constitutes moderate-intensity walking and they concluded that >100 steps per minute is an acceptable minimal threshold value for adults. This translated to between 3,000-4,600 steps per day averaged over the week for older adults or those with chronic disease to 7,100 steps per day averaged over the week for healthy adults to achieve 150 minutes of MIAPA per week. Therefore participants were advised to aim to achieve 7,100 steps per day.

Additionally, translation of 'moderate intensity' of PA was communicated to participants (as recommended by the Breast Cancer Network of Australia) as *"exercise that makes breathing a bit harder but does not make you feel completely out of breath. For example walking briskly where you can talk but not sing."* (p7) [86].

Participants were given a Fitbit Alta HR Monitor (pedometer) at the commencement of the study to record their daily step count. In addition, they were instructed to wear the monitor (wristband) for as long as comfortable each day. Wearable step-count tracker monitors are a feasible method for recording PA levels. Furthermore, in studies involving fBCS, they are reported to be a user-friendly method to measure step count [19, 93], an effective tool to enhance PA engagement [91, 95] and less prone to recall bias [91, 92].

The average daily step count was retrieved from the participant's online Fitbit app for the seven days preceding each of the time-points (T1=Week 1, T2=Week 12, T3 = Week 24). The highest and lowest step count were excluded, and the average of the remaining five daily step count amounts was used to formulate the final average daily step count. A recent analysis reports that the minimum amount of days required to accurately reflect an individual's PA levels is three to four days for wrist-worn pedometers, [216] hence the average of five days-worth of data was deemed sufficient. Participants were also required to recall the average amount of time they wore the Fitbit in the preceding week (hours per day and days per week) to help contextualise the average daily step count within that time-point.

3.3.10.3. Quality of Life

The Functional Assessment of Cancer Therapy-Breast (FACT-B + 4; version 4) (Appendix 11) was used to collate data on the participants' QoL. It is a 37-item questionnaire consisting of five different subscales; Physical Wellbeing (7 items), Social/Family Wellbeing (7 items), Emotional Wellbeing (6 items), Functional Wellbeing (7 items) and an Additional Concerns subscale (10 items) pertaining to breast cancer-specific concerns.
There are eight scores derived (five subscales and three summary scores):

- Physical Well Being (PWB) = score range 0-28
- Social/Family Well Being (SWB) = score range 0-28
- Emotional Well Being (EWB) = score range 0-24
- Functional Well Being (FWB) = score range 0-28
- Additional Concerns – Breast Cancer Subscale (BCS) = score range 0-40
- Trial Outcome Index (TOI) = PWB + FWB + BCS (score range 0-96)
- FACTG Total Score = PWB + SWB + EWB + FWB (score range 0-108)

- FACTB Total Score = PWB + SWB + EWB + FWB + BCS (score range 0-148)

Each of the first four subscales contain items that relate to cancer issues commonly found to be prevalent within that domain. For example PWB contains items such as *'I am forced to spend time in bed',* SWB contains items such as *'I am satisfied with family communication about my illness',* EWB contains items such as *'I feel nervous'* and FWB contains items such as *'I am enjoying the things I usually do for fun'.* The BCS contains items that cover a range of the four well-being domains mentioned before however in the context of breast cancer-specific issues such as *'One or both of my arms are swollen or tender'* and *'I feel sexually attractive'.* TOI is an indication of total functional status of an individual as it is the summary score of all subscales that pertain to physical and functional status (remembering that the BCS contains items pertaining to these domains). The FACTG Total Score is an indication of the general QoL of the cancer individual whereas the FACTB Total Score is the same yet contains the additional subscale score of the BCS.

The scoring is via a 5-point Likert-scale answering system with 0 = not at all and four = very much. The questions within the SWB and FWB subscales contain positively worded questions which translates into the higher the score, the higher the QoL for that question. Questions within the PWB subscales contain negatively worded questions which translates to the higher the score the lower the QoL for that question. Questions within the EWB and BCS subscales are a mixture of both positively and negatively worded. According to FACT scoring guidelines, every completed questionnaire was scored [217] and entered into an excel spreadsheet. The scoring process included adding 0 to all the scores from positively worded questions and subtracting from 4 all the scores from negatively worded questions. Following this first step, all of these 'scored' values within one subscale were added to get the 'sum individual item score'. This total score was multiplied by the number of questions within that subscale and then divided by the number of questions answered resulting in the final score for that subscale. An illustration of this scoring process can be seen in Figure 19. The last two steps of multiplying the 'sum individual item score' by the number of questions within the subscale and then dividing by the number of questions within the subscale, accommodating for any missing data.

FACT-B Scoring Guidelines (Version 4) – Page 2

Subscale	Item Code	Reverse item?		Item response	Item Score
BREAST CANCER SUBSCALE (BCS)	B1	4	-	_____	=_____
	B2	4	-	_____	=_____
	B3	4	-	_____	=_____
	B4	0	+	_____	=_____
	B5	4	-	_____	=_____
Score range: 0-40	B6	4	-	_____	=_____
	B7	4	-	_____	=_____
	B8	4	-	_____	=_____
	B9	0	+	_____	=_____
	P2	4	-	_____	=_____

Sum individual item scores: _____
Multiply by 10: _____
Divide by number of items answered: _____ =**BC Subscale score**

Figure 19. BCS score – FACT-B (version 4) Scoring Guidelines

The FACT-B (version 4) questionnaire is a reliable and valid measuring tool, in English, for QoL in other breast cancer studies with reports of high overall alpha coefficients (internal consistency) of 0.90 [218, 219]. This questionnaire was also available in various languages such as Vietnamese, Greek, Chinese and Macedonian (internal reliability values are not available). A clinically meaningful change is between 3 and 7 points for the FACTG Total score and between 6 and10 points for the FACTB Total score [208].

3.3.10.4. Exercise Barrier and Task Self-Efficacy

The Exercise Barrier and Task Self-Efficacy questionnaire contains two subsections: i) Barrier self-efficacy, which contains nine items pertaining to the individual's perceived level of confidence to perform the PA when presented with possible barriers and ii) Task self-efficacy, which contains four items relating to an individual's perceived level of confidence to perform a particular PA task. The scoring sheet has a 10-point scale with 0% indicating 'Not at all' (low level of confidence) to 100% indicating 'Extremely' (high level of confidence). Each item describes a situation, and the participant is required to answer how confident they are in doing the exercise in certain situations. For example, the fourth item within the barrier self-efficacy section describes a situation; *"When the weather is bad"* – and the participant is required to score anywhere between 0% = not at all (confident to do exercise when the weather is bad) or 100% = extremely (confident to do exercise when the weather is bad). Therefore, the higher the score the greater the confidence to a) overcome barriers and b) perform the task. The mean of all scores within each subsections will be calculated at each of the three time-points and the mean for each item within each subsection. Internal consistency for this questionnaire is good with a

Cronbach's alpha for the barrier self-efficacy scale being 0.96 and the task self-efficacy scale being 0.89 [144].

3.3.10.5. Behavioural Regulation in Exercise 2

The Behavioural Regulation in Exercise Questionnaire 2 (BREQ2) is a 19-item questionnaire with five different subscales that represent the different types of motivation (except for 'integration regulation' type) that exist within a continuum from extrinsic (involving less autonomous regulatory type) motivation to intrinsic (involving more autonomous regulatory types) motivation. This continuum is based on the Self-Determination Theory (SDT) proposed by Ryan and Deci [136]. It proposes that by increasing an individual's sense of control over their behaviour (autonomy), one can develop more intrinsic motivators, thus leading to more effective and sustainable change.

Each of the five subscales has four items (except for Introjection, which has three) all assessed by a 5-point Likert scale (0 = not true for me, 4 = very true for me):

- Amotivation (Items 5, 9, 12 and 19): Avolition to PA
- External regulation (Items: 1, 6, 11 and 16): Motivation via external persons advice or encouragement to engage in PA
- Introjection regulation (Items: 2, 7 and 13): Internal motivation derived from external expectations and pressures to engage in PA, commonly involving feelings of guilt
- Identified regulation (Items: 3, 8, 14 and 17): Motivation from a desire to achieve a goal that PA may assist in attaining e.g. losing weight
- Intrinsic regulation (Items: 4, 10, 15 and 18): Motivation due to enjoyment of PA behaviour.

The Cronbach's alpha reliabilities were good for each of these subscales: Amotivation (0.83), External Regulation (0.79), Introjected Regulation (0.80), Identified Regulation (0.73) and Intrinsic Regulation (0.86) [220]. The multidimensional scoring method for this questionnaire is to calculate the mean scores for the set of items within each subscale. This outcome will indicate the individuals' preferred motivation style for performing the PA at various time-points. The MI intervention aims to enhance one's autonomy over their behaviour, thus favouring a move towards the more intrinsic regulatory types following the intervention.

3.3.11. Statistical analysis

All original data for the outcomes mentioned above were entered into an excel spreadsheet where they were coded and subscale scores calculated. Data was then transferred into a JASP software 2022 (Version 0.16.3) [Computer software] where all analyses were conducted. Descriptive statistics were used with demographic and adherence data to calculate the mean, standard deviation and range for continuous variables (age and time since diagnosis) and number and percentage for categorical variables (all others). To assess variance between demographic data between groups, independent *t*-tests were conducted on continuous and categorical data.
For assessing any effect of MI on step count, QoL subscales and scores, self-efficacy and self-regulatory types, period-adjusted linear mixed modellings were used. The alpha value was set as 0.05, with p values < 0.05 considered statistically significant.

Chapter 4

Physical Activity Outcome Results

Step count Outcome Results

4.1. Overview

Physical inactivity levels in fBCS are lower than their healthy cohorts, due to unique barriers, such as musculoskeletal pain [52], depression and anxiety [105] and fear of injury [101], which can occur as a result of diagnosis or treatment. This can become problematic as PA has been shown to be a safe [79] and effective strategy to improve various health outcomes in fBCS, including reduced risk of cancer recurrence and improved physical and mental health [59, 69, 71]. Developing the motivation to overcome such barriers becomes pivotal in achieving overall optimal health [76]. MI is a psychological tool designed to discover the factors responsible for an individuals' ambivalence to change [148]. The MI intervention used in this study was underpinned by the self-determination theory which was directed towards increasing PA levels (as measured by average daily step count) within a cohort of fBCS. The interview identified current motivators, benefits and barriers to PA and established goals and strategies to increase PA levels [136].

Two of the specific research questions of this pilot study were: 1) Is there an effect of MI on self-directed PA levels (as measured by step count) in fBCS? and, 2) Is there an effect of MI on self-efficacy and self-regulatory types in fBCS? The results from the above mentioned outcome data will be presented and related to other relevant evidence within the literature. For a detailed description of the study design, methodology, outcome measures and synthesis of results, refer to Chapter 3. Study Design.

4.2. Results

The original raw data for the outcomes presented within this chapter is presented within Appendix 16.

4.2.1. Demographic data

Table 5 outlines the demographic characteristics of each group. The *p* values of all domains are > 0.05 indicating no significant differences between the groups. The mean age of the cohort was 49.7 years of age (SD 9.49), with the IIG consisting of slightly younger participants (32-65 years of age) with a greater spread of ages (SD 10.22). The majority of participants have had more than one pregnancy (73.7%, n = 14) and 21.1% (n = 4) have had none. However, there was a higher proportion who have not had any pregnancies in the IIG with 27.3% (n = 3) compared to

the DIG with 12.5% (n = 1). 63.2% (n = 12) of combined participants experienced menarche between 12-14 years of age and 79% (n = 15) had their last period over 40 years of age. Most of combined participants had a diagnosis of stage two breast cancer (73.7%, n = 14) with the remaining 26.3% (n = 5) having a stage three diagnosis with not much variation between groups.

Mean time since cancer diagnosis was 18.5 months (SD 8.17). All participants had undergone some form of surgery. However, half of the women in the DIG had a mastectomy compared to 27.3% (n = 3) in the IIG. The majority of women in both groups had received chemotherapy with more in the IIG with 81.9% (n = 9) compared to 75% (n = 6) within the DIG. However, with respect to receiving radiotherapy, those in the DIG had a higher proportion with 87.5% (n = 7), compared to 81.9% (n = 9) in IIG. Finally, 63.6% (n = 7) of women in the IIG were receiving ongoing hormonal treatment, of which 28.4% (n = 2) were taking aromatase inhibitors with the rest taking Tamoxifen. The DIG group had significantly less percentage of women, 37.5% (n = 3), receiving ongoing hormonal treatment, of which two thirds were taking aromatase inhibitors with the last third taking Tamoxifen.

Table 5. Baseline participant characteristics (by group allocation)

Demographic characteristic	**IIG (n=11)**	**DIG (n=8)**	**Combined (n=19)**	***P* value**
Age, years	48.6 ± 10.22 (32-65)	51.4 ± 8.78 (41-69)	49.7 ± 9.49 (32-69)	0.537
Pregnancies				
- **None**	3 (27.3%)	1 (12.5%)	4 (21.1%)	0.337
- **One**	1 (9.1%)	-	1 (5.2%)	
- **More than one**	7 (63.6%)	7 (87.5%)	14 (73.7%)	
Age at first period				
- **Less than 12 years**	3 (27.3%)	2 (25%)	5 (26.3%)	0.846
- **12-14 years**	7 (63.6%)	5 (62.5%)	12 (63.2%)	
- **More than 14 years**	1 (9.1%)	1 (12.5%)	2 (10.5%)	
Age at last period				
- **In reproductive period**	1 (9.1%)	-	1 (5.2%)	0.539
- **Less than 39 years**	2 (18.1%)	1 (12.5%)	3 (15.8%)	
- **40-49 years**	4 (36.4%)	5 (62.5%)	9 (47.4%)	
- **More than 50 years**	4 (36.4%)	2 (25%)	6 (31.6%)	
Stage of Cancer				
- **One**	-	-	-	0.373
- **Two**	9 (81.9%)	5 (62.5%)	14 (73.7%)	
- **Three**	2 (18.1%)	3 (37.5%)	5 (26.3%)	

- **Four**	-	-	-	
Period (of time) since diagnosis (months)	16.7 ± 8.82 (6-36)	20.9 ± 7.02 (10-30)	18.5 ± 8.17 (6-36)	0.287
Surgery - **No** - **Yes (lumpectomy)** - **Yes (mastectomy)**	- 8 (72.7%) 3 (27.3%)	- 4 (50%) 4 (50%)	- 12 (63.2%) 7 (36.8%)	0.338
Chemotherapy - **No** - **Yes**	2 (18.1%) 9 (81.9%)	2 (25%) 6 (75%)	4 (21.1%) 15 (78.9%)	0.737
Radiotherapy - **No** - **Yes**	2 (18.1%) 9 (81.9%)	1 (12.5%) 7 (87.5%)	3 (15.8%) 16 (84.2%)	0.754
Current Hormonal Treatment - **None** - **Tamoxifen** - **Aromatase Inhibitors** - **Herceptin**	4 (36.4%) 5 (45.5%) 2 (18.1%) -	5 (62.5%) 1 (12.5%) 2 (25%) -	9 (47.4%) 6 (31.5%) 4 (21.1%) -	0.163

IIG = Immediate Intervention Group, DIG = Delayed Intervention Group
**Values presented as mean ± standard deviation (range) or n (%)*

4.2.2. FitBit usage data

Usage of the FitBit for each group and combined values are illustrated in Table 6. There was complete adherence during the day and night (considered 22 hrs to allow for water-based activities such as showering and washing where the monitor was required to be removed) for seven days of the first week. There were similar adherence levels between the 12-week and 24-week time-points for the IIG with an average of 18.4 (SD 5) and 19.1 (SD 6.8) hours per day, respectively. Comparatively, within the DIG there was lower adherence at the 12-week time-point with an average of 13.9 (SD 5.4) hours per day. However, by the 24-week time-point, the average hours had increased to 19 (SD 5), which was similar to the IIG. The number of days per week was similar across all time-points for both groups being between 6.8-7 days per week which was mainly skewed by one participant in each group (IIG1 and DIG11) whose adherence was five days per week at both time-points (except for DIG11 which increased to 7 days by week 24).

Table 6. FitBit usage data

Adherence in FitBit usage **Hours per day/days per week**	**Week 1**	**Week 12**	**Week 24**
IIG (n=11) - **Hours per day** - **Days per week**	22 ± 0 (22) 7 ± 0 (7)	18.4 ± 5 (8-22) 6.8 ± 0.6 (5-7)	19.1 ± 6.8 (6-22) 6.8 ± 0.6 (5-7)
DIG (n=8) - **Hours per day** - **Days per week**	22 ± 0 (22) 7 ± 0 (7)	13.9 ± 5.4 (7-22) 6.8 ± 0.7 (5-7)	19 ± 5.2 (8-22) 7 ± 0 (7)
Combined (n=19) - **Hours per day** - **Days per week**	22 ± 0 (22) 7 ± 0 (7)	16.5 ± 5.5 (7-22) 6.8 ± 0.6 (5-7)	18.9 ± 5.2 (6-22) 6.9 ± 0.5 (5-7)

IIG = Immediate Intervention Group, DIG = Delayed Intervention Group
**Values presented as mean ± standard deviation (range)*

4.2.3. Outcome data

Table 7 shows the means values at each time-point in both groups for outcome measures.

	IIG			**DIG**		
	Week 1	**Week 12**	**Week 24**	**Week 1**	**Week 12**	**Week 24**
Average daily step count	8,350 (±3417)	10,369 (±5653)	9,334 (±4967)	9,526 (±4308)	10,107 (±4098)	9,662 (±5424)
EB&TSE - EB (score range 0-100%)	38.5 (±23.1)	41.2 (±22.7)	34.2 (±27.2)	37 (±13.3)	43.8 (±19.6)	60.4 (±18.3)
- TSE (score range 0-100%)	63.6 (±21.4)	60.9 (±24.2)	62.3 (±24.3)	59.4 (±33.4)	69.4 (±28)	76.9 (±27.3)
BREQ2 (score range: 0 = not true for me, 4 = very true for me) -Amotivation	0.6 (±0.8)	0.5 (±0.8)	0.3 (±0.5)	0.2 (±0.4)	0 (0)	0 (0)
- External regulation	0.9 (±0.7)	0.6 (±0.9)	0.6 (±1.1)	0.8 (±1)	0.6 (±1.1)	0.2 (±0.4)

- Introjection regulation	1.8 (±1.2)	2.1 (±1.1)	2.5 (±1)	2.2 (±1.5)	2 (±1.2)	2.4 (±1.1)
- Identified regulation	3 (±0.6)	3.3 (±0.7)	3.5 (±0.5)	3.1 (±0.3)	3.3 (±0.3)	3.3 (±0.4)
- Intrinsic regulation	3 (±0.8)	3.1 (±1)	3.2 (±0.8)	3.1 (±0.9)	3.1 (±0.5)	3.3 (±0.8)

Table 7. Outcome data (by group allocation and time-point)
IIG = Immediate Intervention Group, DIG = Delayed Intervention Group
EB&TSE = Exercise Barrier & Task Self-Efficacy, BREQ2 = Behavioural Regulation in Exercise Questionnaire 2.
**Values presented as mean (standard deviation)*

The period-adjusted linear mixed modelling demonstrated that there was no significant effect of motivational interviewing on either of; step count (p=0.652) (*Figure 20*), amotivation (p=0.447) (*Figure 21*), external regulation (p=0.384) (*Figure 22*), introjection regulation (p=0.872) (*Figure 23*), identified regulation (p=0.472) (*Figure 24*), intrinsic regulation (p=0.994) (F*igure 25*), barrier self-efficacy (p=0.069) (*Figure 26*) or task self-efficacy (p=0.277) (*Figure 27*).

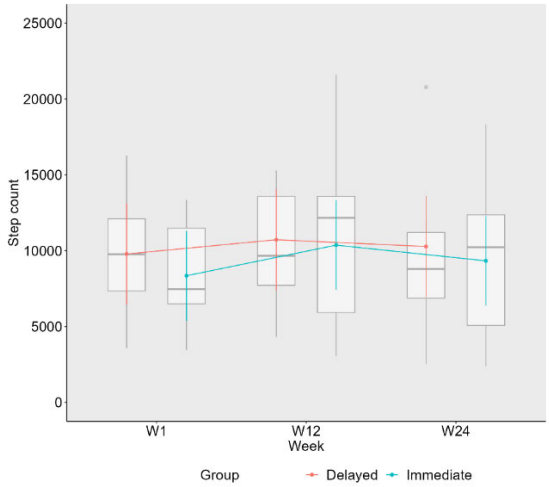

Figure 20. Step count data (by group allocation)

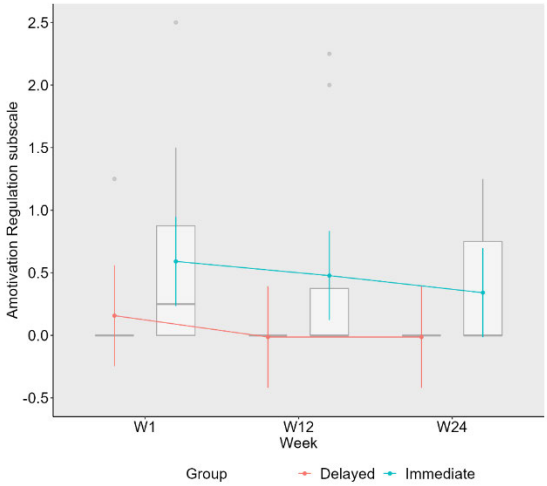

Figure 21. Amotivation (by group allocation)

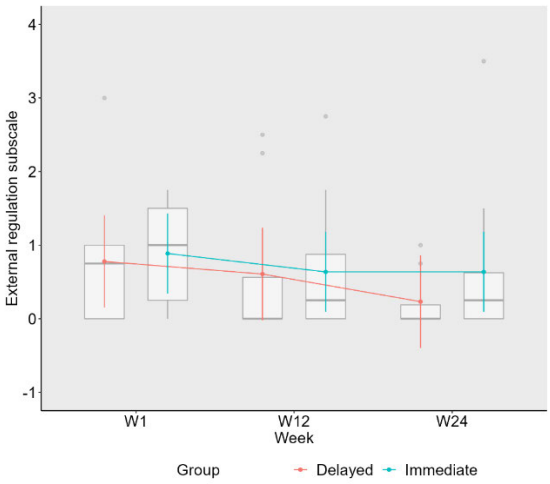

Figure 22. External Regulation (by group allocation)

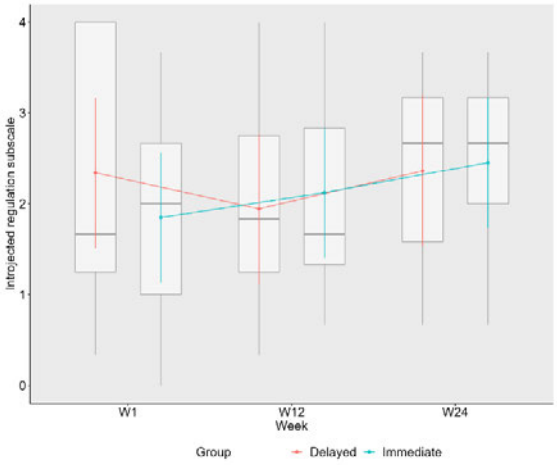

Figure 23. Introjection Regulation (by group allocation)

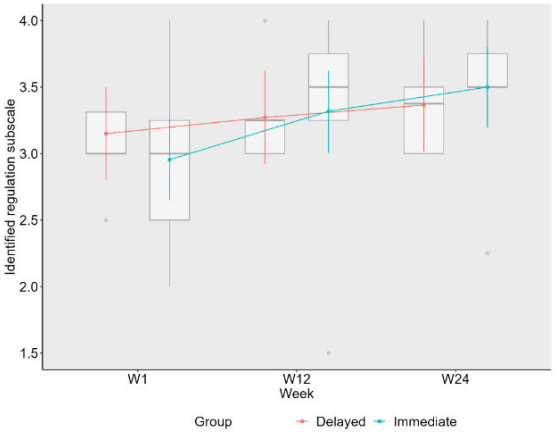

Figure 24. Identified Regulation (by group allocation)

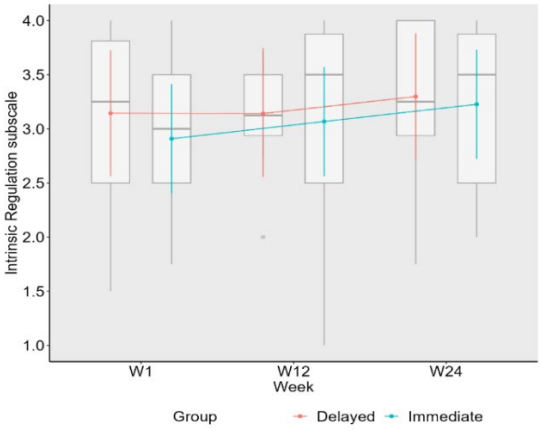

Figure 25. Intrinsic Regulation (by group allocation)

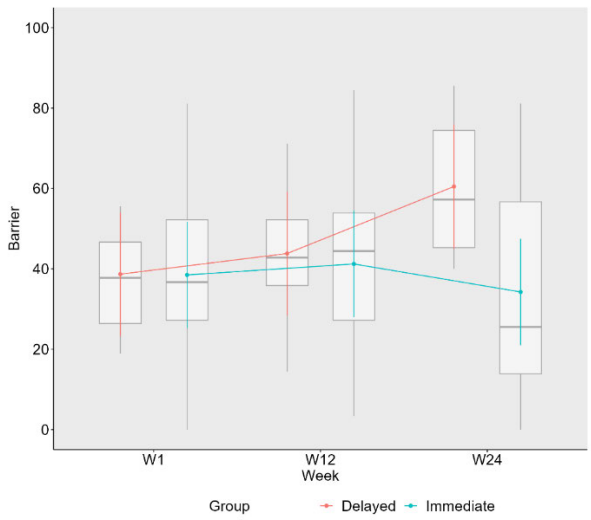

Figure 26. Barrier Self-Efficacy (by group group allocation)

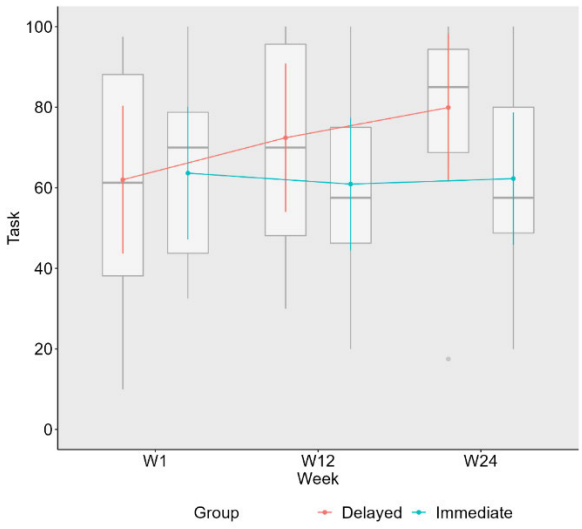

Figure 27. Task Self-Efficacy (by allocation)

** Coloured dot = group mean value, vertical coloured line = 95% confidence intervals, horizontal grey line = group median value, top and bottom end of boxes = Q1 and Q3, vertical grey lines = minimum and maximum group values, grey dots = outliers*

4.3. Discussion

Initiating, and sustaining, a change in behaviour is a challenging task for many adults. However, for fBCS, effecting a change in health behaviours such as PA, can be even more overwhelming given the inherent obstacles that can occur as a result of diagnosis and treatment. Finding strategies that can enhance engagement in healthy behaviours as well as empowering an individual's level of self-efficacy and more autonomous self-regulatory types can be the key to facilitate long-term effective change [118]. Two of the specific research questions of this study was to determine whether MI aimed at increasing PA levels in fBCS had an effect on both PA behaviour (as measured by step count) and associated levels of self-efficacy and self-regulatory types. The results presented earlier within this chapter will attempt to answer these questions.

This cross-over randomised pilot study showed no effect of MI on levels of step count in fBCS. In addition, there was no effect of MI on levels of task or barrier self-efficacy nor on any of the five components of behavioural regulation in exercise (amotivation, extrinsic regulation, introjection regulation, identification regulation or intrinsic regulation).

Motivational Interviewing and step count

The results from this pilot study show that there was no effect of MI on changes in step count levels in fBCS irrespective of the timing of the intervention. Contrary to these findings, some systematic reviews and meta-analyses indicate small to moderate effects of behavioural change strategies on PA levels in cancer patients and survivors [76, 96, 150, 162]. The authors of these reviews and analyses reported the sources of the significant heterogeneity found between their included studies were mostly intervention characteristics, outcome measures used and demographic characteristics of participants which may have influenced their results.

In-person, interactive behavioural change coaching sessions were found, in some meta-analyses, to have a greater impact in promoting PA than remote or passive delivery such as via phone or email [76, 96]. However, two other meta-analyses found that mode of delivery (in-person or via phone) was not a moderating factor in the effect of MI on health and behavioural outcomes [155, 158]. The two meta-analyses that found greater effect from in-person sessions were conducted in cohorts of cancer patients and survivors. One of these meta-analyses also found that a higher qualification of the interviewer was predictor of improved outcomes [158]. Furthermore, a RCT that used a combination of highly qualified health professionals and other fBCS peers to deliver the MI to fBCS participants showed significant improvements in PA levels, BMI, cardiovascular function and dietary intake [151]. This study also measured feasibility outcomes such as acceptability of the intervention by participants which rated high (85%) with specific reports of high levels of trust in the interviewer [151]. This supports the key tenets of the SDT and MI process that building a strong rapport between the interviewer and the participant is pivotal. However, methods of how to achieve that may lay in the mode of MI delivery and background of the interviewer. The MI sessions within this study were mostly via phone consultations due to COVID-19 pandemic restrictions and without the inclusion of other fBCS peers, which may have translated into poorer rapport with the interviewer thus reducing the effect of the MI on PA levels.

The fidelity and frequency of MI sessions may have influenced the efficacy of the intervention within our study. A similar pilot study in 2014 showed that weekly MI (one initial in-person followed by phone calls), over 16 weeks in a cohort of fBCS produced significant improvements in PA levels [221]. The study also incorporated fidelity measures, via regular reviews by a supervising MI instructor, to ensure consistency of the MI intervention over the 16 weeks. Some meta-analyses have found evidence to support improved outcomes when objective measures are taken to ensure fidelity of the MI intervention [155, 157, 158]. Whilst some measures were taken to ensure fidelity of MI delivery in our study i.e. the same counsellor delivered all the MI sessions using the same script of questions, perhaps the use of objective reviews by more

qualified MI persons would have resulted in a higher effect of the intervention. The weekly delivery of MI sessions within the 2014 study may suggest that the four MI sessions used within our study, over 12 weeks, was not enough to produce an effect of the MI on step count in our participants. This suggested dose-response relationship between MI and increases in PA levels is a relationship that was observed by the authors of two meta-analyses however, it was stated that it was more of a trend and further evidence was needed to report if dosage was an actual moderator [149, 157]. The 2014 study mentioned earlier also incorporated a home-based, highly structured combined aerobic and resistance exercise intervention component which the authors identified as being an influential factor in improved PA outcomes [221]. Two meta-analyses found significant improvements in PA levels following the use of a MI intervention using studies that incorporated added component of either structured home-based exercise programs or supervised exercise sessions [149, 158]. This suggested that a lack of a structured exercise intervention component in our study may have also explained the no change in PA levels.

The supplemental use of print materials to the MI intervention, in the form of either diaries or informative documents, has been shown in systematic reviews and meta-analyses to contribute to improved PA outcomes within studies [76, 96, 150, 162]. Two RCTs that used a combination of MI and detailed, bespoke printed information (including culturally appropriate images and terminology) notebooks and diaries to improve healthy behaviours in fBCS found a significant improvement in PA levels post-intervention compared to the control group [151, 185]. Interestingly, the control groups within each of these studies had also received print materials albeit at a very basic level of general health information. This suggests that the additional use of print materials, specifically those that are detailed and tailored to the aim of the study and specifics of the cohort, improve PA outcomes. The lack of inclusion of print materials within our study may have limited improvements to the PA outcomes.

The use of digital monitors (wearable device or smart-phone application) has been reported to act as a tool that facilitates active feedback, motivation and accountability, thus enhancing PA outcomes in studies [76, 162]. Whilst our study utilised a wearable step count tracker, it did not seem to impact PA levels. A RCT that used a combination of MI, informative print materials and a pedometer in fBCS found significant improvements in PA levels post-intervention compared to controls [181]. However, the authors concluded that the pedometer may not have contributed to this impact given the device readings were low, with six of the 13 participants using the pedometer more than three times over 12 months. Also there may be an element of reporting bias, given the participants recorded their PA levels either through data from the pedometer or self-estimation. However, reporting bias is a common issue with studies that use self-reported outcome measures as illustrated by a meta-analysis that found that the use of self-reported

outcome measures was a moderator of MI efficacy in medical care settings [157]. The authors of this meta-analysis rationalised this finding as a result of reporting bias rather than a true moderator of MI. Whilst our study used objective measures of PA (step count via pedometer), there are still reporting biases that can occur with such measures. A RCT that used a MI intervention, in fBCS, aimed at increasing self-directed PA levels and required the participants to wear two activity monitors: one worn on the wrist which recorded step count in number per week and one worn on the waist and hip which measured MIVPA in minutes per week. The authors found that whilst there was a statistically significant increase in levels of MIVPA immediately post-intervention (within the intervention group), the step count change was not significant. Similarly, when comparing control and intervention, the increase in MIVPA was significant but not when looking at step count [154]. Therefore, PA outcomes in our study may have been underestimated given the pedometer used to measure step count was a wrist monitor and the only tool used to assess PA outcomes. Inaccurate reporting of PA levels using wrist-worn pedometers have been shown to be more prevalent especially in unsupervised settings [222] and during moderate walking speeds where discrepancies of between 700-1800 steps per day could be seen [223]. In contrast to these reports, three recent studies provided evidence that there is high accuracy of step count measurements via wrist worn monitors when used in supervised environments [224-226]. This could potentially mean that our results were a reflection of underestimation of step count given the participants within our study were using a wrist worn monitor in an unsupervised setting of self-directed walking.

The impact of the COVID-19 pandemic on participants' ability to perform self-directed PA is another factor that may have impacted step count outcomes within this study. On January 25 2020, Australia identified the first case of COVID-19 which was followed by a number of lockdowns in very quick succession on various states, in an attempt to contain the virus. Within the state of Victoria, the metropolitan region of Melbourne was reported to be the most 'locked-down' city in the world with a cumulative total of 263 days between the dates of March 30th, 2020 to October 21st, 2021 [227]. Some of the lockdowns involved restrictions that impacted an individuals' ability to engage in PA especially when an 8pm – 5am curfew restricted exercise to a maximum of one hour per day, with only one other person, within a 5km radius of their home [228]. In addition, all sporting and recreational facilities were closed for the entirety of the lockdown. In a report released by KPMG (a leading global accounting firm) in July 2021, Brimbank, Hume, Melton and Wyndham were found to be the most impacted local government areas (LGA's) within Metropolitan Melbourne during the pandemic [229]. All four of these LGA's are serviced by the local public government funded health service called Western Health. Therefore, considering all participants in this study were patients of Western Health and

recruitment commenced in February 2020 and ceased in May 2021, pandemic restrictions would have undoubtedly had an impact on participants' PA behaviour. The impact of pandemic restrictions on PA levels in other exercise oncology studies has been contradictory. One study conducted in Brazil found there was reduction in PA levels as a result of pandemic restrictions [230]. However, contrary to this, researchers conducting PA intervention studies (two in Italy and one in the United States) reported that home-based exercise programs combined with regular support via mobile apps, phone calls or video-conferencing methods are just as effective in increasing PA levels and other health outcomes during the pandemic despite restrictions [172, 231, 232]. Paradoxically, the pandemic restrictions have been shown within some studies to be related to an increase in PA levels. Authors of these studies reported that a lockdown can be a perfect time when breast cancer patients and survivors are not faced with barriers they normally would experience such as time restrictions, distance to activity locations and work requirements [231, 233].

Motivational Interviewing and self-efficacy

The MI intervention did not affect levels of self-efficacy within this study. Similar to these findings, two other studies used MI interventions aimed at improving PA behaviour, by establishing goals and strategies to overcome barriers, and measured self-efficacy as an outcome. Both studies found no significant effect following the intervention when compared to baseline and controls [180, 188]. The authors reasoned that small sample sizes and the generic nature of the self-efficacy questionnaire could potentially explain the lack of effect. However, another probable reason may be due to the focus of the MI intervention. In three other studies that found significant improvements in self-efficacy outcomes [183, 187, 194], there was a specific focus in the MI intervention on self-efficacy in the context of management of adverse symptoms in addition to improving general healthy behaviours. This could suggest that MI is more effective at improving self-efficacy when the focus (of the MI) is on managing the adverse symptoms that may be forming the barriers to PA such as pain, fatigue, anxiety and depression. Admittedly, all of these studies (including the two mentioned before) were conducted in cohorts of cancer patients either actively receiving treatment or were in advanced stages where adverse symptoms were most prevalent. Whilst the participants within our study were in fBCS, symptoms such as pain, fatigue, anxiety and depression have all shown in the literature to be present in the breast cancer survivorship period [16, 17, 19, 22] and are reported barriers to PA [101, 104, 106]. Furthermore, pain and fatigue are common side effects of some ongoing hormonal treatments [52, 53] which 52.6% of participants within our study (Table 5) were currently taking.

Whilst the MI intervention used within this study incorporated elements of self-efficacy, under the general principles of MI, there was no focus on self-efficacy of management of any possible adverse symptoms which may explain the lack of improvement in self-efficacy outcomes.

Motivational Interviewing and self-regulation

The results showed no impact of MI on levels of self-regulation types (in any of the five subscales) irrespective of group allocation. Very few studies measure these outcomes within the breast cancer cohort utilising MI as an intervention. Two earlier cohort studies identified that cancer survivors who achieved higher levels of PA, had higher levels of intrinsic regulation and lower levels of amotivation and extrinsic regulation [139, 234]. Other studies that looked for causative links, by utilising MI interventions and measuring regulation subscales, showed results that do not mirror this of this pilot study's results. These studies reported intrinsic motivation subscales significantly increased post-MI intervention [235, 236] along with increases in PA, however they also involved healthy adult cohorts who may not be faced with similar barriers experienced by cancer survivors.

The MI intervention used within this study was designed using the SDT as the underlying theoretical framework which aims to increase levels of intrinsic self-regulation for more effective long-term behavioural change. Therefore, the lack of increase in levels of intrinsic self-regulation may be reflective of the non-effect of the underlying SDT rather than the MI tool itself. Two other studies that used the TTM to inform their MI intervention found significant improvements in their outcomes [182, 194]. However, there were no outcome measures used to assess the constructs from the TTM like there was within this study.

The impact of the COVID-19 pandemic on PA levels has been discussed earlier, however there is some evidence to suggest there was an impact on the motivation type (or self-regulatory style) to engage in PA during this time. An observational, longitudinal study of PA and autonomous motivation levels in French and Swiss adults during the 2020 lockdowns showed some interesting results [237]. The authors found that autonomous motivation was not necessarily associated with higher PA levels by the end of the lockdown, whereas it was before the lockdown. This was suggested to be due to the lack of control (less autonomy) associated with not being able to participate in activities that would normally bring great enjoyment to an individual (intrinsic motivation) such as swimming pools and gymnasiums. Therefore, engagement in PA behaviour was more due to extrinsic motivators such as perceived benefits to certain health outcomes such as depression or anxiety – which has been shown to be negatively affected during this period [238, 239]. Contrary to this, a cross-sectional study in New Zealand

reported the intrinsic (more autonomous) motivational levels of adults (as measured by the same questionnaire used within our study) were high during the 2020 COVID19 pandemic [240].

In summary, we found no impact of MI on changing health behaviour in this cohort of fBCS. Further to this, there was no impact on self-efficacy or self-regulatory types. These results highlight the strengths and weaknesses of intervention design and can help inform promotional strategies that may facilitate breast cancer survivor's engagement in PA.

In the following chapter, results for MI's effect (if any) on QoL outcomes will be discussed.

Chapter 5

Quality of Life Outcome Results

Quality of Life Outcome Results

5.1. Overview

As the incidence and survival rates of breast cancer increases [5], there are more fBCS living with long term adverse effects as a result of diagnosis or treatment [16, 19]. It is well recognised that the QoL of fBCS is poorer than those of age-matched healthy women worldwide [54]. Further to this, the literature also outlines many predictors that are associated with lower levels of QoL in fBCS including lower socioeconomic status [241, 242], type of cancer treatment [53] and younger age at the time of cancer diagnosis [21]. Another reported predictor of poorer QoL in fBCS outlined in the literature is self-efficacy levels, particularly in relation to the management of long-term adverse effects of cancer diagnosis and treatment [243]. Additionally, self-efficacy levels have been seen to have a mediating effect of fatigue on PA levels and subsequently improve QoL [244]. Thus self-efficacy is proposed to have both direct and indirect impacts on QoL. A counselling tool that can indirectly enhance self-efficacy through the improvement of levels of autonomy and competency is MI particularly when it is designed with the SDT as its underpinning framework [178]. In the previous chapter, the principles of SDT and MI were outlined in the context of improving PA behaviour in fBCS. However, the core premise of the SDT is more generalist in nature and encapsulates the theory underpinning the growth and change that occurs during human development in a number of fields such as education, socialisation, relationships and technology use and can be applied to various topics such as emotional regulation, psychopathology, socialisation and vitality [245]. Therefore, MI can be designed to enhance an individual's capacity to manage adverse symptoms in the case of cancer patients and survivors [187, 193].

As highlighted in Chapter 2: Systematic Review and Meta-Analysis, MI has been used within studies as an intervention aimed at improving self-management of symptoms in cancer patients and survivors such as fatigue [221], fear of cancer recurrence [246], depression [184], insomnia [154], nausea [194] and pain [193]. However, the results are variable depending on many factors related to the participant characteristics, intervention design and outcome measures.

One of the key research questions of this study was: 1) Is there an effect of MI on QoL domains in fBCS? Even though the target of the MI intervention was increasing self-directed PA questions, a possible indirect effect of the intervention could be a change in QoL. This chapter will present the results from these outcome data and discuss how it is situated within the current literature. For a detailed description of the study design, methodology, outcome measures and synthesis of results, refer to Chapter 3. Study Design. The results of this study can help understand MI's working processes and their impact on QoL.

5.2. Results

The original raw data for the outcomes presented within this chapter is presented within Appendix 17.

5.2.1. Demographic data

A summary of the demographic characteristics of each group has been summarised in Table 5 within Chapter 4.

5.2.2. Outcome data

Table 8 shows the means values at each time-point in both groups for outcome measures.

	IIG			DIG		
	Week 1	**Week 12**	**Week 24**	**Week 1**	**Week 12**	**Week 24**
QoL:						
- PWB (score range 0-28)	21 (±5.3)	22 (±5.6)	22 (±6.3)	21 (±4.7)	22 (±4.3)	24 (±5.1)
- SWB (score range 0-28)	18 (±7.7)	17 (±6.8)	20 (±6.5)	24 (±5.1)	24 (±6.6)	24 (±4.5)
- EWB (score range 0-24)	16 (±5)	19 (±4)	19 (±5.2)	18 (±5.4)	18 (±5.7)	19 (±5.5)
- FWB (score range 0-28)	19 (±5.1)	20 (±5)	20 (±5.6)	22 (±5)	23 (±5.5)	24 (±4.7)
- BCS (score range 0-40)	22 (±8.2)	23 (±7.8)	26 (±9.6)	23 (±7.2)	25 (±6.9)	24 (±7.7)
- TOI (score range 0-96)	62 (±16.9)	65 (±15.8)	68 (±18.9)	65 (±14.6)	69 (±13)	72 (±15.4)
- FACTG (score range 0-108)	74 (±16.2)	78 (±16)	81 (±19)	84 (±17)	86 (±16.4)	90 (±16.8)
- FACTB (score range 0-148)	96 (±23.3)	101 (±23)	107 (±27.8)	106 (±22.4)	110 (±22.1)	114 (±22.9)

Table 8. Outcome data (by group allocation and time-point)
IIG = Immediate Intervention Group, DIG = Delayed Intervention Group
QoL = Quality of Life, PWB = Physical Wellbeing, SWB = Social/family Wellbeing, EWB = Emotional Wellbeing, FWB = Functional Wellbeing, BCS = Breast Cancer Subscale, TOI = Trial Outcome Index, FACTG = Functional Assessment of Cancer Therapy General, FACTB = Functional Assessment of Cancer Therapy Breast
**Values presented as mean (standard deviation)*

The period-adjusted linear mixed modeling demonstrated that MI led to a significant improvement in the BCS subscale score ($p<0.05$) (*Figure 32*), however there were no significant changes in any of the PWB subscale score ($p=0.155$) (*Figure 28*), SWB subscale score ($p=0.144$) (*Figure 29*), EWB subscale score ($p=0.232$) (*Figure 30*), FWB subscale score ($p=0.588$) (*Figure 31*), FACTB TOI ($p=0.867$) (*Figure 33*), FACTG total score ($p=0.672$) (*Figure 34*) or FACTB Total Score ($p=0.669$) (*Figure 35*).

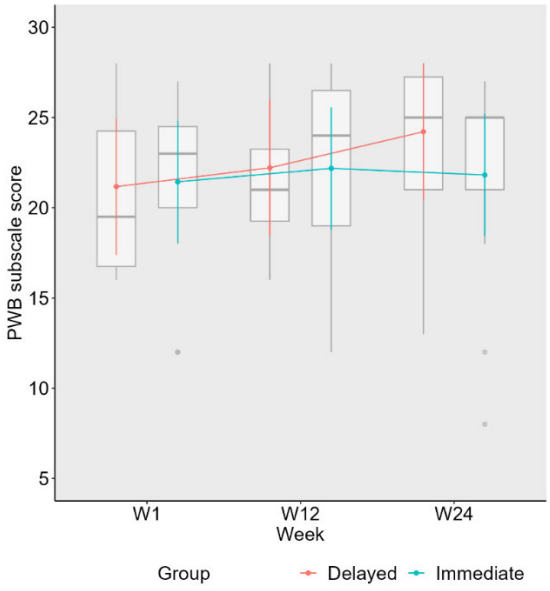

Figure 28. Physical Wellbeing Subscale (by group allocation)

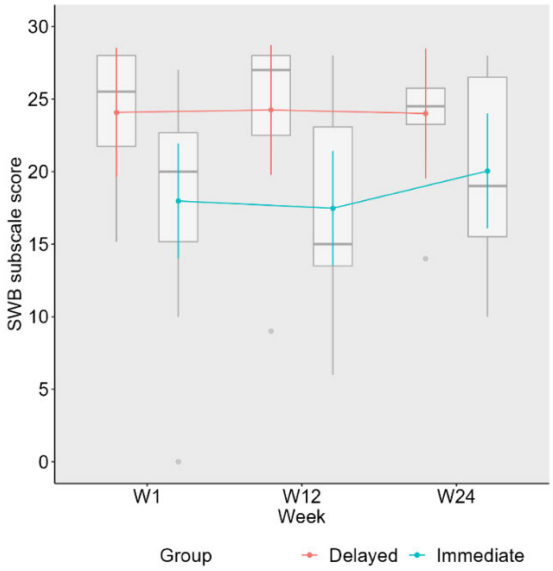

Figure 29. Social/Family Wellbeing Subscale (by group allocation)

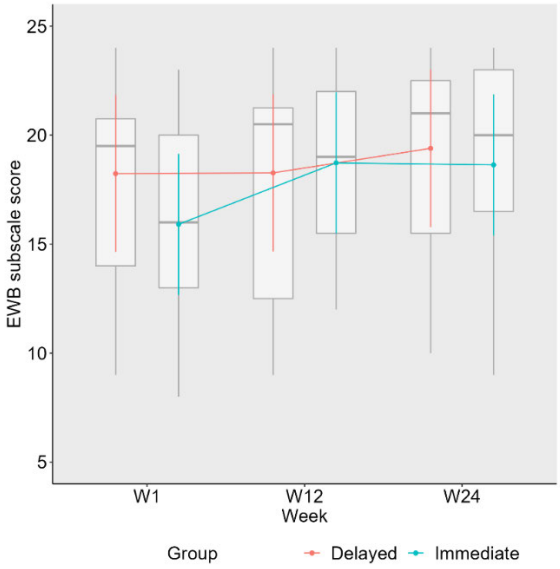

Figure 30. Emotional Wellbeing Subscale (by group allocation)

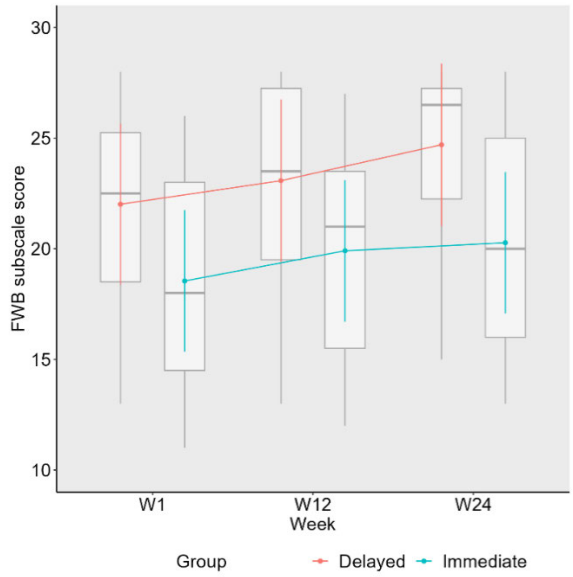

Figure 31. Functional Wellbeing Subscale (by group allocation)

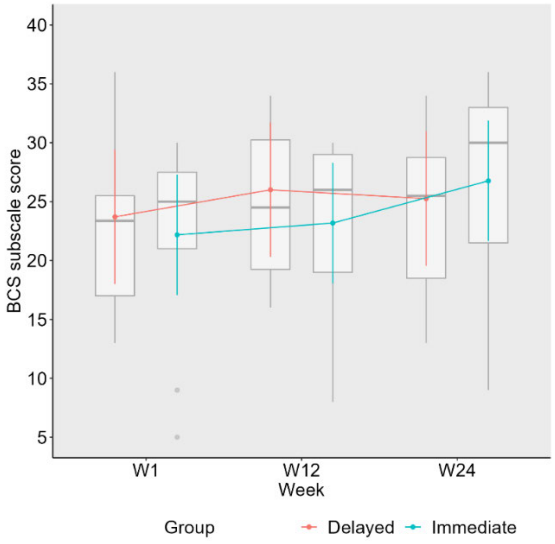

Figure 32. Breast Cancer Subscale (by group allocation)

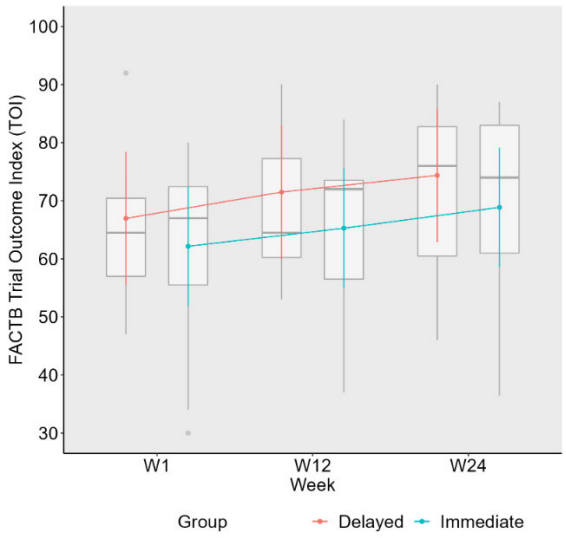

Figure 33. Trial Outcome Index Score (by group allocation)

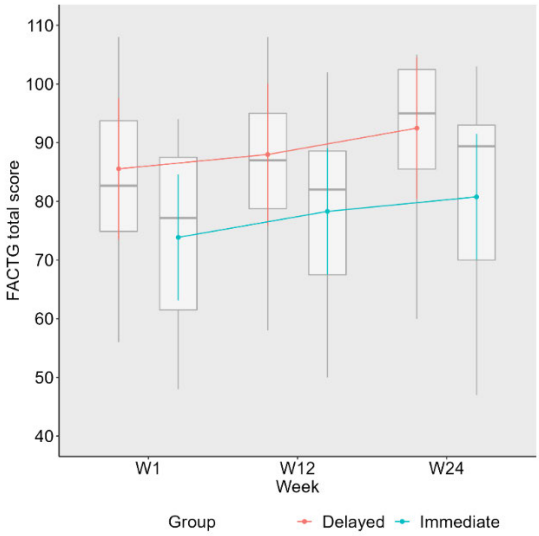

Figure 34. FACTG Total Score (by group allocation)

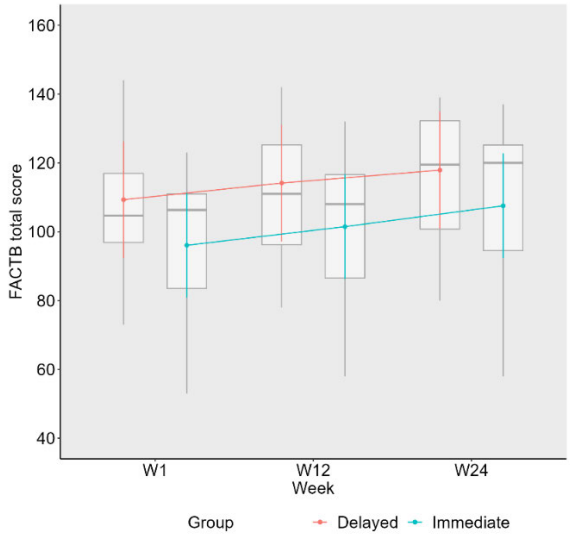

Figure 35. FACTB Total Score (by group allocation)

** Coloured dot = group mean value, vertical coloured line = 95% confidence intervals, horizontal grey line = group median value, top and bottom end of boxes = Q1 and Q3, vertical grey lines = minimum and maximum group values, grey dots = outliers*

5.3. Discussion

Surviving breast cancer can be an enormous feat for many women, and unfortunately, there can be long lasting negative impacts on QoL that can affect many aspects of their lives. Utilising tools that facilitate confidence and emotional resilience in a sustainable and autonomous way can

help to improve their overall physical, mental, social and emotional well-being. One specific research question of this current study is whether there is an effect of MI on QoL outcomes in a cohort of fBCS. The results presented earlier within this chapter will aim to answer this research question. This study's results can give insight into the benefits and associated use of MI for improving QoL in fBCS cohorts.

This pilot study showed a significant effect of MI on the QoL - breast cancer subscale in fBCS. However, there was no effect of MI on all other QoL subscales (PWB, SWB, EWB, FWB, TOI, FACTG total score and FACTB total score).

A systematic review of studies investigating the effect of MI on various behavioural and health outcomes in mixed cancer patients and survivors found that most studies reported a small to negligible improvement in QoL outcomes using the FACT-G and FACT-B surveys [150]. The authors highlight that the main source of the large heterogeneity seen in their included studies was specific characteristics of the intervention used.

To answer the key research question of this study of whether MI affects QoL outcomes in fBCS, the discussion will be sub-grouped into studies that fall into one of two categories. The two categories are: 1) Studies that use a MI intervention to enhance adherence to recommended PA levels and measure both PA and QoL outcomes, and 2) Studies that use an intervention that combines MI and exercise components (supervised or home-based) and measure adherence (to the PA and MI components) and QoL outcomes.

Category 1)

A RCT by Kvale et al, used a single one hour MI session, in a cohort of fBCS, to develop a survivorship care plan aimed at improving health goals, medication adherence and follow up screening, symptom management and general health behaviours [184]. Despite the outcome measure used to quantify QoL in this study was not breast cancer-specific, there was a significant improvement in the domains of physical role, bodily pain, and emotional roles within the SF-36 which were not seen in our study. An explanation for this could be lower baseline QoL levels given the mean time since completion of primary treatment for the participants within this study was 116 days (4.1 months). In contrast, there was a mean time of 18.5 months post-diagnosis within our study. Another survivorship care plan study used a similar methodology (the same focus of MI, a cohort of fBCS, over a 12-week intervention period with a similar mean time since completion of primary treatment) to the Kvale et al study except for a higher frequency of MI sessions (five) and use of FACT-B QoL outcome measure [247]. A significant improvement in FACT-B total score was found. The PWB and BCS subscales were stronger contributing drivers to this result (given that all subscales within the FACT-B contribute to the total FACT-B

score). Whilst our study did not see an impact of MI on the physical and emotional domains mentioned within these two survivorship care plan studies, as mentioned before, this could be due to the point within the cancer continuum or the choice of outcome measure used. Alternatively, the BCS is the only subscale within the FACTB questionnaire that contains items specifically related to breast cancer-specific issues and also covers all physical, social, emotional and functional domains of QoL. Therefore, in regard to the results of our study, it could be argued that MI does have an effect on all other domains of QoL however only in the context of breast cancer-specific issues. However, given the small sample size, these inferences should be interpreted with caution.

The type of QoL measure used within studies should accurately reflect the stage of cancer the participant is currently in. For example, applying a questionnaire that contains items relating to active treatment phases such as 'I experience hair loss' and 'I experience nausea' to a cohort of fBCS in a 5 years post-treatment phase may produce a score that indicates higher QoL outcome. Whereas if items relating to the survivorship period such as 'I fear recurrence of my cancer' were used it may result in a lower QoL outcome. There has been much discussion within the literature as to what defines the 'survivorship' period (in the context of QoL changes) and thus what components of a questionnaire accurately captures a survivor's QoL status. A piece of literature reviewed many commonly used QoL questionnaires to develop a questionnaire specific for fBCS [15]. They criticised the FACT-B questionnaire saying, whilst specific to breast cancer issues, is not specific to the survivorship cohort. It still has questions that mostly pertain to the active stages of treatment, such as nausea and loss of appetite (present within the PWB section). This could explain the results seen within our study, given items used within our QoL measure (FACT-B) may not have been relevant in the survivorship period.

Interestingly, when evaluating other studies that measure the impact of MI on individual constructs within QoL measures in cancer cohorts, there are varying results. For example, one study noted significant improvements in 'overall symptom distress' [194], whereas two other studies showed no significant improvements in fatigue [187] and pain [193]. Whilst these studies are in cancer patients actively receiving treatment, where these symptoms would be heightened, the results were still adjusted for baseline values. Interestingly, two studies [187, 194] measured self-efficacy as an outcome to see if it was the 'active' agent of the MI intervention. Both reported a significant improvement post-MI intervention. Unfortunately, as described within the previous chapter, this was not mirrored in the results of our study, in which there was no impact of MI on self-efficacy outcomes.

An RCT that used an MI intervention aimed at improving fBCS' body image and sexual satisfaction levels in post-mastectomy, found that there were significant improvements, both

within and between groups, in sexual satisfaction scores but not in body image [190]. These results were similar to our study results, as the breast cancer subscale score of the FACTB questionnaire contained questions about sexual satisfaction. However, they also contained questions relating to body image. In addition, whilst the questionnaires for both studies (theirs and ours) was quantitative, with answers scoring on a 5-point Likert scale, their questionnaires did not incorporate other aspects of QoL, such as physical or social well-being. This importance of the use of QoL questionnaires was highlighted earlier in Chapter 1, whereby they help the individual consider how individual constructs impact their overall well-being [18].

Category 2)

Our results are consistent with two other studies which measure QoL as a primary outcome, where the intervention consisted of MI and PA components. These studies report significant improvements in adherence to PA levels and in some QoL subscales and summary scores [152, 221]. One study reported statistical improvement in the BCS and TOI scores [221], and the other showed significant improvement in BCS, TOI, FACT-B total score and FWB subscale [152]. These two studies are methodologically similar to our study such as participants were fBCS, similar mean age, had received similar cancer treatment and the MI sessions were targeting increasing PA levels. However, the two studies contained specific structured exercise interventions which either satisfied or exceeded the 2010 global recommended minimum PA thresholds needed to achieve significant improvements in QoL for cancer survivors (150 minutes of moderate intensity PA per week) [63]. A detailed analysis to identify the moderator of the improved QoL outcome in one of the aforementioned studies showed that the exercise component of the intervention was partially responsible (80% likelihood of a beneficial effect) when compared to the control group. Therefore, the absence of a structured exercise intervention component within this current study may explain the lack of improvement found within the functional and physical well-being domains of the QoL outcomes.

This chapter has highlighted that MI can have varying impacts on QoL outcomes depending on certain factors such as PA components to the intervention, type of outcome measuring tool used and stage of cancer treatment of the participant. Irrespective of these factors, the results of our study shows that there are potential benefits of MI on breast cancer-specific concerns of fBCS however given the small sample size these results should be considered with care.

The next chapter will bring together the results and discussions from the previous two data chapters to form conclusions for the overall aims of this study. In addition, limitations within the study will be outlined and form suggestions for future research directions.

Chapter 6

Conclusion

Conclusion

This chapter will summarise the discussion sections of the previous two chapters which addressed the three specific research questions. This summary will also outline the study limitations, overall conclusion and recommendations for future research.

6.1. Summary discussion

This study investigated the use of a motivational tool (MI), using the SDT as the underpinning framework, and measured its effects on levels of self-directed PA (as measured by step count), QoL, self-efficacy and self-regulatory types.

The MI used within this study was targeting an increase in self-directed step count however its inability to produce a significant effect on any of the outcomes, except the breast cancer subscale of the QoL measure, was interesting. Primarily these results are highly unlikely to be a true reflection of the effect of MI given the small sample size and thus under-powering the results however there is still great value in this study as it gives insight to other aspects of MI and study design. Other possible explanations for the results in step count were reasoned to be due to a number of variations ranging from MI characteristics and other supplementary tools (or lack thereof) to the suitability of the underpinning behavioural theory (given the lack of effect on self-regulatory types and self-efficacy) for this cohort of fBCS. The lack of increase in PA levels could also explain the lack of improvement in the non-breast cancer-specific QoL domains and self-efficacy, especially given there was no focus on adverse symptom management in the MI which was discussed to potentially be a key factor in overcoming barriers to engaging in PA as demonstrated by other literature. However, the improvement seen within the BCS potentially highlights that MI may have an effect in QoL outcomes but only when measured through breast-cancer specific outcome measures. But nonetheless future studies, with larger sample sizes, would be able to produce higher-quality evidence to either confirm or refute these results.

In summary, there are design, cohort, intervention and outcome variables that can help rationalise the findings of this pilot study. Whilst the results of this pilot study may not have been a reflection of the real efficacy of MI, there are still insights that can be gained from this study.

6.2. Limitations

The main limitation of this study was the global pandemic. Ethics for the larger trial was obtained in 2019 and participant recruitment commenced a few months prior to the onset of the

pandemic and subsequent restrictions. This resulted in unforeseen and significant negative impacts on recruitment, attrition, MI delivery modes and participants' capacity to perform self-directed PA. The small sample size meant that the study was underpowered. Actions were taken to attempt to circumvent these adverse effects such as amendments to ethics to include approved remote methods for recruitment such as social media avenues and remote delivery of the MI. However, despite these attempts, recruitment failed to significantly increase and continued restrictions resulted in limitations becoming present for the duration of this pilot study. Another limitation of the study was the potential reporting inaccuracies of the FitBit step count monitor which may have resulted in under-representation of actual PA levels.

6.3. Conclusion

When investigating methods to improve behaviours and health outcomes in cohorts of fBCS who face unique physical, emotional and cultural challenges, it is vital to utilise feasible and effective methods. Facilitating an environment that improves health literacy (the why), establishing goals (the what), strategies to achieve goals (the how) using methods that are empowering, autonomous and sustainable are key to attaining improvements in long-term overall health. Despite the low statistical power, the study design provides insights and shows promise in the positive effect that MI may have on breast cancer-specific QoL components in fBCS. However, it is important for further research into this topic to be conducted to optimise further the health and wellbeing of fBCS.

6.4. Future directions of research

The insights gained from this pilot study can greatly inform the future directions of research. Suggestions for future study design include the use of a two-arm RCT, providing recruitment is high, rather than a cross-over design to best cater for the use of a psychological intervention tool. Additionally, using a MI that has a focus on adverse symptom management in addition to improving PA behaviour may be more effective. Providing MI sessions that are initially in-person and then conducted more frequently (such as weekly) for the purpose of building a stronger rapport would be beneficial. Using aspects of other behavioural frameworks such as the TPB in the MI intervention to strengthen an individual's intention and possibly a component of the SCT to increase social aspects of the self-directed exercise such as group walking sessions or online peer encouragement forums. Incorporating objective measures to ensure the fidelity of the MI sessions may also contribute to an intervention that closely aligns with any singular or

combination of selected behavioural theories. Other suggestions that could improve outcomes can be additional supplemental use of tools such as culturally appropriate print materials such as information booklets to help improve the health literacy fBCS and with goal setting. Furthermore, to increase the accuracy of PA outcomes, inclusion of a self-reporting measure of PA (in addition to the pedometer use) which can also act as a diary or workbook that also provides improved feedback and motivation. Also inclusion of prior levels of PA and other socioeconomic indicators can help to contextualise motivational influences of participants. Additionally, the selection of a QoL measure that closely reflects the survivorship stage of the cohort whilst remaining breast cancer-specific could give more accurate results of the QoL status of a fBCS cohort. Finally, the global pandemic has highlighted the importance of designing interventions and data collection that can be adapted to remote delivery.

More generally, research into interventions that can enhance the health and well-being in the most at-risk groups of fBCS (mostly from disadvantaged backgrounds) is vital. These interventions must be founded in established behavioural change theories and be designed with feasibility, transferability and sustainability in mind to help inform clinical recommendations for health professionals in the field.

Chapter 7

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Chapter 8

Appendices

Appendix 1

MELBOURNE HEALTH

Office for Research
The Royal Melbourne Hospital
Level 2 South West
300 Grattan Street
Parkville VIC 3050
Australia

Telephone: +61 3 9342 8530
Facsimile: +61 3 9342 8548
Email: research@mh.org.au
thermh.org.au
ABN 73 802 706 972

MELBOURNE HEALTH HUMAN RESEARCH ETHICS COMMITTEE

ETHICAL APPROVAL

Dr. Meron Pitcher
Western Hospital
Department of Medical Oncology
Gordon Street
FOOTSCRAY VIC 3011

01 May 2019

Dear Dr. Meron Pitcher,

HREC Reference Number: HREC/45268/MH-2018
Melbourne Health Site Reference Number: 2018.339

Project Title: Physical activity adherence, psychological health and immunological outcomes (PAPHIO study) in breast cancer survivors

---

I am pleased to advise that the above project has **received ethical approval** from the Melbourne Health Human Research Ethics Committee (HREC). The HREC confirms that your proposal meets the requirements of the National Statement on Ethical Conduct in Human Research (2007). This HREC is organised and operates in accordance with the National Health and Medical Research Council's (NHRMC) National Statement on Ethical Conduct in Human Research (2007), and all subsequent updates, and in accordance with the Note for Guidance on Good Clinical Practice (CPMP/ICH/135/95), the Health Privacy Principles described in the Health Records Act 2001 (Vic) and Section 95A of the Privacy Act 1988 (and subsequent Guidelines).

HREC Approval Date: 29 April 2019

Ethical approval for this project applies at the following sites:

Site
Western Health • Sunshine Hospital • Footscray Hospital

Approved Documents:

The following documents have been reviewed and approved:

Document	Version	Date
Protocol	7	15 April 2019
Participant Information Sheet/Consent Form	3	16 April 2019

Letter of invitation to colleagues	3	16 April 2019
Letter of invitation to potential participants	3	16 April 2019
International physical activity questionnaire	2	01 February 2019
Daily step count record and pedometer adherence	2	01 February 2019
Demographic health history record	2	01 February 2019
Letter of invitation to doctor	2	01 February 2019
Dialog of face-to-face motivational interviewing at week 0 (T1) for IIG group and at week 13 (T13) for DIG group (20 minutes)	2	01 February 2019
Dialog of phone call motivational interviewing (15 minutes) at week 1, week 4 and week 9 for IIG group and at week 14, week 17 and week 22 for DIG group	1	01 February 2019
Advertising Poster	3	15 April 2019
Aerobic fitness test and anthropometry	1	03 September 2018
Biomarkers record form	1	03 September 2018
Daily step count record form	1	03 September 2018
Exercise barrier and task self-efficacy	1	2006
Exercise self-regulation BREQ2	2	2004
FACT-B	4	16 November 2007
DASS 21	1	03 September 2018

Governance Authorisation:

Governance Authorisation is required at each site participating in the study before the research project can commence at that site.

You are required to provide a copy of this HREC approval letter to the principal investigator for each site covered by this ethics approval for inclusion in the site specific assessment application.

Conditions of Ethics Approval:

- You are required to submit to the HREC:
    - An Annual Progress Report (that covers all sites listed on approval) for the duration of the project. This report is due on the anniversary of HREC approval. Continuation of ethics approval is contingent on submission of an annual report, due within one month of the approval anniversary. Failure to comply with this requirement may result in suspension of the project by the HREC.
    - A comprehensive Final Report upon completion of the project.
- Submit to the reviewing HREC for approval any proposed amendments to the project including any proposed changes to the Protocol, Participant Information and Consent Form/s and the Investigator Brochure.
- Notify the reviewing HREC of any adverse events that have a material impact on the conduct of the research in accordance with the NHMRC's Safety Monitoring and Reporting in Clinical Trials Involving Therapeutic Goods (2016) guideline.
- Notify the reviewing HREC of your inability to continue as Coordinating Principal Investigator.
- Notify the reviewing HREC of the failure to commence the study within 12 months of the HREC approval date or if a decision is taken to end the study at any of the sites prior to the expected date of completion.

- Notify the reviewing HREC of any matters which may impact the conduct of the project.
- If your project involves radiation, you are legally obliged to conduct your research in accordance with the Australian Radiation Protection and Nuclear Safety Agency Code of Practice 'Exposure of Humans to Ionizing Radiation for Research Purposes' Radiation Protection series Publication No.8 (May 2005)(ARPANSA Code).

Please note: Template forms for reporting Amendments, safety reporting, Annual/Final reports, etc. can be accessed from: https://www2.health.vic.gov.au/about/clinical-trials-and-research/clinical-trial-research/monitoring-reporting

The HREC may conduct an audit of the project at any time.

Yours sincerely,

[redacted]

Prof Peter Colman
Chair – Melbourne Health Human Research Ethics Committee (HREC)

Appendix 2

Western Health

GOVERNANCE AUTHORISATION
SITE SPECIFIC ASSESSMENT (SSA) APPROVAL TO CONDUCT A RESEARCH PROJECT AT
Western Health04 December 2019

04 December 2019

Doctor Meron Pitcher
Surgery Department – Breast Unit
Western Health

Dear Dr Pitcher,

HREC Reference Number: HREC/45268/MH-2018 **ERM ID Reference Number:** 45268

Project Title: Physical activity adherence, psychological health and immunological outcomes (PAPHIO study) in breast cancer survivors

Western Health Site: Sunshine Hospital and Footscray Hospital

Principal Investigator: Dr. Meron Pitcher

Associate Investigators: Miss Supa Pudkasam and Ms Sara Jorgensen

I am pleased to advise that the above project has been authorised to be conducted at Western Health. This authorisation is subject to compliance with any conditions imposed by the reviewing HREC.

Research governance:

As Principal Investigator, you are required to:

1. Comply with the Investigator's responsibilities as outlined in the *Note for Guidance on Good Clinical Practice (CPMP/ICH/135/95).*
2. Notify the Office for Research details of:
    - The actual start date of the project at Western Health.
    - Any amendments to the project after these have been approved by the reviewing HREC.
    - Any adverse events involving patients of Western Health, in accordance with the NHMRC Position Statement: *Monitoring and reporting of safety for clinical trials involving therapeutic products May 2009*.
    - Any changes to the indemnity, insurance arrangements or Clinical Trial Research Agreement for this project. This includes changes to the project budget or other changes which may have financial or other resource implications at Western Health.
    - Your inability to continue as Principal Investigator or any other change in research personnel involved in this project.
    - Failure to commence the study within 12 months of the Governance authorisation date or if a decision is taken to end the study at this site.
    - Any other unforeseen events.
    - Any other matters which may impact the conduct of the project at Western Health.

3. Ensure that HREC approval remains current for the entire duration of the project. Investigators undertaking projects without current Reviewing HREC approval risk their indemnity, funding and publication rights.
4. Submit an annual progress report every 12 months for the duration of the project. This report is due on the anniversary of HREC approval. Continued SSA approval is contingent on receipt of an annual report by the RGO. In addition, a comprehensive final report should be submitted to the RGO upon completion of the project.
5. Ensure that the Clinical Trial Research Agreement (CTRA) and Indemnities (or other research agreements as applicable) are fully executed, i.e. signed by all parties; and an original version (or copy) placed in the study file.

Authorised Documents:

Document	Version	Date
HREC Approval Letter		29 April 2019
Protocol	7	15 April 2019
Human Research Application Form (HREA); Submission code; HREC/45268/MH/2019-165232	2	14 February 2019
Site Specific Assessment Form (SSA); Submission code; SSA/45268/MH/2019-195703	3	29 November 2019
Statement of Approval – Breast Cancer Service Clinic		07 June 2019
Pathology Clinical Trial Research Application Form and Pathology Approval		13 June 2019
Victorian Specific Module		01 February 2019
Master Participant Information Sheet/Consent Form	3	16 April 2019
Western Health Site Specific Participant Information Sheet/Consent Form	1	09 September 2019
Budget	2	07 July 2019
Letter of invitation to colleague - Master	3	16 April 2019
Letter of invitation to participant - Master	3	16 April 2019
Letter of invitation to doctor - Master	2	01 February 2019
Letter of invitation to colleague – Western Health Site Specific	1	10 September 2019
Letter of invitation to participant - Western Health Site Specific	1	10 September 2019
Letter of invitation to doctor - Western Health Site Specific	1	10 September 2019
Aerobic fitness test and Anthropometry	1	03 September 2018
Current physical activity - IPAQ	2	01 February 2019
Daily step count record form	1	03 September 2018
Biomarkers record form	1	03 September 2018
Daily Step count record and pedometer adherence	2	01 February 2019
Dialog of face to face motivational interviewing	2	01 February 2019
Dialog of phone call motivational interviewing	1	01 February 2019
Demographic - health history data	2	01 February 2019
Questionnaire BREQ2	2	2004
Exercise Barrier and task self	1	2006
Questionnaire FACT-B	4	16 November 2007
Questionnaire DASS_21	1	03 September 2018
Advertisement poster (revised logo)	3	15 April 2019
Clinical Trial Research Agreement for an Investigator Initiated Study between Victoria University and Western Health		03 December 2019
ICH Good Clinical Practice Certificate – Meron Pitcher		29 October 2017

Curriculum Vitae & WH Research Code of Conduct (2018) • Meron Pitcher • Supa Pudkasam • Sara Jorgensen		13 May 2019 06 Septemebr2018 09 October 2019

Please note: Template forms for reporting Amendments, Adverse events, Annual/Final reports, etc. can be accessed from: https://www2.health.vic.gov.au/about/clinical-trials-and-research/clinical-trial-research/how-to-make-an-hrec-application-for-clinical-trials.

The Office for Research may conduct an audit of the project at any time.
The Office for Research Western Health wishes you and your colleagues every success in your research.

Yours sincerely,

[redacted]

Ms Meera Senthuren
Ethics and Governance Administration Officer
Western Health Office for Research
Email: ethics@wh.org.au

Appendix 3

VICTORIA UNIVERSITY

MEMO

TO	Prof Vasso Apostolopoulos Victoria University	DATE	18/10/2022
FROM	Associate Professor Deborah Zion Chair Victoria University Human Research Ethics Committee		
SUBJECT	Ethics Application – HREC Approved Application External to Victoria University		

Dear Prof Apostolopoulos,

Thank you for submitting this request for ethical approval of the project entitled:

Physical activity adherence, psychological health and immunological outcomes (PAPHIO study) in breast cancer survivors

Project approved by Melbourne Health HREC
HREC Reference Number: HREC/45268/MH-2018
Melbourne Health Site Reference Number: 2018.339

The proposed research project has been accepted and deemed to meet the requirements of the National Health and Medical Research Council (NHMRC) 'National Statement on Ethical Conduct in Human Research (2018)' by the Chair of the Victoria University Human Research Ethics Committee. Approval has been granted from **17th May 2019 to 17th May 2023**. Any variations to the protocol must be approved through the original approving HREC and notified to VUHREC.

Approval for this project was granted by the Chair of the Victoria University Human Research Ethics Committee from 17th May 2019. Both Melbourne Health HREC and Western Health HREC have approved the final amendments for the PICF on the 15th March 2021 to include the COVID-19 updates as requested by Victoria University.

Please note that the Human Research Ethics Committee must be informed of the following: any changes to the approved research protocol, project timelines, any serious events or adverse and/or unforeseen events that may affect continued ethical acceptability of the project. In these unlikely events, researchers must immediately cease all data collection until the Committee has approved the changes. Researchers are also reminded of the need to notify the approving HREC of changes to personnel in research projects via a request for a minor amendment. It should also be noted that it is the Chief Investigators' responsibility to ensure the research project is conducted in line with the recommendations outlined in the National Health and Medical Research Council (NHMRC) 'National Statement on Ethical Conduct in Human Research (2018).'

On behalf of the Committee, I wish you all the best for the conduct of the project.

Kind regards,

Associate Professor Deborah Zion
Chair
Victoria University Human Research Ethics Committee

Appendix 4

Date of amendment	Approving body	Amendment details
26th June 2020	Melbourne Health Human Research Ethics Committee (MHHREC)	-Protocol version 8 -Master Adult PICF -Recruitment by email -Recruitment by phone call -Recruitment by social media
26th June 2020	MHHREC	-Addition of recruiting site -Advertisement poster -Letter of invitation to participant IPC Health
11th August 2020	Western Health Office for Research (WHOR)	Site-Specific Authorisation for all study documents
18st December 2020	MHHREC	-Addition and removal of personnel -Protocol version 9 -Recruitment by social media -Advertisement poster -Patient Informed Consent Form (PICF)
14th January 2021	WHOR	-Site-specific authorisation for certain amendment documents -Change of personnel -Katherine Harkin signed documents
15th March 2021	MHHREC	-PICF
25th March 2021	MHHREC	-Application for an annual progress report (still awaiting approval)
7th April 2021	WHOR	-Master and WH site-specific PICF
1st October 2021	WHOR	-Approval of annual progress report
18th October 2022	Victoria University Human Research Ethics Committee (VUHREC)	- Approval of ethics documents from MHHREC and WHHREC

Appendix 5

PROVIDING A VOICE FOR PATIENTS WORLDWIDE

FUNCTIONAL ASSESSMENT OF CHRONIC ILLNESS THERAPY (FACIT) LICENSING AGREEMENT

The Functional Assessment of Chronic Illness Therapy System of Quality of Life questionnaires and all related subscales, translations, and adaptations ("FACIT System") are owned and copyrighted by David Cella, Ph.D. The ownership and copyright of the FACIT System resides strictly with Dr. Cella. Dr. Cella has granted FACIT.org ("Licensor") the right to license usage of the FACIT System to other parties. Licensor represents and warrants that it has the right to grant the License contemplated by this agreement to the party listed below ("Licensee") for use of the measure and languages listed below in the study listed below ("Study").

Institution ("Licensee"): Katherine Harkin, Associate Investigator

Measurement: FACT-B

Language(s): English

Study Title ("Study"): Physical Activity, Psychological Health and Immunological Outcomes in Female Breast Cancer Survivors - The PAPHIO Study

This current license is only extended to Licensee's Study subject to the following terms:

1) Licensee agrees to provide Licensor with copies of any publications resulting from this study or produced as a result of collecting data with any FACIT questionnaire.

2) Due to the ongoing and evolving nature of questionnaire development, treatment modalities and cross-cultural linguistic research, Licensor reserves the right to make adaptations or revisions to wording in the FACIT, and/or related translations as necessary. If such changes occur, Licensee will have the option of using either previous or updated versions according to their own research objectives.

3) Licensee may not change the wording or phrasing of any FACIT document without previous permission from Licensor. If any changes are made to the wording or phrasing of any FACIT item without permission, the document cannot be considered the FACIT, and subsequent analyses and/or comparisons to other FACIT data will not be considered appropriate. Permission to use the name "FACIT" will not be granted for any unauthorized translations of the FACIT items. Any analyses or publications of unauthorized changes or translated versions may not use the FACIT name. Any unauthorized translation will be considered a violation of copyright protection.

4) Licensor reserves the right to withdraw this license if Licensee engages in scientific or copyright misuse of the FACIT questionnaires; provided, however, that Licensor shall give Licensee 30 days' notice and opportunity to cure such misuse.

5) In all publications and on every page of the FACIT used in data collection, Licensor requires the copyright information be listed precisely as it is listed on the questionnaire itself. Licensee also agrees to publish the following statement in any publications, documents, CD-ROMS or any other media which include the FACT-

G: The FACIT and all related works are owned and copyrighted by, and the intellectual property of David Cella, Ph.D. Permission for use of the FACT-G is obtained by contacting Dr. Cella at information@facit.org

6) This license is not extended to electronic data capture by third party vendors of Licensee. Electronic versions by third party vendors of the FACIT questionnaires are considered derivative works and are not covered under this license. Permission for a third party to migrate and administer the FACIT electronically must be covered under separate agreement between the electronic data capture vendor and FACIT.org.

7) This license is only extended for use on the internet on servers internal to Licensee. In no cases may any FACIT questionnaire be placed on the internet without password protection. To do so is considered a violation of copyright.

8) There are no fees associated with this license.

9) This Agreement shall be effective for the license period from the commencement of the study until the final analysis is completed. Either party may terminate this Agreement in the event of a material breach of its terms by the other party or any of that party's agents by written notice delivered at least thirty (30) days prior to the effective date of the termination.

10) Neither party shall use the name of the other party in any publicity, advertising or announcement without the consenting party's prior written approval.

11) Licensor warrants and represents that the terms of this Agreement are not inconsistent with any other contractual and/or legal obligations it may have or with its policies or the policies of any institution with which it is associated.

Victoria University

[redacted]

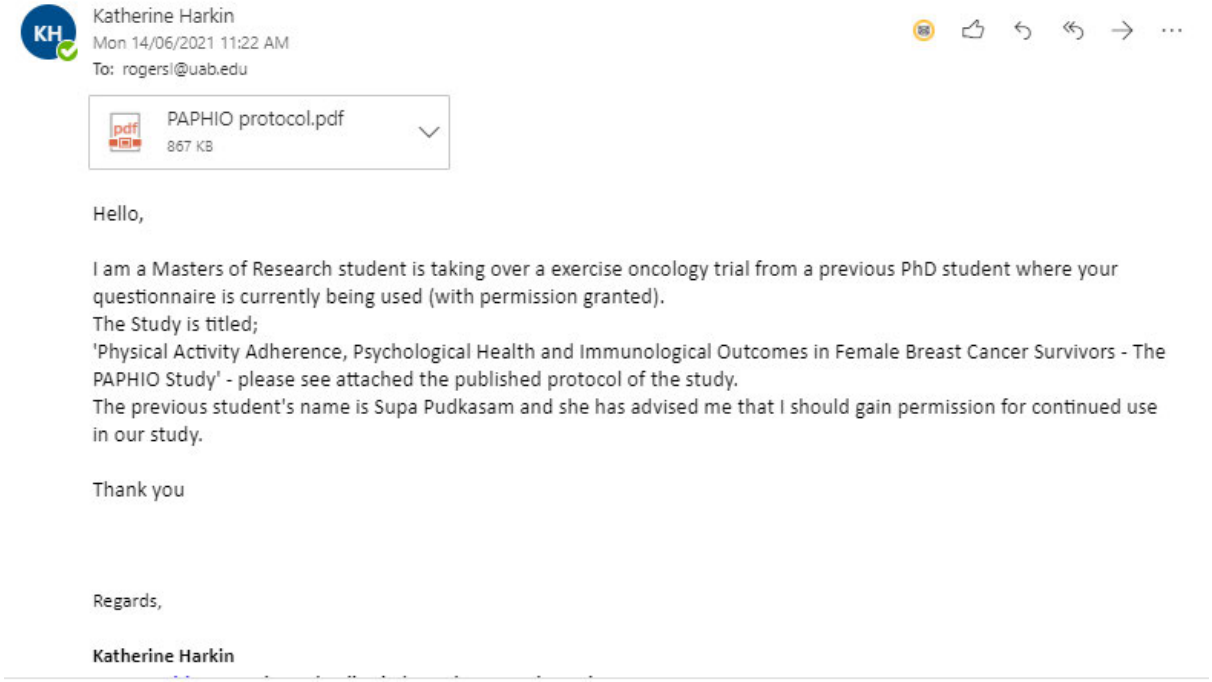
Katherine Harkin (Jun 15, 2021 07:59 GMT+10)

Katherine Harkin

Associate Investigator

Jun 15, 2021

Appendix 6



Katherine Harkin
Mon 14/06/2021 11:22 AM
To: rogersl@uab.edu

PAPHIO protocol.pdf
867 KB

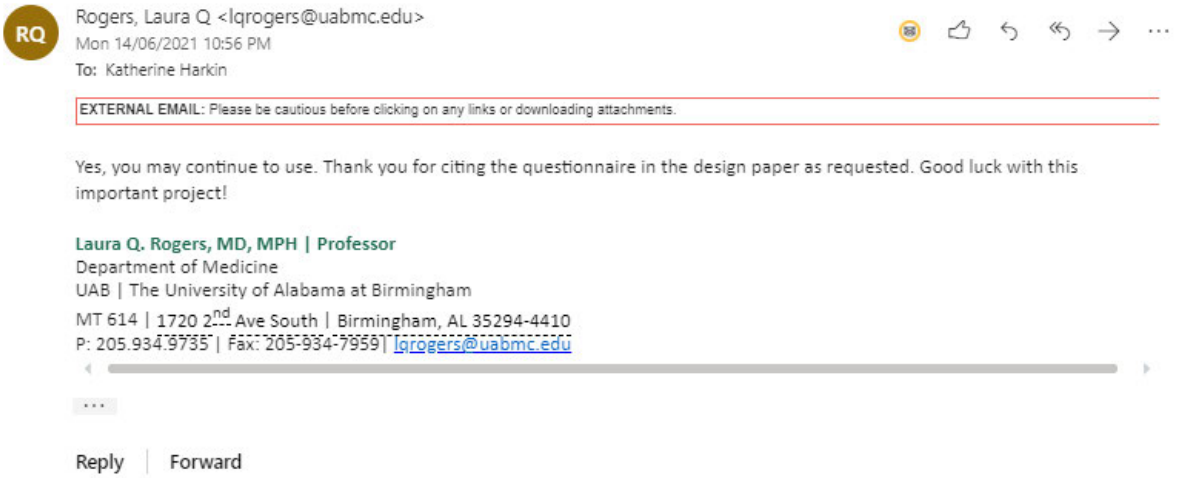
Hello,

I am a Masters of Research student is taking over a exercise oncology trial from a previous PhD student where your questionnaire is currently being used (with permission granted).
The Study is titled;
'Physical Activity Adherence, Psychological Health and Immunological Outcomes in Female Breast Cancer Survivors - The PAPHIO Study' - please see attached the published protocol of the study.
The previous student's name is Supa Pudkasam and she has advised me that I should gain permission for continued use in our study.

Thank you

Regards,

Katherine Harkin



Rogers, Laura Q <lqrogers@uabmc.edu>
Mon 14/06/2021 10:56 PM
To: Katherine Harkin

EXTERNAL EMAIL: Please be cautious before clicking on any links or downloading attachments.

Yes, you may continue to use. Thank you for citing the questionnaire in the design paper as requested. Good luck with this important project!

Laura Q. Rogers, MD, MPH | Professor
Department of Medicine
UAB | The University of Alabama at Birmingham
MT 614 | 1720 2nd Ave South | Birmingham, AL 35294-4410
P: 205.934.9735 | Fax: 205-934-7959| lqrogers@uabmc.edu

Reply | Forward

Appendix 7

PRAXIS AUSTRALIA

Promoting Ethics and Education in Research

Sophie Mepham GCP

This is to certify that

Katherine Harkin

has satisfactorily completed the following module

MODULE

Principles of GCP

This ICH E6 GCP Investigator Site Training meets the Minimum Criteria for ICH GCP Investigator Site Personnel Training identified by TransCelerate BioPharma as necessary to enable mutual recognition of GCP training among trial sponsors.

C5.01

September 12, 2020

The equivalent of 2 hours of study was completed.

[redacted]

IAN KERRIDGE

Director, PRAXIS Australia Ltd.

Version Number	Modified By	Modifications Made	Date Modified	Status
2.0	Praxis Australia	Redevelopment for Trans Celerate	14th June 2017	Current

Appendix 8

Western Health
Office for Research
3rd Floor, WCHRE Sunshine Hospital
Furlong Rd. St Albans VIC 3021
Tel. +61 3 8395 8074
Fax. +61 3 8395 8259
ABN 61 166 735 972

WESTERN HEALTH OFFICE FOR RESEARCH
APPOINTMENT AS AN HONORARY RESEARCHER

29 September 2020

Ms. Katherine Harkin
23 Fuchsia Street
Blackburn VIC 3130

Dear Ms. Harkin,

The Office for Research is responsible for the review and endorsement of Research Honorary Appointments, to enable the involvement of non WH staff in the conduct of research utilising Western Health facilities and /or involving Western Health patients and their data.

I am pleased to offer you a Research honorary position within the Division of Perioperative and Critical Care Services at Western Health. The terms of this appointment are:

Project Ref: HREC/45268/MH-2018
Scope: Data Collection, Data Analysis, Ethics and Governance Submissions, Consent, Interviews, Recruitment, Specimen Processing.
Reporting to: Dr Meron Pitcher
Period: 01 Nov 2020 to 31 Dec 2021
Employment Status: Fixed-Term Honorary
Conditions of Appointment:

- You are required to maintain current Allied Health registration in accordance with the Health Practitioner Regulation National Law Act 2009, and provide evidence of such an appointment, and then annually upon renewal.
- You agree to abide by the Western Health's Privacy Policy and relevant legislation as it applies to the organisation e.g. Confidentiality of patient information.
- You agree to be bound by and adhere to all other organisational Regulations and Policies as may apply.
- Your commencement date is subject to a satisfactory police check, immunisation status clearance and governance authorisation. You may not commence at Western Health until a satisfactory police check and immunisation status has been cleared; and you may not commence until research governance authorisation has been issued.

The Western Health Policy Manual may be viewed on the Western Health Intranet site http://info.wh.org.au/

Please sign this letter and return via email to ethics@wh.org.au. A copy of this letter is enclosed for your records. Please return the attached document at your earliest convenience, the honorary appointment will not be finalised until a signed copy of this letter is received.

Congratulations on your appointment at Western Health.

[redacted]
estern Health
C.c.: Dr. Meron Pitcher – Surgeon – Department of Surgery
Mr. Jason Plant – Divisional Director – Perioperative and Critical Care Services

I, Ms. Katherine Harkin accept the offer of employment according to the conditions outlined in this letter.

Signed: [redacted] Date: 29/09/2020

WH HRAF Letter of Offer Template Apr19

Appendix 9

Booklet

WHCOR26

Western Health

VICTORIA UNIVERSITY
MELBOURNE AUSTRALIA

PATIENT LABEL

Participant Information Sheet/Consent Form

Interventional Study - Adult providing own consent

Title	Physical activity adherence, psychological health and immunological outcomes in breast cancer survivors
Short Title	PAPHIO study
Project Number	2018.339
Project Sponsor	Victoria University
Principal Investigator	Dr Meron Pitcher
Associate Investigator(s)	Ms Lisa Matar, Dr Sara Holton, Professor Vasso Apostolopoulos, Ms Anne O'Connor, Professor Remco Polman, Emeritus Professor Lily Stojanovska, Ms Katherine Harkin
Location	Western Health VIC - Sunshine Hospital - Footscray Hospital

Part 1 What does my participation involve?

1 Introduction

You are invited to take part in this research study. This is because you have breast cancer and have received standard treatments such as surgery, chemotherapy, hormone therapy. The research project aims to assess how physical activity using a step count tracker improves mental health, quality of life and the body's immune function in breast cancer survivors. The new activity is called motivational interviewing (MI) with a health coach which provides directive and patient-centred counselling to help explore and improve motivation to undertake physical activity

Please read this information carefully. If you have any questions or would like to know more about the research please contact the project officer listed below. Before deciding whether or not to take part, you may want to talk about the research with a relative, friend or your local doctor.

Participation in this research is voluntary. If you do not wish to take part, you do not have to. You will receive ongoing best care whether or not you take part in this research
If you decide you wish to take part in the research project, you will be asked to sign the consent form attached. By signing you are advising us that you:

- Understand what you have read
- Consent to take part in the research project
- Consent to have the tests and treatments that are described
- Consent to the use of your personal and health information as described.

You will be given a copy of this Participant Information and Consent Form to keep for your records.

2 What is the purpose of this research?

Exercise or physical activity has been shown to improve the physical and mental health in breast cancer survivors whilst also reducing the risk of breast cancer recurrence. However, there is little research on how exercise improves the body's immune function and improve breast cancer outcomes. This study will determine how self-directed exercise using a step count tracker together with a collaborative conversation method for exercise motivation can improve these outcomes. If proven, this program could be implemented more widely at a low cost for future physical activity promotion within this population group.

This research has been funded by Victoria University, Melbourne, Australia. This research is being conducted by Western Health in collaboration with Victoria University.

3 What does participation in this research involve?

You will be participating in a randomised, two armed controlled research study. In order to best determine the effectiveness of a program we need to compare different treatments/programs. We allocate participants into two groups and give each group a different treatment at different times. The results are compared to see if one group is better than the other and whether overall the treatment/program implementation is effective. To try and make the groups the same, each participant is assigned to a particular group by chance (what is referred to as randomisation).

In this study, all participants will be provided with a step counter (Fitbit alta HR) and you will be asked to record your steps daily over a 24 week period. You will be randomly assigned to 1 of 2 program groups (like flipping a coin); Group 1 will receive motivational interviewing counselling from a health coach for exercise motivation during the first 12 weeks of the study. Group 2 will receive motivational interviewing counselling for the second 12 weeks. Each motivational interviewing counselling session will last 15 to 20 minutes in which time we will find out how you are progressing with your physical activity and enhance your motivation. You will receive 1 time conversation for exercise motivation interviewing by face-to-face (20 minutes) and 3 times by phone call (10 minutes). You will meet the research team at Sunshine Hospital 3 times: week 1 (Visit 1), week 12 (Visit 2), and week 24 (Visit 3). At this time you will be asked to complete 3

questionnaires regarding your mental health and quality of life. We will withdraw 10 mls of blood from your arm at these times to test your body's immune function.

These visits will take approximately 1 hour.

During the physical activity period, participants will be given a step-count tracker (Fitbit alta HR) and the researcher will explain how to use the prescribed step count tracker-based activity. At this time you will be advised to do activity at your own pace and as tolerated whilst wearing the Fitbit during waking hours throughout the 24 weeks. The researcher will track the participants' step count and tracker usage time via the Fitbit connect application. You will be advised to record your own daily step count throughout the 24 weeks You will have 3 times of 10 ml blood withdrawal (about 2 teaspoons each time) for testing of substances that help your body to fight cancer cells, 3 times answering questionnaires about mental status, QoL, your exercise motivation and your confidence to do exercise.

It is desirable that your local doctor be advised of your decision to participate in this research project. If you decide to participate in this research project, the researchers will inform your local doctor.

4 What do I have to do?

You will need to comply with all study requirements and assessments and attend the visits as outlined. You will be advised to wear the step count device every day during the study and record your own steps during waking hours for 24 weeks. You will be asked to complete a number of questionnaires at each study visit. You must complete as accurately and truthfully as you can. There are no dietary restrictions it is important for your own safety that you inform us of your complete medical history and all medications/supplements/herbal presentation that you are taking. If you notice any health problems, please notify your study doctor immediately. You will not be eligible for taking part of this study if you are currently undergoing breast surgery, chemotherapy and radiation therapy or if you are less than 6 months post active treatments. You are eligible if you are currently receiving hormone therapy or Herceptin.

5 Other relevant information about the research project

The study will recruit 64 females who are breast cancer survivors from Western Health (They will be randomly allocated into two groups (32 participants per group); immediate intervention group (group-1) and delayed intervention group (group-2). All participants will undertake physical activity and wear a step count tracker (Fitbit alta HR) to record daily steps at the first week to week 24. The participants in group 1 will receive motivational interviewing counselling for exercise motivation by face-to-face 1 time and by phone 3 times over the first 12 weeks. Group 2 will receive the same motivational interviewing counselling between week 13 and 24. The study will

test the effects of the 12-week-physical activity by self-management combined with motivational interviewing counselling on mental health, quality of life and the body's immune function. This study is a collocation between Victoria University and Western Health, with recruitment of participants from Western Health.

There are no additional costs associated with participating in this research project, nor will you be paid. All tests and procedures required as part of the research project will be provided to you free of charge
You may be reimbursed for any reasonable travel and car parking associated with the research visits.

6 Do I have to take part in this research project?

Participation in any research project is voluntary. If you do not wish to take part, you do not have to. If you decide to take part and later change your mind, you are free to withdraw from the project at any stage.

If you do decide to take part, you will be given this Participant Information and Consent Form to sign and you will be given a copy to keep.

Your decision whether to take part or not to take part, or to take part and then withdraw, will not affect your routine treatment, your relationship with those treating you or your relationship with Western Health

7 What are the alternatives to participation?

You do not have to take part in this research project to receive treatment at this hospital. Other options are in the decision of your local doctor. Your study doctor will discuss these options with you before you decide whether or not to take part in this research project. You can also discuss the options with your local doctor.

8 What are the possible benefits of taking part?

We cannot guarantee or promise that you will receive any benefits from this research though the possible benefits of taking part in this study may include improvement in your overall well-being, mental health and quality of life. We also predict that there will be an improvement in your immune function which helps your body to fight cancers cells. The results of this research may be useful for health care providers in order to provide motivational interviewing counselling for exercise adherence in breast cancer survivors.

9 What are the possible risks and disadvantages of taking part?

Physical activity by ones person's own management combined with the motivational interviewing counselling may have side effects. You may have none, some or all of the effects listed below, and the symptoms may be mild to moderate. If you have any of these side effects, or are worried about the adverse effects, talk with your study doctor. Your study doctor will also be looking out for side effects.

There may be side effects that the researchers do not expect or do not know about and that may be serious. Tell your study doctor immediately about any new or unusual effects that you get.

Many side effects go away shortly after physical activity program ends. However, sometimes side effects can be serious, long lasting or permanent. If a severe side effect or reaction occurs, your study doctor may need to stop your treatment. Your study doctor will discuss the best way of managing any side effects with you.

The table of possible side effects of this study

Side Effect	How often is it likely to occur?	How severe might it be?	How long might it last?
Discomfort from talking about confidence for behavioural change in motivational interviewing	Sometimes	Mild to moderate	12 weeks
Body aches, due to physical activity	Following physical activity. Rare	MIld	Up to 24 weeks
Fatigue	Rare	Mild	12 weeks
Infection due to blood withdrawal	Rare	Mild to moderate	1 week

While the possibility of this happening is very low, you should still be aware of the possibility. We will try to decrease the chances of this event occurring, but if something unexpected happens. If you feel uncomfortable, you can inform the researcher team. Having a blood taken may cause some discomfort, bruising, skin inflammation, rash or hives.

If you become upset or distressed as a result of your participation in the research, the study doctor will be able to arrange for counselling or other appropriate support. Any counselling or support will be provided by qualified staff who are not members of the research project team. This counselling will be provided free of charge.

If you do become pregnant whilst participating in the research project, you should advise your study doctor immediately. Your study doctor will withdraw you from the research project and advise on further medical attention should this be necessary. You must not continue in the research if you become pregnant.

COVID-19 can spread easily in the community and it can have severe consequences. We will take any practical precautionary measure to reduce the risk of you been infected in COVID19 while in our facilities during your participation in the research, however, we cannot guarantee that you will not be infected. To minimise the risk we will ask you to notify us if you have been recently diagnosed (less than 14 days) with COVID-19, have been identified as a close-contact of someone with COVID-19, or have signs or symptoms suggestive of COVID-19. You will be phone screened for these criteria 24 hours prior to each in-person visits and will also complete the form again on arrival.
If you have been diagnosed with COVID19 you will not be allowed to participate in the study until you will be cleared of COVID-19 and your medical doctor will provide us a letter of approval

10 What will happen to my test samples?

We will take blood from a vein at your arm by using a syringe and needle times at the first and 12 and 24 weeks to test the body's immune function. Each time we will take approximately 10 ml of blood *(*2 teaspoons). In total, we will take 6 teaspoons in 24 weeks during physical activity period. At the end of the research, we will analyse substances in your blood within 1 year, any leftover blood sample will be destroyed. Your blood will not be kept for future research.
Your blood will be collected into a tube containing substance for clotting prevention and quickly spin after collection or on the same day approximately 7 hours later. Liquid portion of blood will be stored at a cool container like refrigerator up to one year prior to analysis for substances-related inflammation.

White blood cells will be used to analyse the substances which help your body to fight cancer cells. These white blood cells will be stored in a very cold freezer (-80 °C) not longer than one day before analysis.

The data will be kept and reported in code (no name indicated). All data of participants will be recorded adequately and stored in databank with secure format for re-checking of research results and discussion among research team. This study has planned to hold this research data for 15 years or more based on circumstances. They will be kept in files of hard copy and saved on a computer disk between Western Health and Victoria University. More specifically, the researchers will have a backup or reserved storage.

You will be asked to provide additional consent for the collection of your blood during the research project.

Samples of your blood obtained for the purpose of this research project may/will be transferred to Victoria University. Your tissue will not be sold by Western Health, however Western Health may

charge study doctors a fee to recover some of the costs of storing and administering the tissue samples.

11 What if new information arises during this research project?

Sometimes during the course of a research project, new information becomes available about the treatment that is being studied. If this happens, your study doctor will tell you about it and discuss with you whether you want to continue in the research project. If you decide to withdraw, your study doctor will make arrangements for your regular health care to continue. If you decide to continue in the research project you will be asked to sign an updated consent form.

Also, on receiving new information, your study doctor might consider it to be in your best interests to withdraw you from the research project. If this happens, he/ she will explain the reasons and arrange for your regular health care to continue.

12 Can I have other treatments during this research project?

You should tell your study doctor about any new medical diagnosis, treatments or medications during your participation in the research project. The study doctor may need to consider your withdrawal from the research study. The study doctor will explain to you for the reason of this withdrawal.

13 What if I withdraw from this research project?

If you decide to withdraw from the project, please notify a member of the research team before you withdraw. This notice will allow that person or the research supervisor to discuss any health risks or special requirements linked to withdrawing.

If you do withdraw your consent during the research project, the study doctor and relevant study staff will not collect additional personal information from you, although personal information already collected will be retained to ensure that the results of the research project can be measured properly and to comply with law. You should be aware that data collected by the sponsor up to the time you withdraw will form part of the research project results. If you do not want them to do this, you must tell them before you join the research project.

14 Could this research project be stopped unexpectedly?

This research project may be stopped unexpectedly for a variety of reasons. These may include reasons such as:

- Unacceptable side effects of self-directed physical activity
- Decisions made in the commercial interests of the sponsor or by local regulatory/health authorities.

15 What happens when the research project ends?

The knowledge that we get from doing this research will be shared with you through community meetings or the research finding newsletter for participants by mail before it is made widely available to the public. Confidential information will not be shared.

Part 2 How is the research project being conducted?

16 What will happen to information about me?

By signing the consent form you consent to the study doctor and relevant research staff collecting and using personal information about you for the research project. Any information obtained in connection with this research project that can identify you will remain confidential. We will not be sharing the identity of those participating in the research. The information that we collect from this research project will be kept confidential in a safe cabinet and computer at the research office of Western health and Victoria University. Information about you that will be collected during the research will be put away and no-one but the researchers will be able to see it. Any information about you will be allocated a unique study number instead of your name. Only the study doctor will know what the study number list linked to your name, which will be kept in a safe place to ensure that if needed you can be identified and contacted. Your information will only be used for the purpose of this research project and it will only be disclosed with your permission, except as required by law. You can request to know your own information or data as a result of this research study. The study doctor will share about your blood test (immune function) and any personal research results during the follow-up period. This study will keep data for 15 years after research publication and then all information will be disposed. Hard copy data will be shredded by the hospital and university office's shredder. Digital information will be destroyed by deleting or overwriting the files.

Your health records will be self-reported and any information obtained during the research project will again be subject to reasonable measures to keep your personal health information confidential. Absolute confidential cannot be guaranteed. By signing the consent, you agree to the transfer of you self-reported personal health information.

It is anticipated that the results of this research project will be published and/or presented in a variety of forums. In any publication and/or presentation, information will be provided in such a way that you cannot be identified, except with your permission. The knowledge that we get from doing this research will be shared with you through community meetings or the research finding newsletter before it is made widely available to the public. Confidential information will not be shared.

Information about your participation in this research project may be recorded in your health records.

In accordance with relevant Australian and/or Victoria privacy and other relevant laws, you have the right to request access to your information collected and stored by the research team. You also have the right to request that any information with which you disagree be corrected. Please contact the study team member named at the end of this document if you would like to access your information.

Any information obtained for the purpose of this research project in Section 16 that can identify you will be treated as confidential and securely stored. It will be disclosed only with your permission, or as required by law.

17 Complaints and compensation

If you suffer any injuries or complications as a result of this research project, you should contact the study team as soon as possible and you will be assisted with arranging appropriate medical treatment. If you are eligible for Medicare, you can receive any medical treatment required to treat the injury or complication, free of charge, as a public patient in any Australian public hospital.

In the event of loss or injury, the parties involved in this research project have agreed to provide compensation to you for any injury suffered because of your participation in the research project.

18 Who is organising and funding the research?

This research project is being conducted by Western Health in collaboration with Victoria University. The project is being funded by Victoria University student research project.

Western Health and Victoria University may benefit financially from this research project if, for example, the project assists Western health and Victoria University to obtain approval for a new self-directed physical activity program combined with motivational interview counselling.

By taking part in this research project you agree that samples of your blood or tissue (or data generated from analysis of these materials) may be provided to Western Health and Victoria University.

You will not benefit financially from your involvement in this research project even if, for example, your samples (or knowledge acquired from analysis of your samples) prove to be of commercial value to Western Health and Victoria University.

In addition, if knowledge acquired through this research leads to discoveries that are of commercial value to Western Health and Victoria University the study doctors or their institutions, there will be no financial benefit to you or your family from these discoveries.

No member of the research team will receive a personal financial benefit from your involvement in this research project (other than their ordinary wages).

19 Who has reviewed the research project?

All research in Australia involving humans is reviewed by an independent group of people called a Human Research Ethics Committee (HREC). The ethical aspects of this research project have been approved by the HREC of Melbourne Health.

This project will be carried out according to the National Statement on Ethical Conduct in Human Research (2007). This statement has been developed to protect the interests of people who agree to participate in human research studies.

20 Further information and who to contact

The person you may need to contact will depend on the nature of your query. If you want any further information concerning this project or if you have any medical problems which may be related to your involvement in the project (for example, any side effects), you can contact or any of the following people:

Clinical contact person

Name	Ms Lisa Matar
Position	Breast care nurse consultant, Breast cancer service clinic, Western Health
Telephone	0383456896
Email	Lisa.Matar@wh.org.au

For matters relating to research at the site at which you are participating, the details of the local site complaints person are:

Local HREC Office contact (Single Site - Research Governance Officer)

Name	Mr Bill Karanatsios
Position	Research Program Director, Western Health Office for Research
Telephone	(03) 8395 8073
Email	ethics@wh.org.au

If you have any complaints about any aspect of the project, the way it is being conducted or any questions about being a research participant in general, then you may contact:

Reviewing HREC approving this research and HREC Executive Officer details

Reviewing HREC name	Melbourne Health Human Research Ethics Committee
HREC Executive Officer	Jessica Turner
Telephone	(03) 9342 8530
Email	research@mh.org.au

Consent Form - *Adult providing own consent*

Title	Physical activity adherence, psychological health and immunological outcomes in breast cancer survivors
Short Title	PAPHIO study
Project Number	2018.339
Project Sponsor	Victoria University
Principal Investigator	Dr Meron Pitcher
Associate Investigator(s)	Ms Lisa Matar, Dr Sara Holton, Professor Vasso Apostolopoulos, Ms Anne O'Connor, Professor Remco Polman, Emeritus Professor Lily Stojanovska, Ms Katherine Harkin
Location	Western Health VIC - Sunshine Hospital - Footscray Hospital

Consent Agreement

I have read the Participant Information Sheet or someone has read it to me in a language that I understand. I understand the purposes, procedures and risks of the research described in the project. I give permission for my doctors, other health professionals, hospitals or laboratories outside this hospital to release information to Victoria University concerning my disease and treatment for the purposes of this project. I understand that such information will remain confidential. I have had an opportunity to ask questions and I am satisfied with the answers I have received. I freely agree to participate in this research project as described and understand that I am free to withdraw at any time during the study without affecting my future health care.
I understand that I will be given a signed copy of this document to keep.

Declaration by Participant – for participants who have read the information

Name of Participant (please print) _____

Signature _____ Date _____

Declaration - for participants unable to read the information and consent form

Witness to the informed consent process
Name (please print) _____
Signature _____ Date _____
* Witness is not to be the investigator, a member of the study team or their delegate. In the event that an interpreter is used, the interpreter may not act as a witness to the consent process. Witness must be 18 years or older.

Declaration by Study Doctor/Senior Researcher†

I have given a verbal explanation of the research project, its procedures and risks and I believe that the participant has understood that explanation.

Name of Study Doctor/
Senior Researcher† (please print) _____

Signature _____ Date _____

† A senior member of the research team must provide the explanation of, and information concerning, the research project.

Note: All parties signing the consent section must date their own signature.

Form for Withdrawal of Participation - *Adult providing own consent*

Title	Physical activity adherence, psychological health and immunological outcomes in breast cancer survivors
Short Title	PAPHIO study
Project Number	2018.339
Project Sponsor	Victoria University
Principal Investigator	Dr Meron Pitcher
Associate Investigator(s)	Ms Lisa Matar, Dr Sara Holton, Professor Vasso Apostolopoulos, Ms Anne O'Connor, Professor Remco Polman, Emeritus Professor Lily Stojanovska, Ms Katherine Harkin
Location	Western Health VIC - Sunshine Hospital - Footscray Hospital

Declaration by Participant

I wish to withdraw from participation in the above research project and understand that such withdrawal will not affect my routine treatment, my relationship with those treating me or my relationship with Western Health.

Name of Participant (please print) _____

Signature _____ Date _____

In the event that the participant's decision to withdraw is communicated verbally, the Study Doctor/Senior Researcher will need to provide a description of the circumstances below.

Declaration by Study Doctor/Senior Researcher†

I have given a verbal explanation of the implications of withdrawal from the research project and I believe that the participant has understood that explanation.

Name of Study Doctor/
Senior Researcher† (please print) _____

Signature _____ Date _____

† A senior member of the research team must provide the explanation of and information concerning withdrawal from the research project.

Note: All parties signing the consent section must date their own signature.

Appendix 10

The Royal Melbourne Hospital

Office for Research
The Royal Melbourne Hospital
Level 2 South West
300 Grattan Street
Parkville VIC 3050
Australia

Telephone: +61 3 9342 8530
Facsimile: +61 3 9342 8548
Email: research@mh.org.au
thermh.org.au
ABN 73 802 706 972

Approval of Amendment

Melbourne Health Human Research Ethics Committee

15 March 2021

Dear Dr Meron Pitcher

HREC Reference Number: HREC/45268/MH-2018
Local Project Number: 2018.339
Research Title: Physical activity adherence, psychological health and immunological outcomes (PAPHIO study) in breast cancer survivors

Type of review: Ethics Review Only

I am pleased to advise that the amendment to the above project has been reviewed and approved by the Melbourne Health HREC. This approval applies to all sites for which the Melbourne Health HREC has issued ethical approval. This HREC is organised and operates in accordance with the National Health and Medical Research Council's (NHRMC) National Statement on Ethical Conduct in Human Research (2007), and all subsequent updates, and in accordance with the Note for Guidance on Good Clinical Practice (CPMP/ICH/135/95), the Health Privacy Principles described in the Health Records Act 2001 (Vic) and Section 95A of the Privacy Act 1988 (and subsequent Guidelines).

Amendment Approval Date: 15 March 2021

Approved Documents:

- Master Participant Information Sheet/Consent Form, version 3 dated 16 April 2019

Please refer to the Melbourne Health Office for Research website to access guidelines and other information and news concerning research at: https://www.thermh.org.au/research/researchers

Please Note: Template forms for reporting Amendments, Adverse Events, Annual Report/Final Reports, etc. can be accessed from: https://www2.health.vic.gov.au/about/clinical-trials-and-research/clinical-trial-research/monitoring-reporting

For any queries about this matter, please contact the HREC Manager on 03 9342 8530 or via email on: research@mh.org.au

Yours sincerely,

[redacted]

Professor Peter Colman
Chair – Melbourne Health Human Research Ethics Committee (HREC)

PO BOX 2155
Parkville VIC 3050 Australia
thermh.org.au
ABN 73 802 706 972

FACT-B (Version 4)

Appendix 11. Functional Assessment of Cancer Therapy – Breast

Name _____ Code (for researcher only) _____

Date of data collection _____

Below is a list of statements that other people with your illness have said are important. **Please circle or mark one number per line to indicate your response as it applies to the <u>past 7 days</u>.**

	PHYSICAL WELL-BEING	**Not at all**	**A little bit**	**Some-what**	**Quite a bit**	**Very much**
GP1	I have a lack of energy	0	1	2	3	4
GP2	I have nausea	0	1	2	3	4
GP3	Because of my physical condition, I have trouble meeting the needs of my family	0	1	2	3	4
GP4	I have pain	0	1	2	3	4
GP5	I am bothered by side effects of treatment	0	1	2	3	4
GP6	I feel ill	0	1	2	3	4
GP7	I am forced to spend time in bed	0	1	2	3	4

	SOCIAL/FAMILY WELL-BEING	**Not at all**	**A little bit**	**Some-what**	**Quite a bit**	**Very much**
GS1	I feel close to my friends	0	1	2	3	4
GS2	I get emotional support from my family	0	1	2	3	4
GS3	I get support from my friends	0	1	2	3	4
GS4	My family has accepted my illness	0	1	2	3	4
GS5	I am satisfied with family communication about my illness	0	1	2	3	4
GS6	I feel close to my partner (or the person who is my main support)	0	1	2	3	4

FACT-B (Version 4)

Q1	*Regardless of your current level of sexual activity, please answer the following question. If you prefer not to answer it, please mark this box* ☐ *and go to the next section.*					
GS7	I am satisfied with my sex life	0	1	2	3	4

FACT-B (Version 4)

Please circle or mark one number per line to indicate your response as it applies to the past 7 days.

	EMOTIONAL WELL-BEING	Not at all	A little bit	Some-what	Quite a bit	Very much
GE1	I feel sad	0	1	2	3	4
GE2	I am satisfied with how I am coping with my illness	0	1	2	3	4
GE3	I am losing hope in the fight against my illness	0	1	2	3	4
GE4	I feel nervous	0	1	2	3	4
GE5	I worry about dying	0	1	2	3	4
GE6	I worry that my condition will get worse	0	1	2	3	4

	FUNCTIONAL WELL-BEING	Not at all	A little bit	Some-what	Quite a bit	Very much
GF1	I am able to work (include work at home)	0	1	2	3	4
GF2	My work (include work at home) is fulfilling	0	1	2	3	4
GF3	I am able to enjoy life	0	1	2	3	4
GF4	I have accepted my illness	0	1	2	3	4
GF5	I am sleeping well	0	1	2	3	4
GF6	I am enjoying the things I usually do for fun	0	1	2	3	4
GF7	I am content with the quality of my life right now	0	1	2	3	4

FACT-B (Version 4)

Please circle or mark one number per line to indicate your response as it applies to the past 7 days.

	ADDITIONAL CONCERNS	Not at all	A little bit	Some-what	Quite a bit	Very much
B1	I have been short of breath	0	1	2	3	4
B2	I am self-conscious about the way I dress	0	1	2	3	4
B3	One or both of my arms are swollen or tender	0	1	2	3	4
B4	I feel sexually attractive	0	1	2	3	4
B5	I am bothered by hair loss	0	1	2	3	4
B6	I worry that other members of my family might someday get the same illness I have	0	1	2	3	4
B7	I worry about the effect of stress on my illness	0	1	2	3	4
B8	I am bothered by a change in weight	0	1	2	3	4
B9	I am able to feel like a woman	0	1	2	3	4
P2	I have certain parts of my body where I experience pain	0	1	2	3	4

Appendix 12

EXERCISE BARRIER AND TASK SELF-EFFICACY

NAME _____ CODE (for researcher only) _____

Date of data collection _____

This questionnaire asks you about how much your confidence is for doing exercise in each of the following situations. Using the scale from 0-100%, indicate your confidence level ('exercise' is planned physical activity undertaken for health benefits, e.g. jogging, planned walks, weight lifting). Even if you have not been exercising now, please read and answer to each question by marking one number for each situation

Level of confidence	Not at all		Slightly		Moderate			Very		Extremely	
	0%	10%	20%	30%	40%	50%	60%	70%	80%	90%	100%
Barrier self-efficacy											
When I lack discipline to exercise											
When I am nauseated											
When exercise is not a priority											
When the weather is bad											
When I am tired											
When I am not interested in exercising											
When I lack time											
When I do not enjoy exercising											
When I do not have someone to encourage me to exercise											
Task self-efficacy											
I can walk briskly for 20 min without stopping											
I can run or jog for 10 min without stopping											

	Not at all		Slightly		Moderate			Very		Extremely	
	0%	10%	20%	30%	40%	50%	60%	70%	80%	90%	100%
I can climb three flights of stairs without stopping											
I can exercise for 20 min at a level hard enough to cause a large increase in heart rate and breathing											

Rogers, L.Q., et al., *Exercise barrier and task self-efficacy in breast cancer patients during treatment.* Supportive care in cancer, 2006. **14**(1): p. 84-90.

Appendix 13

EXERCISE REGULATIONS QUESTIONNAIRE (BREQ-2)

Name_____ **Code** (for researcher only) _____

Date of data collection _____

WHAT ARE YOUR REASONS IN EXERCISE ADHERENCE?

This questionnaire is used for asking you about your reasons to do or not do physical activity or exercise. This simply ask how you are feeling about exercise. Using the scale below, please mark to the score each of the following items that is true for you. Please note that there are no right or wrong answers. Your answers will be held in confidence and only used for our research purposes.

		Not true for me		**Sometimes true for me**		**Very true for me**
1	I exercise because other people say I should	0	1	2	3	4
2	I feel guilty when I don't exercise	0	1	2	3	4
3	I value the benefits of exercise	0	1	2	3	4
4	I exercise because it's fun	0	1	2	3	4
5	I don't see why I should have to exercise	0	1	2	3	4
6	I take part in exercise because my friends/family/partner say I should	0	1	2	3	4
7	I feel ashamed when I miss an exercise session	0	1	2	3	4
8	It's important to me to exercise regularly	0	1	2	3	4
9	I can't see why I should bother exercising	0	1	2	3	4

		Not true for me		Sometimes true for me		Very true for me
10	I enjoy my exercise sessions	0	1	2	3	4
11	I exercise because others will not be pleased with me if I don't	0	1	2	3	4
12	I don't see the point in exercising	0	1	2	3	4
13	I feel like a failure when I haven't exercised in a while	0	1	2	3	4
14	I think it is important to make the effort to exercise regularly	0	1	2	3	4
15	I find exercise a pleasurable activity	0	1	2	3	4
16	I feel under pressure from my friends/family to exercise	0	1	2	3	4
17	I get restless if I don't exercise regularly	0	1	2	3	4
18	I get pleasure and satisfaction from participating in exercise	0	1	2	3	4
19	I think exercising is a waste of time	0	1	2	3	4

Appendix 14

Motivational Interview Question Script

Engage:

How are you?

How is your exercise going using the step count tracker?

Have you found any change in the amount of exercise you are doing by using the step count tracker?

Focus:

How do you feel about that?

How might doing this exercise affect how you feel (physically and/or mentally)?

What impact might that have on the 'bigger picture' of your life (e.g. more productive at work, better relationships etc)?

Evoke:

What are your motivations for continuing and/or increasing your exercise?

On a scale of 0 to 10, how confident are you at sustaining your exercise?

Plan:

Going forwards, what are your expectations for your daily step count for the next 3 weeks?

What factors (physical, environmental, emotional etc) could help motivate you to achieve these exercise expectations?

Appendix 15

Name _____ **Code** (for researcher only) _____

Date of data collection _____

1. Demographic data

1.1 What was your date of birth? (dd/mm/yyyy) _____

1.2 Number of pregnancies

□ None

□ One

□ More than one

1.3 Age at first period

□ Less than 12 years

□ 12-14 years

□ More than 14 years

1.4 Age at last period

□ in reproductive period

□ Less than 39 years

□ 40- 49 years

□ More than 50 years

2. Health history: Breast cancer and treatments

2.1 Type of breast cancer

□ Ductal carcinoma in situ

□ Lobular carcinoma in situ

□ Invasive ductal carcinoma

□ Invasive lobular carcinoma

□ Inflammatory breast cancer

□ Paget's disease of the nipple

2.2 Stage of breast cancer

□ Stage I

□ Stage II

□ Stage III

□ Stage IV

2.3 Period since diagnosis _____Year(s) _____Month(s)

2.4 Surgery

□ Lumpectomy

□ Mastectomy

2.4 Treatment received and the latest date receiving

□ Chemotherapy Date receiving_____

□ Radiotherapy Date receiving_____

□ Chemotherapy combining radiotherapy Date receiving_____

□ None

2.5 Treatment receiving at the moment

□ Herceptin

□ Tamoxifen

□ Aromatase inhibitors

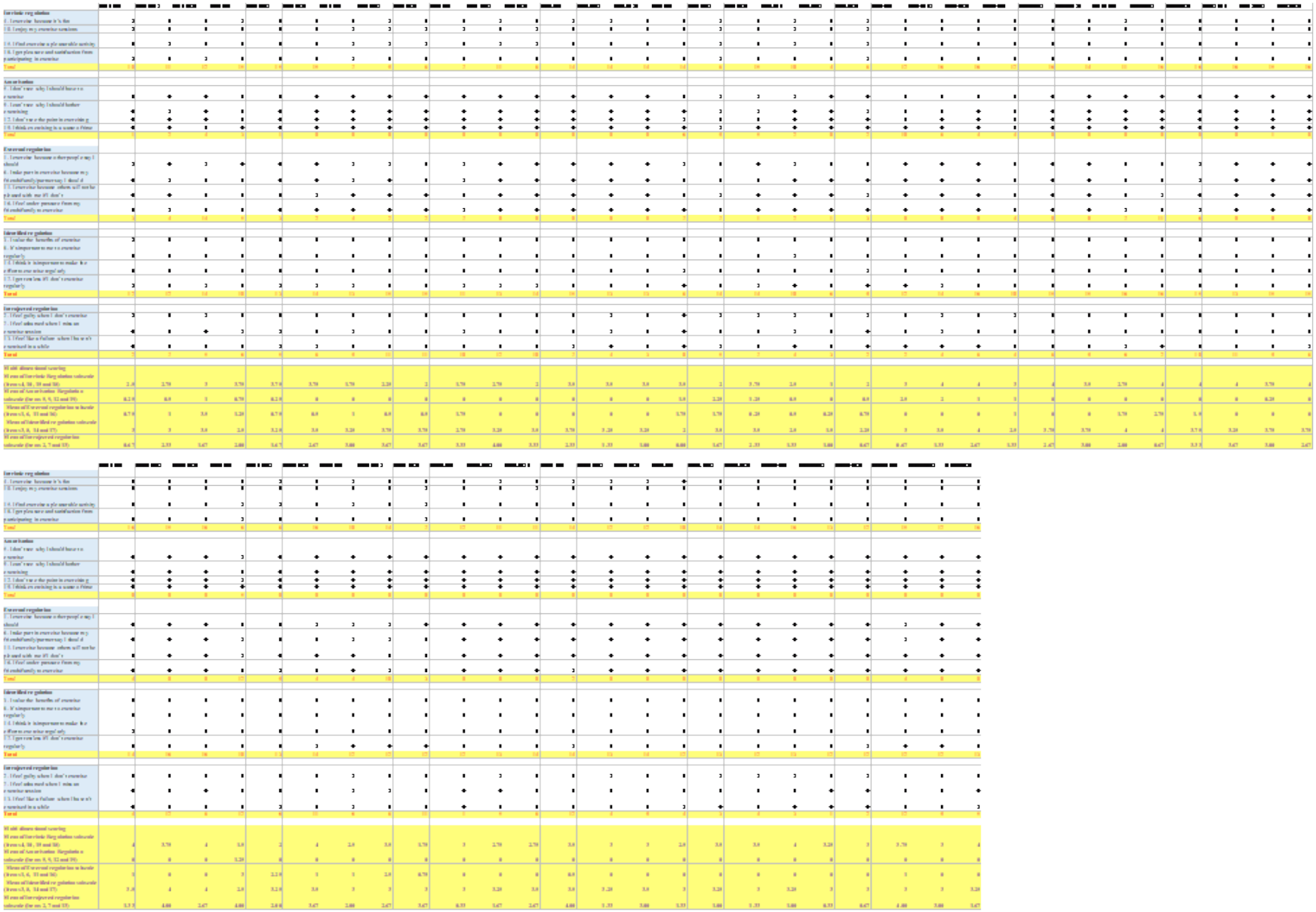
□ None

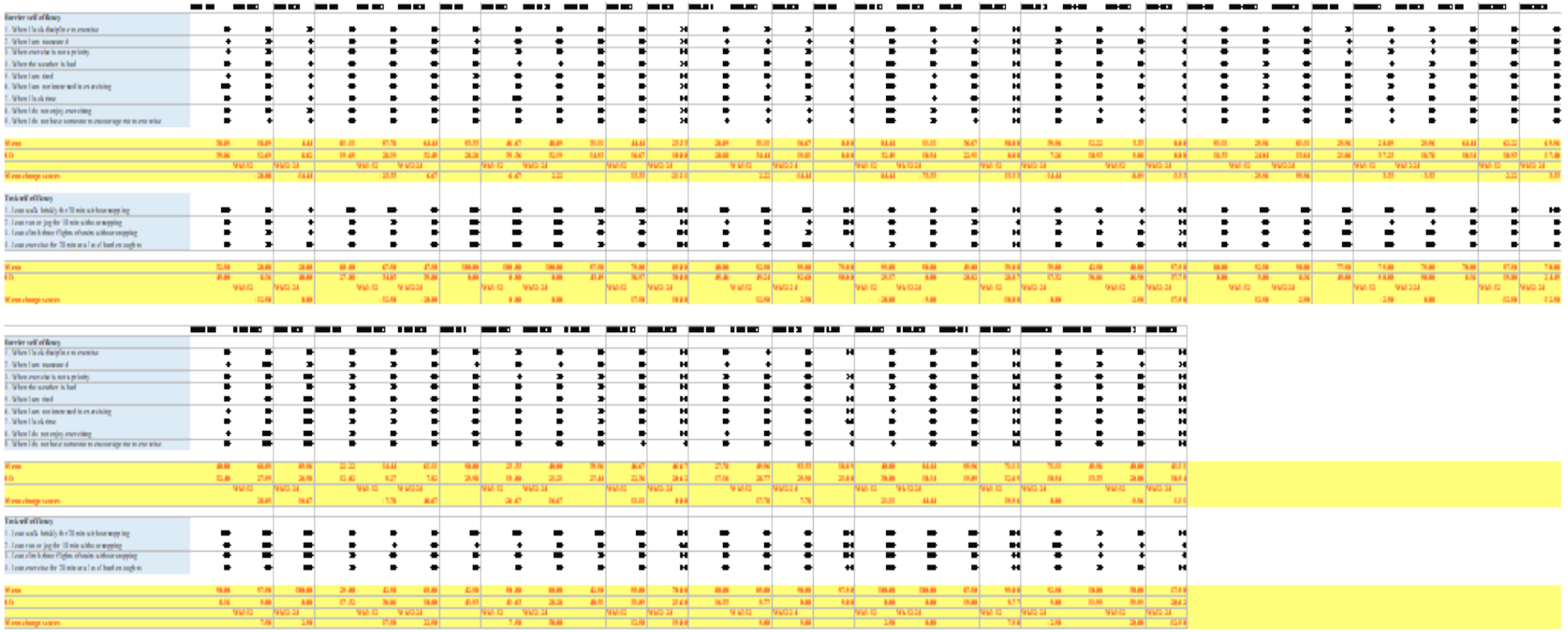
Appendix 16

	Code	Age (years)	Number of pregnancies	Age at first period	Age at last period	Stage of breast cancer	Period (of time) since diagnosis (months)	Surgery	Chemotherapy	Radiotherapy	Current hormonal
1	IIG1	46	more than one	less than 12 years	40-49 years	2	12	yes (L)	yes	no	Tamoxifen
2	IIG3	47	more than one	12-14 years	40-49 years	2	23	yes (L)	yes	yes	none
3	IIG4	35	none	12-14years	Less than 39	2	36	yes (L)	yes	yes	Tamoxifen
4	IIG5	41	more than one	12-14 years	Less than 39	3	22	yes (M)	yes	no	Tamoxifen
5	IIG6	58	more than one	12-14 years	more than 50 years	3	11	yes (L)	yes	yes	Aromatase Inhibitor
6	IIG7	32	none	less than 12 years	in reproductive period	2	18	yes (L)	yes	yes	None
7	IIG8	46	one	12-14 years	40-49 years	2	12	yes (L)	yes	yes	Tamoxifen
8	IIG9	65	more than one	less than 12 years	more than 50 years	2	9	yes (L)	no	yes	Tamoxifen
9	IIG10	52	more than one	12-14 years	more than 50 years	2	11	yes (M)	yes	yes	none
10	IIG11	60	none	12-14 years	40-49 years	2	6	yes (L)	no	yes	none
11	IIG12	52	more than one	more than 14 years	more than 50 years	2	24	yes (M)	yes	yes	Aromatase Inhibitor
12	DIG1	41	more than one	more than 14 years	40-49 years	2	27	yes (L)	yes	yes	None
13	DIG4	52	more than one	12-14 years	more than 50 years	2	10	yes (L)	no	yes	Tamoxifen
14	DIG5	52	more than one	12-14 years	40-49 years	2	24	yes (L)	yes	yes	None
15	DIG6	52	more than one	less than 12 years	40-49 years	3	24	yes (M)	yes	no	None
16	DIG7	43	none	12-14 years	40-49 years	3	15	yes (M)	yes	yes	None
17	DIG8	56	more than one	less than 12 years	more than 50 years	2	14	yes (L)	no	yes	Aromatase Inhibitor
18	DIG10	46	more than one	12-14years	Less than 39	3	23	yes (M)	yes	yes	Aromatase Inhibitor
19	DIG11	69	more than one	12-14 years	40-49	2	30	yes (M)	yes	yes	none

Key and Categories:	Age in years:	Pregnancies:	Age at first period:	Age at last period:	Stage of Cancer:	Period (of time) since diagnosis (months)	Surgery:	Chemotherapy:	Radiotherapy:	Current Hormonal Treatment:
IIG- Immediate Intervention Group DIG- Delayed Intervention Group		- None - One - More than one	- Less than 12 years - 12-14 years - More than 14 years	- In reproductive period - Less than 39 years - 40-49 years - More than 50 years	- One - Two - Three	-	- No - Yes (Lumpectomy) - Yes (Mastectomy)	- No - Yes	- No - Yes	- None - Tamoxifen - Aromatase Inhibitors - Herceptin

Healthy-pond cooks	Rs million shop-counsel						FRBM mapp e		Week: 33 shop counsel						FRBM mapp		Week: 34 shop counsel						FRBM s mapp	
	day 1	day2	day 3	day4	day5	Average	Shares per day	Shops per week	day 1	day2	day 3	day4	day5	Average	Shares per day	Shops per week	day 1	day2	day 3	day4	day5	Average	Shares per day	Shops per week
BG1	4,207	2,754	3,085	1,855	5,501	3463.8	22.0	7.0	3,021	2,984	2,628	3,452	3,155	30480	8.0	5.0	5901.0	7195.0	4636.0	4185.0	5142.0	5411.4	6	5
BG3	7,988	7,898	8,512	8,618	8,498	8302.8	22.0	7.0	13,853	15,062	9,938	10,477	11,504	121 66.8	20.0	7.0	17742	13760	15708	11150	12694	14210.8	22	7
BG4	12,120	12,322	13,355	12,154	12,271	12444.4	22.0	7.0	14,202	15,502	13,938	13,430	14,111	138 36.6	22.0	7.0	10110	10474	10298	10220	10068	102.34	22	7
BG5	5,053	6,904	7,793	8,617	8,940	7461.4	22.0	7.0	10,999	7,675	9,892	8,757	6,522	87 69.0	16.0	7.0	7966	10511	6455	8664	7869	82.49	14	7
BG6	7,607	6,830	7,583	6,045	6,978	7088.2	22.0	7.0	10,385	13,936	15,701	16,175	12,272	136 93.8	12.0	7.0	8006	8775	9852	12283	16248	1 1032.8	22	7
BG7	8,080	6,499	5,554	6,225	7,447	6757	22.0	7.0	10,928	10,026	5,102	6,147	6,029	76 46.4	14.0	7.0	1664	2568	3820	2951	7654	3731.4	14	7
BG8	5,568	3,391	4,915	2,842	2,528	3848.8	22.0	7.0	4,153	6,788	3,989	3,595	2,658	42 18.6	22.0	7.0	5224	6876	1759	5784	3995	4727.6	22	7
BG9	11,807	10,475	9,807	10,853	9,993	10587	22.0	7.0	13,399	15,970	11,984	11,019	11,789	124 32.2	22.0	7.0	13758	14086	12953	14627	13095	1 3703.8	22	7
BG10	14199	11388	11942	11143	13291	12392.6	22	7	18022	22051	21099	23216	23645	216 02.6	22	7	15235	22222	17912	19624	18653	1 8329.2	22	7
BG11	4846	5888	9746	4066	6678	6244.8	22	7	6887	2257	1944	2282	2496	31 73.2	22	7	3378	1653	2790	2217	1887	2385	22	7
BG12	10702	15318	16949	8205	15542	13342.8	22.0	7	20476	11067	10129	10232	15474	13475	22.0	7	10178	11965	10702	10847	9547	1 0663.4	22	7
Mean						8358.33	22.00	7.00						1036 9.29	18.36	6.82						9 334.48	19.09	6.82
SD						3416.67	0.00	0.00						565 3.18	5.05	0.60						4967.85	5.39	0.60
DIG1	18,837	17,309	10,995	17,130	17,051	16264.4	22.0	7.0	15,049	15,050	19,496	10,383	14,267	148 49.0	10.0	7.0	10049	12859	11752	10030	10056	1 0949.2	8	7
DIG4	6,174	3,643	2,524	2,466	4,120	3785.8	22.0	7.0	2,205	5,034	3,490	4,623	6,223	43 15.0	7.0	7.0	4886.0	9 9470	5 2880	6028.0	6095.0	6448.8	18	7
DIG5	8,161	10,654	11,407	9,606	8,530	9671.6	22.0	7	9,751	8628	8692	10,107	11962	98 27.2	20.0	7	3658	5409	8556	10096	7783	7096.4	22	7
DIG6	13,380	13,958	12,457	9,213	10,782	11958.0	22.0	7	12,486	8,690	7,395	9957	9041	95 13.8	16.0	7	8592	6306	6681	7850	5624	7010.6	22	7
DIG7	10655	6322	6777	8252	10724	8546.2	22.0	7	15,515	12,522	13252	12118	12446	131 70.6	14.0	7	14475	11613	11191	11978	10610	11973	22	7
DIG8	6181	10302	14918	15520	15771	12538.8	22.0	7	14948	17120	14698	19180	16501	152 89.4	14.0	7	24688	27910	15617	22835	12871	24784.2	14	7
DIG1 0	9089	9334	10573	10305	10086	9875.4	22.0	7	9949	8340	10085	5795	8540	85 01.8	22.0	7	9628	11085	11205	10436	10084	1 0487.6	22	7
DIG1 1	2222	4806	2774	5712	4728	3568.4	22.0	7	7336	5055	5462	5218	3839	5386	8.0	5	1056	5152	1042	5173	2313	2547.2	22	7
Mean						9525.83	22.00	7.00						1010 6.60	13.88	6.75						9 662.13	18.75	7.00
SD						4301.50	0.00	0.00						489 8.28	5.61	0.71						5 424.02	5.23	0.00
						[illegible]								[illegible]	[illegible]	[illegible]						[illegible]	[illegible]	[illegible]
						[illegible]								[illegible]	[illegible]	[illegible]						[illegible]	[illegible]	[illegible]
Combine dMean						8965.27								1025 8.68	16.47	6.79						9 472.39	18.95	6.89
Combine dSD						3749.66								492 9.93	5.54	0.63						5017.49	5.18	0.46





Appendix 17