Physical activity motivation and self-directed physical activity in female breast cancer survivors

A thesis submitted for the degree of

Doctor of Philosophy

by

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Institute for Health and Sport

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ABSTRACT

1. The PAPHIO study protocol: a randomized controlled trial with a 2 x 2 crossover design of Physical Activity adherence, Psychological Health and Immunological Outcomes in breast cancer survivors

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Summary. The PAPHIO study; a randomized controlled trial with 2X2 crossover design implements a self-directed physical activity program in which participants engage in self-monitoring and receive motivational interviewing (MI) to enhance physical activity adherence. The study aims to determine the effects of 24 weeks self-directed activity combined with MI on (i) psychological health, (ii) quality of life (QoL) and (iii) immune function in female breast cancer survivors. During my PhD, I was involved in writing of the PAPHIO protocol, submission of ethics applications, informed consent, information to participants and advertising materials, acquiring site specific approvals, submission of ethics amendments, adding a new recruitment site, and, submission of ethics progress reports. The trial has been registered via the Australian New Zealand Clinical trials Registry- ACTRN12619001271190. Prospectively registered on 13 September 2019
http://www.ANZCTR.org.au/ACTRN12619001271190.aspx

2. The effect of physical activity motivation by step tracker and motivational interviewing in self-directed physical activity on quality of life and psychological health in female breast cancer survivors

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Background. Regular physical activity (PA) or exercise in female breast cancer survivors is well known to promote their clinical outcomes and quality of life (QoL), as well as importantly reducing their mortality rate. However, few breast cancer survivors achieve PA recommendations. Those prescribing PA or exercise programs for breast cancer survivors must be aware of its safety and effectiveness, as well as their physical ability and clinical conditions.

This thesis aims to assess the efficacy of two motivational strategies - step tracker and motivational interviewing (MI) - for promoting adherence to self-directed physical activity in breast cancer survivors. The thesis reports the feasibility of the clinical trial "**P**hysical **A**ctivity adherence, **P**sychological **H**ealth and **I**mmunological **O**utcomes in breast cancer survivors (PAPHIO study)" conducted in collaboration with Western Health, Melbourne VIC Australia. Additionally the thesis reports a systematic review and meta-analysis comparing the efficacy of step tracker and MI in promoting adherence to self-directed PA in breast cancer survivors.

A 12-week feasibility study of a randomized controlled trial

The pilot study presented herein, involved the recruitement of female breast cancer surviors who were randomly allocated into intervention group (Immediate intervention group; IIG) or control group (delayed intervention group; DIG) between February and December 2020. All participants were prescribed a 12 week self-directed PA program, alongside a pedometer (Fitbit Alta HR) for daily step self-monitoring. Paricipants in the IIG were provided MI once face-to-face at week 1 and three times via telehealth (phone call) at weeks 2, 4 and 9. The participants in the DIG were not provided with MI, but received the same PA intervention. The feasibility of the study was assessed by the recruitment and retention rate as well as the preliminary efficacy of the pedometer and MI interventions, evaluated by analysing PA adherence, daily step counts, and scores in QoL, psychological health, exercise self-regulation, exercise barriers and task self-efficacy at week 12.

Results. Seventeen participants were recruited over an 11 month period. The recruitment rate was 1.5 participants per month, with a retention rate of 82.35 % (14/17). Three participants dropped out (17.65%), with one withdrawal (5.89%) in the IIG group and two (11.76%) in the DIG losing contact with the study. No effects of group by time on daily steps, or scores in QoL, psychological health, exercise self-regulation, exercise barriers and task self-efficacy were noted at week 12 of the intervention.

3. A systematic review on self-monitoring vs Motivational Interviewing: Motivation techniques in self-directed physical activity to improve adherence in breast cancer survivors

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Background / Methods. The systematic review was registered with PROSPERO on 22nd January 2020 (Registration number CRD42020148542). The study included studies implementing self-directed PA programs, alongside step tracker or MI for motivation in female breast cancer survivors from the following databases: CENTRAL, Pubmed, CINAHL, PsycINFO, and Sportdiscuss without date of publication limitation. Search results were collected using the online software Covidence. The primary intervention of the study was self-directed PA, the comparisons were motivation strategies between step tracker and MI and the outcome was adherence. Two reviewers independently screened titles and abstracts, before individually assessing full-texts of the relevant articles for eligibility criteria. Data of individual trials were extracted into custom data extraction forms.

Results. The search identified 7,921 potential studies published between 1980 and 2020. Of these, 91 underwent full-text screening, of which 16 studies were included for data extraction. The review found that self-directed PA program applying step tracker and MI in breast cancer survivors were heterogenous in interventional designs and duration across the studies. PA adherence was reported with significant heterogeneity; for example, some studies report percentage of participants who met PA recommendations while some studies use repeated measures such as weekly duration or intensity of PA or daily step count. Overall, they reported a positive effect of step tracker or MI intervention on adherence and physical or psychological outcomes. The studies which clearly indicated the PA recommendations or minimum requirements of the project as meeting guidelines for participants can report the percent of participants who meet the criteria. However, studies which declared that participants would be motivated to direct themselves to increase their PA (no minimum requirement) reported the average of repeated activity measures in participants.

Conclusion. This systematic review illustrates the benefit of applying step tracker and MI in self-directed PA programs, to improve adherence. The pilot study shows the feasibility of a 12-

week self-directed physical activity program using a Fitbit and MI intervention in female breast cancer survivors. However, the pilot study showed the low acceptability of the effect of group by time on physical activity adherence, QoL and psychological health in breast cancer survivors due to the limitations of recruitment during the outbreak of COVID-19 leading to small numbers in this pilot study. A larger randomized controlled with 2x2 crossover design study (two groups each receiving the intervention and control conditions by random order of conditions) under the project PAPHIO study is currently in progress.

Doctor of Philosophy Student Declaration

Doctor of Philosophy Declaration
"I, Supa Pudkasam, declare that the PhD thesis entitled Physical activity motivation and self-directed physical activity in female breast cancer survivors is no more than 80,000 words in length including quotes and exclusive of tables, figures, appendices, bibliography, references and footnotes. This 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 my research in alignment with the Australian Code for the Responsible Conduct of Research and Victoria University's Higher Degree by Research Policy and Procedures.

Signature [redacted] Date 27/02/21

Declaration regarding Ethics Approval
If a candidate has had ethics approval over the course of their candidature, the candidate must include the following declaration in the thesis, underneath the Student Declaration:

"All research procedures reported in the thesis were approved by the Melbourne Health Human Research Ethics Committee on 29 April 2019, HREC reference number: HREC/45268/MH-2018

Signature [redacted] Date 27/02/21

DETAILS OF INCLUDED PAPERS: THESIS WITH PUBLICATION

Please list details of each scholarly publication and/or manuscript included in the thesis submission. Copies of published scholarly publications and/or manuscripts submitted and/or final draft manuscripts should also be included in the thesis submission.

This table must be incorporated in the thesis before the Table of Contents.

Chapter no.	**Publication Title**	**Publication Status** **□Published** **□Accepted for publication** **□In revised and resubmit stage** **□Under review** **□Manuscript ready for submission**	**Publication Details** **□Citation, if published** **□Title, Journal, Date of acceptance letter and Corresponding editor's email address** **□Title, Journal, Date of submission**
1	1a Breast cancer and exercise: the role of adiposity and immune markers 1b Physical activity and breast cancer survivors: Importance of adherence, motivational interviewing and psychological health 1c Work it out: Exercise as an anti-cancer intervention	1a Published 25 April 2017 1b Published 18 July 2018 1c Published July 2021	1a Maturitas (2017) *105*, 16-22. Impact Factor 3.63 Q1 1b Maturitas (2018) *116*, 66-72. Impact Factor 3.63 Q1 1c Nova Science Publishers (2021) ISBN: 9781536197129 Highly reputable
2	Self-monitoring vs Motivational Interviewing: Motivation techniques in self-directed physical activity to improve adherence in breast cancer survivors: A protocol for a systematic review and meta-analysis	Manuscript ready for submission	

Chapter no.	Publication Title	Publication Status □Published □Accepted for publication □In revised and resubmit stage □Under review □Manuscript ready for submission	Publication Details □Citation, if published □Title, Journal, Date of acceptance letter and Corresponding editor's email address □Title, Journal, Date of submission
3	Motivational strategies to improve physical activity adherence in breast cancer survivors: A systematic review and meta-analysis	Published June 2021	Maturitas ,Published online 24 June 2021, In Press Impact Factor 3.63 Q1
4	4a. The PAPHIO study protocol: a randomised controlled trial with a 2 x 2 crossover design of Physical Activity adherence, Psychological Health and Immunological Outcomes in breast cancer survivors	4a Published 01 May 2020	BMC public health (2020) *20*, 1-8. Impact factor 2.69 Q1

Declaration by [candidate name]: [redacted] 27/02/2021

Supa Pudkasam Signature: Date:

For each chapter in the thesis which is based on publication(s)/manuscript(s), the declaration of co-authorship must be incorporated in thesis and it is recommended it be placed in the appendices.

Acknowledgments

My PhD research and thesis would not have been possible without the support of my principal supervisor; Professor Vasso Apostolopoulos. She provided me with a great opportunity to be involved in a clinical trial that I could translate my research skills. Being involved in the clinical trial enabled me to collaborate with physicians, breast care nurses, and especially I was able to approach female breast cancer survivors and encourage them to engage in physical activity. Professor Apostolopoulos is well connected with oncology health care groups and she is very enthusiastic in research process which inspires me in my research training. Her advice and support while I was proceeding with the human research ethics applications and conducting the research study was a great help for the success of my research project.

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I wish to acknowledge the help provided by the breast care nurses atWestern Health, Melbourne; Melanie Fisher, Lisa Matar, Sue Komp, and Darcie Vogan regarding participant recruitment and facilitating participant's blood collections. I appreciate the support from Anne O'Connor, IPC Health and in charge of the breast care support group for her involvement in participant recruitment.

Special thank you should be given to the following colleagues who provided guidance and assistance in the systematic review process and meta-analysis; Kristina Vingrys, Jack Feehan and Jason Talevski. In addition, thank you to Jack Feehan who edited all the chapters for grammatical errors. I also thank Brigitte Pascal for her great effort and help with the Motivational interviewing aspects of the clinical study. I am grateful that Katherine Harkin, an enthusiastic MSc candidate will continue with the project. I would also like to thank Suzanne Poliness, Victoria University librarian, for her assistance in search strategies development using MeSH and related terms as well as useful databases.

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I wish to acknowledge the Institute for Health and Sport at Victoria University for providing PhD research funds which were used to conduct my research project, and in addition for providing tuition fees waiver for my last two semesters due to my candidature extension and my financial issues.

Finally, I wish to thank my parents for their love, support and encouragement throughout my study.

Publications

Pudkasam, S., Tangalakis, K., Chinlumprasert, N., Apostolopoulos, V., & Stojanovska, L. (2017). Breast cancer and exercise: The role of adiposity and immune markers. *Maturitas*, *105*, 16-22. doi:https://doi.org/10.1016/j.maturitas.2017.04.022 (IF=3.63, Q1)

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Pudkasam, S., Vingrys, K., Polman, R., Chinlumprasert, N., Stojanovska, L., & Apostolopoulos, V. (2021). Self-monitoring vs Motivational Interviewing: Motivation techniques in self-directed physical activity to improve adherence in breast cancer survivors: A protocol for a systematic review and meta-analysis.(To be submitted).

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Pudkasam, S., Poonraksa, S., & Chinlumprasert N. Exercise and psychological health in Middle-life. In Apostolopoulos, Feehan, & Tripodi (Eds.).*Exercise throughout the lifespan*. Elsevier. (Submitted)

Pudkasam,S & Apostolopoulos V. Exercise and immunity. In Apostolopoulos, Feehan, & Tripodi (Eds.) *Exercise throughout the life span.* Elsevier. (Submitted)

Peer review

Maturitus Journal Manuscript number MAT_2018_698

Title “A scoping review and meta-synthesis of behaviour change theories to develop the ‘PHYT in dementia’, an integrated model promoting physical activity in people with dementia"

Maturitus Journal Manuscript number MAT-D-21-0041

Title " Effect of post-diagnosis physical activity on breast cancer recurrence: A systematic review and meta-analysis"

European Journal of Physiotherapy Manuscript number SPHY-2021-0066

Title " Effects of physical activity changes induced by behavior change interventions on inflammation and patient-centered outcomes in breast cancer survivors: A systematic review"

Presentations

PhD student presentation “Effects of exercise on the immune system in breast cancer” in 2nd Immunology Summit on 7 December 2016 at Room 1108, Victoria University, 300 Flinders St Campus

Postgraduate presentation “The Effect of Self-Directed Physical Activity Combining Exercise Motivation on Exercise Adherence and Well-being in Culturally Diverse Women with Breast Cancer” in Postgraduate Research Conference on 7 December 2017 at St Albans Campus, Victoria University

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Chapter 1

Chapter I

Literature Review

Chapter preface:

This chapter is a combined literature review, consisting of three published works which were created during the candidature of this thesis.

Authorship declarations:

The three manuscripts included in this chapter have benefitted from the valuable contribution of a number of co-authors, who provided guidance, editorial assistance and advice. However, the conception, execution and initial draft of the publications were performed by the candidate. Specific contributions by co-authors are detailed in the declarations

Chapter 1

Literature Reviews

Review paper manuscript - 1

1a. Breast cancer and exercise: the role of adiposity and immune markers

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ABSTRACT

Currently, breast cancer forms a quarter of all cancers and 15% of cancer-specific deaths amongst females. The global occurrence of breast cancer increased between 2008 and 2012, while the mortality rate decreased. Exercise can be beneficial to breast cancer patients through mechanisms of adiposity and immune responses. Herein, we identify the effects of exercise programs on adiposity and immunological markers which can improve breast cancer outcomes. Even though there is some evidence supporting the improvement of fat metabolism and immune function after an exercise program in breast cancer, the randomized control studies published are limited and require further comprehensive analysis in this population group.

Keywords: Breast cancer, Exercise, Biomarkers, Adiposity, Immune biomarkers, Outcome

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DECLARATION OF CO-AUTHORSHIP AND CO-CONTRIBUTION: PAPERS INCORPORATED IN THESIS

This declaration is to be completed for each conjointly authored publication and placed at the beginning of the thesis chapter in which the publication appears.

1. PUBLICATION DETAILS (to be completed by the candidate)

Title of Paper/Journal/Book: Breast cancer and exercise: the role of adiposity and immune markers

Surname: Pudkasam First name: Supa

Institute: Institute for Health and Sport Candidate's Contribution (%): 76%

Status:

Accepted and in press: ☐ Date:

Published: ☑ Date: 25 /4/2017

2. CANDIDATE DECLARATION

I declare that the publication above meets the requirements to be included in the thesis as outlined in the HDR Policy and related Procedures – policy.vu.edu.au.

[redacted] 24 February 2021

Signature **Date**

3. CO-AUTHOR(S) DECLARATION

In the case of the above publication, the following authors contributed to the work as follows:

The undersigned certify that:

1. They meet criteria for authorship in that they have participated in the conception, execution or interpretation of at least that part of the publication in their field of expertise;
2. They take public responsibility for their part of the publication, except for the responsible author who accepts overall responsibility for the publication;

3. There are no other authors of the publication according to these criteria;
4. Potential conflicts of interest have been disclosed to a) granting bodies, b) the editor or publisher of journals or other publications, and c) the head of the responsible academic unit; and
5. The original data will be held for at least five years from the date indicated below and is stored at the following **location(s)**:

Name(s) of Co-Author(s)	Contribution (%)	Nature of Contribution	Signature	Date
Supa Pudkasam	76%	Creating the topic and layout of article, writing of article	[redacted]	24/2/21
Kathy Tankalakis	2%	Editing the manuscript		26-2-21
Nanthaphan Chinlumprasert	2%	Editing the manuscript		01/03/21
Vasso Apostolopoulos	15%	Revising the topic and layout of article, editing and formating, supervision		25/02/21
Lily Stojanovska	5%	Editing the manuscript		25/02/21

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Review

Breast cancer and exercise: The role of adiposity and immune markers

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ARTICLE INFO

Keywords:
Breast cancer
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Breast cancer outcome

ABSTRACT

Currently, breast cancer accounts for a quarter of all cancers and 15% of cancer-specific deaths amongst females. The global occurrence of breast cancer has increased in the last decade whilst the mortality rate has decreased. Exercise can be beneficial to breast cancer patients through changes in adiposity and immune responses. Even though there is some evidence supporting the improvement of fat metabolism and immune function after an exercise program in breast cancer, randomized controlled studies are limited and require further comprehensive analysis in this population group. Herein, we identify the known effects of exercise programs on adiposity and immunological markers which can improve breast cancer outcomes.

1. Introduction

Breast cancer leads to physical and mental distress [1] which is linked with increased prevalence of malignancy-related mortality amongst females worldwide [2]. The World Health Organization [3] mandates that exercise improves physical and mental wellbeing in general and that consistent moderate-intensity exercise decreases the risk of cardiovascular disease, diabetes and cancer. Interestingly, exercise programs for breast cancer have been reported to contribute to positive outcomes with increased survival rates [4]. This article gives an overview of the current trend for global breast cancer, possible risks factors and the benefits of exercise programs on breast cancer prevention and outcomes, with specific emphasis on adiposity and immunological biomarkers. It has been shown that certain biomarkers are improved with physical activity; for example, adipokines, estrogen, insulin resistance, C-reactive protein [5,6], T helper (Th) cells [7] and cytotoxic activity of NK cells [8]. These biological changes following exercise training have been associated with improved breast cancer outcomes and reduced mortality rates [6].

2. Methodology

This review article summarizes the existing knowledge of the benefits associated with exercise on breast cancer outcomes through adiposity and immunological mechanisms using related articles published between 2000 and 2017 in Medline and PubMed. The key terms of this review consists of breast cancer OR breast neoplasms AND exercise OR physical activity, breast cancer OR breast neoplasms AND biomarkers for adiposity OR obesity-related biomarkers, breast cancer OR breast neoplasms AND immunological biomarkers.

3. The global incidence of breast cancer

Breast cancer is one of the leading health issues of women worldwide. Currently, breast cancer is ranked as the most common diagnosed cancer with an estimated 1.7 million cases and over 520,000 deaths worldwide [9]. It accounts for one quarter of all cancer types and 15% of all cancer related deaths in females. The higher developed countries such as USA, Europe (northern and western), Australia and New Zealand have higher incidence rates of breast cancer as compared to the intermediate developed countries of Europe (central), Latin America and the Caribbean; the lowest incidence rates of breast cancer being in low developed countries, Africa and Asia [10]. However, the highest death rate is observed in parts of Africa and South Asia [11], with the death rate being lowest in USA, Europe (northern and western), Australia and New Zealand [11]. Data from the World Health Organization shows that the occurrence of breast cancer has increased rapidly in 22 of 39 observed countries between 2008 and 2012, whilst the global mortality rate has decreased [11].

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[1] These authors contributed equally to this paper.

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3.1. The incidence trends by age

In the 1980s, the incidence of breast cancer dramatically increased in US women aged over 40 years [12]. This may have resulted from improvements in mammography screening. The incidence remained constant for women who were in their 40s through the 1990s but gradually increased in women above 50 [12]. This upward trend is likely due to increased rates of obesity in older women and the use of hormonal replacement therapy to alleviate menopausal symptoms [13]. In the early 2000s, following the publication of the Women's Health Initiative study [14] the incidence rate decreased in women aged over 50, possibly due to the decreased use of hormone replacement therapy. More recently, the incidence of breast cancer has been reported as stable for US women in their 40s and 50s. However, it has increased by 1 % and 1.2 % annually for women aged 60 and 70 years since 2004 and 2005, respectively. For women aged in their 40s, the incident rate of breast cancer has been stable since 1986, whereas for women aged between 20-39 years the incidence rate increased 0.6 % per annum from 1994-2012 [12]. The incidence of breast cancer in younger women is higher in less developed countries in Africa and Asia comparing with Europe and North America [2].

3.2. The incidence trends by race and ethnicity

Age-standardised rate of breast cancer incidence in developed continents, ie. Australia and Northern America are greater than developing continents i.e Asia and Africa (71.7 vs 29.3/100,000) [2]. The incidence and mortality rates of breast cancer in relation to race and ethnicity in the US suggests that non-Hispanic women have the highest incidence (128.1 (white) and 124.3 (black) / 100,000) than Alaska native/American Indian, Hispanic (91.9/100,000) and Asian Pacific women (88.3/100,000) [12]. Even though, the incidence rate in white women is slightly higher than black women, the mortality rate in black women is 42 % higher than in white women [12]. The lower incidence of breast cancer in

Alaska native/American Indian, Hispanic and Asian Pacific women may represent the variation of the risk factors associated with decreased risk, ie. younger age having their first child and breast feeding for over 12 months [12]. The continuing higher rate of breast cancer incidence has been found in more developed regions such as Northern America, Europe and Australia [11].

4. Risk factors of breast cancer

The presence of risk factors does not denote that a woman will develop breast cancer, just as the absence of risk factors does not necessarily prevent breast cancer [15]. However, it is very important for a woman to understand her risks for breast cancer and specific interventions to reduce the risks, in addition to the benefits of breast cancer screening [15]. Known risk factors have a strong association with ageing, reproductive history, exogenous hormone exposure and family history [15]. Indeed, some risk factors can be controlled but others are difficult to manage. The possibility of breast cancer in American women dramatically increases every 10 years. For example, the breast cancer risk of a woman aged 30 is 0.44 %, whereas a woman aged 70 has a risk of 3.89 % [12]. Some data suggests that the impact of lifestyle and reproductive patterns are on the upward trend of breast cancer incidence; for instance, agricultural countries changing to industrial societies [16], menarche at younger age and menopause at a later age [17]. In addition, the use of hormone replacement therapy pre- and post-menopause [15], the use of oral contraceptives and primiparous women with the first full-term pregnancy at a later age are linked to rising breast cancer occurrence [15, 18, 19]. In fact, a female that is periparous or multiparous at a younger age lowers the relative risk of breast cancer at or after menopause compared to nulliparous women [17]. Interestingly, women who breastfed have a hazard ratio of 0.75 for premenopausal breast cancer compared to women who never breastfed; although this phenomenon is associated to those with a family history of breast cancer [20]. Moreover, the presence of BRCA1 and BRCA2 gene mutations are associated with higher risk of breast cancer [21]. As a consequence, counselling and timely screening procedures are provided to women who carry these genetic mutations [21].

In the last decade research studies have alluded to chronic low grade inflammatory responses being one of the major contributing factors leading to chronic diseases such as diabetes, cardiovascular disease and cancer. One of the major culprits of low grade inflammation is obesity [22]. In fact, in obese animals there is a

correlation between adipocyte hyperplasia and tumor progression [23]. It is likely that in obesity, poor functional adipose tissue secretes higher levels of pro-inflammatory factors and inhibits the release of adiponectin. This alteration may explain the link between obesity, type-2 diabetes, metabolic syndrome and cancer [23].

4.1. Breast cancer and obesity

Obesity is likely to be associated with increased risk of breast cancer, especially in postmenopausal women [24]. Body weight gain of every 3.2 kg in women above 18 years of age increases the risk factor for breast cancer with an estimated relative risk of 2.85, increasing their mortality rate by 7 % [25]. This attribute can be related to several mechanisms through the increase of adiposity consisting of increased blood circulation of estrogen, insulin and insulin-like growth factor (IGF [26] as well as endocrine disrupting compounds (organic pollutants, such as, organochlorines which accumulate and are stored in fatty tissues, including that of adipose mammary tissue [27]. In addition, adipokines and leptin, produced and secreted by adipocytes, are higher in obese individuals and may contribute to postmenopausal breast cancer [6]. Moreover, the association between obesity and activation of immune cells (M1 macrophages, B cells, T cells), chemokines, pro-inflammatory cytokines (IL-1, IL-6, TNF-α) and pro-angiogenic factors, change the body milieu contributing to increased risk of breast cancer [28].

5. Effects of exercise on overall health and disease prevention

The ancient Greek physician, Hippocrates, stated in the 5th century BC that if individuals lack their energy expenditure, they would be liable to disease, deteriorated growth and quicker ageing [29]. The observational studies conducted between 1940 and 1950 noticed that employees who were more active, such as bus conductors, had lower incidence of heart disease than bus drivers [30]. Exercise training reduces the precedence of some chronic diseases due in part to its effects on anti-inflammatory processes [31]. Regular and long term moderate aerobic exercise enhances fat metabolism which results in the reduction in adipokine secretion [31]. Physical activity has been shown to decrease IL-6, IL-8 and IL-15 cytokines, whereas IL-1 receptor antagonist and soluble TNF-alpha receptor which are released during muscle contraction, may contribute to anti-inflammatory processes [32]. Likewise, in a 10 week combined walking and weight training program dramatically reduced C-reactive protein

in hypercholesteremic people with inactive lifestyles [33]. It is recommended by the World Health Organization that an active lifestyle improves overall health in adults aged 18-64 years. Active lifestyle includes that of leisure physical activity (gardening, walking, dancing, swimming), transportation (cycling, walking), occupational work, household tasks and contributing to game play, sports or planned exercise. This leads to improved heart function, muscular fitness and bone health, as well as contributing to reduced risk of developing chronic disease [34]. Generally, an adult should participate in at least 150 minutes of moderate intensity aerobic activity or at least 75 minutes of vigorous intensity aerobic activity per week [34]. Indeed, a prospective cohort study of 3,918 subjects conducted in England between 1990 and 2014 reported that the mortality rate of people who lived sedentary lifestyles was highest at approximately 42/1,000 persons per year risk (PYR) and lowest amongst those who met the recommended activity levels at approximately 6/1,000 PYR. Hence, activity reduces the mortality rate by 25 % [35]. As the representative population adhering to exercise guidelines would significantly reduce mortality rates, a strategy to involve the general population in engaging in an active lifestyle could be emphasized for public health promotion [35]. The implication of positive effect of regular exercise on anti-inflammatory response can support exercise recommendation for people living with chronic diseases such as cancers [31].

5.1. Effects of exercise on immunological parameters

Acute exercise releases the stress hormone cortisol which upregulates major histocompatibility complex (MHC) class II expression IL-12 production, neutrophils and natural killer (NK) cells have been noted in the circulation during bouts of acute exercise [36]. In addition, a short bout of heavy cycling increases pro- and anti-inflammatory responses, including cytokines (TNF-alpha, IL-6 and IL-4), T cells, B cells, monocytes and growth factors [37]. Likewise, immediately following brief exercise, gene expression of some monocytes involved in vascular diseases like angiogenesis, asthma and arthritis are altered [36]. More specifically, a single bout of vigorous exercise at approximately 80 % VO_2max alters the expression of a number of NK cell genes which are involved in cancer [36]. These findings suggest that exercise may contribute to chronic disease prevention via the innate immune system. Moreover, long term exercise and/or high-intensity training in young swimmers exhibits greater leukocyte transcriptional changes in some genes which are related to mitochondrial energetics and protein production, as well as downregulating genes that are involved in inflammation [38]. The effects of exercise on immune functions in cancer patients involves the changes of NK cells, neutrophils, T cells, monocytes and cytokines. However, more research studies in

immunological biomarkers responding to exercise are required [36].

6. Epidemiological studies linking exercise with the incidence of breast cancer

Physical activity in adulthood tends to reduce the risk of breast cancer. In a systematic review and meta-analysis study associating physical activity to chronic disease outcomes between 1980-2016, noted that there was a strong correlation between those who achieved total physical activity several times higher than the recommended minimum to the risk of 5 chronic diseases including, breast cancer; the other chronic diseases being colon cancer, diabetes, ischemic heart disease and ischemic stroke events. Thirty five prospective cohort studies (involving 50,949,108 cases of breast cancer) reported 14 % reduction in the risk of breast cancer for those in the highly active category (over 8,000 metabolic equivalent (MET) minutes/week) with relative risk of 0.863 [39]. Exercise appears to reduce the risks of breast cancer through a number of mechanisms including, reducing body fat which in turn reduces estrogen and insulin concentrations. Indeed, these biological substances have mitogenic effects on mammary cells [6]. Likewise, leptin released from adipose tissue which is associated to post-menopausal breast cancer, significantly decreases following aerobic activity [6]. Furthermore, exercise may have positive effects in reducing the incidence of breast cancer, by improving the immune system. Indeed, exercise has been shown to increase circulatory NK cells by 5-fold which play a key role in the defense against pathogens and cancer immune-surveillance [36]. Moreover, there is evidence to suggest that physical activity during adolescence or young adulthood may lower the risk of pre-menopausal and post-menopausal breast cancer [40]. Overall, the decreased risk of breast cancer associated with physical activity differs according to age; 16 % for adolescence, 8 % for early adulthood, 15 % for middle adulthood and 17 % for over the age of 50 [41]. Importantly, breast cancer prevention efforts must start from the early stages of a woman's life [16].

A prospective cohort study in 78,733 women conducted between 1997-2011 [42], assessed the degree of physical activity during adolescent and adult life. It was noted that moderate physical activity in women aged 14-22 reduced the risk of pre-menopausal breast cancer considerably. High intensity physical activity in these young women (over 4,320 MET minutes/week) showed a modest correlation with breast cancer risk reduction. The association is likely stronger in breast cancer patients with estrogen receptor negative tumors and in younger pre-menopausal women. However, there was no correlation between physical activity in early life to the risk of developing post-menopausal breast cancer [42]. The likely mechanism involved in reduced breast cancer risk for an adolescent who regularly performs exercise could

be due to delayed onset in menarche and/or reduced menstrual cycles, shortening reproductive hormone exposure [43].

6.1. Exercise as an adjuvant therapy following breast cancer diagnosis

Physical activity, especially moderate intensity aerobic exercise for females following breast cancer diagnosis, has been noted in a number of studies to be advantageous in regards to breast cancer outcomes (decreased mortality rate by >30 % [4] and decreased recurrence rates). As a result of exercise, total body fat reduces as well as a number of inflammatory biomarkers which could contribute to better outcomes in patients with breast cancer [47]. Likewise, in a cohort-longitudinal study, it was clear that fast walking (3 hours/week) prior to and following breast cancer diagnosis in postmenopausal women reduced the mortality rate by 40 % [44]. In addition, an aerobic exercise regime prescribed to women with breast cancer during early treatment in the Netherlands between 2010-2013, reduced fatigue and increased overall fitness [1]. Furthermore, sleeping disturbance, mood disturbance and anxiety declined following a 12 week aerobic exercise program in Thai women undergoing adjuvant chemotherapy [45]. Most importantly, reports in previous systematic reviews, suggested that aerobic exercise with moderate-high intensity (50-85 % of maximal heart rate), 3 times/week ranging between 8-24 weeks to be the most frequent mode for breast cancer patients and survivors as this program may also have a positive effect on the cardiovascular, muscular and neurological systems. As a consequence this can lead to improvements in quality of life, such as the ability to deal with daily tasks [46]. Improvements in clinical outcomes in breast cancer patients following different exercise regimes are shown in Table 1. Although the American College of Sports Medicine has identified safety and benefits of exercise programs to breast cancer outcomes, there are a limited number of randomized controlled trials that have assessed the positive effects of exercise to breast cancer outcomes. Hence, the need for clarity on the mechanisms that may be related to exercise and cancer prognosis [47].

Table 1. The effects of different exercise regimes on breast cancer clinical outcomes

Types of exercise	Effects on clinical outcome	Reference
Regular exercise, occupational and leisure activities	- Reduce cancer-specific and all-cause mortality (Hazard ratio in survival rate)	[47]
Fast walking (3 hours/week) before and after diagnosis	- Exercise before diagnosis can lower all-cause mortality by 39% - Exercise after diagnosis can reduce all-cause mortality by 46% and reduce breast cancer-specific mortality by 39%	[44]
Moderate to high intensity aerobic exercise (50-85% of maximal heart rate) for 3 time/week and range between 8-24 weeks	- Improved quality of life, ability to deal with daily tasks	[46]
Two aerobic and strength sessions per week; 60 minutes per session including 5 min-warming-up, 25 min-progressive aerobic exercise, 25-min weight training and 5 min-cool down, for 18 weeks (start early after diagnosis)	- Lower physical and mental fatigue - Increase leg muscles strength	[1]
Self-directed exercise (during treatment period) : 12-week progressive aerobic exercise (low to moderate intensity	- Decline sleeping disturbance - Improved emotional status - Reduced symptoms of distress	[45]

walking; at least 20 min each day)

6.2. Effect of aerobic training on obesity-related cancer risk biomarkers in breast cancer

Obesity is an important contributing factor to the generation of low grade chronic inflammation leading to chronic conditions, including metabolic diseases, immune dysfunction and cancer; as a result of improper fat metabolism [22]. This condition however, can increase the recurrence and mortality rates of breast cancer survivors [48]. Adipose tissue produces high levels of pro-infammatory cytokines (IL-1, IL-6, TNF-alpha) and monocyte chemo attractant protein, which are known to be associated with insulin resistance [49]; an adverse effect well known for mammary cell proliferation [5]. However, further randomized clinical trials are required in order to ascertain appropriate exercise regimes on adiposity that may influence breast cancer survival [47].

In a systematic review it was clear that alterations in adiposity related biomarkers as a result of physical activity, are likely to lower the risk of postmenopausal breast cancer; adiposity biomarkers included, body mass index (BMI), leptin, adiponectin, sex hormone binding globulin (SHBG), estrogen, androgen, insulin resistance, IL-6, TNF-alpha and C-reactive protein (CRP) [5]. In addition, long term exercise has been shown to decrease estradiol levels and increase SHBG in postmenopausal women who reduced more that 0.5 % of body fat [50]; in fact, those who did not lose body fat showed increase levels of estrogen [50]. In addition, exercise reduces testosterone levels by decreasing adiposity or by increasing SHBG [51], as well as improving insulin sensitivity, reduces adipokines and CRP which directly influence the risk of breast cancer [5].

Furthermore, in a 10-year prospective cohort study involving 603 breast cancer patients [52] showed that levels of insulin to be strongly associated with C-peptide levels which leads to higher mortality rate for breast cancer in post-menopausal women. Insulin levels are also associated with waist-hip ratio and BMI, and negatively correlates with SHBG levels. However, there is no relation between leisure-time physical activity and mortality rate [52]. A pragmatic lifestyle for breast cancer survivors in the early stages of breast cancer with obesity

(BMI $\geq$25 kg/m^2) including 3 weekly supervised sessions of moderate-intensity (65-85% estimated VO_2max) aerobic exercise and hypocaloric eating program through randomized clinical trial has shown a reduction in body weight, waist-hip ratio and resting diastolic blood pressure after 6-months of intervention [53]. As a consequence, decrease in leptin levels and decreased total cholesterol levels were also noted. In addition, decreased body weight is associated with reduction in CRP. Change in waist circumference is also positively correlated with a change in CRP. These biological markers are likely to have a positive outcome to the mortality and overall health outcomes to patients with breast cancer [53]. In a 6-month counselling program (face to face and telephone) for breast cancer patients with obesity, a recommended daily caloric intake of 1,200-2,000 kcal combined with a home-based physical activity program (150 mins/week of moderate intensity) significantly reduced body weight and waist-hip circumference compared to patients who received only usual care [54]. Those patients who lost > 5% of body weight also showed decreased levels of leptin, insulin, IL-6 and CRP [54]. These biomarkers are hypothesized to facilitate the risk and mortality of breast cancer [55]. Moreover, a 12-month weight training regime has been reported to be a safe exercise program to breast cancer survivors resulting in decreased body weight, percent body fat and insulin growth factor levels [56]. However, further randomized trials are required to assess the benefits of reducing weight in obese breast cancer survivors to prevent breast cancer recurrence. Weight management strategies especially the optimal exercise program and diet control are required to understand the mechanisms which are beneficial for survival outcomes [57].

6.3. Effect of exercise on the immune biomarkers in breast cancer

Aerobic exercise activity has been shown to improve immunological biomarkers in breast cancer patients, although there are no reports showing improvement in inflammation and immunological markers in breast cancer patients during chemotherapy or radiation treatment [58]. In fact, chemotherapy used to treat breast cancer decreases the number of B and T cells suppressing overall the immune system [59]. In a 6 month moderate aerobic exercise regime in breast cancer patients after completion of chemotherapy improves T cell recovery by increasing the percentage of CD4+ CD69+ T cells. In addition, in a randomized controlled trial, a 15 week moderate-high intensity exercise regime (70-75 % VO_2max) in postmenopausal breast cancer patients, increased the cytotoxic activity of NK cells which should be beneficial to overall survival [8]. A previous study noted that the cytotoxic activity of NK cells to be

significantly higher in tumor-free survivors compared to those who had tumor-related mortality [60]. Interestingly, vasoactive intestinal peptide (VIP), an autocrine growth factor regulating cell proliferation, survival and differentiation in human breast cancer cells is blocked by the generation of natural anti-VIP antibodies stimulated by regular exercise. As a consequence, exercise programs may be important to prevent breast cancer recurrence [61].

Furthermore, twelve-week aerobic exercise training (home-based exercise) in breast cancer survivors reduces pro-inflammatory cytokines ie. IL-8 and epithelial neutrophil activating protein levels (angiogenesis and apoptosis related markers). This suggests that aerobic exercise program is likely related to angiogenesis and apoptosis which may be beneficital to cancer prognosis [62]. A single bout of strenous exercise such as, a half marathon illustrates the similarity of immune recovery between breast cancer survivors and healthy group [63]. The effects of this acute exhaustive endurance exercise on immune response such as the proportion of overall immune cells, T-cell subsets and pro-inflammatory cytokine levels are not different between the survivors and healthy subjects. However, the survivors show significantly lower baseline levels of monocytes, T helper cells, and naive T-cell populations, whereas cytotoxic and memory T-cells are higher than the control group [63]. The reduction in baseline overall immune cells of the experimental subjects can be explained by the previous bone marrow suppressive treatments such as chemotherapy and radiation [63]. However, it can be hypothesized that the survivors of breast cancer after treatment and healthy subjects have the same recovery behavior and immune response after a single bout of endurance exercise [63]. Immune biomarkers in breast cancer can also be improved by resistance training. In fact, a16 week-machine based weight training exercise in 20 breast cancer survivors resulted in lower levels of TNF-alpha indicating that resistance training is likely to be advantageous in promoting an anti-inflammatory profile amongst breast cancer survivors [64]. The influence of various types of exercise training on biomarkers and physical changes are shown in Figure 1.

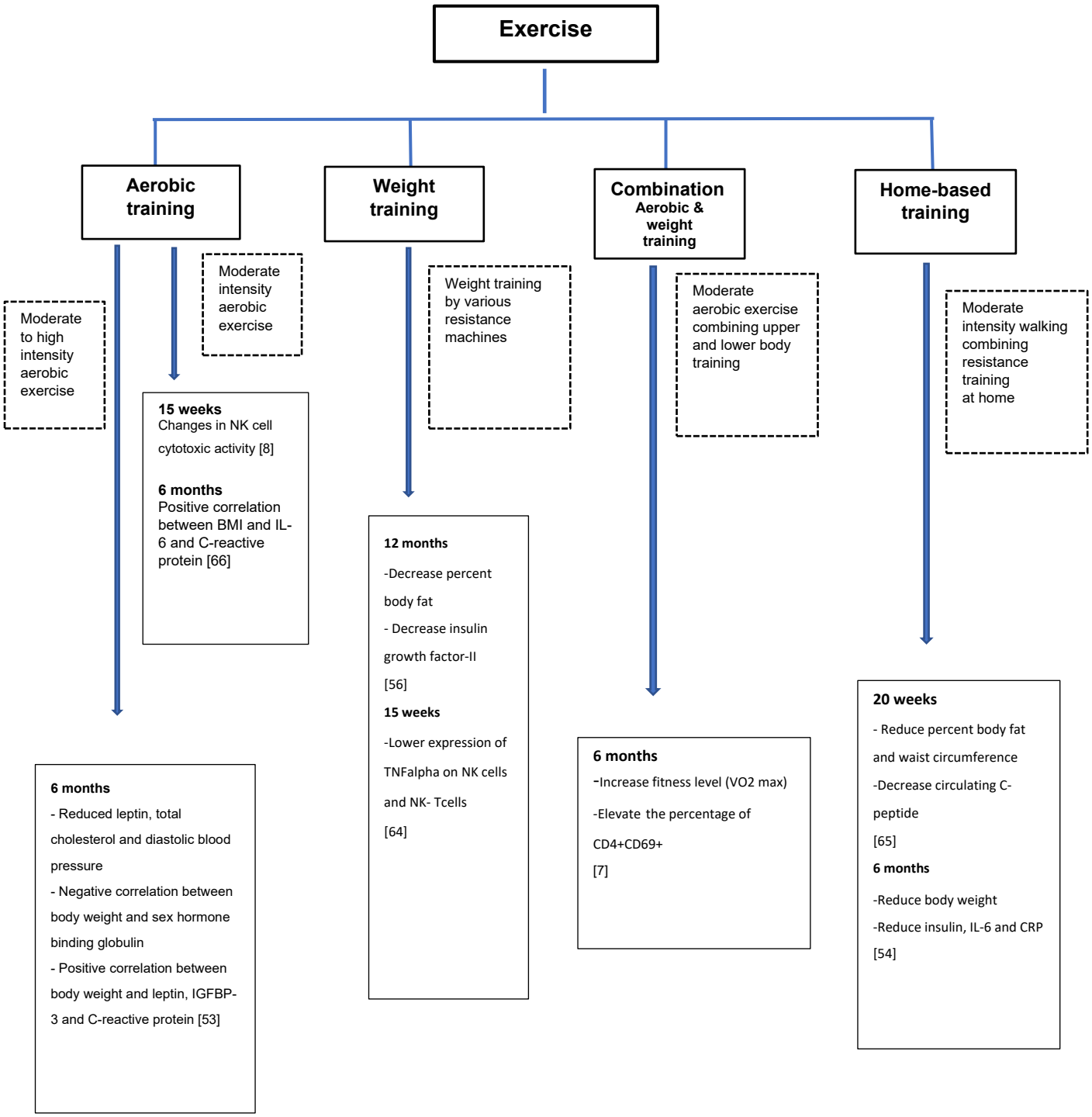

Figure 1. The influence of exercise on immune biomarkers and physical change in breast cancer patients

7. Conclusion and future prospects

Breast cancer affects women's well-being. The incidence rate tends to increase year by year, whereas mortality is likely to decrease worldwide. The possible risk factors of breast cancer are age, lifestyle, reproductive history, use of hormonal therapy and genetic mutations. Obese women are predisposed to developing breast cancer as a result of chronic pro-inflammatory milieu and hypoxic conditions of breast tissue. Furthermore, weight gain after diagnosis has been evident to increase mortality rate of breast cancer. Some biomarkers associated with adiposity and immune responses are used to correlate breast cancer prognosis. Biochemical substances related to fat metabolism such as insulin, adipokines and estrogen can precipitate mammary cell proliferation and cancer progression. Additionally, the alteration of immune functions both overreaction and suppression can be accepted predictors of breast cancer risks and breast cancer outcome. Exercise programs such as aerobic and weigh training have been reported to benefit breast cancer survival through adiposity and immune response. Several studies suggest that exercise can significantly reduce the mortality rate and improve the quality of life of breast cancer patients; as a consequence, exercise and physical activities have been recommended as an adjuvant therapy for breast cancer survivors.

Although numerous research studies support a significant role of exercise on immune function in cancer patients and some randomized clinical trials argue that an exercise program which reduces body fat can diminish breast cancer death rate, further mechanisms related to adiposity and immune responses to cancer outcomes still need to be determined. More specifically, studies of an appropriate exercise program for breast cancer survivors are needed with more clear comprehensive analysis of the adiposity and immune biomarker changes which are anticipated for positive health outcomes.

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Review paper manuscript - 2

1b. Physical activity and breast cancer survivors: Importance of adherence, motivational interviewing and psychological health

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ABSTRACT

Physical activity programs based on behavioural change theories have been implemented for physical activity motivation and adherence in breast cancer survivors. Most of the programs can improve psychological health-related quality of life. Depressive and anxious symptoms in their life seem to be associated with some stressors such as, their perception towards breast cancer, prognosis, long-term treatment related side effects and fear of cancer recurrence. Beyond physical fitness, several physical activity programs for breast cancer survivors have been reported to improve psychosocial wellness and life satisfaction. However, many physical activity programs have failed to motivate breast cancer survivors engaging in the program due to barriers including general health issues, and lack of time. More specifically, women may have low confidence towards the benefits of physical activity on breast cancer outcomes. Therefore, the strategy for physical activity engagement in breast cancer survivors is challenging for health care professionals. The review aims to identify cancer-related mental distress, coping style and behavioural theories applied to physical activity programs in breast cancer survivors. More specifically, we discuss the effectiveness and limitation of 3 psychological theories and 2 concepts related to behavioural change including the theory of planned behaviour, social cognitive theory, self-determination theory, transtheoretical model and motivational interviewing for physical activity adherence in breast cancer survivors.

Keywords: Breast cancer survivors, Physical activity adherence, Psychological health, Theory related behavioural change, Motivational interviewing

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Physical activity and breast cancer survivors: Importance of adherence, motivational interviewing and psychological health

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ABSTRACT

Behavioral change theories have been used to support interventions that increase both motivation for and adherence to physical activity programs for breast cancer survivors. Most of the programs can improve psychological health-related quality of life. Depressive and anxious symptoms seem to be associated with some stressors, such as the perception of breast cancer, prognosis, long-term treatment-related side-effects and fear of cancer recurrence. Beyond physical fitness, several physical activity programs for breast cancer survivors have been reported to improve psychosocial wellness and life satisfaction. However, many physical activity programs have failed to motivate breast cancer survivors due to barriers such as general health issues and lack of time. More specifically, women may have little confidence in the benefits of physical activity and breast cancer outcomes. Therefore, engaging breast cancer survivors in physical activity is challenging for health care professionals. Herein, we identify cancer-related mental distress, coping style and behavioral theories applied to physical activity programs in breast cancer survivors. More specifically, we discuss the effectiveness and limitations of 3 psychological theories and 2 concepts related to behavioral change, including the theory of planned behavior, social cognitive theory, self-determination theory, transtheoretical model and motivational interviewing for physical activity adherence in breast cancer survivors.

1. Introduction

Psychosocial distress in patients with different types of cancer and needs of supportive care are likely to depend on the stage of cancer [1]. Many women at diagnosis and early treatment phase of breast cancer are stressed due to physical, mental, working, social and sexual problems. Breast cancer survivors, on the other hand, are more likely concerned about the risk of cancer recurrence and mortality [1]. Exercise programs have also been shown to enhance mental health-related quality of life (QoL) amongst breast cancer survivors who have completed cancer therapy [2,3]. However, some breast cancer survivors have low confidence and understanding towards the benefits of exercise to their cancer outcomes following treatments [4,5]. A number of psychological theories and techniques related to motivation have been used to understand and enhance exercise uptake and adherence in the population in general and cancer survivors in particular [6]. For example, motivational interviewing (MI) has been shown to be an effective technique used to decrease resistance against behavioral change in general cancer survivors by facilitating decision making [6]. So far, studies promoting physical activity behavior in breast cancer survivors have been of high interest in the cancer field due to their good prognosis and outcomes [7]. Herein, we aim to identify the psychological struggles of breast cancer survivors coping with their illness-related stress and physical activity programs applied to enhance mental health-related QoL. We discuss the efficacy of 3 psychological theories and 1 model related to behavioral change, as well as the concept of MI which have been effectively utilized to enhance physical activity adoption and adherence in breast cancer survivors.

2. Methodology

This review presents studies on mental health in breast cancer survivors and the effectiveness of physical activity programs using psychological change theories on adherence to the program. Searches

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1. Introduction

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2. Methodology

This review expresses the previous studies on mental health in breast cancer survivors and the effectiveness of physical activity program using psychological change theories on their adherence to the program which published between 2007 and 2018 in Medline and PubMed. The key terms of this review are breast cancer survivor AND psychological health OR mental health, breast cancer survivor AND physical activity OR exercise, breast cancer survivor AND physical activity adherence OR exercise adherence.

3. Psychological health in breast cancer survivors

During the transition from active treatment to follow-up care or survivorship, breast cancer survivors, in this respect, may experience mental suffering such as fear, depression and anxiety towards their cancer prognosis, body image disturbance, sexual dysfunction, work and family life problems [1]. These issues may influence their coping ability and QoL [8]. Younger breast cancer survivors experiencing menopausal symptoms have been reported for more mood disturbance than older ones due to vasomotor effects (night sweating and hot flash) [9] and urogenital symptoms (vaginal dryness and decreased libido) after chemotherapy and radiation [10]. These adverse symptoms including altered body image are likely to impact their intimate relationship with partner [10]. Thirty percent of breast cancer survivors have reported the feelings of abandonment because of transitions in their care (from curative to supportive treatment) [11].

The current review of breast cancer survivors asserts that acute and long-term stressors after diagnosis are related to physical symptoms, side effects of treatment (e.g., tiredness, nausea, pain, sexual problem) and spousal relationship disturbance [12]. The degree of stress in breast cancer survivors is likely associated with mental well-being and may result in changes to social roles and uncertainty of their future [13]. For breast cancer, more than 30% of survivors has experienced mental distress especially depression and anxiety around one year before diagnosis. Furthermore, the incidence of mental disorders involving stress and mood disturbance in this population reached a peak within a month post-diagnostic period [14].

3.1. Factors affecting psychological distress and coping in breast cancer survivors

Generally, psychological health of cancer survivors is highly associated with age, gender, education, marital status and type of cancer [15]. Psychological disturbance such as anxiety, depression, poorer spirituality and less sexual satisfaction in breast cancer survivors have been greatly affected by their age [16]. The research focusing on breast cancer survivors urges that around 50% of survivors aged less than 50 may manifest depressive symptoms [17]. Younger breast cancer survivors possibly have more mood distress and worse psychological adjustment than older survivors which may be due to reproductive disturbances [18] and impaired sexual partnership [10]. Fear of disease recurrence in breast cancer survivors may be positively correlated to their anxious personality but longer period after treatment and radiation therapy may lower this unpleasant feeling [19].

The coping styles have been categorized into positive and negative adjustment [21]. Adaptive psychological coping is characterized by fighting spirit (e.g., seeking social support and information) and may lead to reduction of recurrence and extension of survival time amongst breast cancer survivors [22]. Fatalism (having passive acceptance of a problem) or helplessness and hopelessness (being overwhelmed by a problem) used by breast cancer survivors probably increases relative risks of death [22].Some females who are breast cancer survivors express that even though they courageously fight with cancer, they feel stressed [23]. However, support from their family is a crucial factor to help them passing through the cancer journey [23]. Many breast cancer survivors have been reported using avoidance coping because they may have social constraint problems especially with their loved one [24]. Difficulty in expression of their breast cancer issues-related feeling, in turn, make worse their mental condition such as greater stress, depression and anxiety [24]. Dealing with breast cancer not only affects the survivors but also their spouse or partner. For example, they may express the concerns-related cancer problems together and collaborate in problem solving [25, 26]. Psychological response to breast cancer and attitude towards coping of individual survivors needs to be identified by health care professionals for mental health promotion improving QoL and survival [22].

4. Exercise adherence in breast cancer survivors

Motivating cancer survivors to exercise is, however, still challenging because there are some strong exercise barriers hindering adoption and adherence to cancer rehabilitation programs [27]. Some of these barriers in women with breast cancer include low confidence in the benefits of exercise to minimize long-term breast cancer and treatment effects [4]. One study found that 32 % of breast cancer survivors quit exercise at 12 months' follow-up. Some of the reasons reported are a lack of exercise prior to diagnosis, less education, being postmenopausal as well as physical and psychological problems [28]. In addition, in older breast cancer survivors, shortage of time, and general health issues are common obstacles reported [29]. Furthermore, barriers to exercise amongst minority women groups (Hispanic and African) of breast cancer survivors in the USA included, tiredness, family responsibilities, physical problems, work, transportation, and negative attitude towards exercise [5]. Breast cancer survivors are likely to need additional motivation after finishing a prescribed exercise program which may enhance their exercise adherence following completion of the program [28]. It would be helpful to use

theoretical models of exercise behavior. These include the theory of planned behavior, social cognitive theory, self-determination theory and trans-theoretical model [6]. Implementation of exercise programs based on these theories have shown some benefits to adherence. Additionally, motivational interviewing (MI) has been shown to be an effective approach to support behavioral change, and to motivate cancer survivors to continue an exercise program [30]

4.1. Theories and other approaches related to behavioural change for physical activity in breast cancer survivors

The evaluation of theories used has been done for effectiveness and extensiveness in physical activity program analysis in breast cancer survivors after treatments [31]. However, many studies are less likely to completely explore the critical determinants of program effectiveness such as factors influencing behavior of breast cancer survivors regarding behavioural change model application [31]. In order to develop such programs for breast cancer survivors we would suggest the researcher make use of Intervention Mapping (IM) [32, 33]. IM is a framework which assists researchers in developing intervention programs based on the best theories for certain populations and also includes a suitable evaluation framework [32].

Existing theories like Theory of Planned Behavior (TPB) [34], Social Cognitive Theory (SCT) [35], Self-Determination Theory (SDT) [36] and the Transtheoretical Model (TTM) [35] have been used to guide physical activity intervention in breast cancer survivors. In particular TTM and SCT have been used extensively between 2005-2013 [31]. In addition to these theoretical frameworks intervention programs have made use of strategies like self-monitoring, social support, problem solving and participative goal-setting to enhance the uptake and adherence [31]. Finally, studies have examined the efficacy of alternative supervisory models like email and phone counselling on program effectiveness [31]. Below we outline some of the theories which have been used to enhance the motivation of breast cancer survivors to engage and adhere to physical activity programs and discuss their effectiveness and limitations.

4.1.1. The theory of planned behavior (TPB)

TPB suggest that the intention to perform a behavior is anticipated by attitude, subjective norm and perceived control [37]. Attitude represents the behavioural performance evaluation of an individual; subjective norm is the perceived belief regarding the rules of behavior, and

perceived control is the belief of an individual in management of the behavior [6]. Previous studies using TPB have indicated that intention to exercise and perceived control are the major determinants of exercise engagement in a variety of groups of cancer patients especially amongst breast cancer survivors [6]. The other factors such as support from an important person and confidence are likely to enable them to sustain exercise [6]. However, a previous meta-analysis appraised the weakening of association between intention, attitude and physical activity behavior when it involved genuine barriers such as an individual past behavior [38]. For example previous habits can lessen the effect of attitude on exercise intention in a similar vein as intention on exercise behavior [38]. Using TPB for physical activity promotion studies have reported varying degree of intention and physical activity behavior and the variation is probably affected by percieved self-efficacy [38]. Additionally, not all studies have been supportive of TPB in enhancing exercise behavior. One study, for example, found only a weak association between intention, planning and exercise implementation at 12 weeks in breast cancer survivors [34]. As such, other theories need to be considered when considering development of intervention programs to promote uptake and adherence to exercise and physical activity programs in women during the different stages of breast cancer.

4.1.2. Social cognitive theory (SCT)

SCT is based on the reciprocal influence of human behavior, its environment and personal factors such as physical characteristics, emotions and social support [6]. One of the main factors of SCT is the concept of self-efficacy [39]. Research has demonstrated that self-efficacy believes are a determinant of exercise behavior [39].

In addition, professionals should focus on a participants' improvement and use positive reinforcement [6]. A physical activity promotion program providing information about self-efficacy and social supports through weekly phone call and newsletters for Hispanic breast cancer survivors showed increased levels of exercise self-efficacy believes which were related to physical activity intensity [40]. A SCT-based physical activity project has also been successfully conducted for breast cancer survivors (improved physical fitness and social well-being) using both supervision and self-monitoring strategies (activity recorded by accelerometer) [41, 42]. Although a 3 months intervention program can improve self-efficacy and reduce perceived barriers to physical activity, there is no interrelationship amongst exercise intensity level and the determinants of theory constructs (e.g., self-efficacy, outcome expectation, perceived barriers and goal setting) [42]. Likewise, other SCT-based study has

suggested that there is no effect of task self-efficacy, social support and role models on physical activity behavior in breast cancer survivors [43]. Therefore, future studies, in particular through qualitative process evaluations, should explore how SCT can enhance physical activity behavior and to explore the role of the underlying mechanisms to increase uptake and adherence in cancer patients [42].

4.1.3. Self-determination theory (SDT)

SDT is based on the premise that the motivation of an individual to engage in behavior is based on the satisfaction of their basic human needs of competence, relatedness and autonomy [36]. Motivation to engage in any behavior is based on a continuum, from extrinsic to intrinsic motivation [6]. When individuals engage in exercise behavior for extrinsic reasons it means they do this because of external demands (e.g., health professional told them so) and/or rewards [36]. Intrinsically motivated behavior, on the other hand, is executed because it is enjoyable, pleasurable or of interest to the individual [36] . From an SDT perspective interventions should try to engage individuals in exercise because of intrinsic reasons. Hence, intrinsically motivated behavior is more likely to become habitual and maintained over time [36].

A study using SDT found that breast cancer survivors who meet physical activity recommendations have higher scores of autonomous regulation and intrinsic motivation than those who are not reaching physical activity guideline [36]. Also, there appears to be close associations between motivational orientation (intrinsic vs. extrinsic) and levels of social support. Greater levels of social support resulting in enhanced levels of intrinsic motivation in breast cancer survivors are needed [48]. As such, it would be recommended to increase social support for exercise behaviour in future interventions.

4.1.4. Transtheoretical model (TTM)

The Transtheoretical model of behavioural change suggests that a person is likely to move through 6 phases of motivational willingness to change health behaviours. These phases have been labelled: pre-contemplation, contemplation, preparation, action, maintenance, and termination [6]. However, the 6 stages of behavioural change are dynamic and can be both stable and variable or relapsing [44].

Based on the stage individuals find themselves in, intervention can be developed to either move from one stage to the next (e.g., from no intention to willingness; plan for making start

to action; sustaining the behaviour to stop changing behavior). Hence, it is likely that the stage an individual is in will influence the efficacy of different intervention theories and strategies [6]. Participants should receive appropriate guidance on exercise programs for their decision making depending on the stage they are in [44].TTM integrated into physical activity program for breast cancer survivors has been successful in lowering the negative attitude towards physical activity and increasing self-efficacy [45]. The intervention program provided lectures and discussions about behavioural change and used self-monitoring as a strategy for physical activity motivation [45]. The result suggests that the breast cancer survivors in the intervention group transitioned to a more advanced stage of change than the survivors in the usual care group (action and maintenance vs preparation and action) [45]. Stage of changing progression was also positively related to the level of self-efficacy [45]. However, this study was unable to find the association between perceived negative impact of exercise and stage of behavior transition [45].

4.1.5. Other approaches and motivational interviewing (MI)

A number of additional approaches have been successful in promoting physical activity and exercise behavior in breast cancer survivors. These include the introduction of social support and interpersonal interactions as well as participative approaches [32]. Physical activity intervention programs for breast cancer survivors have included supervised center based, community, and home based programs [46, 47]. However, alternative delivery formats, including email and phone counselling have also been shown to be effective [31]. Finally, self-monitoring devices like pedometers and accelerometer have been introduced effectively to promote adherence [48, 49].

In addition, motivational interviewing has been used successfully in physical activity interventions across multiple groups of patient and non-patient populations. Motivational interviewing (MI), a client-centered approach, has been shown to be an effective techniques to instigate health behavioral change [6]. Although there is no clear theoretical framework for the insight of MI process, the same assumption between MI and SDT is the belief of human's innate ability for individual development through psychological aspects [50]. An intervention which used nurses to use MI to motivate breast cancer survivors to engage in regular exercise to prevent lymphedema showed significant improvements in the survivors ability to self-care [51]. Additionally, MI can paralleled worked with TTM for the stage of behavioral change [50].

The study of intervention adoption for exercise adherence such as MI with behavioral change-related theory can be worthy for cancer survivors' active lifestyle sustainability [6], especially as it has been mostly conducted in breast cancer patients and survivors for healthy life style and physical activity improvement [52]. Physical activity programs using psychological theory-based behavioral change techniques for physical activity adherence in cancer survivors are presented in Table 1.

Table 1. Psychological theory-based physical activity program and adherence in cancer survivors.

Theory and intervention technique used	**Theory-based program scrutiny**		**Research study**	**Participants and Cancer type**	**Exercise adherence**	**Ref.**
	Determinants	**Process relation**				
Social cognitive theory (SCT) Cognitive behavioral technique Exercise therapy sessions (Consciously decisional making, goal setting and increasing self-regulation)	Self-regulation Goal setting	Intervention technique	Randomized controlled trial: 8 weeks aerobic exercise; 30 minutes moderate intensity: 3 sessions per week	Breast cancer survivors aged 18-65, completed initial treatment (after 12-36 months)	70-80% exercise adherence of participants completing target program (≥ 70 % of program prescription)	[56]
Theory of planned behavior	**TPB :** Intention, behavioral	Intervention technique	Randomized controlled trial: 12 weeks	African American breast	70% exercise adherence	[30]

(TPB), social cognitive theory (SCT) and **motivational interviewing (MI)** Group education session Phone IM session; every two weeks (Personal implementation plan, family involvement and increasing self-efficacy)	attitude, subjective and cultural norm **SCT :** Perceive control Self-efficacy Role model Barrier to exercise	Intervention technique Evaluation (perceived control)	multimodal activity (30 minutes for supervised exercise and 60 minutes for health education every two weeks; individual telephone coaching every other week)	cancer survivors aged 54.7 on average, 6 months to 5 years post initial treatments	of participants completing target program	
Transtheoretical model (TTM) and **Social cognitive theory (SCT)** (Telephone, email, in-person visits and support groups)	Exercise stage of change Exercise self-efficacy	Evaluation (stage of change and self-efficacy)	Cross sectional study	Breast cancer (aged 56.8) and prostate cancer (aged 66.6) survivors	Stage of change and self-efficacy is independent associated with exercise activity and diet program adherence	[57]

Social cognitive theory (SCT) (15 telephone counselling sessions)	Social support	Intervention technique	Randomized controlled trial: a yearlong self-monitoring program (exercise and diet control)	Mixed cancer survivors (breast, prostate and colorectal cancer); aged >65; post diagnosed > 5 years	Telephone attendance correlates with exercise adherence and health related outcomes	[58]
Motivational Interviewing (MI) based on transtheorethical theory and SCT (3 months counselling and weekly telephone calls for 12 weeks	Motivational readiness Self-report Self-monitoring Self-efficacy	Intervention technique (Outcome expectation and increase self-efficacy) Evaluation (Stage of change, motivational readiness)	Randomized controlled trial; 12 weeks home-based exercise program	Colorectal cancer survivors aged 57.3 on average	64.7%, 38.9% and 31.6% exercise adherence of participants completing target program at 3, 6 and 12 months, respectively (higher than control group) Physical activity outcome is strongly associated with	[59]

					motivational readiness	
Theory of planned behavior (TPB) Print materials (exercise guidelines) and step count pedometer	Intention to exercise Attitude Subjective norm Perceived behavioral control	Intervention technique Evaluation	Randomized controlled trial; 12 weeks moderate to vigorous PA	Breast cancer survivors aged 58 on average	93% retention at 4 weeks 90% retention at 12 weeks Intervention group can increase intention to exercise	[34]
Social cognitive theory (SCT) Culturally home-based exercise (pedometer and exercise guidebook)	Exercise self-efficacy Social support	Intervention technique (social support and self-monitoring) Evaluation (self-efficacy)	16 weeks randomised controlled trials	Hispanic American breast cancer survivors aged 58.5 on average	Increase PA time and self-efficacy Social support is associated with vigorous exercise time	[40]
Social cognitive theory (SCT) Behavioral change theory based exercise program (12	Self-efficacy Outcome expectation Goal-setting Perceived barrier	Intervention technique (self-efficacy and goal setting) Evaluation	3 months randomised controlled trials	Breast cancer survivors	98% adherence for exercise session, increase self-efficacy and goal, reduce	[42]

supervised sessions; 6 group discussion sessions; face to face couselling) Accelerometer for self-monitoring		(self-efficacy, outcome expectation, goal setting, perceived barriers)			perceived barrier through 3 months No relationship amongst the determinants of SCT	
Self-determination theory (SDT) Supervised combined exercise program 3 times a week and 1 hour per time (centered base) Phone call every three weeks Self-report assessment	Autonomy Competence Relatedness Motivational continuum Self-regulation Self-directed exercise behavior	Intervention technique (Self-directed, Self-report) Evaluation (Behavioral regulation for exercise)	12 weeks randomised controlled cross over trials	Breast cancer survivors aged 55.1 on average	61% exercise adherence rate; Self-determines regulation, Autonomy, Competence, and Relatedness increase through exercise program	[46]
Transtheorethical model (TTM) Group based program for	Self-efficacy Stage of change	Intervention technique (Self-efficacy, cognitive	6 months randomised controlled trials	Breast cancer survivors aged 55.7 on average	Increase self-efficacy and greater stage progression	[45]

self-efficacy, cognitive and behavioral strategies for physical activity Print materials (booklets) Behavioral change methods beased on the steps in TTM Self-monitoring for PA (Self-record or pedometer)	Decisional balance	and behavioral strategies) Evaluation (Stage of change)			in intervention group over the program Self-efficacy is associated with stages of change Perceived fewer cons in intervention group	
Motivational interviewing (MI) Counselling (1 time in-person and 2 times phone call)	Self-efficacy	Evaluation (Self-efficacy)	6 months randomised controlled trials	Breast cancer survivors 42 months after completed treatments	Increase exercise intensity (energy expenditure per week) and self-efficacy in intervention group	[54]

5. The use of MI in promoting physical activity adherence for breast cancer survivors

MI over 6 individual telephone calls (15 minutes every 2 weeks) has been reported to improve self-efficacy in a 12-week exercise participation and diet control amongst overweight African-American breast cancer survivors after active treatments. Indeed, this intervention showed adherence rates of up to 70 percent [30]. Additionally, a pilot study over 16 weeks of a home-based approach combining aerobic and weight training increased weekly exercise time, aerobic fitness and QoL when using MI through face-to-face and phone calls to encourage exercise adherence in breast cancer survivors [53]. Promoting self-efficacy and self-confidence are crucial determinants for program adherence [53]. Six months of an exercise program with MI (1 face-to face counselling and 2 phone calls) can increase weekly exercise intensity in long-term breast cancer survivors who have high self-efficacy beliefs regarding their exercise behavior [54]. In addition, MI can be effectively applied for exercise motivation in breast cancer patients during treatments. In fact, MI by telephone counseling for 12 months correlated with a positive outcome in encouraging patients with breast cancer to reduce their body weight through exercise and dietary control during chemotherapy [55]. Although it is not clear what the optimal practice of MI is, MI has been recognized as an effective tool to promote individual behavior change [52]. However, further studies are required to explore the best MI practice and related determinants for exercise adherence in breast cancer survivors [53].

6. Conclusion and Future Prospects

Regular exercise participation has significant benefits to cancer survivors. As such, it is important to develop programs and use strategies to help these individuals to initiate and adhere to exercise or physical activity programs. A number of theories and process models can help with this including, TPB, SCT, SDT and TTM. MI seems to be a proven strategy to enhance adherence. Researchers might use MI and the theories, models and strategies described for the development of efficacious exercise programs. When developing these programs it is also important to consider the specific barriers and issues faced by individuals with breast cancer and the stage they are in.

Approximately half of breast cancer survivors report psychological alterations including mood, spiritual and social distress. They experience fear, anxiety and depression with regard to their long-term cancer diagnosis, prognosis, adverse effects of treatment and fear of cancer

recurrence. In addition, breast cancer is likely to impact body image, physical and sexual functionality, socialization and intimacy with partners. These cancer-related stressors are strongly associated with illness perception; as a result, their attitude towards breast cancer may affect their coping style and adjustment. Breast cancer survivors with positive views of illness management seem to apply a proper coping style to deal with stress and lessen their cancer-related stress. For example, they use fighting spirit driving their motivation for healthy program engagement; as a result, their mental health-related QoL is better, especially receiving family and social support.

These theoretical frameworks and MI concepts applied in physical activity programs are likely to enhance key determinants of behavioural change such as perceived control, self-regulation and self-efficacy for physical activity engagement. However, there are some limitations in using these frameworks to explain the link between key determinants of each framework for behavioural changes in breast cancer survivors. Understanding the factors influencing breast cancer survivors, specifically psychological stress, is a crucial key to create a motivational strategy in the development of physical activity engagement. Even though psychological theories used for health promotion in breast cancer survivors are advantageous to change behavior, more research with clear determinants is required to understand the elements of physical activity sustainability and adherence.

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Review paper manuscript - 3

1c. Work it out: Exercise as an anti-cancer intervention

ABSTRACT

Exercise or physical activity can be regarded as either an intervention for cancer prevention or an intervention for health promotion in people living with cancer. Here we discuss the effects of exercise and physical activity in reducing cancer risk and the clinical benefits for cancer patients and survivors. It is acknowledged that exercise can reduce the incidence of breast, colon and endometrial cancer, however the efficacy in reducing the incidence of some other cancer types such as prostate, ovarian, lung, gastric and haematological, is limited due to time limitation in randomized controlled studies and inaccurate measurements in observational studies. In general, it has been shown that exercise can prevent cancer cell proliferation, reduce oxidative damage, improve fat metabolism, reduce chronic inflammation and enhance immune functions. Research studies exploring the benefits of exercise in patients with breast and colon cancer have shown improved physical health and quality of life and a prolonged survival period. Likewise, exercise also provides good clinical outcomes for those living with prostate, endometrial, lung, gastric and hematological malignancies, although further research regarding exercise type and biological pathways are required. On the other hand, exercise may generate some adverse effects such as increased blood pressure, headache, muscle pain, physical accidents, severe discomfort, and dizziness amongst patients with cancer and survivors, especially those who are older and overweight or having hematological pathology following primary treatment with chemotherapy and/or radiation. As the benefits on clinical outcomes greatly outweigh the adverse effects, exercise for health in cancer patients and survivors should be recommended. However, considering the significant high rate of non-compliance to exercise in this cohort of individuals, the implementation of motivational strategies is vital otherwise any outcome benefits can be lost.

Keywords: exercise, physical activity, cancer patients, survivors, health promotion, physical health, psychological health, quality of life, biological pathway, biomarkers, adverse effects, motivation, exercise adherence

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Supa Pudkasam	70%	Creating the topic and layout of manuscript, writing and making a table	[redacted]	24/2/21
Katherine Harkin	15%	Writing one section and making a table		1/3/21
Kathy Tangalakis	5%	Editing the manuscript		26-2-21
Jack Feehan	5%	Formating and creating a figure		28/02/21
Vasso Apostolopoulos	5%	Conceptualising topic, editing and revising the manuscript		25/02/21

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Chapter 2

Chapter 2

Systematic Review Protocol : The Methodology Section of Chapter 3 Systematic Review and Meta-analysis

Chapter preface:

This chapter presents the protocol for the systematic review presented in chapter 3 This protocol has been registered with PROSPERO and it is ready to be submitted for publication.

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Lily Stojanovska	5%	Advising systematic review protocol Editing the manuscript		25/02/21
Vasso Apostolopoulos	5%	Advising systematic review protocol, searching key terms editing, supervision		25/02/21

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MANUSCRIPT READY FOR SUBMISSION

Self-monitoring vs Motivational Interviewing: Motivation techniques in self-directed physical activity to improve adherence in breast cancer survivors: A protocol for a systematic review and meta-analysis

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Chapter 3

Chapter 3

Systematic Review and Meta-analysis

Chapter preface:

This chapter presents the result of the systematic review and meta-analysis. The data has been submitted for publication in Maturitas.

Chapter 3

Motivational strategies to improve physical activity adherence in breast cancer survivors: A systematic review and meta-analysis

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ABSTRACT

Two behavioral change-based strategies for promoting adherence to physical activity (PA) suggested to have the greatest potential are the pedometer and Motivational Interviewing (MI). However, there are no comparisons between these two strategies identifying which one is more effective for improving PA adherence. This systematic review and meta-analysis aimed to determine which PA motivation strategy is more effective for promoting adherence to self-directed PA in female breast cancer survivors. Studies implementing self-directed PA which used step tracker and/or MI for motivation in female breast cancer survivors were identified from the following databases: CENTRAL, PubMed, CINAHL, PsycINFO, and Sportdiscuss at two timepoints in September 2019 and June 2020. Sixteen randomized controlled trials (RCTs) were recruited for data extraction, whereas ten RCTs were included in meta-analysis. Meta-analysis was performed on pooled data to estimate the standardized mean difference and 95% confidence intervals of PA duration and step count. Analysis of the number of participants meeting PA recommendations was also performed. Subgroup analysis was performed for three motivational strategies (pedometer combined with counselling, print material or combining with motivational interviewing). Meta-analysis showed that pedometer combined with another intervention on behavioral change theory has a small effect on step count ($p = 0.03$) and a moderate effect on moderate-vigorous physical activity (MVPA) duration ($p = <0.0001$) compared to controls. Additionally, motivational strategies increase the number of participants who meet PA goal ($p = 0.005$). The findings of this review advocate for the use of step tracker combined with counselling, print material or MI based on behavioral change theory. This approach provided the most consistent positive effect on PA adherence in self-directed PA among breast cancer survivors. Future studies should specifically evaluate the

differences between PA adherence measurements in self-directed PA, to identify the best motivation strategy for improving patient adherence and health outcomes.

Systematic review registration: PROSPERO Registration number CRD42020148542

Keywords: Breast cancer survivors, physical activity, exercise, self-directed, behavioural change strategies, step count tracker, wearable technology, pedometer, accelerometer, motivational interviewing, adherence, compliance

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2. They take public responsibility for their part of the publication, except for the responsible author who accepts overall responsibility for the publication;

3. There are no other authors of the publication according to these criteria;
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Name(s) of Co-Author(s)	Contribution (%)	Nature of Contribution	Signature	Date
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Jack Feehan	10%	The second reviewer, help with meta-analysis and revising the manuscript		28/02/21
Jason Talevski	10%	Revising data extraction sheet Helping with meta-analysis		01/03/21
Kristina Vingrys	5%	Advising data extraction, advising risk of bias assessment, editing		02/03/21
Remco Polman	2%	Advising data analysis, editing the manuscript		26/02/21
Nanthaphan Chinlumprasert	2%	Editing the manuscript		01/03/21
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Motivational strategies to improve adherence to physical activity in breast cancer survivors: A systematic review and meta-analysis

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ABSTRACT

Two behavioral change-based strategies for promoting adherence to physical activity (PA) suggested to have the greatest potential are the pedometer and Motivational Interviewing (MI). However, there are no comparisons between these two strategies identifying which one is more effective for improving PA adherence. This systematic review and meta-analysis aimed to determine which PA motivation strategy is more effective for promoting adherence to self-directed PA in female breast cancer survivors. Studies implementing self-directed PA which used a step tracker and/or MI for motivation in female breast cancer survivors were identified from the following databases at two timepoints, September 2019 and June 2020: CENTRAL, PubMed, CINAHL, PsycINFO, and Sportdiscuss. Sixteen randomized controlled trials (RCTs) were selected for data extraction, whereas ten RCTs were included in meta-analysis. Meta-analysis was performed on pooled data to estimate the standardized mean differences in PA duration and step count, and 95% confidence intervals. The number of participants meeting PA recommendations was also analyzed. Subgroup analysis was performed for three motivational strategies (pedometer combined with counselling, with print material or with motivational interviewing). Meta-analysis showed that pedometer combined with another intervention has a small effect on step count ($p = 0.03$) and a moderate effect on duration of moderate-vigorous physical activity (MVPA) ($p = <0.0001$) compared to controls. Additionally, motivational strategies increase the number of participants who meet a PA goal ($p = 0.005$). The findings of this review endorse the use of a step tracker combined with counselling, print material or MI based on behavioral change theory. This approach provided the most consistent positive effect on adherence to self-directed PA among breast cancer survivors. Future studies should evaluate differences between measures of adherence to self-directed PA, to identify the best motivation strategy for improving patient adherence and health outcomes.

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Motivational strategies to improve physical activity adherence in breast cancer survivors: A systematic review and meta-analysis

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1. Introduction

Breast cancer was the leading cause of cancer morbidity and mortality in women across the world in 2018 with 2.1 million females diagnosed and 626,679 deaths [1]. In 2017, the disability-adjusted life-years (DALYs) was 17.7 million [2]. The significant health impacts of breast cancer make a strong argument to develop interventions which reduce the burden on both patients and healthcare systems. Breast cancer survivors are also vulnerable to significant mental distress [3]. There are a number of factors which can cause psychological stress, including their cancer related illness, fear of cancer recurrence, difficult work-life balance, lost feminine body image and dysfunctional intimate relationships with partner [4]. These psychological burdens can reduce coping with daily life issues and affect quality of life (QoL) [5].

A cohort study acknowledged that adherence to regular PA can improve mental health-related quality of life in breast cancer survivors [6]. PA adherence has been defined by an individual's behaviour in meeting exercise recommendations [7]. PA adherence is typically measured by two methods: determining total activity by ratio or percentage of exercise session attendance or physical measures such as step count, exercise duration and intensity [7]. It can be reported by threshold of exercise prescription (e.g., the percentage of participants who perform at least 50% of exercise sessions) [8] or as the percentage of participants meeting a level of exercise goal of duration and intensity [9, 10]. Some studies suggest that adherence can be measured by PA frequency (number of sessions), duration (mean minutes), and intensity (mean RPE) completed per week and report a weekly trend [11]. For the measurement of exercise volume, technology such as activity trackers are commonly used to record participants' exercise intensity and duration [12].

Adherence to PA or exercise programs is known to be associated with positive breast cancer outcomes such as enhancement of QoL, physical and mental health [13]. A year-long supervised home-based exercise program in breast cancer survivors reported that the exercise group adhered to 115 minutes and 119 minutes of aerobic exercise weekly on average at six and twelve months, respectively [10]. While only 33 % of the women met exercise recommendations (150 minutes weekly) in the year-long program, they still increased their aerobic fitness over the follow-up period [10]. PA or exercise programs are typically classified as self-directed if more than 50% of the program is implemented without close supervision (e.g. at a laboratory or clinic) [14]. Self-directed PA programs for cancer survivors often consist of a partially supervised and home-based program, with exercise classes or group support walking [15]. Many trials applying self-directed PA in cancer survivors achieve high

levels of adherence to PA [15]. In breast cancer survivors, a one year-self-directed weight training at a clinical setting and at home resulted in high percentage adherence to the program [16]. PA or exercise promotion in breast cancer survivors can be improved by integrating behavioral change theories or models such as Social Cognitive Theory (SCT) [17], Self-determination Theory (SDT) [18], Theory of Planned Behavior (TPB) [19] or the Transtheoretical Model (TTM) [17]. Theory-based PA programs employ strategies such as social or peer support, participative goal-setting, self-efficacy promotion and self-monitoring to promote adherence [20]. More specifically, these behavioral change theory-based strategies have been implemented through PA counselling focused on supportive approach by an exercise coach (in person or by phone) or group session [20]. A systematic review reported that adherence to home-based PA programs was associated with self-motivation and social support, highlighting the importance of these strategies [21].

Motivation is a vital factor in individual behaviour change; for example, people with more intrinsic motivation have more engagement in weight management programs [22]. SDT identifies some factors influencing human motivation such as individual characteristics and their interaction with the social world [23, 24] and represents the significance of autonomous self-regulation [25]. Two most potential strategies used for exercise motivation in clinical research are self-monitoring [26] and Motivational Interviewing (MI) [27]. Step count trackers or pedometers have been used to enhance PA adherence in many research studies [12, 28, 29]. Similarly, MI can increase PA behavior in cancer survivors [30]. MI, a patient-focused interview, aims to empower a person by counselling for behavioral change [31]. A counsellor who provides MI should apply four principles: (1) empathy expression (2) understanding of individual's current behavior and their goal (3) attention to resistance and (4) self-efficacy promotion [31].There is evidence that MI through both phone call and in-person counselling can reduce sedentary and increase active behaviors in breast cancer survivors [30]. Phone based MI integrated into a twelve-week diet control and exercise program in breast cancer survivors resulted in 70% of participants to adhere to the program [32].

Self-monitoring, one of the key concepts in Self-regulation Theory, is an individual evaluating their personal performance with reference to their perceptions, beliefs, and emotions [33]. PA promotion through self-monitoring can be made more pragmatic by making use of technological devices [34]. Step trackers can accurately detect PA behavior as daily steps and it can be used for PA motivation [35] in cancer patients and survivors [36, 37]. A previous study found that step trackers helped in PA self-monitoring and resulted in long-term PA adherence in post-menopausal women [12].

This systematic review and meta- analysis examined whether step count tracker and MI are effective motivational strategies to promote adherence to self-directed exercise in breast cancer survivors. The study does not include RCTs applying accelerometers (by attachment at participant's thigh) for weekly moderate-vigorous physical activity (MVPA) assessment which is not for PA self-motivation. We will explore the effectiveness of these motivational strategies in exercise interventions by comparing the adherence rates of participants in participating in self-directed PA.

2. Objective

The objective of this systematic review and meta-analysis was to compare PA adherence to self-directed PA in programs applying step tracker and MI in female breast cancer survivors. The study aimed to identify whether either of these behavioral change techniques is more effective in promoting adherence to self-directed PA in breast cancer survivors.

3. Methods

3.1. Protocol and Registration

The protocol was written using the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analysis Protocols (PRISMA-P) 2015 [38]. The protocol of this systematic review was registered with the International Prospective Register of Systematic reviews (PROSPERO) (CRD42020148542).

3.2. Eligibility criteria

Participants

Studies were considered eligible for the review if: 1) they included female breast cancer survivors aged 18 and older diagnosed with stage 0 to III tumors; 2) participants had completed primary treatments (surgery, chemotherapy and radiotherapy) at least three months prior to recruitment and had no evidence of cancer recurrence [39]; and 3) participants were on continuing hormonal therapy (e.g. Tamoxifen) as well as immune targeted therapy (e.g. Herceptin).

Studies were excluded if participants were currently receiving primary treatments of breast cancer and those who were diagnosed with metastatic breast cancer. We also excluded studies that involved male breast cancer survivors, unless the results of females could be separately extracted.

3.3. Intervention

The review included RCTs that evaluated self-directed PA or exercise as defined by the World Health Organization (WHO) compared to usual care [40]. Exercise is deemed a subcategory of PA which is well-organized and aims deliberately to improve physical fitness [40]. RCTs with PA or exercise implementation were considered self-directed and included if more than half of the program duration was independently implemented without strict control or close supervision in a controlled unit [14]. We included partially supervised or non-supervised programs, home-based programs, exercise class sessions that participants choose or group support walking [15]. The interventions were not limited by exercise or PA type, duration or intensity.

4. Outcome

The primary outcome of this systematic review was PA or exercise adherence. The study included studies which assessed the adherence by using the following criteria:

- Percentage of participants who completed a specified number of sessions (full adherence).
- Percentage of participants who attended at least a defined threshold of exercise sessions (partial adherence).
- Percentage of participants who achieved a given exercise volume recommendation such as weekly duration and intensity.
- The average of repeated measures such as exercise duration, intensity and step count.

PA adherence can be affected by the duration of PA program [41]. Therefore, PA or exercise adherence was reported at the end of the follow-up period of the program.

5. Report characteristics

The review included peer-reviewed articles with available full-texts. There were no limitations to the language of the publication. However, all eligible studies were reported in English. Literature reviews, conference abstracts, theses and book chapters were excluded from the review.

6. Information sources

The literature search made use of relevant medical subject headings (MeSH) and terms related to breast cancer, physical activity, self-directed, behavioral change and adherence to developed searching strategies in electronic databases (Appendix 1). The literature search includes studies published up to June 2020 available on the following databases; the Cochrane Breast Cancer Group's Specialised Register, the review identified relevant studies and trials which were outlined at http://www.mrw.interscience.wiley.com/cochrane/clabout/articles/BREASTCA/frame.html, Cochrane Central Register of Controlled Trials (CENTRAL) (Appendix 2), Pubmed (Appendix 3), Cumulative Index to Nursing and Allied Health Literature (CINAHL) with full text (EBSCOhost) (Appendix 4), PsycINFO (EBSCOhost) (Appendix 5) and Sportdiscuss with full text (EBSCOhost) (Appendix 6).
Searches were performed at two timepoints; firstly, September 2019, and with an update in June 2020 for studies published from September 2019 to June 2020. The literature was limited to human research.

7. Search Strategy

The search strategy was designed in collaboration with an experienced college librarian, College of Health and Biomedicine, Victoria University. A trial search with key words and related terms was conducted on Pubmed (advance search) in May 2019 for feasibility of the number of potential articles. The trial search on Pubmed is in Appendix 3.

8. Study selection

Search results from the five databases were exported to Covidence with following reviews working in the software [42]. The reviewers utilized Covidence screening tools for assessment of articles based on keywords for inclusion and exclusion criteria.

A summary of study inclusion and exclusion at each phase is described in Figure 1. Two reviewers (SP and JF) independently screened the titles and abstracts yielded by electronic key-term searching. Full-texts of the included studies were then uploaded and reviewed in full by the same reviewers independently. During screening any conflicts between reviewers were reviewed finally by a deciding third reviewer (VA).

9. Data extraction

Data from included studies was extracted manually and entered into a collection tool built in Microsoft Excel developed specifically for the current review. After data was extracted by the first reviewer (SP), the data was independently verified by a second and third reviewer (JF and JT). Where required, study authors were contacted by email for additional clarification regarding PA adherence measurement.

The review extracted the following data: Publication related information (Authors, year, Titles), Type of study or research design, number and age of participants, intervention characteristics (types and period of self-directed physical activity), PA or exercise motivation techniques (pedometer, MI and other behavioral change theory-related interventions) and measurements of PA or exercise adherence.

10. Risk of bias

Two reviewers (SP and JF) independently used Cochrane's assessment tool for the risk of bias in the recruited studies [43]. Relevant domains for risk assessment were: Selection bias (random sequence generation and allocate concealment); performance bias (blinding of participants and researchers); detection bias (blinding of outcome assessment); attrition bias (completeness of outcome data including exclusion from analysis); and reporting bias (selective reporting). All decisions were reported as low, high, and unclear risk. Any disagreements were resolved by discussion with the reviewer team and then by consensus. The result of the risk of bias assessment is reported and discussed in the review findings.

11. Synthesis of results

The review reported the outcomes of included studies consisting of repeated measures of PA duration (minutes per week of MVPA) and step count (daily or weekly steps) in standardized mean difference. Additionally, the number of participants who meet PA recommendation was reported by odds ratio (OR). A meta-analysis was performed on pooled data to estimate the standardized mean difference and 95% confidence intervals of PA duration (weekly minutes MVPA) and step count. The pooled difference in number of participants meeting PA recommendations between control and intervention groups was also performed. This analysis method was suitable for the comparison of data from the relevant scales [44]. The primary outcome was exercise or PA adherence in female breast cancer survivors which was reported by dichotomous data (e.g., the number of participants who met and did not meet the

exercise/PA targets) and continuous data (e.g., mean of duration attending exercise and mean of daily steps). The outcomes of each study were displayed in forest plots to identify the effect of motivational strategies on PA adherence. The score of standardized mean difference was considered as a small, moderate and large effect with scores of <0.20, between 0.20 and 0.80 and >0.80, respectively [45]. Subgroup effect analyses were conducted for each outcome regarding to the characteristics of PA motivational strategies of each study (e.g., pedometer combining with counselling or pedometer combining with motivational interviewing).

The I square (I^2) statistic for heterogeneity was also calculated, with a threshold of > 50% was identified as significant. A random-effects model was used to account for heterogeneity and extended variation in the pooled data [45], otherwise fixed-effect models were used [46]. All statistical analyses were conducted by using Review Manager, version 5.3.

12. Results

12.1. Study selection

The database search returned 7,921 articles which underwent abstract screening, with 7,830 excluded for irrelevance to topic. The remaining 91 studies underwent full-text screening, resulting in a final 16 studies included for data extraction.
The search and selection of articles are represented in Figure 1.

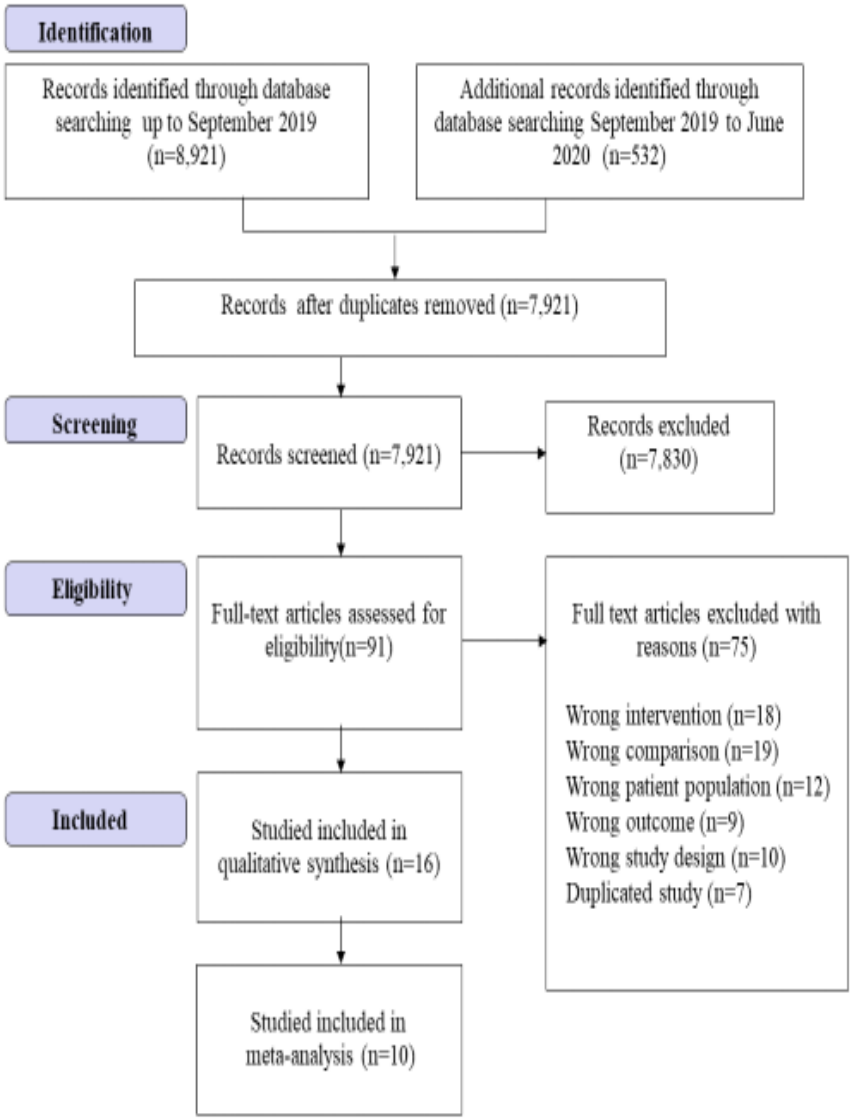

Figure 1. Flow of information through the different phases of a systematic review

12.2. Study characteristics

The sixteen included RCTs had a median duration of follow-up of twelve weeks (range: ten weeks to nine months). There was a total of 1,668 participants (953 intervention and 715 control) and the mean age across studies ranged from 49.50 - 61.90 years. Self-directed PA types consisted of home-based PA, walking programs and supervised tapering to home-based PA. The interventions studied could be grouped based on PA motivational strategy by five classifications as following 1) pedometer combining counselling, 2) pedometer combining

MI, 3) pedometer combining print material, 4) pedometer combining social media and 5) MI. The first three groups were included in the meta-analysis. Groups 4 and 5 could not be included in the meta-analysis as there was only one trial of the intervention.

There were thirteen trials providing usual care of breast cancer, standard PA recommendation or maintaining usual activity in waiting list as control interventions, while three trials provided standard care with pedometer [47, 48] or accelerometer for daily use [37].

PA adherence was reported as weekly intensity of PA (MET), weekly minutes of MVPA, daily steps (one study reported weekly steps [48], the numbers of participant who met PA goals and percent of participant who met PA recommendations (% PA adherence). The adherence measures of all included studies are illustrated in Table 1.

Table 1. Characteristics of included studies

No.	Author, Year	Study site (Country)	PA program	Follow-up	Participant Number and Age	Motivation strategies	Control condition	PA adherence measurement
Pedometer + Counselling								
1	Basen-Engquist et al, 2006	USA	6 months PA at moderate intensity such as walking at home	6 months	Intervention group N= 35 Age= 55.7± 11.1 Control group N= 25 Age= 54.4± 11.7	Pedometer + 21 sessions lifestyle counselling based on Transtheoritical Model	Receiving Standard care	●S-MVPA (min/week)
2	Pinto et al., 2005	USA	12 weeks home-based moderate intensity PA	12 weeks	Intervention group N= 43 Age= 53.42 ± 9.08 Control group N= 43 Age= 52.86 ± 10.38	Pedometer +PA counselling based on Transtheoretical Model (weekly phone call)	Receiving weekly phone call about Breast cancer care	●S-MVPA (min/week) ● Daily steps ●% PA adherence
3	Pinto et al., 2015	USA	12 weeks MVPA such as brisk walking at home	12 weeks	Intervention group N= 39 Age= 55.64 ± 8.59 Control group N= 37 Age= 55.59 ± 10.59	Pedometer +PA counselling based on Transtheoretical Model (weekly phone call)	Receiving Standard care	●S-MVPA ●O- MVPA (min/week) ●% PA adherence
4	Roger et al., 2015	USA	3 months supervised tapered to 12 weeks home-based PA	24 weeks	Intervention group N= 110 Age= 54.9± 9.3 Control group N= 112 Age= 53.9 ± 7.7	Accelerometer + Counselling based on Social Cognitive Theory (3 Face-to-face sessions)	Accelerometer +Standard PA	●S-MVPA ●O-MVPA (min/week) ●% PA adherence
Pedometer + Motivational Interviewing								
5	Hartman et al., 2018	USA	12 weeks walking with pedometer	12 weeks	Intervention group N= 43 Age= 58.2± 11.37 Control group N= 44 Age= 56.2 ± 9.30	Pedometer + MI (1 time in-person session and 2 phone calls)	Wait listed control	●O-MVPA (min/week, min/day) ●% PA adherence

No.	Author, year	Study site (Country)	PA program	Follow-up	Participant Number and age	Motivation strategies	Control condition	PA adherence measurement
6	Lynch et al., 2019	Australia	12 weeks wearable technology-based PA	12 weeks	Intervention group N= 40 Age= 61.3± 5.9 Control group N= 40 Age= 61.9 ± 7.0	Pedometer + MI (1 face-to-face session and 5 phone calls)	Wait listed control	●O-MVPA (min/week) ●Daily steps
Pedometer + Print materials								
7	Short et al., 2015	Australia	4 months home-based PA support	4 months	Intervention (SCT) N= 109 Age= 56 (34-74) Intervention (TPB) N= 110 Age= 55 (36-82) Control group N= 111 Age= 55 (33-75)	Pedometer + Print materials (2 groups) based on • Social Cognitive Theory • Theory of Planned Behaviour	Pedometer + Standard PA guideline	●S-MVPA (min/week) ●Daily steps ●% PA Adherence
8	Singh et al., 2020	Australia	12 weeks follow-up pedometer and guideline-based PA after 12 weeks supervised exercise	12 weeks	Intervention group N= 26 Age= 49.5 ± 8.6 Control group N= 26 Age= 52.8 ± 9.5	Pedometer + Booklet based on Theory of Planned Behaviour	Standard PA guideline	●S-MVPA ●O-MVPA (min/week) ●Daily steps ●% PA adherence
9	Vallance et al., 2007	Canada	12 weeks step tracker and guideline-based PA	12 weeks	Intervention (pedometer + booklet) N= 93 Age= 58 (38-86) Intervention (pedometer + PA advice) N= 94 Age= 58 (34-75) Control group N= 96 Age= 57 (37-90)	Pedometer + Booklet based on Theory of Planned Behaviour	PA recommendation	●S-MVPA (min/week) ●Daily steps
10	Hirschey et al., 2018	USA	12 weeks home-based PA	12 weeks	Intervention group N= 29 Age= 59 ± 10.0 Control group N= 29 Age= 57 ± 12.0	Pedometer + Booklet based on Social Cognitive Theory (self-efficacy and expected outcome)	Pedometer +Booklet based on diet	●Weekly steps
Pedometer + Counselling								
11	Baruth et al, 2015	USA	12 weeks home-based walking program	12 weeks	Intervention group N= 20 Age= 57.4 ± 6.1 Control group N= 12 Age= 54.9 ± 6.5	Pedometer + Counselling based on Social Cognitive Theory (goal setting, social support and reward) (1 in-person session and 5 phone calls)	Maintain usual activity	●MET (hr/week)
12	Pinto et al., 2013	USA	12 months PA at least at moderate intensity (received in person advice)	12 months	Intervention group N= 106 Age= 56.1 ± 9.9 Control group N= 86 Age= 55.9 ± 9.9	Pedometer + PA counselling based on Transtheoretical Model and Social Cognitive Theory (8 phone calls)	8 phone call about Breast cancer symptoms	●S-MVPA (min/week)
13	Pinto et al., 2008	USA	Follow-up 6 and 9 months after 12 weeks home-based PA	6 and 9 months	Intervention group N= 43 Age= 53.42 ± 9.08 Control group N= 43 Age= 52.86 ± 10.38	Pedometer + PA counselling based on Transtheoretical Model (weekly Phone call for	Receiving phone call about Breast cancer symptoms	●S-MVPA (min/week)

No.	Author, Year	Study site (Country)	PA program	Follow-up	Participant Number and Age	Motivation strategies	Control condition	PA adherence measurement
						first 3 months and then monthly phone calls for 3 months and then last 3 months they were ask for maintain PA by themselves)		
Pedometer + Social support								
14	Vallance et al., 2008	Canada	6 months follow-up after 3 months step tracker and print material guideline-based PA	6 months	Intervention (pedometer + booklet) N= 93 Age= 58 (38-86) Intervention (pedometer + PA advice) N= 94 Age= 58 (34-75) Control group N= 96 Age= 57 (37-90)	Pedometer + Booklet based on Theory of Planned Behaviour	PA recommendation	●S-MVPA (min/week)
15	Pope et al., 2018	USA	10 weeks home-based PA	10 weeks	Intervention group N= 16 Age= 50.6 ± 7.4 Control group N= 14 Age= 54.9 ± 11.0	Pedometer + Social media: Facebook Based on Social Cognitive Theory	Separated, content identical Facebook	●O-MVPA (min/day) ●Daily steps
Motivational Interviewing								
16	Lahart et al., 2016	UK	6 months moderate intensity of home-based PA program	6 months	Intervention group N= 40 Age= 52.4± 10.3 Control group N= 40 Age= 54.7 ± 8.3	MI (1 face-to-face session + 3 phone calls)	Standard PA guideline	●MET (min/week)

Abbreviations: USA: United States of America, UK: United Kingdom, N: the numbers of participant, Age: reported in years (mean ± standard deviation or mean and range), PA: Physical activity, S-MVPA: Subjective (self-report) moderate vigorous physical activity, O-MVPA: Objective moderate vigorous physical activity, min/week: Minutes per week, MET: Metabolic equivalent of task, MI: Motivational Interviewing

12.3. Risk of bias within the studies

All included studies indicated randomization of participants into study groups but only 50% declared allocation concealment [37, 47, 49-54]. There were no trials which blinded participants, assessors, and outcomes assessment. One trial reasoned that they did not blind participants and staff due to the nature of intervention [53]. Ten of sixteen trials [37, 47, 49, 51, 52, 54-58] reported low risk of attrition bias (presenting the methods to deal with missing data). One of sixteen trials [55] had high risk of reporting bias as they did not report all outcomes stated in the protocol; the frequency, duration of walking and MET were not reported at the follow-up. Most of studies reported the potential of other sources of bias which may affect the results as they had the limitation in generalisation of participants, small sample size, and type 1 error control. Most of participants were willing to participate in an exercise program that may result in the positive effects of intervention.

The review could not assess non-reporting bias across included trials by evaluating the symmetry of funnel plot and Egger's test because there were not more 10 trails included in meta-analysis for each PA adherence outcome [59]. However, the review implemented comprehensive searching from 5 databases and included studies with peer review publication. Risk of bias is summarized in Figure 2 and Figure 3.

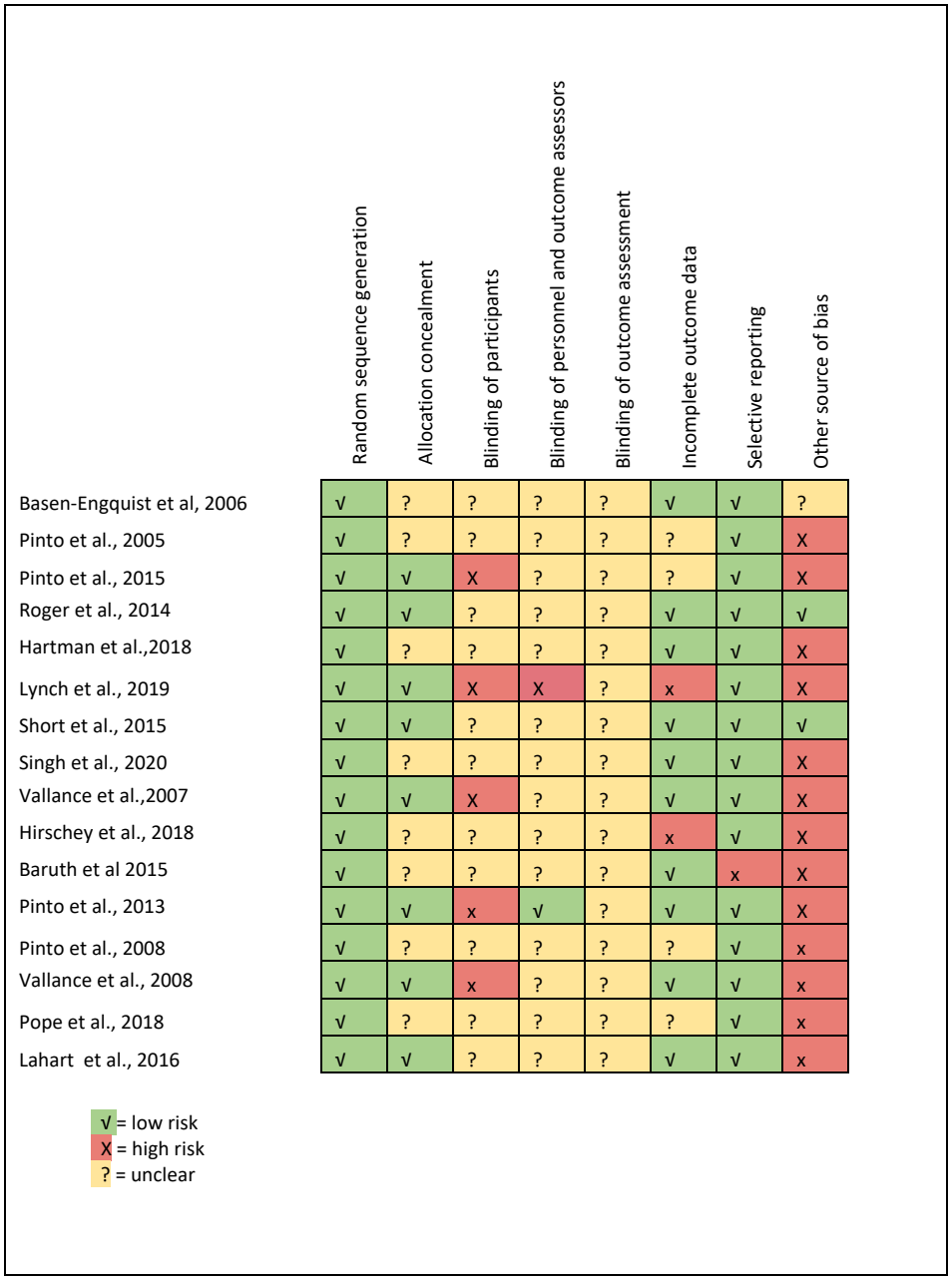

Figure 2. Risk of bias summary

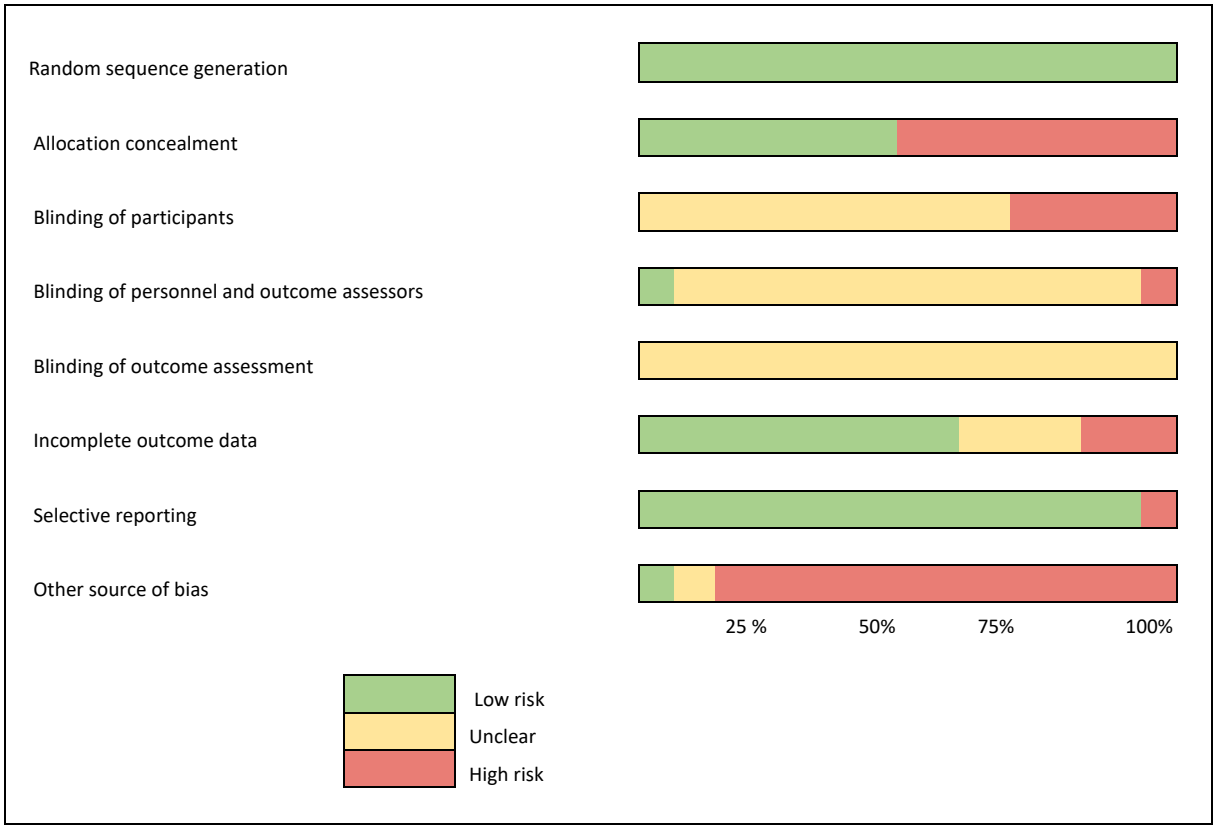

Figure 3. Risk of bias graph

12.4. Synthesis of results

Ten studies with eleven intervention arms (one study had two parallel intervention arms [47]) were included in the meta-analysis [37, 47, 48, 50, 51, 53, 56-58, 60]. Overall, intervention group involved in meta-analysis can be categorised into three groups consisting of 1) pedometer + counselling, 2) pedometer + MI, and 3) pedometer + print material.

12.4.1. MVPA duration

Nine trials [37, 47, 50, 51, 53, 56-58, 60] were included in meta-analysis of MVPA duration (minutes per week). There was significant heterogeneity between studies (I^2 =77%). When a random effects analysis was applied, the intervention group achieved a moderate improvement in MVPA duration compared with the usual care group (SMD=0.55, 95% CI 0.30,0.79). Results were consistent in the three subgroup analyses (Figure 4).

12.4.2. Step count

Five studies were included in meta-analysis of step count; four studies [47, 51, 53, 57] reported in daily steps but one study [48] reported in weekly steps. There was no heterogeneity between studies (I^2 =0%). Overall, a small effect of the intervention was detected compared to the control groups (SMD= 0.16, 95% CI 0.02, 0.29; Figure 5). There were two subgroups meta-analysis of step count; 1) the intervention group applying pedometer and print material [47, 48, 51, 57] showed a small effect in improvement of step count; SMD 0.15, 95% CI 0.01, 0.30, p =0.04, I^2=0%, 2) the intervention group applying pedometer and motivational interviewing [53] shown small effect; SMD 0.19, 95% CI -0.26, 0.64, p =0.40 (Figure 5).

12.4.3. The number of participants who meet physical activity recommendation

Overall, six studies [37, 47, 50, 57, 58, 60] were included in the meta-analysis measuring participants meeting PA recommendations. There was significant heterogeneity between studies (I^2 =77%). When a random effects analysis was applied, the intervention group had a significantly higher odds of meeting physical activity recommendations compared with the usual care group (OR=2.66, 95%CI 1.34, 5.27). This was consistent in all subgroup evaluations (Figure 6).

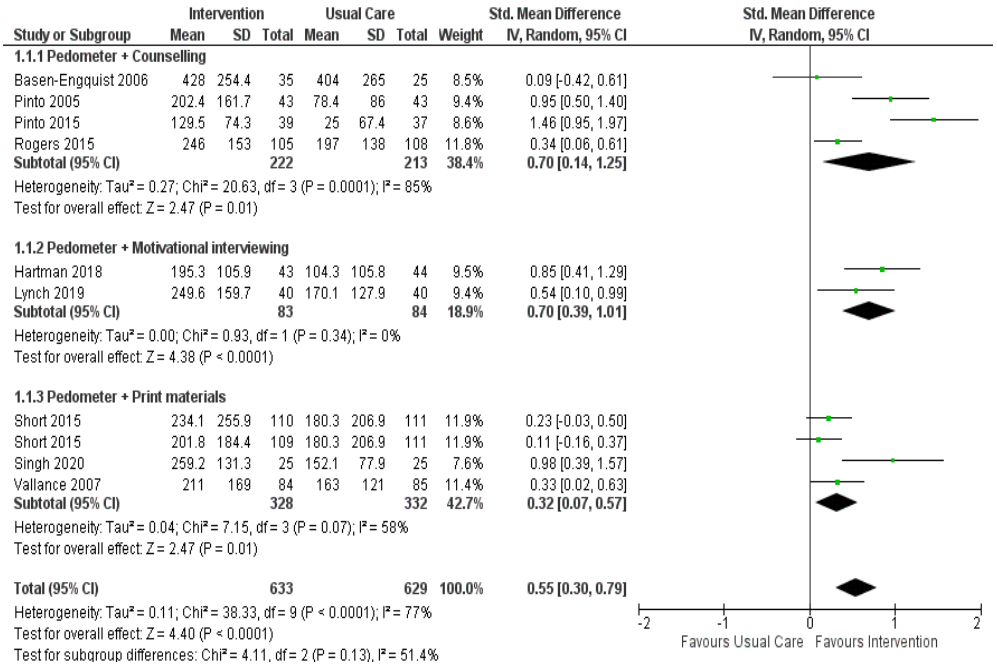

Figure 4. Meta-analysis of MVPA duration

Abbreviations: IV: inverse variance, Std: standardized, Total: number of participants in the study group

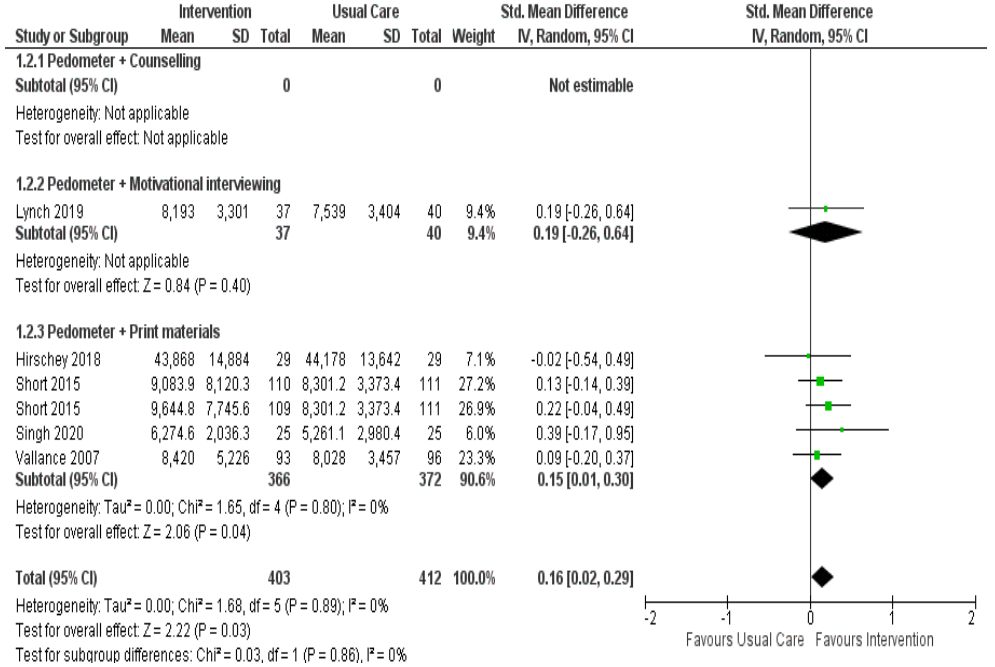

Figure 5. Meta-analysis of daily steps

Abbreviations: IV: inverse variance, Std: standardized, Total: number of participants in the study group

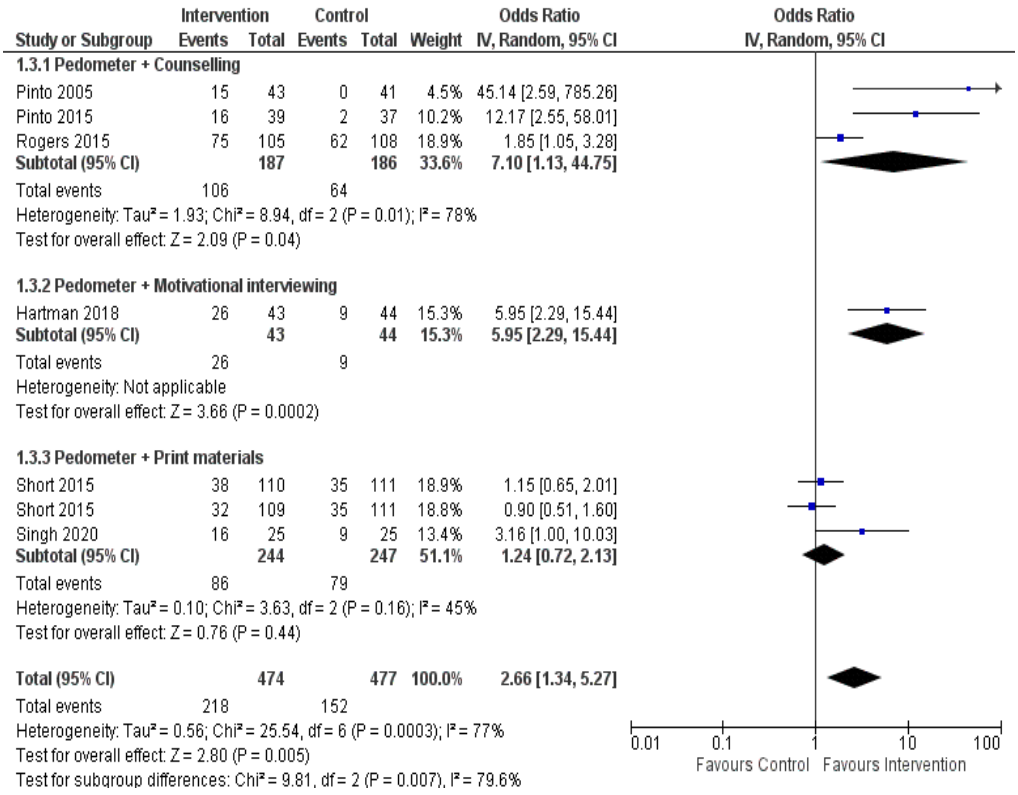

Figure 6. Meta-analysis of meeting PA recommendation (Odds Ratio)

Abbreviations: IV: inverse variance, Std: standardized, Total: number of participants in the study group

13. Discussion

Summary of evidence

This review and meta-analysis provides new evidence of improved adherence to self-directed PA in breast cancer survivors through application of two motivational strategies; pedometer (strep tracker) and MI. Overall, pedometer combined with another motivational strategy based on behavioral change theory provides small to moderate effect on step count and MVPA duration when compared to control receiving standard PA recommendation or usual care. Additionally, motivational strategies increased the number of participants who meet PA goal. Though there was significant heterogeneity among trials, the improvements of PA adherence were mostly consistent across the subgroups of motivational strategy.

Among sixteen included trials, there were a number of commonalities in the application of pedometer (step tracker) and/or MI for PA motivation. Fifteen of the studies used step tracker

(fourteen trials used pedometer [47-53, 55-58, 60-62] and one trial [37] used accelerometer for weekly self-monitoring over the trial duration. No trial utilized step tracker alone, with all fifteen trials combining them with another behavioral change theory informed strategy such as counselling, print material, social media, and MI.

Three trials used MI for PA motivation; two combining MI with pedometer [53, 58], and trial applying MI alone [54]. Additionally, there were a variety of behavioral change theories applied to interventions including Social Cognitive Theory (SCT), Transtheoretical Model (TTM) and Theory of Planned Behavior (TPB). However, among the ten studies included in meta-analysis, the review could not analyze these subgroups due to the small number of trials using a particular theoretical framework.

There was also heterogeneity of PA duration among the included studies. A twelve-week self-directed PA regimen was the most widely used program, with durations ranging from ten weeks to nine months. Subgroup analyses on programs of different durations could not be conducted due to low numbers.

There was also heterogeneity in the methods used to assess MVPA between the included studies. The review included six studies [47, 50, 51, 56, 57, 60] assessing MVPA by self-reported questionnaire and three studies using objective measurements obtained by accelerometer [37, 53, 58]. Of the studies using self-reported PA questionnaires; three [50, 56, 60] applied the Seven Day Physical Activity Recall Questionnaire (7 Day PAR), two [47, 51] used the Godin Leisure-Time Exercise Questionnaire, and one study used The Active Australia Survey [57].

Among the sixteen included trials of self-directed PA and motivational strategy there were two principal measurements of PA adherence, which have been identified in previous work [7]. The first was percentage of participants who met PA recommendations and the other was the average of repeated measure such as PA intensity, duration and step count. Six trials [37, 47, 50, 57, 58, 60] reported the number and percentage of participants who met PA recommendations. All six of these used a benchmark of at least weekly 150 minutes of MVPA as a minimum recommendation, in line with common guidelines for breast cancer survivors. The remaining ten trials did not report a percentage of PA adherence, instead reporting the average of repeated measure such as intensity (MET), duration (weekly minutes of MVPA) and step count described above. The corresponding authors of these trials were contacted by email for percentage of PA adherence data, if available, however no additional data was

acquired through this despite several responses from the authors. PA adherence was determined to be an individual's behavior in responding to PA goals in accordance with previous definitions [7].

The findings of this review highlight the potential role of incorporating self-directed PA in the treatment of breast cancer survivors by using an affordable step tracker for PA self-monitoring at their home or in the community. Additionally, combining the use of a pedometer with another PA motivational strategy based on behavioral change theories such as counselling, MI, or print materials (handout or brochure) will likely enhance PA adherence in this population.

Given the noticeable heterogeneity of PA adherence outcome assessment in self-directed PA in breast cancer survivors, the review would suggest that the appropriateness of PA adherence outcome measurements in self-directed PA needs to be standardized in trials to provide accurate reporting standards and allow for effective comparison between trials. This will allow for identification of optimal interventions to improve PA adherence in this patient cohort, and so improve health outcomes.

14. Limitation

The recommendation of this meta-analysis are limited by the significant heterogeneity of the trials included in this review. Firstly, there were a variety of PA motivation strategies and behavioral change theories that informed them, making it difficult to recommend a single intervention over another. There was also significant variability in the duration of the self-directed PA regimens. This is important, as participant adherence is strongly impacted by program duration [41]. The included trials in this review all show the potential risk of bias. The nature of the intervention led to unavoidable issues with blinding participants, exposing the trials to risks of bias.

15. Conclusions

This review found that step tracker combining with counselling, print material or MI based on behavioral change theory provided a consistent positive effect on adherence to self-directed PA among breast cancer survivors. This emphasizes the importance of applying motivational improvement strategies in this cohort to improve their health outcomes over time. While there was heterogeneity in the application of step tracker and/or MI among included trials, the improvements were consistent across studies, so while confidence can be

received in the results, no single intervention could be identified as having an optimal outcome. The review highlights opportunities for health care professionals to improve patient outcomes through the application of motivational strategies to increase PA adherence. Future studies should assess and report PA adherence outcomes consistently, to allow for more effective examination of motivational interventions.

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Appendices

Appendix 1. MeSH terms

1. **Breast cancer**

Tumors or cancer of the human breast
Entry Terms:
Breast Neoplasm
Neoplasm, Breast
Breast Tumors
Breast Tumor
Tumor, Breast
Tumors, Breast
Neoplasms, Breast
Breast Carcinoma
Breast Carcinomas
Carcinoma, Breast
Carcinomas, Breast
Mammary Neoplasms, Human
Human Mammary Neoplasm
Human Mammary Neoplasms
Neoplasm, Human Mammary
Neoplasms, Human Mammary
Mammary Neoplasm, Human
Breast Cancer
Cancer, Breast
Mammary Cancer
Cancer, Mammary
Cancers, Mammary
Mammary Cancers
Malignant Neoplasm of Breast
Breast Malignant Neoplasm
Breast Malignant Neoplasms
Malignant Tumor of Breast
Breast Malignant Tumor
Breast Malignant Tumors
Cancer of Breast
Cancer of the Breast

2. **Physical activity**

Physical activity which is usually regular and done with the intention of improving or maintaining PHYSICAL FITNESS or HEALTH. Contrast with PHYSICAL EXERTION which is concerned largely with the physiologic and metabolic response to energy expenditure.
Entry Terms:
Exercises
Physical Activity
Activities, Physical
Activity, Physical
Physical Activities
Exercise, Physical

Exercises, Physical
Physical Exercise
Physical Exercises
Acute Exercise
Acute Exercises
Exercise, Acute
Exercises, Acute
Exercise, Isometric
Exercises, Isometric
Isometric Exercises
Isometric Exercise
Exercise, Aerobic
Aerobic Exercise
Aerobic Exercises
Exercises, Aerobic
Exercise Training
Exercise Trainings
Training, Exercise
Trainings, Exercise

3. Motivational Interviewing

It is a client-centered, directive method for eliciting intrinsic motivation to change using open-ended questions, reflective listening, and decisional balancing. This nonjudgmental, non-confrontational interviewing style is designed to minimize a patient's resistance to change by creating an interaction that supports open discussion of risky or problem behavior.

Entry Terms:

Interviewing, Motivational

4. Fitness tracker

Devices used for measuring physical activity as an indication of HEALTH STATUS.

Entry Terms:

Fitness Tracker
Tracker, Fitness
Trackers, Fitness
Physical Fitness Trackers
Fitness Tracker, Physical
Fitness Trackers, Physical
Physical Fitness Tracker
Tracker, Physical Fitness
Trackers, Physical Fitness
Activity Trackers
Activity Tracker
Tracker, Activity
Trackers, Activity
Personal Fitness Trackers
Fitness Tracker, Personal
Fitness Trackers, Personal
Personal Fitness Tracker
Tracker, Personal Fitness
Trackers, Personal Fitness

5. Wearable Electronic Devices

Electronic implements worn on the body as an implant or as an accessory. Examples include wearable diagnostic devices, wearable ACTIVITY TRACKERS, wearable INFUSION PUMPS, wearable computing devices, SENSORY AIDS, and electronic pest repellents.

Entry Terms:

Device, Wearable Electronic
Devices, Wearable Electronic
Electronic Device, Wearable
Electronic Devices, Wearable
Wearable Electronic Device
Wearable Technology
Technologies, Wearable
Technology, Wearable
Wearable Technologies
Wearable Devices
Device, Wearable
Devices, Wearable
Wearable Device
Electronic Skin
Skin, Electronic

6. Adherence

Patient Compliance

Voluntary cooperation of the patient in following a prescribed regimen.

Entry Terms:

Compliance, Patient
Patient Adherence
Adherence, Patient
Patient Cooperation
Cooperation, Patient
Treatment Compliance
Compliance, Treatment
Treatment Compliances
Therapeutic Compliance
Compliance, Therapeutic
Compliances, Therapeutic
Therapeutic Compliances

Appendix 2. Draft CENTRAL search

#1 MeSH descriptor: [Breast Neoplasms] explode all trees
#2 breast near cancer
#3 (breast near cancer) OR (breast near neoplasm) OR (breast near carcinoma)
#4 MeSH descriptor: [Exercise] explode all trees
#5 physical next activity*
#6 ("physical activity")
#7 (physical next activity*)
#8 (physical next activity*) OR exercise OR sport
#9 ("self directed") OR ("home based") OR ("community based") OR ("non supervised") OR ("partial supervised") OR ("low supervised")
#10 ("behavioral change") OR (motivation) OR ("self monitoring") OR ("fitness next tracker*) OR (pedometer) OR (accelerometer) OR ("step count tracker") OR ("step next tracker*)
OR ("wearable device") OR ("digital device") OR ("wearable technology")
#11 ("motivational interviewing")
12 MeSH descriptor: [Motivational Interviewing] explode all trees
13 MeSH descriptor: [Treatment Adherence and Compliance] explode all trees
14 adherence
15 (adherence) OR (compliance) OR (engagement) OR (participation)
16 #8 OR #9 OR #10 OR #11
17 #3 AND #16 AND #15

Appendix 3. Draft Pubmed search

53	Search (((((breast cancer) OR breast neoplasm) OR breast carcinoma)) AND (((((((((physical activity) OR physical activities) OR exercise) OR exercises) OR sport) OR sports)) OR ((((((self-directed program) OR home-based program) OR community-based program) OR non-supervised program) OR partial supervised program) OR low-supervised program)) OR ((((((((((((((((((behavioural* change strategy) OR behavioural* change strategies) OR physical activity motivation) OR exercise motivation) OR self-monitoring) OR fitness tracker) OR pedometer) OR accelerometer) OR step count trackers) OR step count tracker) OR step counter) OR step counters) OR wearable device) OR wearable devices) OR digital device) OR digital devices) OR wearable technology)) OR motivational interviewing))) AND ((((adherence) OR compliance) OR engagement) OR participation)
52	Search (((((((physical activity) OR physical activities) OR exercise) OR exercises) OR sport) OR sports)) OR ((((((self-directed program) OR home-based program) OR community-based program) OR non-supervised program) OR partial supervised program) OR low-supervised program)) OR ((((((((((((((((((behavioural* change strategy) OR behavioural* change strategies) OR physical activity motivation) OR exercise motivation) OR self-monitoring) OR fitness tracker) OR pedometer) OR accelerometer) OR step count trackers) OR step count tracker) OR step counter) OR step counters) OR wearable device) OR wearable devices) OR digital device) OR digital devices) OR wearable technology)) OR motivational interviewing)
51	Search ((((((((((((((((((behavioural* change strategy) OR behavioural* change strategies) OR physical activity motivation) OR exercise motivation) OR self-monitoring) OR fitness tracker) OR pedometer) OR accelerometer) OR step count trackers) OR step count tracker) OR step counter) OR step counters) OR wearable device) OR wearable devices) OR digital device) OR digital devices) OR wearable technology)) OR motivational interviewing
50	Search (((adherence) OR compliance) OR engagement) OR participation
49	Search ((((((((((((((((behavioural* change strategy) OR behavioural* change strategies) OR physical activity motivation) OR exercise motivation) OR self-monitoring) OR fitness tracker) OR pedometer) OR accelerometer) OR step count trackers) OR step count tracker) OR step counter) OR step counters) OR wearable device) OR wearable devices) OR digital device) OR digital devices) OR wearable technology
48	Search (((((self-directed program) OR home-based program) OR community-based program) OR non-supervised program) OR partial supervised program) OR low-supervised program
47	Search (((((physical activity) OR physical activities) OR exercise) OR exercises) OR sport) OR sports
46	Search participation
45	Search engagement
44	Search compliance
43	Search adherence

42 Search motivational interviewing
41 Search wearable technology
40 Search digital devices
39 Search digital device
38 Search wearable devices
37 Search wearable device
36 Search step counters
35 Search step counter
34 Search step count trackers
33 Search step count tracker
32 Search accelerometer
31 Search pedometer
30 Search fitness tracker
29 Search self-monitoring
28 Search exercise motivation
27 Search physical activity motivation
26 Search behavioural* change strategies
25 Search behavioural* change strategy
24 Search low-supervised program
23 Search partial supervised program
22 Search non-supervised program
21 Search community-based program
20 Search home-based program
19 Search self-directed program
18 Search (sport) OR sports
17 Search sports
16 Search sport
15 Search (exercises) OR exercise
14 Search exercises
13 Search exercise
12 Search (physical activities) OR physical activity
11 Search physical activities
10 Search physical activity[MeSH Terms]
9 Search physical activity
7 Search breast cancer[MeSH Terms]
8 Search breast neoplasm[MeSH Subheading]
6 Search ((breast cancer) OR breast neoplasm) OR breast carcinoma
5 Search breast carcinoma
2 Search (breast cancer) OR breast neoplasm
4 Search (breast cancer) AND breast neoplasm
3 Search breast neoplasm
1 Search breast cancer

Appendix 4. CINAHL with full text (EBSCOhost)

S1 (MH "Breast Neoplasms+")
S2 breast cancer
S3 breast neoplasm
S4 breast carcinoma
S5 S2 OR S3 OR S4
S6 (MM "Physical Activity")
S7 physical activity
S8 physical activity OR exercise OR sport
S9 self-directed OR home based OR community based OR non-supervised OR partial supervised OR low supervised
S10 behavioral change OR motivation OR self-monitoring OR (fitness tracker or activity tracker or sport tracker) OR pedometer OR accelerometer OR step count tracker OR step tracker OR wearable devices OR digital devices
S11 (MM "Motivational Interviewing")
S12 motivational interviewing
S13 adherence OR compliance OR engagement OR participation
S14 S8 OR S9 OR S10 OR S12
S15 S5 AND S13 AND S14

Appendix 5 PsycINFO (EBSCOhost)

S1 breast cancer
S2 MM "Breast Neoplasms"
S3 breast neoplasms
S4 breast carcinoma
S5 S1 OR S3 OR S4
S6 MM "Exercise" OR MM "Aerobic Exercise" OR MM Weightlifting"
OR MM "Yoga" OR MM "Physical Activity" OR MM "Actigraphy" OR MM "Exercise"
S7 exercise
S8 MM "Physical Activity" OR MM "Actigraphy" OR MM “Exercise"
S9 physical activity
S10 sport
S11 MM "Sport Psychology"
S12 S7 OR S9 OR S10
S13 self-directed OR home based exercise OR community based OR non supervised OR partial supervised OR low supervised
S14 behavioral change OR motivation OR self-monitoring
OR (fitness tracker or activity tracker or sport tracker) OR
(pedometer or activity monitor or daily steps)
OR (accelerometer or accelerometry or actigraphy) OR
step tracker OR step count tracker OR
(wearable devices or wearable technology) OR digital devices
S15 motivational interviewing
S16 MM "Motivational Interviewing"
S17 S12 OR S13 OR S14 OR S15
S18 MM "Treatment Compliance"
S19 adherence
S20 adherence OR compliance OR (engagement or involvement or participation)
S21 S5 AND S17 AND S20

Appendix 6. SPORTDiscus with full text (EBSCOhost)

S1 DE "BREAST cancer"
S2 breast cancer OR breast carcinoma OR breast neoplasms
S3 DE "PHYSICAL activity" OR DE "EXERCISE"
S4 (DE "PHYSICAL activity" OR DE "EXERCISE") OR sports
S5 DE "SPORT for all"
S6 S3 OR S5
S7 physical activity OR exercise OR sports
S8 self-directed OR home based exercise OR community based OR non supervised OR partial supervised OR low supervised
S9 behavioral change OR motivation OR self-monitoring OR (fitness tracker or activity tracker or sport tracker) OR (pedometer or activity monitor or daily steps) OR accelerometer OR step tracker OR step counter OR (wearable technology or wearable devices) OR digital devices
S10 motivational interviewing or mi or motivational interview
S11 DE "MOTIVATIONAL interviewing"
S12 (adherence or compliance) OR engagement OR (participation or engagement or involvement)
S13 DE "PHYSICIAN adherence" OR DE "EXERCISE adherence"
S14 S7 OR S8 OR S9 OR S10
S15 S2 AND S12 AND S14

Chapter 4

Chapter 4
PAPHIO study protocol

Chapter preface:

This chapter, consists of a published paper which was created during the candidature of this thesis.

Authorship declarations:

The manuscript included in this chapter has benefitted from the valuable contribution of a number of co-authors, who provided guidance, editorial assistance and advice. However, the conception, execution and initial draft of the publication was performed by me. Specific % contributions by co-authors are detailed in the declaration

Chapter 4

PAPHIO study protocol

4a. The PAPHIO study protocol: a randomised controlled trial with a 2 x 2 crossover design of Physical Activity adherence, Psychological Health and Immunological Outcomes in breast cancer survivors

---

ABSTRACT

Background. The PAPHIO study; a randomized controlled trial with 2X2 crossover design will implement a self-directed physical activity program in which participants will engage in self-monitoring and receive motivational interviewing to enhance physical activity adherence. The study aims to determine the effects of 24 weeks self-directed activity combined with motivational interviewing (MI) on (i) psychological health, (ii) quality of life (QoL) and (iii) immune function in female breast cancer survivors.

Methods. The study will recruit 64 female breast cancer survivors within three years of diagnosis and at least six months post primary treatments at Western Health Sunshine Hospital, Melbourne, Australia. They will be randomly allocated to immediate intervention (IIG group) or delayed intervention groups (DIG group) in a 1:1 ratio. All participants will be given a wearable device (Fitbit Alta HR) and undertake self-directed physical activity for 24 weeks and will receive MI for 12 weeks (IIG; during week 0 to week 12 and DIG; during week 13 to week 24). Participants' daily step count and the changes of immune cell functionality will be assessed at the beginning (week 1: T1), week 12 (T2) and week 24 (T3) of the program. Physical activity adherence will be assessed at T2 and T3. Participants will also complete four questionnaires assessing exercise self-regulation (BREQ2), exercise barrier and task self-efficacy, mental health (DASS-21) and QoL (FACT-B) at three time points (T1 to T3). Linear-mixed models will be used to assess the relationship between physical activity volume by step counting and mental health (DASS-21), QoL (FACT-B), immune biomarkers, self-regulation (BREQ2) and self-efficacy at T1, T2 and T3;between 2 groups.

Discussion. We expect this physical activity intervention to be acceptable and beneficial to the participants in terms of psychological and immunological well-being with the potential outcomes to be implemented more widely at relatively low cost to these or other patient populations.

Trial registration Australian New Zealand Clinical trials Registry-ACTRN12619001271190. Prospectively registered on 13 September 2019 http://www.ANZCTR.org.au/ACTRN12619001271190.aspx

Keywords: Breast cancer survivor, self-directed physical activity, physical activity adherence, motivational interviewing, pedometer, quality of life, psychological health, and immunological biomarker

OFFICE FOR RESEARCH TRAINING, QUALITY AND INTEGRITY

DECLARATION OF CO-AUTHORSHIP AND CO-CONTRIBUTION: PAPERS INCORPORATED IN THESIS

This declaration is to be completed for each conjointly authored publication and placed at the beginning of the thesis chapter in which the publication appears.

1. PUBLICATION DETAILS (to be completed by the candidate)

Title of Paper/Journal/Book:	The PAPHIO study protocol: a randomised controlled trial with a 2 x 2 crossover design of physical activity adherence, psychological health and immunological outcome in breast cancer survivors
Surname:	Pudkasam
First name:	Supa
Institute:	Institute for Health and Sport
Candidate's Contribution (%):	70%

Status:

Accepted and in press:	☐	Date:	
Published:	☑	Date:	1/5/2020

2. CANDIDATE DECLARATION

I declare that the publication above meets the requirements to be included in the thesis as outlined in the HDR Policy and related Procedures – policy.vu.edu.au.

[redacted]	24 February 2021
Signature	**Date**

3. CO-AUTHOR(S) DECLARATION

In the case of the above publication, the following authors contributed to the work as follows:

The undersigned certify that:

1. They meet criteria for authorship in that they have participated in the conception, execution or interpretation of at least that part of the publication in their field of expertise;
2. They take public responsibility for their part of the publication, except for the responsible author who accepts overall responsibility for the publication;

3. There are no other authors of the publication according to these criteria;
4. Potential conflicts of interest have been disclosed to a) granting bodies, b) the editor or publisher of journals or other publications, and c) the head of the responsible academic unit; and
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The PAPHIO study protocol: a randomised controlled trial with a 2 x 2 crossover design of physical activity adherence, psychological health and immunological outcomes in breast cancer survivors

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Abstract

Background: The PAPHIO study; a randomized controlled trial with 2X2 crossover design will implement a self-directed physical activity program in which participants will engage in self-monitoring and receive motivational interviewing to enhance physical activity adherence. The study aims to determine the effects of 24 weeks self-directed activity combined with motivational interviewing (MI) on (i) psychological health, (ii) quality of life (QoL) and (iii) immune function in female breast cancer survivors.

Methods: The study will recruit 64 female breast cancer survivors within 3 years of diagnosis and at least 6 months post primary treatments at Western Health Sunshine Hospital, Melbourne, Australia. They will be randomly allocated to immediate intervention (IIG group) or delayed intervention groups (DIG group) in a 1:1 ratio. All participants will be given a wearable device (Fitbit Alta HR) and undertake self-directed physical activity for 24 weeks and will receive MI for 12 weeks (IIG; during week 0 to week 12 and DIG; during week 13 to week 24). Participants' daily step count and the changes of immune cell functionality will be assessed at the beginning (week 1: T1), week 12 (T2) and week 24 (T3) of the program. Physical activity adherence will be assessed at T2 and T3. Participants will also complete four questionnaires assessing exercise self-regulation (BREQ2), exercise barrier and task self-efficacy, mental health (DASS-21) and QoL (FACT-B) at three time points (T1 to T3). Linear-mixed models will be used to assess the relationship between physical activity volume by step counting and mental health (DASS-21), QoL (FACT-B), immune biomarkers, self-regulation (BREQ2) and self-efficacy at T1, T2 and T3;between 2 groups.

Discussion: We expect this physical activity intervention to be acceptable and beneficial to the participants in terms of psychological and immunological well-being with the potential outcomes to be implemented more widely at relatively low cost to these or other patient populations.

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1. Background

Breast cancer is a common malignant disease leading to physical and psychological distress in females worldwide [1, 2]. Approximately 2.1 million women suffered from this disease and 626,000 deceased across the world in 2018 [3]. The occurrence rate of breast cancer has dramatically increased in 22 out of 39 countries from 2008 to 2012, whereas the global death rate has gradually dropped [4]. The global trend of breast cancer increases awareness in the availability of breast cancer care program [4]. Breast cancer survivors may have mental distress mainly due to long-term treatments [5]. Currently, survivorship programs, especially physical activity programs have emphasised strategies to enhance psychosocial well-being [6, 7]. Psychological interventions including emotional ventilation, adjustment skill training and self-efficacy promotion techniques have been applied in improving their mental wellness over the decades [6, 8].

Physical activity, especially moderate intensity aerobic exercise for female breast cancer survivors, have been noted in a number of studies to be beneficial to breast cancer outcomes, decreasing the mortality rate by >30% and reducing the recurrence rate [9]. As a result of physical activity, there is a reduction in the total body fat as well as a number of inflammatory and immunological biomarkers which could contribute to better outcomes in breast cancer survivors [10, 11]. Moderate aerobic exercise and combination of aerobic and resistant training in breast cancer women ranging between 15 and 24 weeks could possibly activate immune cells such as NK cell cytotoxic activity and lymphocytes [12, 13]. Furthermore, a 12-weeks aerobic exercise training at home in breast cancer survivors reduces the level of epithelial neutrophil activating protein and pro-inflammatory cytokines [14].

Approximately one third of patients with cancer reduce their physical activity after diagnosis and almost 70% of them will not reach the exercise recommendation for cancer patients [15]. 30% Of of breast cancer survivors with early phase (stage 0 to 3) breast cancer have reported physical activity cessation during twelve months follow-up after participation in a six months RCT [16]. The cessation may be associated with the resumption of their previous domestic tasks and work [16]. Physical activity barriers in older breast cancer survivors are related to physical tiredness and lack of time management skills [17]. In addition, some breast cancer survivors have low confidence in the benefits of physical activity in minimizing adverse effects of breast cancer and treatment [18]. The challenge of recruiting

patients with advanced stage of cancer is to deal with their cancer-related fatigue in particular the side effect of treatments [15].

2. Physical activity and motivation for activity adherence in breast cancer survivors

Adoption and adherence to physical activity programs amongst cancer survivors are challenging due to their physical and mental vulnerability [22]. As such, in this study we developed an intervention which maximizes feasibility, sustainability and generalisability. This study will prescribe self-directed physical activity to breast cancer survivors. Many of self-directed techniques for physical activity adherence in participants with advanced stage of heterogeneous cancers have been used in research studies, such as partially advised and home-based program, exercise class teaching and peer support walking group programs [23]. Many of the programs have achieved high percentages of exercise adherence, reducing fatigue and improving QoL [23].

An important factor to adopt and adhere to a physical activity program is an individual's motivation. To this end, a number of behavioural change strategies have been reported which enhance motivation and adherence [24]. Two of these strategies are Motivational Interviewing (MI) and self-monitoring. MI is a conversation technique used by a professional during consultation when making health behaviour changes [25], and has been effectively used to bring about behavioural change in health promotion programs for the general population. This includes changes in eating behaviour, alcohol cessation and adoption of an active life style [26]. More specifically, face-to-face and phone-based MI has been implemented successfully to enhance self-efficacy and reduce resistance against physical activity in breast cancer survivors [27, 28].. On the other hand, self-monitoring, one of the important concepts in self-regulation theory, is an auditing mechanism of individual performance in relation to an individual's cognitions, beliefs and emotions [29]. Some digital devices have the ability to promote physical activity through self-monitoring concept [30]. For example, step counting gadgets including pedometers, can effectively monitor physical activity in terms of daily steps. Such devices have been utilised for promotion of physical activity in clinical trials [31] especially in breast cancer patients and survivors [32, 33]. Step counters help in monitoring individual's physical activity behaviour and can result in increased motivation and ultimately adherence to long-term physical activity behaviour [34].

To understand participants' motivation to self-directed physical activity, self-determination theory (SDT) has been effectively used to enhance insight in physical activity behaviour and motivation in breast cancer survivors [35]. According to SDT motivation to engage in behaviour lies on a continuum ranging from extrinsic (controlled by external factors) to intrinsic (individual interest and preference). The theory predicts that intrinsic-motivation might enhance confidence in task accomplishment (competence), independent action (autonomy) and the feeling of connection to others (relatedness) [35]. Our study will assess how self-regulation and motivational interviewing might change participants motivational orientation over the intervention period using the behavioural regulations in exercise questionnaire (BREQ2; [36]).

Self-efficacy, an important concept in social cognitive theory, has been shown to be a predictor for physical activity behaviour and adherence in breast cancer patient [37]. In this project two types of efficacy beliefs will be examined. First, we will explore exercise barriers self-efficacy, which will examine the participants' confidence to overcome or deal with barriers to their exercise participation. Secondly, this project will examine task self-efficacy beliefs In particular, it will examine the self-efficacy beliefs of the participants to engage in exercise behaviour [37]. To measure this, the project will use the nine-item barriers self-efficacy [38] and four-item task self-efficacy questionnaire [38].

3. Study goals and objectives

The study has an overall aim to determine the effects of 24 weeks self-directed activity combined with motivational interviewing on (i) psychological health (depression, anxiety, stress), (ii) quality of life (QoL; physical, social/family, emotional and functional) and (iii) immune function in female breast cancer survivors. In addition, we will explore the dose-response relationship between exercise volume (step count) and the outcome measures.

4. Study design

This study is a randomised crossover trial; a single site research project conducted at Brest Cancer Service Clinic, Western Health (Sunshine Hospital) Australia. Whereas, the project recruited potential participants from two recruiting sites; Sunshine hospital and Improving and Promoting Community (IPC) health, Altona Meadows. Potential participants will be prescribed with a Fitbit Alta HR tracker for a 24-week-self-directed activity and will receive motivational interviewing for 12 weeks

(Immediate intervention group; during week 0 to week 12 and Delayed intervention group; during week 13 to week 24). The study protocol through 24 weeks is illustrated in Figure 1.

4.1. Inclusion criteria. Female breast cancer survivors 18 years and older who are within three years of diagnosis and at least six months post active treatment; operation, chemotherapy and/or radiotherapy [stages 0 to 3 including those with ductal carcinoma *in situ* (DCIS)], will be recruited. Survivors on hormonal therapy such as, tamoxifen and aromatase inhibitors as well as immune targeted therapy (Herceptin) will be eligible to participate because these hormonal and cell surface blockages do not have direct effects on immune cells and adiposity-related biomarkers in breast cancer. The study will also include participants who are unable to read/ write English but are literate and English speaking. For participants with non-English literacy, translators will be used to obtain informed consent and the study will apply the questionnaires that have been validated in other languages such as Vietnamese, Greek, Chinese and Macedonian. This study plans to recruit participants from Breast cancer care service of Sunshine Hospital, Western Health, and IPC health Altona Meadows Melbourne, Australia.

4.2. Exclusion criteria. Participants who are undergoing active treatments (surgery, chemotherapy and radiation) as well as those less than six months post active treatment. Likewise, those individuals with cognitive impairment and unable complete the questionnaires will be excluded. Participants with known metastatic disease will also be excluded from the study. The participant will be withdrawn from the study if they develop cancer recurrence or metastases during the study period.

5. Recruitment

The study will recruit participants who are breast cancer survivors within three years of diagnosis and at least six months post primary treatments. Eligible participants will be randomly allocated to immediate intervention or delayed intervention groups in a 1:1 ratio after completion of informed consent. The participants will be recruited from Breast cancer care service, Western Health Sunshine campus and IPC health, Altona Meadows in Melbourne. Recruitment strategies will include public media (poster advertising or flyer) and individual contact introduced by their physician [39]. All participants have to be physical activity program approved by their physician for engagement in the of this research and the screening process will be conducted before obtaining consent.

The study will commence at Western Health Sunshine campus following ethical approval from Melbourne Health Human Research Ethics Committee (MH HREC) and Western Health research governance authorization [40]. Based on our power calculation we aim to recruit 64 participants.

6. Randomization

The study design is a two-armed RCT with a crossover design. Sequence generation will be conducted by simple randomisation following patient informed consent. The participants will be randomly allocated to either IIG or DIG in 1:1 ratio by computerised number generator. Allocation concealment by enclosing the allocation in sealed envelopes will be used to prevent selection bias [41]. The allocation concealment will be conducted by a third party to prevent researchers from affecting group assignment. The participants in both groups will be prescribed a self-directed physical activity for 24 weeks. The IIG will receive MI from week 1 to week 12, whereas DIG will receive the same MI intervention from weeks 13 to 24. Allocation concealment technique will be applied in process of randomisation. During weeks 1 to week 12, the IIG will perform self-directed physical activity and receive MI. On the other hand, the DIG will perform self-directed physical activity without MI. During week 13 to week 24, DIG will continue self-directed physical activity with MI. Whereas IIG will perform physical activity but will no longer be given MI.

7. Methods of Intervention

7.1. Self-directed physical activity. Participants will perform a 24-week period of self-directed, pedometer controlled physical activity [42, 43]. A pedometer is user-friendly and affordable for home-based or self-directed physical activity [42]. All participants will be given a step-count tracker devise (Fitbit Alta HR) and investigators will explain the prescribed pedometer-based activity to participants. Fitbit Alta HR is a valid wearable gadget can be used to monitor step count. The participants' activity engagement will accompanied by individual face-to-face and phone call MI [25]. Participants will be taught how to operate the Fitbit and will be taken on a 10-minute walk to experience a moderate level of exertion. At week 1 (baseline or T1), all participants will be prescribed to assess and record their activity using the Fitbit monitoring device through its application via computer or smartphone to establish their baseline physical activity volume by step count. Following this, they will be

advised to perform their activity on their own pace as tolerated and will wear the Fitbit during the daytime or when they are available for physical activity throughout the 24 weeks. Individual participants will be advised and motivated to gradually increase their daily steps on physical activity at moderate intensity exertion or at their perception of taking some efforts but can talk during physical activity (the recommendation by the department of health, Australian government) [45] during face-to-face and over the phone MI. The participants will be advised for safety during physical activity. They will be suggested to stop physical activity if adverse symptoms occur such as chest pain or pain down to arms, dizziness, difficulty breathing, unusual rapid heart rate, and sever fatigue. The researcher will suggest to the participant to inform their family members and take a mobile phone with them before they go out to exercise. They will be also advised to take record of their daily steps in their notebook. All participants will be informed that the researcher will track the participants' step count and tracker usage time via Fitbit connect application. Individual average daily step count, and activity level will be assessed at baseline (T1), week 12 (T2), and week 24 (T3).

7.2. Motivational interviewing. MI will be used in encouraging participants through open-end questions, friendly and supportive communication and induction of behavioral changes [25, 27]. Each MI will be conducted through four phases of conversation comprising: 1) Engage, 2) Focus, 3) Evoke, and 4) Plan [25]. The study will use the dialog of MI guided by Mentha Counselling and will be conducted by a counsellor who experienced MI There will be a 20 minute face-to-face in week 1 and three phone MI sessions (15 min) at weeks 2, 4 and 9 for IIG. For DIG this will take place at weeks 12, 13, 15 and 20.

7.3. Blood collection and storage. Approximately 20 ml of blood will be collected via a venepuncture at T1, T2 and T3 for both groups. Whole blood will be collected into a tube containing anticoagulant and centrifuged immediately after collection or on the same day approximately seven hours later.

Isolation of peripheral blood mononuclear cells (PBMCs) by density gradient configuration using Ficoll-Paque will be used for immune cell functions. PBMCs will be stored in refrigerator not longer than one day and then use flow cytometry to assess the composition of the isolated PBMC populations.

8. Method of data collection and outcome measurements

8.1. Primary outcomes

8.1.1. Psychological health and QoL. Levels of stress, depression and anxiety will be assessed using the DASS 21 [46]. The DASS21 has been validated for breast cancer survivors and has good reliability [47]. In addition, the FACT-B version 4 [48] will be used to measure QoL. This cancer specific questionnaire is well validated and has good reliability and measures physical, social/family, emotional and functional well-being aspects and breast cancer specific conditions [48, 49]. Participant will complete these instruments at baseline; week 1 (T1), week 12 (T2), and week 24 (T3).

8.1.2. Immune function: PBMC cells (white blood cells) will be isolated from blood and PBMC assessed for changes at the cellular level by flow cytometric analysis [50] at baseline; weeks 1 (T1), 12 (T2), and 24 (T3). Cell surface markers, CD40, CD80, CD83, CD86, MHC-I, MHC-II, CD14, CD16, CD206, CD209 will be assessed by flow cytometry technique [50] to determine the changes after the program. In addition, the ratio of type 1 and type 2 T helper (Th1/Th2) cytokines secreted by monocytes and T cells will be determined to understand any cellular changes following exercise activity.

8.2. Secondary outcomes

8.2.1. Average daily step count. Participants will record their own daily steps through the Fitbit Alta HR application, upload their step count on their computer or smartphone and send the data to the researcher by email or phone call weekly. They can also record their steps from the tracker in a provided notebook. Researchers can track an individual's daily step count via Fitbit Alta HR application on a computer or smartphone. The average daily step count will be calculated at baseline at each of the 12 weeks of the intervention program.

8.2.2. Adherence in step tracker usage. The participants' adherence to self-directed physical activity will be evaluated by their compliance by wearing the Fitbit Alta HR. The adherence rate of fitness tracker usage can be an indicator for exercise program feasibility in

breast cancer patients [51]. The adherence will be defined as step count tracker wearing time with data capture (daily
hours and the number of wearing days) [51]. The mean of daily hours and number of wearing

Table 1. Study outcomes measurement for both groups of participants

Outcome measurement	Method	Week 1 Baseline (T1)	Week 12 (T2)	Week 24 (T3)
Primary outcomes				
Psychology health	DASS-21	x	x	x
QoL	FACT-B version 4 questionnaire	x	x	x
Immune cell functions	Isolation of peripheral blood mononuclear cells	x	x	x
Secondary outcomes				
Daily step count/Average activity volume assessment	Step count tracker	x	x	x
Adherence in pedometer usage	Step count tracker wearing time with data capture (daily hours and the number of wearing days)		x	x
Exercise self-regulation;	BREQ2	x	x	x
Exercise barrier and task self-efficacy	Exercise barrier and task self-efficacy rating scale	x	x	x

days per week will be calculated at the end of week 12 and week 24 of self-directed physical activity period [34].

8.2.3. Exercise self-regulation. The participant's self-regulation for exercise will be assessed using the behavioral regulations in exercise questionnaire version 2 (BREQ2) [36] on three occasions. This five level-Likert scale-questionnaire has 19 items assessing exercise self-regulation which consists of five categories: external, introjected, identified, intrinsic and un-motivated[36]. The psychometric properties of the BREQ2 is adequate to assess self-regulation for exercise in breast cancer survivors [52].

8.2.4. Exercise barrier and task self-efficacy. The nine-item rating barrier self-efficacy scale will be used to assess the confidence of participants performing exercise when experienced some difficulties. Task self-efficacy will be assessed with a four items scale. This questionnaire was validated and tested for internal consistency in women with breast cancer during treatment period [37]. Efficacy beliefs will be assessed at the start and end of the trial (see study outcomes measurement in Table 1).

9. Statistical methods

9.1. Sample size estimation and justification

Based on a power of .8, alpha of .05 and large effect size in change in FACT-B (Cohen's d = 2.23) from previous studies [53] we calculated that a minimum of 53 participants are required. Considering a 10-20% drop-out rate in exercise studies we decided to recruit a minimum of 64 participants (n = 32 in each of the two conditions).

9.2. Analysis of data

Baseline descriptive statistics (mean, standard deviation for continuous data and percentage for categorical data) will be used to describe the distribution of personal data and variables between two groups of participants (e.g., age, breast cancer health history, body compositions, and blood pressure). Independent T-test will be used to compare means for continuous data and the Pearson Chi square will be used for testing the difference in distribution of a categorical variable at baseline [54].

Linear-mixed models will be used to identify the relationship between physical activity volume by step counting and mental health (DASS-21), QoL (FACT-B), self-regulation (BREQ2) and self-efficacy at T1, T2 and T3; the relationship between activity volume by step counting and immune biomarker changes at T1, T2, and T3. The models will also be used to control for the effect of covariates or confounding factors and to manage for missing data.

10. Data security and confidentiality

The patient's personal information and health history which are necessary for this research study will be protected for their privacy and confidentiality [55]. All data of participants will be recorded adequately and stored in a secure, password protected databank Agreements involving data ownership and storage will be done between Western health and Victoria University. This study has planned to hold clinical trials research data for 15 years or more based on circumstances [40]. It is possible to keep files of hard copy and electronic files in a research office at Sunshine Hospital. A locked filing cabinet and a computer for research data can only be accessed by agreed members of the research team. More specifically, the researchers will have a backup or reserved storage [40]. For destruction of the data, hard copy will be shredded by hospital and university office's shredder. Digital information will be destroyed by deleting or overwriting the files. According to the protection of participants' privacy, personal, health related data and clinical outcomes will be kept and reported in coded or reversibly anonymised technique. Re-identifiable information will be used for data management (name will be removed and replaced by a code which can be re-identified for relating the different data sets and data verification) [40].

11. Discussion

Self-directed physical activity in this clinical trial is considered a feasible practice in breast cancer survivors. More specifically, the combination of self-monitoring (step count) and MI have been shown to be important strategies for long-term adherence to physical activity behaviour in people living with cancer. This trial, will examine the efficacy of these health behaviour change techniques in self-directed physical activity. This is an important issue because this is a potentially low cost intervention which could be applied and implemented

widely if successful. This study is guided by the Self-Determination Theory [35] and Social Cognitive Theory [29]. We anticipate that those who adhere to the program will be more intrinsically motivated at the end of the trial in comparison to those who do not. We will also explore whether the initial motivational orientation predicts adherence to the physical activity program. In addition, we would anticipate that successful adherence to the physical activity program will be associated with higher levels self-efficacy believes and reduced number of barriers to be physically active.

The primary outcomes of this study focuses on both psychological and physiological changes which can translate positively for their breast cancer clinical outcomes. The study expects the enhancement of their QoL, psychological health and immune biomarkers in 12 to 24 weeks self-directed physical activity by pedometor application combining 12 weeks motivational interviewing.

Abbreviations

PAPHIO study, Physical activity adherence, psychological health and immunological outcomes study; QoL, Quality of life; IIG; Immediate intervention group, DIG; Delayed intervention group; BREQ2, The behavioral regulations in exercise questionnaire version 2; DASS21; A 21-item depression, anxiety and stress scale, FACT-B; the Functional Assessment of Cancer Therapy-Breast, ANOVA; analysis of variance, MI; Motivational interviewing; PBMC; Peripheral blood mononuclear cell; ES; effect size; HREC; Human Research Ethics Committee; CD; Cluster of differentiation

Declarations

Ethics approval and consent to participate.

The research proposal meets the requirements of the National Statement on Ethical Conduct in Human Research (2007). This study protocol (version 7: Date 15 April 2019), participant informed, consent form, recruitment and data collection materials have been approved by Melbourne Health Human Research Ethics Committee (HREC Reference Number: HREC/45268/MH-2018, Melbourne Health Site Reference Number: 2018.339) on 29 April 2019. The study is required to submit annual progress report and any proposed amendment to Melbourne Health HREC. The participants involved in this research must be well-informed and are volunteers. They all will give written consent to participate in this study.

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Chapter 4

PAPHIO study protocol

4b. Amendments to the PAPHIO Study protocol and Adding a new recruiting site

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After the study had suffered the impact of COVID-19 disturbing participant recruitment at breast cancer service clinics in March 2020, we requested two amendments to the study protocol from Melbourne Health Human Research Ethics Committee. The first one was to add a new recruitment site - Improving and Promoting Community Health (IPC Health), in Altona Meadows, Melbourne, Victoria. The other request was for alternative recruitment methods and changes to the brand of pedometer supplied to participants. The details of the protocol amendments and the new recruiting site are described below:

A. The amendment request form for adding a new recruiting site and related documents were submitted on 23 March 2020.

   The definition of the changes included:

   1. The project would like to recruit participants from Breast cancer support group at IPC Altona Meadows by providing the information of project to potential participants. The study is presently occurring at Western Health.

   The reason for change:

   1. There was a low recruitment rate at Western Health over the preceding two months.

B. The amendment request form for alternative recruitment methods and amended protocol were submitted on 12 May 2020.

   The definition of changes included:

   1. The investigators would like to change the brand of material (pedometer) used by participants from Garmin Vivofit2 to Fitbit alta HR.
   2. Adding alternative methods for participant recruitment such as phone calls during scheduled follow-ups by physicians and breast care nurses, as well as social media promotion.
   3. Adding alternative methods for consent and communication with participants during the COVID-19 pandemic, including email, phone call and video call, to

ensure participant safety.

The reason for changes included:

1. The pedometer we proposed to use is out of date and out of stock. So there was a need to order a new brand which is accurate but identical in usage and application as we proposed in the study protocol.
2. During COVID-19 situation that we were required to keep social distancing, the project was unable to recruit new participants by face-to-face meeting.
3. COVID-19 situation and social distancing limited our face-to-face meetings with participants.

The Melbourne Health HREC approved both amendment on 26 June 2020 requests with related documents as the followings:

1. Advertising poster version 4 dated 25 May 2020
2. Letter of invitation to participants at IPC Health version 4 dated 25 May 2020
3. PAPHIO-001 Protocol version 8 dated 20 April 2020
4. Master Adult participant informed consent form version 3 dated 16 April 2019
5. Script of recruitment by email version 1 dated 27 May 2020
6. Script of recruitment by phone call version 1 dated 27 May 2020
7. Script of recruitment by Social media version 1 dated 27 May 2020

The letters of amendment approval from Melbourne Health HREC are illustrated in Figure 1 and 2.

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APPROVAL OF AMENDMENT

03 July 2020

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: 26 June 2020

Addition of Recruiting Site:

- Breast Cancer Support Group- IPC Altona Meadows

Approved Documents:

- Breast Cancer Advertisement Poster, version 04 dated 25 May 2020
- Letter of Invitation to Participant IPC Health, version 04 dated 25 May 2020

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,

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

First in Care, Research and Learning

The Royal Melbourne Hospital · NorthWestern Mental Health · Doherty Institute

Figure 1. The letter of amendment approval from Melbourne Health HREC: Adding IPC Health Altona Meadows as a new recruiting site

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APPROVAL OF AMENDMENT

08 July 2020

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

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Amendment Approval Date: 26 June 2020

Approved Documents:

- PAPHIO-001 Protocol, version 08 dated 20 April 2020
- Master Adult Participant Information Sheet/Consent Form, version 03 dated 16 April 2019
- Recruitment Email, version 01 dated 27 May 2020
- Recruitment by Phone Call, version 01 dated 27 May 2020
- Recruitment by Social Media, version 01 dated 27 May 2020

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

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Figure 2. The letter of amendment approval from Melbourne Health HREC: alternative recruitment methods

Chapter 5

Chapter 5
The pilot results of the PAPHIO study

Chapter preface:

This chapter consists of a pilot analysis, results and discussion of the PAPHIO trial. Additionally, this chapter shows the documents which were approved by the Melbourne Health Human Research Ethics Committee such as the study protocol, participant informed consent form, advertising poster and questionnaires.

Chapter 5

The Pilot results of PAPHIO study

5a. The effect of combined pedometer and motivational interviewing on adherence in self-directed physical activity in breast cancer survivors: A 12 weeks feasibility of randomized controlled trial

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1. Introduction

The American College of Sport Medicine (ACSM) acknowledges that following or adhering to physical activity or exercise recommendation is essential for cancer survivors. However, this also requires testing the safety and effectiveness of specific programs for different populations. The guidelines for the general population for aerobic exercise state, that individuals should engage in at least 150 minutes of moderate-intensity activity or 75 minutes of vigorous-intensity activity weekly. The recommendations for resistance training are a minimum of 2-3 sessions per week [1]. The Clinical Oncology Society of Australia (COSA) state that exercise programs should be included in the standard care of cancer patients [2]. They also recommend that the program should be modified to suit an individual's physical ability, cancer treatment and medical conditions [2].

Despite strong recommendations for physical activity by health care professionals for people living with cancer, some patients and survivors have difficulty adhering to exercise programs [3]. Exercise adherence among breast cancer patients has been shown to be influenced by fatigue, work responsibilities, cancer prognosis, lack of exercise interest and perceived lack of exercise benefit [4].

As such it has been suggested that exercise program for people living with cancers should not be too strict or controlled [3]. In a local community, a simple activities such as walking at light intensity, with a gradually increase to a moderate workload is practical form of exercise for cancer survivors to adhere to [5]. Therefore, the current study, the Physical Activity adherence, Psychological Health and Immunological Outcomes in breast cancer survivors study (PAPHIO study) utilizes a self-directed physical activity program in which breast cancer survivors engage

in self-monitoring and receive motivational interviewing to enhance physical activity adherence.

A self-directed physical activity program in a research study enables an individual to autonomously perform physical activity independent of the supervision by an exercise trainer [6]. However, there is a need for researchers to explain the exercise program clearly to the participant and requires participants to take responsibility in completing the prescribed activity [7]. Although partially supervised home-based exercise, one common self-directed physical activity program, for cancer patients seems to be flexible for adherence to the program, this partial coaching -based exercise program can in fact promote exercise adherence through social or peer support [8].

Physical activity or exercise programs which integrated behavioural change strategies are effective in promoting short-term exercise adherence in breast cancer surviors. For example, phone counselling and self-monitoring have been shown to produce larger improvements in physical activity behaviour or adherence [9].

Self-monitoring is an important element of self-regulation theory and effective self-monitoring can enhance task performance and exercise engagement [10]. Exercise using a technological device such as mobile phone application for self-monitoring can increase weekly exercise duration in adults [11]. Some studies have used pedometers or accelerometers for physical activity self-monitoring and self-record [9]. Likewise, motivational interviewing (MI) can support individuals' behavioural change in tandem with self-monitoring and self-evaluation [12]. Application of MI in a 12-week multifaceted lifestyle program was reported to improve physical activity behaviour and aerobic fitness in overweigh breast cancer survivors [13].

Physical activity adherence, a critical factor in achieving the outcomes ~~in~~ of physical activity promotion projects [14], has been defined as an individual's behaviour regarding a physical activity recommendation [4]. Besides the benefits to physical activity motivation, step trackers can be used to track adherence to exercise goals of participants in research studies [15]. The step tracker can also be used for the assessment of a dose-response relationship. For example, some studies use activity trackers to record participants' daily step count, exercise intensity and time spent being active [15]. A randomised controlled study reported the median percentage of the days wearing activity tracker at least 10 hours per day as a proxy for physical activity adherence in postmenopausal women [15].

This pilot study is a preliminary analysis of the PAPHIO trial, approved by the Melbourne Health Human Research Ethics Committee on 29 April 2019 (HREC reference number: HREC/45268/MH-2018) and authorised to be conducted at Western Health Hospital, Melbourne, Australia by the Western Health, Office for Research on 4 December 2019. The randomised controlled trial was registered at the Australia New Zealand Clinical Trials Registry (Number: ACTRN12619001271190).

This pilot randomised controlled study aimed to assess the feasibility of two motivation strategies between step tracker and MI for promoting physical activity adherence into a self-directed physical activity in female breast cancer survivors.

2. Materials and Methods

2.1. Study design

The PAPHIO study was designed as a 24 weeks-two armed-randomised-controlled trial with crossover design conducted at the Brest Cancer Service Clinic at Sunshine Hospital, Western Health, Melbourne, Australia [16]. However, the pilot study reported the first phase that was lasting 12 weeks for self-directed physical activity using a pedometer in both intervention and control groups. The participants beginning the trial in the intervention group (Immediate intervention group; IIG) received 4 sessions of MI across 12 weeks (1 by face-to-face interviewing at week 1 and 3 times by phone call at weeks 2, 4 and 9). The participants in the control group (Delayed intervention group; DIG) performed the self-directed physical activity without receiving MI over 12 weeks. The groups then swap interventions, with no extra week washout period in between.

After reading the participant information and giving informed consent each participant was randomly allocated into one of two groups by simple randomisation using a table created by computer software and sealed opaque envelopes. The randomisation was conducted by an associate investigator who was blinded to the health history of participants.

2.2. Participants

The study recruited female breast cancer survivors who were within three years of diagnosis and at least six months after completion of primary treatment, including surgery, chemotherapy and/or radiotherapy. Potential participants were diagnosed with stage 0 to 3 breast cancer or ductal carcinoma *in situ* (DCIS), aged 18 and older. Those who were or had previously been prescribed hormonal therapies such as tamoxifen and aromatase inhibitors, or immune targeted therapies (Herceptin) were elegible to participate. The study also recruited participants who were

unable to read/write English but were literate and English speaking. The researcher would read all documents (informed consent form and questionnaires) for participants who cannot read English.

Exclusion criteria were those who were undergoing active breast cancer treatment (surgery, chemotherapy and radiation), or were less than six months post active treatment, as well as those with cognitive impairment, cancer recurrence or metastasis.

2.3. Recruitment

The pilot study recruitment is ongoing, but this data set represents those recruited in the 11 months between February and December 2020. Surgeons, clinicians, oncologists and breast care nurses were requested to inform potential participants of the study. Researchers provided study flyers to breast care nurses at the Breast Cancer Clinic and asked them to display or give the flyers to eligible survivors.

Recruitment process paused for two months in April to May 2020 due to the global COVID-19 pandemic after which the project started recruitment again by phone call, email and social media in June 2020 when the outbreak of the disease in Victoria, Australia was controlled. The clinicians and breast care nurses were able to introduce the project to eligible survivors during follow-up appointments and asked the potential participants' permission for a researcher's direct contact by phone call or email. The recruitment by phone call, email and social media was approved by amendment by Melbourne Health Human Research Ethics Committee (HREC) in June 2020.

The study also added a new participant recruitment site at Improving and Promoting Community Health (IPC health) Altona Meadows, approved by Melbourne Health HREC in June 2020.

3. Study intervention

3.1 Self-directed physical activity

All participants were given a pedometer (Fitbit Alta HR) and a study researcher prescribed and explained the 24-week pedometer-based activity program. Participants were shown how to operate the Fitbit and its associated application through smartphone or computer. At week 1 (baseline or T1), all participants were advised to assess and record their physical activity using the Fitbit to establish their baseline step count. They were then asked to perform physical activity such as walking and jogging at their own cadence as tolerated and to wear the Fitbit during the daytime or when they performed physical activity throughout the 24 weeks. Then they were advised to progressively increase their daily steps at moderate intensity which was

described as awareness of some exertion but not enough to limit speech during physical activity (in line with recommendations from the department of health, Australian government) [17]. All participants were informed that the researcher would request the participants' step count and tracker usage time records via the Fitbit application at baseline (T1), week 12 (T2), and week 24 (T3).

3.2. Motivational interviewing

MI was used to enhance physical activity motivation in participants by a two-way communication aimed at being friendly and supportive [18, 19]. Each MI session consisted of four defined phases of conversation: 1) Engage, 2) Focus, 3) Evoke, and 4) Plan [19]. The study used the MI dialog protocol designed by Mentha Counselling and sessions were conducted by a counsellor experienced in using MI for behavioural change. There was a 20-minute face-to-face session of MI at week 1 and three 15 minutes phone call sessions at weeks 2, 4 and 9 for the intervention group. The control group initially had no MI, but after crossover, received one face-to-face and three phone calls sessions at weeks 12, 13, 15 and 20, respectively. Face-to-face MI was conducted in a private room at the breast cancer service clinic, Sunshine hospital, Melbourne Australia. Throughout the four phases of MI intervention, the study took note of the conversation by hand-writing during face-to-face MI and phone call MI. However, the study made a formal records of an individual face-to-face MI and interpreted the participants' words representing the change talk and sustain talk in a word document [20]. The project could conduct face-to-face sessions in February 2020 but after COVID-19 outbreak these were conducted via video call (zoom or equivalent applications).

4. Study outcomes

The aim of the pilot study was to assess the feasibility of a 12-week self-directed physical activity program using pedometer and motivational interviewing to enhance physical activity adherence amongst female breast cancer survivors. The second aim was to evaluate the efficacy of pedometer and motivational interviewing on physical activity adherence (assessed by daily steps and the duration of pedometer wearing), quality of life, psychological health, exercise self-regulation (intrinsic and extrinsic motivation) and exercise barrier and task self-efficacy in female breast cancer survivors.

4.1. Feasibility of the study. Number of recruited participants were recorded between February and December 2020 and retention rate and participation in motivational interviewing sessions were recorded through 24 weeks of the study duration.

4.2. The efficacy of pedometer and motivational interviewing. Efficacy of pedometer and motivational interviewing were assessed by analysis of the following outcomes: daily steps, the duration of pedometer wearing, psychological health score, quality of life (QoL), exercise self-regulation and exercise self-efficacy at baseline and week 12.

Daily steps. Participants recorded their own daily steps via Fitbit Alta HR and its application on their smartphone or computer. The researcher requested participants to capture the display of daily steps for seven days and send the records to the researcher via phone or email at weeks 1 and 12.

Daily steps assessed by a pedometer or an accelerometer in general adults was used for classification of individual physical activity levels as followed: 1) sedentary: less than 5,000 steps/day (basal activity less than 2,500 and limited activity between 2,500 and 4,999 steps/day); 2) low active: between 5,000 and 7,499 steps/day; 3) somewhat active: between 7,500 and 9,999 steps/day; 4) active: between 10,000 and 12,499 steps/day and 5) highly active: more than 12,500 steps/day [21].

Self-report daily hours wearing pedometer and number of wearing day per week. The adherence to activity tracker usage can be applied to examine exercise program feasibility in breast cancer survivors [22]. Adherence was defined as time wearing step count tracker with data capture (daily hours and the number of wearing days) [22]. The researcher asked the participants to report daily hours wearing pedometer and the number of days worn weekly at the end of week 12.

Quality of life. The Functional Assessment of Cancer Therapy-Breast (FACT-B) questionnaire version 4 [23] was used to measure participant QoL. This questionnaire is validated and reliable for the measurement of physical, social/family, emotional and functional well-being aspects in breast cancer patients [23, 24]. Participants were asked to complete the questionnaire at baseline; week 1 and week 12. The FACT-B and physical, social/family, emotional and functional well-being and the breast cancer subscale (BCS) scoring were assessed with the functional assessment of chronic illness therapy (FACIT) administration and scoring guidelines, with higher scores indicating better QoL.

Psychological health. The 21-item depression, anxiety and stress scale (DASS-21) was used for assessment of depression, anxiety and stress levels [25]. The DASS21 has been tested for validity and reliability in breast cancer survivors [26]. Participants were asked to complete the questionnaire at baseline; week 1 and week 12. Scoring of each subscale (depression, anxiety

and stress) was performed by summation of each subscale and multiplication by 2. Higher scores in each scale indicates the severity of mental health disturbance.

Exercise self-regulation. The participant's self-regulation of physical activity was assessed using the behavioural regulations in exercise questionnaire version 2 (BREQ2) [27] at baseline, week 1, and week 12. A five level-Likert scale was used with 0 = not true for me and 4 = very true for me [27]. Scoring of each subscale was performed by weighting and summation. Positive scores indicate higher autonomy regulation, whereas negative scores represent more extrinsic control.

Exercise barrier and task self-efficacy. The nine-item rating barrier self-efficacy scale was used to assess participants' confidence in performing physical activity when experiencing obstacles. Task self-efficacy was assessed for the confidence in four physical activity conditions. This questionnaire was validated and tested for internal consistency in women with breast cancer during treatment period [28]. The efficacy beliefs measured as percent confidence in doing exercise under some situations were assessed at baseline; week 1 and week 12.

5. Statistical analysis

Baseline descriptive statistics (mean, standard deviation for continuous data and percentage for categorical data) were used to describe the distribution of personal data and variables between the two participant groups (e.g., age, breast cancer health history and daily steps at week 1). The distribution normality of variables was assessed by Shapiro-Wilk test. Independent T-test or Mann-Whitney U test were used to compare means for continuous data based on their distribution. The Pearson Chi square test was used for testing the differences in distribution of categorical variables at baseline [29].

The effect of the intervention (self-directed physical activity using a pedometer + motivational interviewing) compared to the control group self-directed physical activity using a pedometer) on continuous outcomes including daily steps, mental health (DASS-21), QoL (FACT-B), self-regulation (BREQ2) and self-efficacy over 12 weeks were evaluated by nonparametric test for repeated measures Friedman ANOVA modelling because of low sample size at follow-up 12 weeks. The effect size (ES) for the change from baseline between groups was evaluated by Cohen's effect size; d = (mean of change from baseline of IIG group- mean of change from baseline of DIG group)/ pooled standard deviation.

6. Results

6.1. The Feasibility of the study

Participant flow and baseline comparisons

Over the 11months period of recruitment between February and December 2020, 17 participants gave consent to participate in the study. They were randomly allocated into either IIG (n=9) or DIG (n=8) (Figure 1). They received a pedometer (Fitbit Alta HR) and self-directed physical activity prescription and then they performed baseline assessments at week 1. The recruitment rate was 1.5 participants per month. There were 14 participants recruited from breast cancer clinic service, Western Health, Melbourne (82.35%), 2 participants recruited by social media advertising (11.76%), and 1 participant recruited from breast cancer support group, IPC health Altona Meadows, Melbourne (5.89%).

The retention rate was 82.35 % (14/17). While the intervention period was ongoing, 3 participants dropped out (17.65%). One participant in the IIG withdrew from the study because it was not convenient for her to use a pedometer and its application on a smartphone or computer. Two participants (11.76%) in the DIG were lost to follow-up at 12 weeks of intervention and could not complete the assessments at week 12. A researcher had a chance to communicate with the two dropped out participants in control group (DIG) at week 12 for their second assessment and continuing in phase two with MI intervention. They postponed the assessment several times. Eventually the researcher could not contact them by phone.

Sixteen out of seventeen (94.12%) participants could reliably operate the pedometer and synchronise it with the Fibit application on their smartphone or computer. They could use the pedometer and recorded their steps in the first week. They could show the display of weekly records via the phone application to the researcher at the end of week 1.

Baseline characteristics and daily steps of participants in both groups (intervention group: n = 8; control group: n = 8) are illustrated in Table 1. The average age of participants in the IIG and DIG were 46.4 years ($\pm$ 10.8) and 50.3 years ($\pm$ 5.4) respectively. Five participants (62.5%) in the intervention group and 3 participants (37.5%) in the control group were diagnosed with stage 2 breast cancer, whereas 2 participants (25.0%) in the intervention group and 2 participants (25.0%) in the control group were diagnosed with stage 3 malignancy.

Four participants did not report their stage of breast cancer but were screened for eligibility by a clinician or breast care nurse. The mean daily steps of participants in intervention and control groups were 7,484.18 $\pm$ 3048.11 and 9,941.63 $\pm$ 3918.21 respectively. There were no

significant differences between groups in terms of age, breast cancer health history and daily steps at baseline (week1).

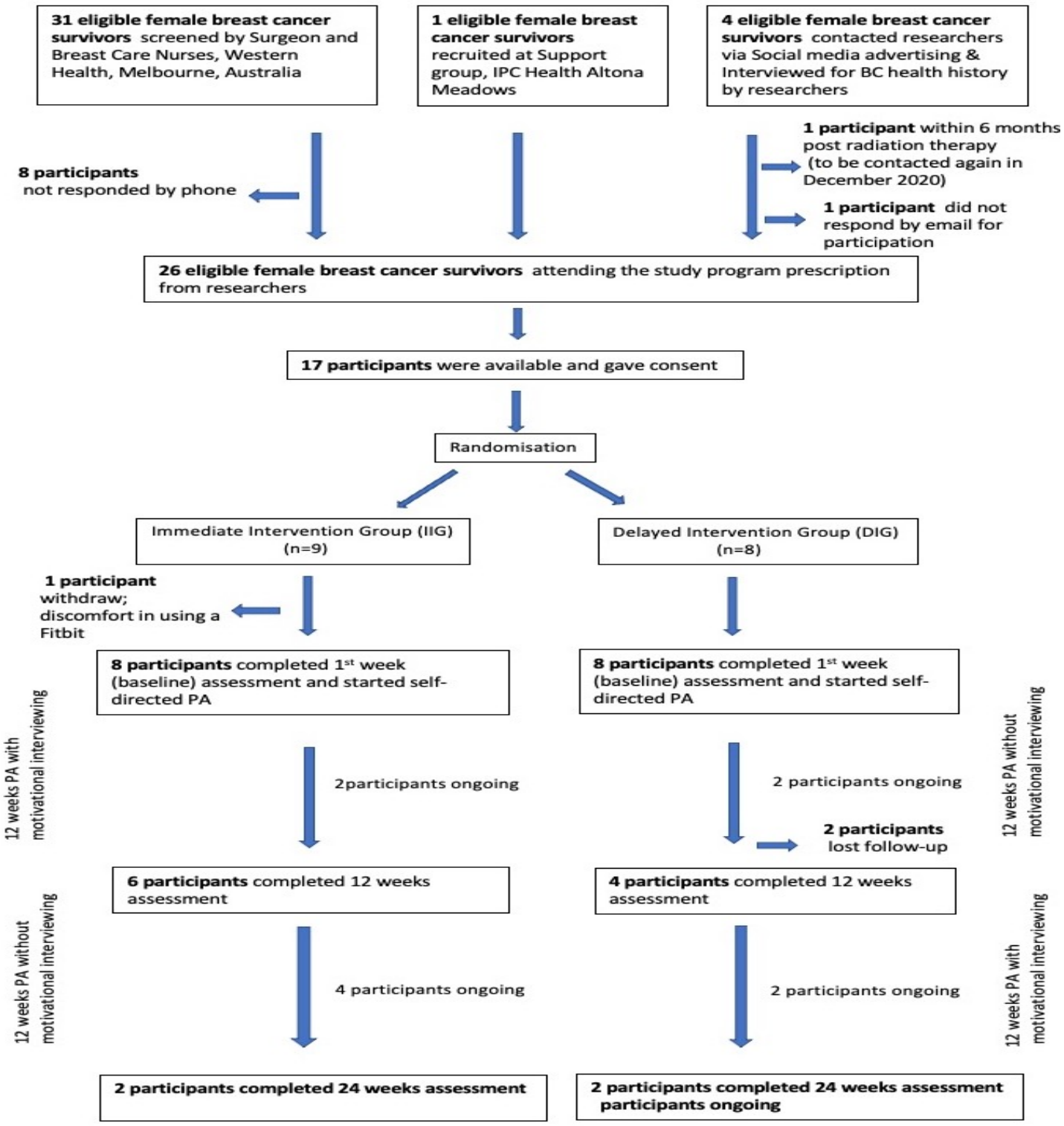

Figure 1. Flow of participants through 24 weeks self-directed physical activity between February and the 2nd week of December 2020

Table 1 Baseline participants characteristics and daily steps

	Intervention group (IIG) (N=8)		Control group (DIG) (N=8)		*p*
	Mean ± SD	**N (%)**	**Mean ± SD**	**N (%)**	
Age (years)*	46.4 ± 10.8		50.3 ± 5.4		0.30
Time since diagnosis (years)*	1.50 ± 0.76		1.67 ± 0.52		0.65
Breast cancer stage#					0.47
Stage 1		0		0	
Stage 2		5(62.5%)		3(37.5%)	
Stage 3		2(25.0%)		2(25.0%)	
Unknown		1(12.5%)		3(37.5%)	
Primary treatment#					0.62
Surgery		8 (100%)		8(100%)	
Chemotherapy		2 (25.0%)		1(12.5%)	
Radiotherapy		1(12.5%)		2(25.0%)	
Combination of chemotherapy and radiotherapy		5 (62.5%		4(50.0%)	
Nether		0		1(12.5%)	
Additional treatment#					0.35
Tamoxifen		5(62.5%)		3(37.5%)	
Aromatase inhibitors		1(12.5%)		1(12.5%)	
None		2 (25%)		4(50.0%)	
Daily steps*	7484.18 ± 3048.11		9941.63 ± 3918.21		0.18

SD= Standard deviation; *Evaluated by independent T-test; # Evaluated by Pearson Chi-square

Table 2 Baseline score of QoL, Psychological health, Exercise self-regulation and Exercise barrier and task self-efficacy between groups

	Intervention group (IIG) (N=8)	Control group (DIG) (N=8)	*p*
	Mean ± SD	**Mean ± SD**	
Quality of life (QoL)			
FACT-B*	92.75 ± 24.89	110.13 ± 24.93	0.19
FACT-G*	72.25 ± 17.20	84.13 ± 17.20	0.19
FACT-B TOI*	59.63 ± 18.34	69.0 ± 16.56	0.30
PWB*	20.29 ± 5.74	21.25 ± 5.20	0.78
SWB*	17.75 ± 9.32	23.16 ± 4.63	0.16
EWB*	16.13 ± 5.14	18.00 ± 5.76	0.50
FWB*	18.63 ± 5.73	21.75 ± 5.20	0.27
BCS*	20.50 ± 8.78	26.00 ± 8.43	0.22
Psychological health (DASS-21)			
Depression#	10.00 ± 10.58	4.25 ± 6.36	0.28
Anxiety#	10.00 ± 9.01	5.75 ± 8.31	0.16
Stress*	15.50 ± 5.63	8.50 ± 11.05	0.13
Exercise self-regulation (BREQ2)			
Amotivation#	-8.25 ± 10.73	-1.88 ± 5.30	0.11
External motivation*	-7.00 ± 5.55	-8.25 ± 8.58	0.74
Introjected motivation*	-5.00 ± 3.59	-5.75 ± 4.10	0.70
Identified motivation*	21.63 ± 5.95	25.00 ± 2.83	0.17
Intrinsic motivation*	33.38 ± 9.41	34.50 ± 8.93	0.81
Exercise barrier self-efficacy*	35.28 ± 24.71	36.82 ± 12.05	0.88
Exercise task self-efficacy*	59.06 ± 23.64	60.94 ± 25.63	0.88

The distribution of data assessed by Shapiro Wilk test. * The data is parametric: assessment between groups using independent T-test; # The data is non-parametric: assessment between groups using independent-samples Mann-Whitney U test.

Abbreviations: QoL=Quality of life, FACT-B= the Functional Assessment of Cancer Therapy Breast Cancer, FACT-G = the Functional Assessment of Cancer Therapy General, FACT-B TOI = FACT-B Trial Outcome Index, PWB= Physical Well-Being, SWB=Social/Family Well-Bbeing, EWB=Emotional Well-Being, FWB= Functional Well-Being, BCS= Breast Cancer Subscale, DASS-21= The Depression, Anxiety and Stress Scale-21 items, BREQ2= Behavioral Regulation in Exercise Questionnaire-2,
FACT-G= PWB+SWB+EWB+FWB; FACT-B= FACT-G +BCS; FACT-B TOI = PWB +FWB +BCS

Baseline score of QoL: the functional assessment of cancer therapy breast cancer (FACT-B) and subscale, psychological health (DASS-21), exercise self-regulation, exercise barrier and task self-efficacy between two groups are shown in table 2. There were no significant differences in mean scores of QoL, psychological health, exercise self-regulation and exercise barrier and task self-efficacy between intervention and control group at baseline.

6.2. The efficacy of pedometer and motivational interviewing:

The effects of 12 weeks of self-directed physical activity applying pedometer and motivational interviewing on physical activity adherence (daily steps and time wearing pedometer between groups) are shown in table 3. The number of participants reporting in the IIG and DIG at 12 weeks of follow-up for physical activity adherence were 6 and 5, respectively. The mean of pedometer wearing time per day in IIG and DIG at week 12 were not different (15.33 hours $\pm$ 5.16 vs 13.0 hours $\pm$ 5.10; p = 0.47). Likewise, participants of both groups wore a pedometer 6-7 days weekly. The mean days wearing the pedometer per week were 6.67 $\pm$ 0.82 and 6.8 $\pm$ 0.45 in intervention and control group respectively, p = 0.75. There was no significant effect of group by time on daily steps (Freidman test chi-squared = 2.5, p =0.47,) at follow-up 12 weeks. However, Cohen's effect size of intervention for the change in daily step from baseline is high (d= 2.1).

There were 6 participants in both groups at 12 weeks follow-up reporting QoL, psychological health, exercise self-regulation and exercise barrier and task self-efficacy. Regarding scores in QoL, no group by time effects were detected for FACT-B (Freidman test chi-squared = 4.0, p =0.26, d= -4.8), FACT-G (Freidman test chi-squared = 5.85, p =0.12, d= -3.84), FACT-B TOI (Freidman test chi-squared = 5.2 p =0.16, d= -2.01) and BCS (Freidman test chi-squared = 5.44, p =0.14, d= -1.36).

There was a significantly higher depression score in IIG group at 12 weeks (chi-squared =5.0, p = 0.025, d=1.53, but there was no difference on anxiety and stress score (chi-squared = 2.5, p = 0.47, d = 3.76 and chi-squared = 7.07, p =0.07, d= 1.26, respectively).

There was no effect of group by time on exercise self-regulation ranging from external to internal motivation; amotivation (chi-squared = 3.0, p = 0.39, d= 0.86), external motivation (chi-squared =0.2.41, p = 0.49, d= -1.47), introject motivation (chi-squared = 1.29, p = 0.73, d= -10.75), identified motivation (chi-squared =2.84, p = 0.42, d= 1.89) or intrinsic motivation (chi-squared = 0.27, p = 0.96, d= -2.21).

Exercise barrier and task self-efficacy were not significantly changed by the effect of group by time at chi-squared = 0.20, p = 0.98, d= 1.28 and chi-squared = 4.2, p =0.24, d= 0.64, respectively.

There was a negative correlation of FACT-B score (QoL) and DASS-21 score (depression, anxiety and stress). Pearson correlation (r) between FACT-B and depression was -0.809 (p=0.00), FACT-B and anxiety was -0.736 (p=0.00), FACT-B and stress was -0.673 (p=0.00). The study also found a reverse correlation between score of FACT-B and amotivation of BREQ2 (negative scoring), r was -0.517 (p=0.005), a negative correlation of depression of DASS-21 and identified regulation of BREQ2 was -0.483 (p=0.009). A negative correlation of stress score of DASS-21 and intrinsic regulation score of BREQ2 was found at r = -0. 376 (p=0.049). There was no correlation of DASS-21 score and exercise barrier and task self-efficacy. The Pearson correlation of DASS-21 score (depression, anxiety and stress) and FACT-B (QoL), exercise self-regulation (BREQ2), and exercise barrier and task self-efficacy was illustrated in Table 4.

Table 3 The descriptive analysis in mean and SD of PA adherence (daily steps and pedometer application), score of QoL (FACT-B and subscales), Psychological health (DASS-21), exercise self-regulation and exercise barrier and task self-efficacy at baseline and 12 weeks follow-up.

	Intervention group (IIG)		**Control group (DIG)**		***P***
	Baseline (N=8)	**Follow-up 12 weeks (N=6)**	**Baseline (N=8)**	**Follow-up 12 weeks (N=6)**	
	Mean ± SD	**Mean ± SD**	**Mean ± SD**	**Mean ± SD**	
PA adherence #					
Daily steps	7484.18 ± 3048.11	9860.10 ± 4203.00	9941.63 ± 3918.21	10615.16 ± 4332.97	0.47
Daily hours wearing pedometer		15.33 ± 5.16		13.00 ± 5.10	0.47
Days per week wearing pedometer		6.67 ± 0.82		6.80 ± 0.45	0.75
Quality of life (QoL)					
FACT-B	92.75 ± 24.89	94.33 ± 21.91	110.13 ± 24.93	121.67 ± 23.76	0.26
FACT-G	72.25 ± 17.20	73.67 ± 15.29	84.13 ± 17.20	93.83 ± 14.80	0.16
FACT-B TOI	59.63 ± 18.34	60.88 ± 13.91	69.00 ± 16.56	78.00 ± 15.96	0.16
PWB	20.50 ± 5.35	21.33 ± 5.05	21.25 ± 5.20	24.17 ± 4.67	0.33
SWB	17.75 ± 9.32	17.00 ± 7.27	23.16 ± 4.63	24.50 ± 2.59	0.1
EWB	16.13 ± 5.14	16.50 ± 3.21	18.00 ± 5.76	19.17 ± 6.55	0.52
FWB	18.63 ± 5.73	18.83 ± 4.45	21.75 ± 5.20	26.00 ± 2.61	0.25
BCS	20.50 ± 8.78	20.67 ± 7.45	26.00 ± 8.43	27.83 ± 9.54	0.14

Psychological health (DASS-21)					
Depression	10.00 ± 10.58	11.33 ± 9.77	4.25 ± 6.36	0.67 ± 1.03	0.025*
Anxiety	10.00 ± 9.01	11.67 ± 8.89	5.75 ± 8.31	2.33 ± 5.72	0.47
Stress	15.50 ± 5.63	14.33 ± 6.38	8.50 ± 11.05	3.67 ± 5.99	0.07
Exercise self-regulation (BREQ2)					
Amotivation	-8.25 ± 10.73	-6.00 ± 10.56	-1.88 ± 5.30	-1.00 ± 2.45	0.39
External motivation	-7.00 ± 5.55	-5.33 ± 5.32	-8.25 ± 8.58	-6.33 ± 9.83	0.49
Introjected motivation	-5.00 ± 3.59	-7.33 ± 3.89	-5.75 ± 4.10	-5.50 ± 4.28	0.73
Identified motivation	21.63 ± 5.95	26.67 ± 2.07	25.00 ± 2.83	25.33 ± 3.93	0.42
Intrinsic motivation	33.38 ± 9.41	34.00 ± 8.20	34.50 ± 8.93	37.00 ± 9.42	0.92
Exercise barrier self-efficacy	35.28 ± 24.72	46.56 ± 22.34	36.82 ± 12.05	40.19 ± 22.06	0.98
Exercise task self-efficacy	59.06 ± 23.64	61.67 ± 26.63	60.94 ± 25.63	60.83 ± 20.17	0.24

SD= Standard deviation

PA adherence at follow-up 12 weeks of DIG group; N=5

* $p < 0.05$

Table 4. The Pearson correlation (r) of DASS-21 score (depression, anxiety and stress) and FACT-B (QoL), exercise self-regulation (BREQ2), and exercise barrier and task self-efficacy

	DASS-21					
	Depression		Anxiety		Stress	
	r	p	r	p	r	p
FACT-B	-0.809***	0.000	-0.736***	0.000	0.673***	0.000
Exercise self-regulation						
Amotivation	-0.517**	0.005	-0.260	0.18	0.189	0.336
External regulation	-0.191	0.331	0.117	0.554	0.081	0.681
Introject regulation	0.209	0.286	0.208	0.287	-0.004	0.984
Identified regulation	-0.483**	0.009	-0.129	0.514	-0.186	0.343
Intrinsic regulation	-0.002	0.99	-0.083	0.676	-0.376 *	0.045
Exercise barrier self-efficacy	0.087	0.66	0.174	0.375	0.056	0.779
Exercise task self-efficacy	0.49	0.806	-0.167	0.395	0.147	0.454

Abbreviations: FACT-B= the Functional Assessment of Cancer Therapy Breast Cancer, QoL=Quality of life, DASS-21= The Depression, Anxiety and Stress Scale-21 items, BREQ2= Behavioral Regulation in Exercise Questionnaire-2.

*** $p < 0.001$, ** $p < 0.01$, *$p < 0.05$

Feasibility of the MI intervention was assessed by the attention rate of participants as schedule. All participants could attend MI sessions. However, some MI sessions were postponed during the intervention phase. Unexpected situations such as mild illness or a minor surgery of participants were the cause of the MI postponement for a few weeks.

The study found that some participants conveyed their change talk by their intention to perform physical activity. For example, participant code IIG1 said "I would like to get back to work and being active like walking after operation. My exercise would start next week" and participant code IIG 4 said "I have committed myself to maintain physical activity at least 2 to 3 times a week".

Some participants showed their change talk by describing the advantages to the change such as participant code IIG 3 said "It's important to stay around longer and control my weight" and participant code IIG6 said "I expect the benefits for my body and mind. GP also suggested to me to stay active. Exercise would improve my immune system. I hope exercise could make me sleep well at night". One participant, code IIG showed her optimism on change by saying "I will keep thinking exercise is a part of me". Sustain talk could also be detected during the MI intervention. Most participants showed some obstacles to change. For example, participant code IIG1 said "but sometimes during exercise I feel tired then I know I need to slow down" and participant code IIG4 said "I sometimes have procrastination which blocks me to do something I already planned like exercise and sometimes I don't want to go out for exercising because the weather is so cold." In addition, participant code IIG6 said "Some days I might not be able to exercise because of my work or my difficulty in sleeping last night". One participant in the control group, participant code DIG2 (after crossing over at week 12) declared in the interview that lockdown in May 2020 stopped her going out for walking. She said "Since the lockdown I can't go out and I have low activity at home, and I gained almost 10kgs in weight.. Next week in New Zealand they will lift lockdown to level 2 so I can go out for jogging or biking" (This participant temporarily moved to New Zealand to care for her parents a few weeks before the lockdown in May 2020).

Change talk or statement with commitment to change and sustain talk or statement with obstacle to change of 12 participants (8 participants from IIG group and 4 participants from DIG group) from their conversation during face-to-face MI by a video call or equivalent applications) was illustrated in table 5.

Table 5. Interpretation of participants' change talk and sustain talk from 30 minutes face-to-face MI (by video call)

Participant	Change talk			Sustain talk
	Intention to change	Advantage to change	Optimism for change	Obstacle to change
IIG1	"I would like to get back to work and being active like walking after operation. My exercise will be started next week."	"I know exercise is good for breast cancer, it can prevent the disease recurrence."	"My reason for exercise is for feeling good about myself (she started crying)." "I don't think exercise is bad, walking with Fitbit can push me to do exercise like it motivates me to do more and more."	"Sometimes during exercise, I feel tired then I know I need to slow down."
IIG3	"If the weather is poor then I will aim to use the treadmill"	"To stay around longer, want longevity and stay active" "It's important to stay around longer and control my weight".	"Feel great if I could do this, it's awesome if I can maintain" "I look forward to it, it's a good aim to target for"	"It can depend on the weather."
IIG4	"I have menopause because of taking medication then I have gained weight. So, I have committed myself to maintain physical activity at least 2 to 3 times a week."	"Exercise makes me healthy, feeling better, more energy and thinking positive"	"I think exercise is my responsibility to take care myself after breast cancer diagnosis.	"I sometimes have procrastination which blocks me to do something I already planned like exercise." "Sometimes I don't want to go out for exercising because the weather is so cold."
IIG5	"I would have a commitment to exercise. I would like to restart my exercise."	"In long term, I think exercise will help my mentally refreshing and lose couples kilogram of body weight."	"I will keep thinking exercise is a part of me and it is fantastic to be motivated to do exercise every day."	"recently, my mom passed away and I was suffering so I stop exercise for several months. It was so sad, I cried every day."
IIG6	"I commit to continue walking, I will do exercise for myself. I expect the benefits on my body and mind. GP also suggests me to stay active."	"Exercise will improve my immune system. I hope exercise can make me sleep well at night"	"I hope I am going well in walking with Fitbit. It is good I like it."	"Some days I might not be able to exercise because of my work or my difficult sleeping last night"
IIG7	"I will be disciplined and strictly for exercise like I can see my self-worth before I got cancer."	"I am aware of my health. Exercise can improve my health and prevent cancer recurrence. My doctor suggested me to exercise at least 30 minutes per day"	"I would like to be active again, to lose 9 to 14 kg of my weight. Bring back my passion is very challenging"	"It may be difficult for me because I know my motivation is very low now." "It seems to be my tough time like I need to do but sometime my body is not ready to do."

Participant	Change talk			Sustain talk
	Intention to change	Advantage to change	Optimism for change	Obstacle to change
IIG8	"I gave 7 to 8 out of 10 for how I am ready to exercise"	"It relieves my lower back pain and help my brain in thought" "I think it should make my life better. It would prevent breast cancer recurrence"	"I feel like when I am more active, I am thinking positive and I am not a down person" "I could enjoy my life, my stuff and taking care kids. I enjoy when going out and do exercise"	"Weather really affects. If it is not too cold, I will go out and walking"
IIG9	"9 out of ten for how I am ready to exercise" "If I want to go, I will go, that is me" "I promise myself for daily active working like planting, gardening and cleaning."	"I expect to lose my weight."	"I can do it by myself, I don't know why other people don't go and work out. They miss it."	"Sometimes so much work to do for my family."
DIG1	"This is my commitment to keep going on exercise." "I have my goal, I will make 15,000 steps a day next week."	"It is good for my health to do exercise. I read some articles saying exercise is good for women with breast cancer"	"I think exercise will make me fit and healthy and then I will be happy."	"I didn't go out for exercise over last 2-3 weeks because I was aware of coronavirus." "Sometimes I was so tired from work because my shift was 8 hours."
DIG2	"I will exercise more next week because the country is lifting lockdown. I am ready to continue exercise with Fitbit."	"When I do exercise, I can lose my weight, and this makes me confident when I meet with other people"	"To make myself looking good. I decide to continue exercise like I have inspiration to do it."	"Someday, I feel too tired to exercise if I have about 8 hours shift working." "Last few weeks, I reduced my movement because of lockdown."
DIG3	"I hope I will do more than 10,000 steps in next few weeks and will go gym for weight training when it re-open. I think I can push myself."	"I know it makes me have well-being and I would like to be healthy for my two kids."	"I am okay, I like exercise. It is good for health. My mood is stable, and I am feeling happy." "I am already confident to do exercise. I have compassion for exercise by myself."	"Sometimes it depends on my energy level. I won't do exercise on the day when I was so tired from work."
DIG4	"My husband would like me to do exercise and he also motivates me to do." "I will continue and increase walking with Fitbit but I need to be motivated."	"I hope if I keep continued exercise, it will be good for my breast cancer and medical conditions. It can prevent my cancer recurrence."	"I am okay with exercise like this" "Exercise can help me change my negative thought to positive outlooks and stay healthy"	"Over the last three months, I slowly increased my steps. I didn't go out for walking because of lockdown and cool weather."

7. Discussion

The results of this pilot randomized study indicate that the feasibility and efficacy of 12 weeks of self-directed physical activity using the step tracker or pedometer (Fitbit Alta HR) and motivational interviewing in female breast cancer survivors are limited by COVID-19 outbreak in 2020. The feasibility which was assessed by recruitment, retention rate and participation in the MI intervention was affected by lockdown in Melbourne between March and December 2020. The study could not detect the efficacy of the 12 weeks self-directed physical activity and MI intervention was evaluated by on physical activity adherence, physical activity volume by weekly step counts and step tracker wearing time (hours per day and days per week), and the improvement of QoL and mental health in female breast cancer survivors due to low number of participants. The pilot study did not analyse immunological biomarkers due to cost effectiveness in assay kit application. We will analyse them when we can achieve the target number of participants.

7.1. The recruitment and feasibility of 12 weeks self-directed physical activity using a pedometer and MI intervention

The recruitment rate in 11 months (February to December 2020) of the current study was low (1.5 participants per months) when compared to similar previous RCT studies with an average recruitment rate of 4 participants per month, ranging from 6 and 14 months [30]. The recruitment in this study was significantly impacted by the global outbreak of COVID-19 in March 2020 of the time the study had only been running for a month. However, COVID-19 was largely able to be controlled over the last 10 months in the state of Victoria, Australia and the project was approved for non-face to face recruitment methods such as phone call, email and social media. Afterwards the project was able to continue recruiting though the recruitment rate was subsequently very low. In addition, some breast cancer survivors refused to participate because of family and work issues.

The main source of participant recruitment over the year was the breast care clinic service of Western Health (14 out of 17 or 82.35% of participants). The clinic limited hospital accessibility of breast cancer survivors but provided a follow up by phone call instead. The study had strong cooperation in participant recruitment from the breast care nurses and clinicians of Western Health, Melbourne, Australia. The nurses and clinicians were able to screen for the eligibility of participants and introduce the project to them. They voluntarily helped in participant recruitment without any incentives. Then the researcher could contact the potential participants by phone or email.

The retention rate of the study was high 82.35 % (14/17). Likewise, similar previous RCT studies could achieve 80 to 90% of 12 weeks retention rate of participants [31, 32]. There was a 17.65% drop out rate (3/17).

One participant (5.89%) in IIG withdrew from the study because she could not operate the pedometer and did not want to wear it. Notably, they were in the older adulthood (63 years old), where technological issues are most likely to provide barriers [33].

Two participants (11.76%) in the DIG were lost to follow-up after 12 weeks of intervention and did not complete the assessments at week 12. 94.12% of participants (16/17) could readily operate the pedometer. The application associated with the pedometer was practical to use for most of the participants. Some participants told the researcher that they would request their offspring for help them with operation of the pedometer.

The MI intervention for physical activity motivation used in this study, was able to detect and interpret change talk, commitment to change, and sustain talk or obstacle to change of participants from their conversation. For change talk, the counsellor could detect words and phrases conveying, possibility, ability or desire to change such as their intention or aims to exercise and their perception towards advantages of physical activity. Sustain talk was identified by wording about lack of interest, inability to change and there were some obstacles to change [20]. The change talk and sustain talk phrases of participants is illustrated in table 5.

The MI intervention in this study is beneficial for the understanding of participants' feeling towards their self-directed physical activity. They could explore their determination of physical activity, as well as their barriers. MI could help them make and meet their own exercise goal.

7.2. The efficacy of 12 weeks of self-directed physical activity using a pedometer and MI intervention

Previous pilot studies have reported that 12 weeks of home-based walking monitored by a pedometer could improve physical activity behaviour (the duration of weekly moderate to vigorous physical activity) and QoL (physical and mental well-being); small to medium of Cohen's effect size (d=0.3-0.6) in breast cancer survivors [34, 35]. However, these pilot studies reported their results with larger numbers of participants than the present study. In the current study, we did not observe effects of group by time on daily steps, QoL (FACT-B and subscales),

exercise self-regulation (BREQ2) and exercise barrier and task self-efficacy in breast cancer survivor. This is likely to be explained by the current study having low numbers of participant recruitment and low number of participants completing the 12 weeks self-directed physical activity and assessments over the 10 months. In addition, the impact of COVID-19 restriction probably limited our participants' physical activity as evidenced by sustain talk of DIG1, DIG2 and DIG4 (table 5).

However, the study found the significant difference of depression score in psychological health (DASS-21) between groups at 12 weeks. The participants in the IIG group had higher depression score than the DIG group. They were likely to have higher but not significant baseline depression score than the DIG group (p= 0.28). Therefore, this study has tested the correlation of depression score and the FACT-B score and subscale and found that there was a significant negative correlations of depression score of DASS-21 and the score of QoL (Table 5).

There were only 6 participants in the intervention group and 5 participants in the control group completing the 12 weeks program. The low recruitment rates during the global outbreak of COVID-19 are likely contributing factors for the poor reflection of the feasibility of the study had it been conducted in more normal times. However, this study will continue and expects to recruit a sufficient number of participants (64 participants) in 2021 when the situation of COVID-19 in Victoria State, Australia is stable with the roll out of the vaccination programs.

Even though, some participants postponed their scheduled MI intervention, they did managed and completed it before the participants crossed to the control intervention. Overall, participants agreed and were willing to participate in the MI intervention. Some participants remarked that they needed more physical activity motivation and appreciated receiving MI from an experienced counsellor.

Indeed, 30 minutes of moderate to vigorous physical activity is comparable to 10,000 steps/ day as demonstrated in healthy older adults [36], and as a result, this was the accepted recommendation for physical activity when monitored using a step tracker device. For breast cancer survivors, their daily-living steps from five previous research studies using a waist-mounted gadget were approximately 7,409 steps/day [37].

One RCT study reported that participants who were breast cancer survivors using a pedometer in 12 weeks walking program had the mean of daily steps equal to 8,476 ± 3,248 steps at baseline and 8,420 ± 5,226 steps at the follow-up 12 weeks [38]. Similarly, the current study found that the overall baseline daily steps of the participants across the two groups was 8,457.84 ± 3,596.09.

At the baseline, 18.75% of participants (3/16) were in the limited activity group (between 2,500 and 4,999 steps/day), 25% (4/16) were in the low active group (between 5,000 and 7,499 steps/day), 18.75% (3/16) were in the somewhat active group (between 7,500 and 9,999 steps/day), 25% (4/16) were in the active group (between 10,000 and 12,499 steps/day) and 12.5% (2/16) were in the highly active group (more than 12,500 steps/day). Although the study could not detect the statistical improvement of daily step counts by the effect of MI and time, at 12 weeks it was noticeable that there were 5 participants in IIG group (5/6) stepping up their level of activity. Whereas one participant in DIG group (1/5) was able to increase her activity level.

This interim analysis has shown that MI had no positive effect after 12 weeks of self-directed physical activity using a pedometer on daily steps, QoL and psychological health, likely due to the low sample size. The strength of our study is the randomised controlled trial design with allocation concealment by sealed envelop. However, the study did not blind participants and outcome assessments due to the research design and human research ethics issue. Other potential risks of bias are the limitation in generalisation of participants and false positive results or type 1 error. All recruited participants were willing to perform self-directed physical activity program. Therefore, there was the likelihood of positive outcomes in breast cancer survivors after 12 weeks self-directed physical activity.

Table 5 Pearson correlations on DASS-21 depression and QoL score at 12 weeks

	FACT-B	FACT-G	FACT-B TOI	PWB	SWB	EWB	FWB	BCS
DASS-21 depression	-0.81**	-0.83**	-0.80**	-058**	-0.59**	-0.59**	-0.81**	-0.69**
(*p*)	(0.00)	(0.00)	(0.00)	(0.001)	(0.001)	(0.001)	(0.00)	(0.00)

** p-value < 0.01

Abbreviations: QoL=Quality of life, FACT-B= the Functional Assessment of Cancer Therapy Breast Cancer, FACT-G = the Functional Assessment of Cancer Therapy General, FACT-B TOI = FACT-B Trial Outcome Index, PWB= Physical Well-Being, SWB=Social/Family Well-Bbeing, EWB=Emotional Well-Being, FWB= Functional Well-Being, BCS= Breast Cancer Subscale, DASS-21= The Depression, Anxiety and Stress Scale-21 items
FACT-G= PWB+SWB+EWB+FWB; FACT-B= FACT-G +BCS; FACT-B TOI = PWB +FWB +BCS

8. Conclusion

Physical activity motivation strategies regarding self-monitoring by a step tracker and MI intervention are effective to increase physical activity behavior or adherence in breast cancer survivors. However, there were logistical challenges to deal with obstacles or barriers of breast cancer survivors to participate and adhere to a physical activity program. More specifically, this challenge was intensified by the pandemic of COVID-19 over the year 2020.

The limitation of recruitment process during the outbreak of COVID-19 leads to a small sample size in the current pilot study, likely caused by the absences of the effect of group by time on physical activity adherence, quality of life and psychological health in breast cancer survivors. However, the study showed acceptable feasibility of participants recruitment and retention rate even though we were implementing our research study during the restricted times in 2020. The study could show the feasibility of self-directed physical activity by guiding breast cancer survivors to be active by using the Fitbit for their daily steps self-monitoring.

In addition, MI intervention by a video and phone calls during the lockdown periods in Melbourne, Australia was worthy to explore the attitude of the participants towards physical activity and help them decide for their own physical activity plan.

The study will continue with a larger randomized controlled with 2x2 crossover design study described under the project PAPHIO Study and will adjust the recruitment strategy based on the ethical aspects of clinical research study to achieve the sufficient number of participants. The study will analyse immunological biomarkers when the study can meet the target number of participants.

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Chapter 5

The Pilot results of PAPHIO study

5b. PAPHIO Study protocol, informed consent, information to participants, advertisement and questionnaires

The PAPHIO study received ethical approval from Melbourne Health HREC on 29 April 2020. All documents consisting of the study protocol, participant informed consent form, letter of invitation to participants, advertising materials and data collection tools have been reviewed and approved by the committee. There were several versions of each document due to several revisions to address the comments of committee until the project proposal met the ethical requirement and was approved. In addition, the project requested protocol amendments for alternative recruitment methods and the addition of Improving and Promoting Community Health (IPC health) Altona Meadows as a new recriutment site.

This chapter will show the working version of documents as the following:

1. The study protocol, version 8 dated 20 April 2020
2. Participant informed consent form, version 3 dated 16 April 2019
3. Advertising poster, version 4 dated 20 April 2020
4. The letter invitation to participants, version 1 dated 10 September 2019
5. Questionnaire: Quality of life FACT-B
6. Questionnaire: Mental health DASS-21
7. Questionnaire: Exercise barrier and task self-efficacy
8. Questionnaire: Exercise regulation BREQ2

STUDY PROTOCOL APPROVED BY MELBOURNE HEALTH HUMAN RESEARCH ETHICS COMMITTEE

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

Protocol Number (PAPHIO-001)

Version: # 8

Date: 20/04/2020

Principle Investigators:

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Sponsor/s:

Victoria University

CONFIDENTIAL

Statement of Compliance

This study will be conducted in compliance with all stipulation of this protocol, the conditions of the ethics committee approval, the NHMRC National Statement on ethical Conduct in Human Research (2007) and the Note for Guidance on Good Clinical Practice (CPMP/ICH-135/95).

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STUDY SYNOPSIS (please provide brief information)

Title:	Physical activity adherence, psychological health and immunological outcomes (PAPHIO study) in breast cancer survivors
Short Title:	PAPHIO study
Design:	A randomised controlled trial with 2 x 2 crossover design
Study Centres:	Victoria University
Hospital:	Western Health, Sunshine campus's Australia
Study Question:	1. Does 12 weeks self-directed physical activity combined with motivational interviewing (MI) in women who are breast cancer survivors influence psychological health and quality of life (QoL) outcomes? 2. Does 12 weeks self-directed physical activity combined with motivational interviewing (MI) improve immune function in women who are breast cancer survivors? 3. What is the minimum level of step count physical activity required to note significant improvements in psychological well-being, QoL and immune function amongst female breast cancer survivors
Study Objectives:	To determine the effects of 12 weeks self-directed activity combined with motivational interviewing on (i) psychological health, (ii) quality of life (QoL) and (iii) immune function in female breast cancer survivors.
Primary Objectives:	To determine whether a self-directed activity program improves (i) psychological well-being (Depression, Anxiety and Stress), (ii) QoL (physical, social/family, emotional and functional well-being and (iii) immune function, in female breast cancer survivors.
Secondary Objectives	To identify the minimum amount of step count required to note significant improvements to psychological well-

	being, QoL and immune function, amongst female breast cancer survivors
Inclusion Criteria:	- Female breast cancer survivors who are within 3 years of diagnosis and at least 6 months post active treatments [stage 0 to III including those with ductal carcinoma *in situ* (DCIS)] both premenopausal and postmenopausal over the age of 18. - Survivors on hormonal therapy such as tamoxifen or aromatase inhibitors as well as those on Herceptin (immune targeted therapy). - Participants who are unable to read/write English but are literate and can speak English.
Exclusion Criteria:	- Participants who are undergoing active treatment (surgery, chemotherapy, and radiation) and those within 6 months of active treatment. - Known metastatic disease patients. - Individuals with cognitive impairment and illiteracy to complete the questionnaires.
Number of Planned Subjects:	64 (32 per group)
Investigational product:	Self-directed physical activity
Safety considerations:	Safety of physical activity program for breast cancer survivors is based on the recommendation of the American College of Sport Medicine for exercise program training in cancer patients
Statistical Methods:	Descriptive statistics (independent T-test and Pearson Chi square for comparing mean and distribution between two groups), Repeated measures analysis of variance (ANOVA) for comparing mean between groups and times, and Linear-mixed models
Subgroups:	None

1. **Glossary of Abbreviations & Terms**

Abbreviation	Description (using lay language)
PAPHIO study	Physical activity adherence, psychological health and immunological outcomes study
QoL	Quality of life
MI	Motivational interviewing
BREQ2	The behavioral regulations in exercise questionnaire version 2
DASS-21	A 21-item depression, anxiety and stress scale
PBMC	Peripheral blood mononuclear cells
HRT	Hormone Replacement Therapy
FACT-B	the Functional Assessment of Cancer Therapy-Breast
APC	Antigen-presenting cell
IGF	Insulin-like growth factors
CRP	C-reactive protein
PCNA	Proliferating cell nuclear antigen
TNF	Tumor necrosis factor
MHC	Major histocompatibility complex
SHBG	Sex hormone binding globulin
NK cells	Natural killer cells
ACSM	American College of Sport Medicine
MVPA	Moderate-to-vigorous physical activity
TPB	Theory of planned behavior
VO2max	Maximal oxygen consumption

2. Study Sites

2.1 Study Location/s

Site	Address	Contact Person	Phone	Email
Western Health	Furlong Road, Sunshine Hospital, Department of Surgery	Dr Meron Pitcher	(03) 83456910	Meron.pitcher@wh.org.au
Western Health	Furlong Road, Sunshine Hospital, Department of Surgery	Ms Sara Jorgensen	0466449397	sara.jorgensen@wh.org.au
Victoria University	Building 2 west, 215 Hoppers Lane, Werribee, VIC 3030 Australia	Professor Vasso Apostolopoulos	0421374037	vasso.apostolopoulos@vu.edu.au
Victoria University	Western Centre for Health Research and Education	Professor Vasso Apostolopoulos Ms Supa Pudkasam	0421374037	vasso.apostolopoulos@vu.edu.au

	(WCHRE), Western Health, Furlong Road, Sunshine, 3021 VIC Australia		0432400308	supa.pudkasam@live.vu.edu.au
IPC Health	330 Queen Street, Altona Meadows, VIC 3028 Breast Cancer Support Group	Ms Anne O'Connor	(03) 83683030	Anne.o'connor@ ipchealth.com.au

3. Introduction/Background Information

3.1 Lay Summary

The study will explore the short-term benefits of 12 weeks self-directed physical activity for female breast cancer survivors on mental well-being, quality of life (QoL), and body's immune function. Because the study will measure physical activity behavior through a step counting device the study will examine the relationship between step count and mental health, QoL as well as body's immune function. In our study all participants will be provided with a step counter (Fitbit alta HR) and be asked to record their steps daily over a 24 week period. They will be randomized into 2 groups:

Group 1. Has motivational interviewing for the first 12 weeks

Group 2. Has motivational interviewing for the second 12 weeks.

The study will be conducted in Melbourne, Australia amongst women over 18 years of age who are breast cancer survivors.

At the start of self-directed physical activity participants will meet with a researcher to explain the study and provide them with a step-count device (Fitbit alta HR). We acknowledge that the health and safety of this population is paramount. As such, participation in the study requires a clearance from either their general practitioner (GP) or hospital doctor. They will be advised to contact their doctor and the project officer if there are any concerns with regards to their activity.

All participants will undertake self-directed physical activity for 24 weeks and will be given a wearable device (Fitbit alta HR). The researcher will explain the step-count-based activity and how to record their own activity. Each participant average daily step count will be assessed 3 times; at baseline, 12 weeks and 24 weeks during the physical activity. Their mental health and QoL will be assessed by standardized questionnaires at the same 3 times; at baseline and every 12 weeks. Markers of immune function and body fat will be assessed at baseline, 12 weeks and 24 weeks.

To enhance participants' engagement and compliance to the self-directed program we will engage in 1 face-to-face motivational interview (MI). In addition to this the participants will be contacted by phone 3 times to encourage engagement and review progress.

During weeks 1 to 12, the participants in the immediate intervention group (Group 1) do self-directed physical activity using the step tracker and MI whereas, participants in the delayed intervention group (Group 2) will use the step tracker but will not receive MI. During weeks 13 to 24, the participants in the delayed intervention group will continue physical activity with MI provided while the immediate intervention group will perform physical activity but not be given further MI.

In summary:
Weeks 1-12 Group 1 - immediate intervention group → self directed physical activity and MI
Weeks 1-12 Group 2 - delayed intervention group → self directed physical activity
Weeks 12-24 Group 1 - immediate intervention group → self directed physical activity
Weeks 12-24 Group 2 - delayed intervention group → self directed physical activity and MI

Our project will help to understand whether a self-directed physical activity combined with MI can help in enhancing the mental health, QoL and body's immune function in breast cancer survivors. If proven effective this could be rolled out more widely at a low cost of future program implementation in this population group (although we should acknowledge that we do not do an economical evaluation for this project).

3.2 Introduction

Regular physical activity in female breast cancer survivors seems to be an important factor to promote their QoL [1] and decrease mortality rates [2]. However, many women fail to adopt or maintain physical activity guidelines [3] due to barriers such as physical and psychosocial problems [4]. This study, therefore, will through a novel approach try to enhance physical activity participation and mental and physical outcomes. In particular, the study will use a self-directed physical activity program in which participants will engage in self-monitoring and receive motivational interviewing to enhance adherence [3].

Besides the novel intervention strategy this project will also address the relatively lack of evidence on the association between physical activity behavior in cancer survivors and their immune function. This is an important issue because this can provide vital information on how physical activity volume by daily step count can influence biomarkers related to cancer prognosis.

The PAPHIO study aims to determine the effects of 12 weeks self-directed activity combined with motivational interviewing on (i) psychological health, (ii) quality of life (QoL) and (iii) immune function in female breast cancer survivors.

A randomized controlled trial with 2X2 crossover design will test how self-directed activity improves psychological well-being (Depression, Anxiety and Stress) and QoL (physical, social/family, emotional and functional well-being and specific concerns of breast cancer) in female breast cancer survivors. In addition, the study will determine how physical activity affects immune cell functionality (cell surface markers, cytokines) in these women. Participants will complete a number of well validated instruments to assess changes in psychological well-being in terms of depression, anxiety and stress (DASS-21) and QoL (FACT-B). In addition,

participants will complete the behavioral regulations in exercise questionnaire (BREQ2) derived from self-determination theory to assess their exercise regulation and motivation continuum over time.

The study will involve women who are breast cancer survivors to undertake 24 weeks' step tracker-based physical activity program combining 12 weeks' MI for the assessment of physical activity adherence, exercise self-regulation, exercise barrier and task self-efficacy, mental wellness and QoL. The changes of immune cell functionality (cell surface markers and immune cell cytokines) and inflammatory markers (C-reactive protein, serum cytokines) will be assessed at the beginning, week 12 and week 24 of the program.
The research findings are expected to deliver important information on whether a self-directed physical activity using self-monitoring and MI can enhance psychological and immunological health and QoL of women who are breast cancer survivors. Furthermore, if this physical activity is shown to be acceptable and beneficial to the participants in terms of either psychological or immunological well-being it could be implemented more widely at relatively low cost to this or other patient population (although we should acknowledge that will not do an economical evaluation in our project).

3.3 Background information

3.3.1. Global trend of breast cancer

Breast cancer is a common malignant disease leading to physical and psychological distress of females worldwide [5, 6]. Approximately 2.4 million women suffered from this disease and 523,000 deceased across the world in 2015 [7]. The countries in the developed world such as Australia, USA and some European countries are likely to have higher incidence rate than developing countries. Conversely, greater mortality rates have been reported in less industrialized countries such as some parts of Africa and Asia [8]. However, the occurrence rate of breast cancer has dramatically increased in 22 out of 39 countries from 2008 to 2012, whereas the global death rate has gradually dropped [8].

3.3.2. The study of physical activity behavior and stage of breast cancer

Approximately one third of patients with cancer reduce their physical activity after diagnosis and almost 70% of them will not reach the exercise recommendation for cancer patients [9]. The reason behind this phenomenon has been explored mainly in breast cancer and colorectal cancer, especially at the initial phase of the diseases due to their ability of participation in research studies [9]. For breast cancer, physical activity and exercise programs have been reported as an alternative intervention to enhance QoL and physical capacity over three decades especially in stage 0 to III [10]. In addition, physical activity can significantly decrease recurrence rate [2] and reduce breast cancer mortality in the early stage [11]. However, 30% of breast cancer survivors with early phase (stage 0 to 3) breast cancer have reported physical activity cessation during 12 months follow-up after participation in a 6 months RCT [12]. The cessation may be associated with the resumption of their previous domestic tasks and work [12]. The challenge of recruiting patients with advanced stage of cancer is to deal with their cancer-related fatigue in particular side effect of treatments [9].

3.3.3. Psychological disturbance in female breast cancer survivors

Mental stress in patients with cancer can affect the quality of life (QoL) of breast cancer survivors, especially the distress from long-term treatments [13]. Almost half of female breast cancer survivors reported emotional disturbances and lack of coping ability [14]. Common psychosocial issues happening in their life consist of feeling of insecurity, fear of dying, anger, impaired body image, socialised and sexual issues [15]. 30% Of breast cancer survivors have also reported other forms of psychological distress, such as, abandoned feelings because of the transition of cancer care (from medical to supportive treatment) [16]. However, symptoms gradually disappear following psychosocial therapy through the use of relaxation techniques and group support [16]. Currently, survivorship programs have emphasised strategies to enhance psychosocial well-being [17]. Numerous studies in the last couple of decades have developed and applied psychological interventions including emotional ventilation, adjustment skill training and self-efficacy promotion techniques for improvement of their mental wellness [17, 18].

Due to the psychological issues related to breast cancer survivors, it is important to measure these in intervention studies. Therefore, in our project we will use the 21-item depression,

anxiety and stress scale (DASS-21).This questionnaire has been specifically validated in patients with cancer and has shown to have good psychometric properties [19, 20].

One valid and reliable questionnaire to assess health-related QoL in breast cancer patients is the functional assessment for cancer therapy-Breast (FACT-B) [21]. This questionnaire consists of 37 items and 4 general factors (FACT-G; physical, social/family, emotional and functional well-being) [22]. The FACT-B has adequate psychometric properties although the scores are moderated by factors such as economic status, level of education and age of breast cancer survivors [23].

3.3.4. The benefits of physical activity on breast cancer outcomes

Physical activity, especially moderate intensity aerobic exercise for female breast cancer survivors, have been noted in a number of studies to be advantageous in regard to breast cancer outcomes, decreasing the mortality rate by >30 % and reducing recurrence rate [2]. As a result of physical activity, total body fat reduces as well as a number of inflammatory and immunological biomarkers which could contribute to better outcomes in breast cancer survivors [24, 25]. Physical activity has been shown to reduce adiposity related biomarkers (i.e., leptin, adiponectin, IL-6, TNF-alpha and C-reactive protein) [26] and improve immunological functions (i.e., the percentage of CD4+CD69+ T cells) [27] and cytotoxic activity of natural killer cells [28] which can inhibit mammary cell growth [24]. A physical activity program has been shown to enhance psychological well-being and QoL in breast cancer survivors [29]. Reduced depressive symptoms, better sleeping quality and improved self-efficacy for daily tasks have been reported after participation in cancer specific exercise programs of varied duration [30, 31].

3.3.5. Effect of exercise on the immune system in breast cancer survivors

Aerobic activity and weight training have been shown to improve immunological biomarkers in breast cancer patients and survivors [25, 32]. In a 6 month moderate aerobic exercise regime in breast cancer survivors after completion of chemotherapy, there was an improvement in T cell recovery by increasing the percentage of CD4+ CD69+ T cells [27]. In addition, in a randomised controlled trial, a 15 week moderate-high intensity exercise regime (70-75 % VO_2max) in postmenopausal breast cancer survivors, increased the cytotoxic activity of NK

cells which should be beneficial to overall survival [28]. Furthermore, a 12-week aerobic exercise training (home-based exercise) in breast cancer survivors reduced pro-inflammatory cytokines and epithelial neutrophil activating protein levels (angiogenesis and apoptosis related markers). This suggests that aerobic exercise program is likely related to angiogenesis and apoptosis which may be beneficial to cancer prognosis [33]. Immune biomarkers in breast cancer can also be improved by resistance training. A 16 week-machine based weight training exercise in 20 breast cancer survivors resulted in lower levels of TNF-alpha, indicating that resistance training is likely to be advantageous in promoting an anti-inflammatory profile amongst breast cancer survivors [32].

3.3.6. Effect of exercise on adiposity biomarkers in breast cancer survivors

Obesity seems to be associated with breast cancer occurrence, especially in postmenopausal women [34]. An inactive lifestyle and weight gain after diagnosis can predict poorer survival outcomes due to the release of a number of biomarkers from fat cells including estrogen and insulin which have the mitogenic effects on mammary cells resulting in abnormal cell growth [2]. A systematic review showed that alterations in adiposity related biomarkers, including body mass index (BMI), leptin, adiponectin, sex hormone binding globulin (SHBG), oestrogen, androgen, insulin resistance, IL-6, TNF-alpha and CRP, are likely to lower the risk of postmenopausal breast cancer as a result of physical activity [26]. Exercise can reduce testosterone levels by decreasing adiposity or by increasing SHBG [35] as well as improving insulin sensitivity and reducing adipokines and CRP, which directly influence the risk of breast cancer [26]. Long term exercise has been shown to decrease oestradiol levels and increase SHBG in postmenopausal women who reduced more than 0.5 % of body fat [36]. Moderate to high intensity aerobic exercise programs prescribed for breast cancer survivors have been reported to significantly lowering blood leptin levels; consequently, this modifiable behavior is likely to be the key to improve the prognosis and survival rate [37].

3.3.7. Physical activity and motivation for activity adherence in breast cancer survivors

Nevertheless, adoption and adherence to physical activity programs amongst cancer survivors are challenging due to their physical and mental vulnerability [38]. More than 30% of female breast cancer survivors participating in exercise studies abandon exercise during the follow-up period as a consequence of physical and mental problems [12]. Physical activity barriers in

older breast cancer survivors are related to physical tiredness and lack of time management skills [39]. In addition, some breast cancer survivors have low confidence in the advantages of physical activity which can minimize adverse effects of breast cancer and treatment [40].

Although a number of physical activity and exercise RCTs have been successful during the duration of the study period many have been problematic in terms of long term adherence and implementation across populations. In addition, there are numerous problems associated with control groups in RCT's.

It has been reported that participants who do not receive their preferred treatment may experience "resentful demoralisation" [41], may not comply with the program structure proposed, may not report accurate responses on the follow-up appointments and are likely to drop out from the trial [41]. Moreover, when participants of a research intervention are not allocated to their preferred option in the research project (i.e. the exercise intervention group) and end up allocated to a control group, they tend to engage more in other activities (e.g., attend gym sessions, join exercise groups or do more home exercises) [42]. Most participants who volunteer to a research intervention have potentially made a decision about the possibility of becoming more active and taking up more physical activities/exercise into their life (i.e., moved into the action stage as proposed in the Transtheoretical Model of Behavior Change) [43]. In the action stage of this model, making a change in habits is typically overt and observable [43].

As such in this project we developed an intervention which maximized feasibility, sustainability and generalisability. This study will prescribe self-directed physical activity to breast cancer survivors. There are no clear guidelines indicating the definition of self-directed physical activity.. Many of self-directed techniques for physical activity adherence in participants with advanced stage of heterogeneous cancers have been used in research studies such as partially advised and home-based program, exercise class teaching and peer support walking group program [44]. Most of the program can make high percentage of their exercise adherence, reduced fatigue and improve QoL [44].

In addition, if the physical activity program is shown to be effective it could be implemented more widely at relatively low cost. An important factor to adopt and adhere to a physical activity program is an individual's motivation. To this end a number of behavioral change

strategies have been reported which enhance motivation and adherence [45]. Two of these strategies are Motivational Interviewing (MI) and self-monitoring.

3.3.8. Self-Monitoring

Self-monitoring, one of the important concepts in self-regulation theory, is an auditing mechanism of individual performance in relation to an individual's cognitions, beliefs and emotions [46]. Some digital devices have the ability to promote physical activity through self-monitoring [47]. For example, step counting gadgets including pedometers can effectively monitor physical activity in terms of daily steps. In fact, such devices have been utilised for physical activity promotion in clinical trials [48] especially in breast cancer patients and survivors [49, 50]. Step counters help in monitoring and individuals physical activity behavior and can result in increased motivation and ultimately adherence to long-term physical activity behavior [51]. Self-efficacy is one important concept of self-regulation theory which is related to a person's perceptions of their ability. This in turn, influences cognitions, and ultimately behavior [46]. For example, in A 16 weeks exercise program using step tracker (fitbit) was successful in self-monitoring and activity adherence in postmenopausal women [51]. In addition, a short-term physical activity program (10 weeks) based on the theory of self-regulation promoting self-monitoring enhanced the perception of confidence to exercise (self-efficacy) in cancer patients and survivors and resulted in 60% of the participants adhering to the prescribed program [52].

Self-monitoring has been shown to be a suitable strategy to enhance motivation and increased adherence to health behavior changes in heterogeneous groups of cancer patients and survivors. It helps individuals in goal setting, planning, self-reward through goal achievement and program selection [53]. Self-monitoring of physical activity behavior through pedometers in particular has the potential to enhance physical efficacy believes in breast cancer survivors which in turn will enhance motivation to continue the behavior in the future [54]. Combining this with motivational interviewing this can provide a strong signal to adhere to a self-selected exercise program [54].

3.3.9. Motivational Interviewing (MI)

Motivational interviewing is a conversation technique used by a professional for consultation to make health behavior changes [55]. MI has been effectively used to bring about behavioral change in health promotion programs for the general population. This includes changes in eating behavior, alcohol cessation and adoption of an active life style over several decades [54]. More specifically, face-to-face and phone based MI has been implemented successfully to enhance self-efficacy and reduce resistance against physical activity in breast cancer survivors [56, 57]. A study combining self-monitoring of a home based physical activity program combined with MI was successful in enhancing PA, increased adherence and improved QoL in colorectal cancer survivors [58]. In breast cancer survivors, the studies of self-monitoring based physical activity and MI intervention on physical activity engagement need more investigation for the improvement of psychological health and breast cancer outcomes [59].

3.3.10. Understanding physical activity motivation and adherence in breast cancer survivors

To understand participants' motivation to self-directed physical activity, self-determination theory (SDT) has been effectively used to enhance insight in physical activity behavior and motivation in breast cancer survivors [60]. According to SDT motivation to engage in behavior lies on a continuum ranging from extrinsic (controlled by external factors) to intrinsic (individual interest and preference). The theory predicts that self-motivation might enhance confidence in task accomplishment (competence), independent action (autonomy) and the feeling of connection to others (relatedness) [60]. The study will assess how self-regulation and motivational orientations might change over the intervention period using the behavioral regulations in exercise questionnaire version 2 (BREQ2).

Self-efficacy, an important concept in the social cognitive theory, can be a predictor for physical activity behavior and adherence in breast cancer patient [61]. In this project 2 types of efficacy believes will be examined. First, we will explore exercise barriers self-efficacy. This will examine the participants' confidence to overcome or deal with barriers to their exercise participation. Secondly, this project will examine task self-efficacy believes. In particular, it will examine the self-efficacy believes of the participants to engage in exercise behavior [61].

To measure this the project will use the 9-item barriers self-efficacy and 4-item task self-efficacy questionnaire.

4. Study Objectives

4.1 Study Aims

Overall Aim:

To determine the effects of 12 weeks self-directed activity combined with motivational interviewing on (i) psychological health, (ii) quality of life (QoL) and (iii) immune function in female breast cancer survivors.

Specific Aims

Primary Aim

1. To determine whether self-directed physical activity program improves psychological well-being (Depression, Anxiety and Stress) in female breast cancer survivors.
2. To determine whether self-directed physical activity program improves QoL (physical, social/family, emotional and functional well-being) in female breast cancer survivors.
3. To identify whether physical activity improves immune cell functionality and decreases inflammation in female breast cancer survivors

Secondary Aims

4. To identify the minimum amount of step count physical activity is required to note significant improvements to psychological well-being, QoL and immune function, amongst female breast cancer survivors

4.2 Hypothesis

There will be a dose response relationship between levels of physical activity during a 12-week-self-directed physical activity combined with MI and enhanced psychological well-being in terms of reduced symptoms of depression, anxiety and stress as well as QoL in female breast cancer survivors. Following physical activity combined with MI for 12 weeks there will be improvements in immune cell functionality.

4.3. OUTCOME MEASURES

4.3.1. Primary outcomes

4.3.1.1. Psychological health and QoL. The tool used for psychological assessment in participants is DASS-21, a 21-item rating scale to evaluate the level of depression, anxiety and stress [19]. This assessment tool has been validated for breast cancer survivors and the reliability of three scales is sufficient [62]. The study will use FACT-B version 4, a reliable and valid questionnaire consisting of the general parts on cancer (FACT-G) and additionally specific concerns of breast cancer to analyse participants' symptoms and ascertain their QoL. The questionnaire assess physical, social/family, emotional and functional well-being aspects and breast cancer specific conditions [21, 22].

4.3.1.2. Immune function: Immune biomarkers (CRP and cytokines such as TNFα) will be measured from plasma using ELISA kits. ELISA kits are accurate for serum cytokine measurements in the research studies [63, 64]. PBMC cells (white blood cells) will be isolated from blood and PBMC assessed for changes at the cellular level by flow cytometric analysis [65]. Cell surface markers, CD40, CD80, CD83, CD86, MHC-I, MHC-II, CD14, CD16, CD206, CD209 will be assessed by flow cytometry technique [65] to determine the changes after the program. In addition, Th1/Th2 cytokines secreted by monocytes and T cells will be determined to understand any cellular changes following exercise activity.

4.3.2. Secondary outcomes

4.3.2.1. Average daily step count. Participants will record their own daily step through the Garmin Vivofit2 application and upload their step count on their computer or smartphone followed the prescription by researchers and send the data to researcher by email or phone call weekly. They can record their step from the tracker in notebook. Researchers can track an individual's daily step count via Garmin Vivofit2 application on a computer or smartphone. The average daily step count will be calculated at the baseline and every 12 weeks during the program.

4.3.2.2. Adherence in step tracker usage. The participants' adherence to self-directed physical activity will be evaluated by their compliance with Garmin Vivofit2. The compliance rate will be calculated later by researcher. The compliance rate of fitness tracker usage can be

an indicator for exercise program feasibility in breast cancer patients [66].The compliance will be defined as step count tracker wearing time with data capture (daily hours and the number of wearing days) [66]. The mean of daily hours and number of wearing days per week will be calculated at the end of week 12 and week 24 of self-directed physical activity period [51] .

4.3.2.3. Exercise self-regulation. The participant's self-regulation for exercise will be assessed using the behavioral regulations in exercise questionnaire version 2 (BREQ2) [67] questionnaire. This 5 level-Likert scale-questionnaire has 19 items assessing exercise self-regulation which consists of 5 categories: external, introjected, identified, intrinsic and amotivated [67]. The internal consistency of BREQ2 is adequate to assess self-regulation for exercise in breast cancer survivors [68].

4.3.2.4. Exercise barrier and task self-efficacy. This 9 item-scale- rating barrier self-efficacy will be used to assess the confidence of participants performing exercise when experienced some difficulties. Task self-efficacy assessment with 4 items rating scale will be used for the confidence of exercise performance. This questionnaire was validated and tested for internal consistency in women with breast cancer during treatment period [61].

The questionnaires that are validated in other languages such as Vietnamese, Greek, Chinese and Macedonian will also be used.

5. Study Design

5.1. Study Type & Design & Schedule

To achieve the overall aims of determining the effects of 12 weeks self-directed activity combined with MI on psychological health, QoL and immune function in female breast cancer survivors, this study is designed as a randomised crossover trial; a single site research project conducted at Western Health (Sunshine hospitals) Australia. The study will recruit participants who are breast cancer survivors within 3 years diagnosis and at least 6 months post primary treatments. Eligible participants will be randomly allocated to immediate intervention or delayed intervention groups in a 1:1 ratio after completion of informed

consent. Allocation concealment technique will be applied in process of randomisation. During weeks 1 to week 12, the immediate intervention group (IIG, Group 1) will perform self-directed physical activity and receive MI. On the other hand, the delayed intervention group (DIG, Group 2) will perform self-directed physical activity without MI. During week 13 to week 24, DIG will continue self-directed physical activity with MI. Whereas IIG will perform physical activity but will no longer be given MI.

Potential participants will be prescribed with a Fitbit alta HR tracker for a 24-week-self-directed activity but will receive MI for 12 weeks (IIG; during week 0 to week 12 and DIG; during week 13 to week 24). Fitbit alta HR has been reported for the accuracy in monitoring step count in a research study [69]. It is small, lightweight and can be worn around wrist. Fitbit step tracker has been tested for the feasibility of application in several clinical trials [70] and in cancer survivors [71].

5.1.1. Inclusion criteria. Female breast cancer survivors who are within 3 years of diagnosis and at least 6 months post active treatment; operation, chemotherapy and/or radiotherapy [stages 0 to III including those with ductal carcinoma *in situ* (DCIS)] both premenopausal and postmenopausal over the age of 18 will be recruited. Survivors on hormonal therapy such as, tamoxifen and aromatase inhibitors as well as immune targeted therapy (Herceptin) will be eligible to participate in the study because these hormonal and cell surface blockages do not seem to have direct effects on immune cells and adiposity-related biomarkers in breast cancer. The study will also include participants who are unable to read/write English but they are literate and English speaking. For participants with non-English literacy, translators will be used in informed consent process and the study will apply the questionnaires that are validated in other languages such as Vietnamese, Greek, Chinese and Macedonian. This study plans to recruit participants from Western Health Sunshine campus's Australia.

5.1.2. Exclusion criteria. Participants who are undergoing active treatments (surgery, chemotherapy and radiation) as well as those in less than 6 months post active treatment. Likewise, those individuals with cognitive impairment and illiteracy to complete the questionnaires will be excluded. Participants with known metastatic disease will also be excluded from the study.

5.1.3. Self-directed physical activity. Participants will perform a 24-week period of self-directed physical activity. This physical activity is based on a pedometer-controlled activity [72, 73]. All participants will be given a step-count tracker devise (Fitbit alta HR) and the

associated investigator who graduated Master degree in exercise physiologist (SP) will explain the prescribed pedometer-based activity to participants. Fitbit alta HR is a wearable gadget and can be used to monitor step count. The participants' activity engagement will be conducted by individual face-to-face and phone call MI technique [55]. The participants will be taught how the Garmin is operated to monitor their step count and they will be taken on 10 minutes walk around Sunshine hospital with the devise to perceive the level of moderate intensity exertion at their feeling of taking some effort but still able to talk while performing activity [74] or as they can tolerate. At week 1 (baseline or T1), all participants will be prescribed to assess and record their activity using the Fitbit monitoring device through its application via computer or smartphone to establish their baseline physical activity volume by step count. After that they will be supervised to perform their activity on their own pace as tolerated and will wear the Fitbit during the daytime or when they are available for physical activity throughout the 24 weeks. Individual participants will be advised and motivated to gradually increase their daily time spent for physical activity during face-to-face and phone call MI until they can meet 150 minutes of moderate intensity exertion per week (the exercise recommendation by the American College of Sport Medicine (ACSM) for cancer survivors) [75] or at their perception of taking some effort but can talk during physical activity (the recommendation by the department of health, Australian government) [74]. The participants will be advised for safety during physical activity. They will be suggested to stop physical activity if adverse symptoms occur. The researcher will suggest the participant to inform their family members and take a mobile phone before they go out for physical activity. The participants who cannot access computer or smartphone will be informed to use only Garmin vivo fit 2 to detect their current physical activity and display their backlit. They will be advised to take record in their notebook. All participants will be informed that researcher will track the participants' step count and tracker usage time via Fitbit connect application. Individual average daily step count, and activity level will be assessed at baseline (T1), week 6 (T2), and week 12 (T3).

5.1.4. Motivational interviewing. The technique of MI will be used for encouraging participants through open-end questions, friendly and supportive communication and induction of behavioral changes [55, 56]. Each MI will be conducted through 4 phases of conversation comprising: 1) Engage, 2) Focus, 3) Evoke, and 4) Plan [55]. The study will use the dialog of MI guided by Mentha Counselling (3 researchers attended the workshop on MI foundation skills training organized by Mentha Counselling during 27-28 July 2017). MI will be scheduled during self-directed physical activity by 1 time face-to-face (20 minutes per time) at week 1

(T1), and 3 times phone call (15 minutes per time) at week 2, 4, and 9 over the program for IIG group to provide encouragement and review progress. This intervention will also be provided for DIG group as the same schedule at week 12 (T2), for face-to-face interviewing. Three times phone call will be conducted at week 13, 15 and 20.

5.1.5. Data collection.

Individual average physical activity volume (daily step count) will be assessed at T1, T2, and T3.

Participants mental health (DASS-21), QoL (FACT-B v4), exercise self-regulation (BREQ2), Exercise Barriers self-efficacy and task self-efficacy will be assessed at T1, T2, and T3.

Blood will be collected via a venipuncture for immune cell assays at T1, T2 and T3.

The study will be aware of participants' privacy protection. All data collection will be re-identifiable. Personal information, health related data and clinical outcomes will be kept and reported in coded or anonymized technique [76] .

The research procedure timeframe for participants in both groups are shown in 5.1.7 and 5.1.8 The research protocol diagram is shown in 5.1.10.

5.1.6. Data storage and protection

Demographic data, health related information, clinical outcomes and research data which are initially recorded by identifiable technique in hard copies will be stored in a locked filing cabinet [77]. Re-identifiable data and key-code data set will be separately kept in electronic files with password protection by the data custodian of research team (an associated investigator who is Western Health personnel) [77]. Re-identifiable data sets will be also kept separately if it will become identifiable in the combination [77]. The study will hold the clinical trial data for 15 years or more based on circumstances. As a result, researcher team must be concerned for the security of data keeping [78]. It is possibly kept in files of hard copy and saved on a computer disk at research office of Sunshine hospital. More specifically, the

researchers will have a backup or reserved storage [78]. Primary investigator and a data custodian will hold a key of filing cabinet and password for authorized accessing data.

5.1.7. Table of research procedure timeframe for IIG group

Assessment procedure	**IIG**		
	Week 1 Baseline (T1)	**Week 12 (T2)**	**Week 24 (T3)**
Informed Consent	**x**		
Motivational Interviewing (face to face)	**x**		
Psychology health; DASS-21	**x**	**x**	**x**
QoL; FACT-B version 4 questionnaire	**x**	**x**	**x**
Exercise self-regulation; BREQ2	**x**	**x**	**x**
Exercise barrier and task self-efficacy	**x**	**x**	**x**
Daily step count/Average activity volume assessment	**x**	**x**	**x**
Adherence in pedometer usage		**x**	**x**
Blood examination : Immune cell functions	**x**	**x**	**x**

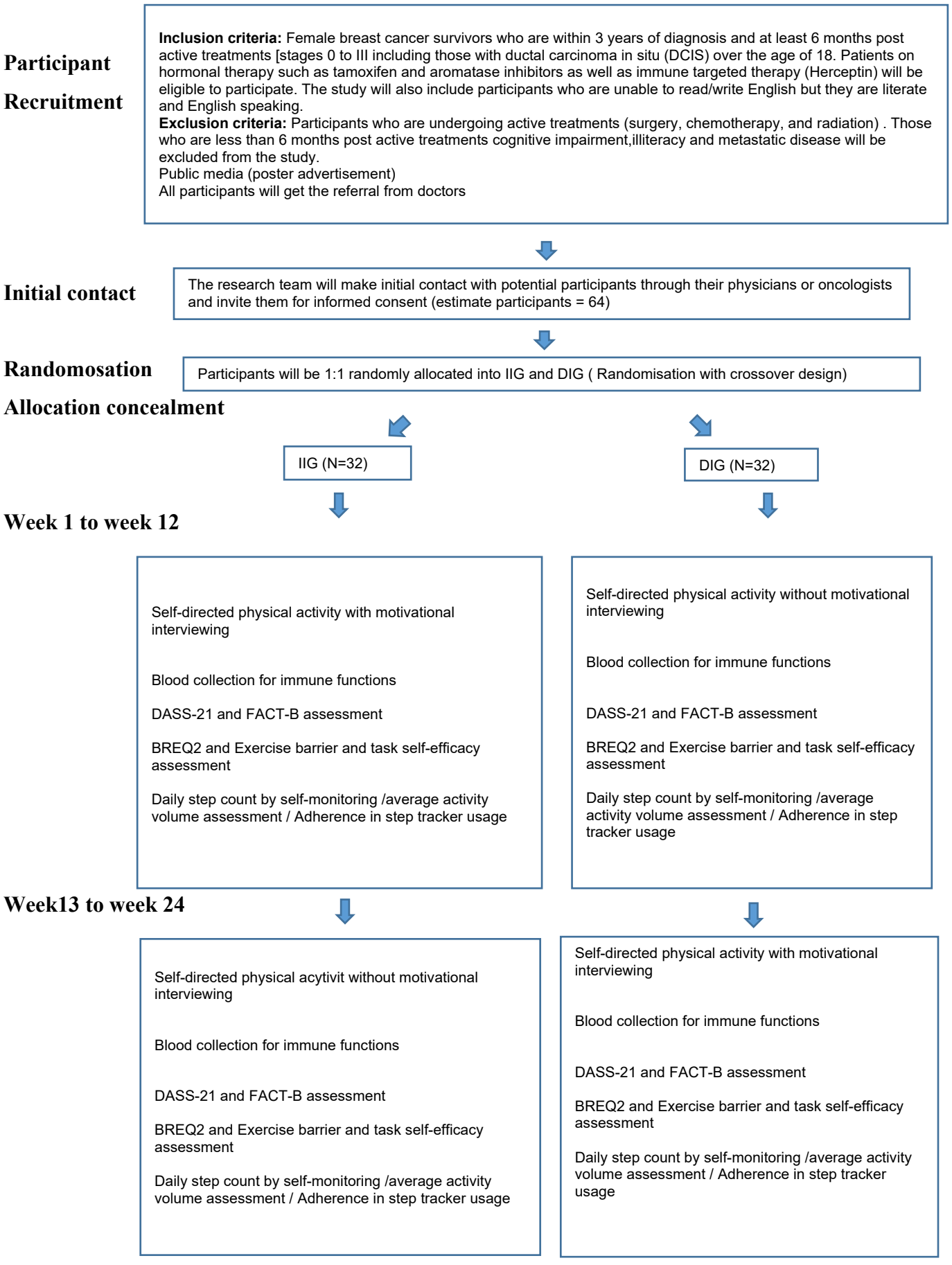
5.1.8. Table of research procedure timeframe for DIG group

Assessment procedure	**DIG**		
	Week 1 Baseline (T1)	**Week 12 (T2)**	**Week 24 (T3)**
Informed Consent	**x**		
Motivational Interviewing (face to face)		**x**	
Psychology health; DASS-21	**x**	**x**	**x**
QoL; FACT-B version 4 questionnaire	**x**	**x**	**x**
Exercise self-regulation; BREQ2	**x**	**x**	**x**
Exercise barrier and task self-efficacy	**x**	**x**	**x**
Daily step count/Average activity volume assessment	**x**	**x**	**x**
Adherence in pedometer usage		**x**	**x**
Blood examination : Immune cell functions	**x**	x	**x**

5.1.9. Research timeframe

Research process	**2017**		**2018**				**2019**			
	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4
Ethics application										
Participant recruitment										
Pedometer-based physical activity (12 weeks)										
MI (Face to face)										
MI (Telephone)										
Psychological assessment										
QoL assessment										
Biomarkers assay										
Data analysis										
Research writing										

5.1.10. Research protocol



5.2. Standard Care and Additional to Standard Care Procedures

Standard Care Procedures		
Procedure	**Time/Visit**	**Dosage/Volume**

Additional To Standard Care		
Procedure	**Time/Visit**	**Dosage/Volume**
Self-directed physical activity	Participant's self-monitoring for 24 weeks	Moderate intensity or by individual ability (their own daily step count and heart rate record)
MI (Face-to-face)	At week 1 (IIG) and week 12 (DIG)	20 minutes
MI (Telephone)	At week2, 4 and 9 (IIG) At week 13,15 and 20 (DIG)	15 minutes
Fasting peripheral blood collection	At week 1, 12, and 24	10 ml

The study procedures are clinical trials for breast cancer survivors. All procedures of the study are additional to standard care procedures. Exercise or physical activity is an adjuvant therapy for improvement of breast cancer outcomes after standard treatments. Self-directed physical activity using self-monitoring concept such as step count tracker is significantly effective to promote physical activity adherence in this population group. Likewise, MI technique used for behavioural change has been developed regarding to psychological theories. This intervention

has been applied for physical activity motivation in breast cancer survivors. Three associated researchers attended 2 days workshop on the foundational skills of MI. All questionnaires assessing participants' quality of life, psychological health, exercise barrier and task self-efficacy have been validated for breast cancer patients and survivors. The questionnaire about participant's personal data was prepared using the Australian Bureau of Statistics guideline for data collecting.

Randomization

The study design is a two-armed and randomised trial with a crossover design. Sequence generation will be conducted by simple randomisation following patient informed consent. The participants will be randomly allocated to either IIG or DIG in 1:1 ratio by computerised number generator. Allocation concealment by enclosing the allocation in sequentially numbered containers or sealed envelopes will be used to prevent selection bias [79]. The allocation concealment will be conducted by a third party to prevent researchers from affecting group assignment. The participants in both groups will be prescribed a self-directed physical activity for 24 weeks. The IIG receive MI from week 1 to week 12, whereas DIG will receive the same MI intervention from weeks 13 to 24.

5.3. Study methodology

5.4.1. Average daily step count. To quantify the volume of participants' physical activity, the mean of daily step count will be assessed and compared between groups and times at T1, T2 and T3. In addition, the participants will be categorised into pedometer-determined physical activity level as follow:

1) basal activity: < 2,500 steps/day, 2) limited activity: 2,500- 4,999 steps/day 3) low active: 5,000-7,499 steps/day; 4) somewhat active: 7,500-9,999 steps/day; 5) active: 10,000-12,499 steps/day and 6) highly active: >12,500 steps/day [48].

5.4.2. Adherence in step tracker usage. To objectively investigate adherence to self-directed physical activity by step tracker, the study will measure the use of Fitbit alta HRof participants through 24 weeks [51]. The mean of daily hours and number of wearing days per week will be calculated and compared between groups and times at the end of week 12 (T2), and week 24 (T3) [51].

5.4.3. Psychological health and QoL. The tool used for psychological assessment in potential participants is DASS-21, a 21-item depression, anxiety and stress scale [19]. This measurement was recently validated to evaluate psychological distress in patients with various cancers [20]. The study will use FACT-B version 4; a reliable and valid questionnaire consisting of the general parts on cancer (FACT-G) and specific concerns of breast cancer scale to analyse participants' symptoms and ascertain their QoL. The participants will respond to 37-item questionnaire which is 5 level of Likert scale and categorised into 4 general domains (physical, social/family, emotional and functional well-being) and additionally specific concerns of breast cancer [21, 22]. DASS-21 and FACT-B will be distributed to participants following physical activity intervention at T1, T2 and T3.

5.4.4. Exercise self-regulation. The participant's self-regulation for exercise will be assessed using the BREQ2 at T1 ,T2, and T3 [67]. This 5 level-Likert scale-questionnaire has 19 items assessing exercise self-regulation which consists of 5 categories e.g., external, introjected, identified, intrinsic and amotivated factors [67].

5.4.5. Exercise barrier and task self-efficacy. The participant's confidence to deal with the most common exercise obstacles in cancer patients will be assessed by 9 item-scale- rating exercise barrier self-efficacy questionnaire. In addition, their confidence of exercise accomplishment will be assessed by 4 items rating scale of task self-efficacy at T1, T2, and T3 [61].

5.4.6. Biological readouts. Blood will be collected via a venipuncture for biological assays at T1, T2 and T3 for both groups. Plasma concentration of inflammatory markers such as TNFα and CRP will be measured using ELISA kit. White blood cells (PBMC) will be isolated from whole blood and immune cells assessed for changes at the cellular level. Cell surface markers such as, CD40, CD80, CD83, CD86, MHC-I, MHC-II, CD14, CD16, CD206, CD209 will be assessed. In addition, cytokines secreted by monocytes and T cells will be determined to understand any cellular changes following exercise activity.

6. Study Population

6.1. Recruitment Procedure

The randomized controlled trial with crossover design plans to recruit participants from Western Health Sunshine campus. Recruitment strategies will include public media (poster advertising or flyer) and individual contact introduced by their physician [80]. All participants have to be approved by their physician for engagement in the physical activity program of this research and the screening process will be conducted before obtaining consent.

The project will be started at Western Health Sunshine campus after the project gets ethical approval from Melbourne Health Human Research Ethics Committee (MH HREC) and Western health research governance authorization [76]. The recruitment process will be conducted after the approval from both authorizations. The process will be ended when the project can recruit 64 participants according to estimated effect size and sample size which can make the influence of exercise on changes in QoL in breast cancer patients [81].

6.2. Inclusion Criteria

Female breast cancer survivors who are within 3 years of diagnosis and at least 6 months post primary treatments; operation, chemotherapy and/or radiotherapy [stages I to III, including those with ductal carcinoma *in situ* (DCIS)] both premenopausal and postmenopausal over the age of 18 will be recruited. Survivors on hormonal therapy such as, tamoxifen and aromatase inhibitors as well as immune targeted therapy (Herceptin) will be eligible to participate in the study because these hormonal blockages do not seem to have direct effects on immune cells and adiposity-related biomarkers in breast cancer. The study will also include participants who are unable to read/write English but they are literate and can speak English. For participants with non-English literacy, translators will be used in informed consent process and the study will apply the questionnaires that are validated in other languages such as Vietnamese, Greek, Chinese and Macedonian.

This study plans to recruit participants from Western Health Sunshine and Footscray campus's Australia.

6.3. Exclusion Criteria

Participants who are undergoing active treatments (surgery, chemotherapy, and radiation) or receiving immunotherapy treatment as well as those in less than 6 months post active treatments, as such treatments have adverse effects on body systems especially immunology and mental status. The study will exclude breast cancer survivors who have concurrent musculoskeletal dysfunctions and cardiovascular diseases that limit mobility and making them potentially unsafe. Participants with known metastatic disease will also be excluded. Likewise, those individuals with cognitive impairment and illiteracy will be excluded to make informed consent and complete the questionnaires.

6.4. Consent

According to World Medical Association Declaration of Helsinki, the participants involving this research must be well-informed and volunteer. The information outlined in the consent form consists of the aims, methods, involvement of participants, data and blood collection, anticipated benefits and potential harm of this research. This process will allow the participants to ask questions and discuss their decision with others. After ensuring the understanding of the participants towards the project, the researcher needs voluntary informed consent from them, which are preferably in writing [82]. The participants will give written consent by self to participate in this study. Western health and Victoria University will collaboratively issue information sheet and consent form. Participants can take time as much as they want for decision making in participation. They can return consent form to researcher directly or a nominated staff of Western health. The consent can be re-negotiated from time to time. The participants will be told if there are any changes from original agreement and given the opportunity to continue or withdraw.

7. Participant Safety and Withdrawal

7.1. Risk Management and Safety

Risk management of this study is based on the recommendation of the American College of Sport Medicine for exercise program training in cancer patients as these following:

- Get approval from their oncologist or hospital doctor before beginning an exercise program

- Stop exercise and contact their doctor if they have any adverse effects [83]

Two associated researchers will be encourage and discuss self-directed activity using step tracker and heart rate monitor to estimate their moderate intensity exertion. We will advise all participants to inform someone and take a phone with before they go out for physical activity. They will be informed to stop physical activity or make an emergency call for urgent medical help if they have some unpleasant symptoms such as chest pain or pain down to arms, dizziness, difficulty breathing, unusual rapid heart rate, and sever fatigue. They are also informed about possible sore muscle when they get a new start of physical activity which should relieve within a few days [84]. The researchers will follow the progression of participants' physical activity and their obstacles by face-to-face and phone call MI throughout 12 weeks.

Researchers will ask all participants about their self-directed physical activity experiences when they have a follow-up by the schedule. In case that they have some adverse effects during their physical activity, the participants will meet a physician for more investigation.

In addition, venous blood collecting will be strictly applied based on aseptic technique and standard precaution to prevent infection of participants [85].

7.2. Handling of Withdrawals

The participants will be informed of their right to withdraw from further involvement in the study, and/or for their data to be extracted [76].

The participants will have the right to stop their participation within the study without giving any reason or legal withdrawal in writing [76]. [76]. The researcher team will observe participants who withdraw their involvement in the program without any disadvantages or consequence for their decision [76]. However at the time of withdrawal, the researcher may request from the participant continued use of their data in the future. If agreeable, the participant will document agreement of continued follow-up and further data usage to the principal investigator [86].

7.3. Replacements

The randomised controlled trial with 2x2 crossover design needs 53 participants for anticipating the changes of QoL in breast cancer survivors after 12 weeks of self-directed physical activity combined with MI because exercise programs have previously been reported

large effect size on this endpoint. To prevent type 2 error, this study estimates 20% inevitable drop-out rate, therefore we have planned to recruit 64 participants. If the drop-out rate is more than 20%, new participants will be recruited.

8. Statistical Methods

8.1. Sample Size Estimation & Justification

To evaluate whether a self-directed activity combined with MI can improve psychological health, QoL, immune function, and adiposity in breast cancer survivors, we will consider statistical power analysis according to Cohen which depends on significance criteria (alpha), sample size (N), and the effect size (ES) [87]. Additionally, we justified the sample size of this study regarding the level of significance, power of study, and estimated effect size [88]. We found that there was large ES of an 12 weeks exercise intervention on the overall score of QoL (by FACT-B assessment) in breast cancer survivors which calculated ES (Cohen's d) = 2.23 (there was same sample size between groups (N=29) in this randomized controlled with crossover study; mean score between-group difference was 27.9) [81].

Regarding to our study design; randomised controlled with 2 x 2 crossover design and the hypothesis test for equality, we calculated sample size using software calculator for crossover study [89]. Within participants' standard deviation of FACT-B score is 13 and minimal difference in mean is 8. Therefore we need a total of 53 participants in this study [81]. We will recruit a total of 64 participants whilst anticipating 20 % drop out rate (32 participants are needed per group). Previous studies illustrated approximately 10-20 % drop-out rate of breast cancer survivors participating exercise program [90-92]. The power of test is set at 0.8 and alpha probability of 0.05 to reject null hypothesis. Recruitment strategies possibly include public media (poster advertising or flyer) and individual contact introduced by their physician [80]. All participants have to be approved by their physician for taking part in the exercise program of this research.

8.2. Power Calculations

To calculate sample size, this study will consider acceptable level of significance, power of the study and expected effect size. The power of test is set at 0.8 to allow only 20% of type 2 error and alpha probability of 0.05 to reject null hypothesis. This study will use the large effect size

d (2.23) and mean difference (27.9) based on a similarly previous study which illustrated significant reduction in physical and mental fatigue after an 18-week exercise program amongst this population group [5]. We should recruit approximately 53 participants but increase to 64 for anticipating 20% drop out rate.

8.3. Statistical Methods To Be Undertaken

Baseline descriptive statistics (mean, standard deviation for continuous data and percentage for categorical data) will be used to describe the distribution of personal data and variables between two groups of participant (e.g., age, breast cancer health history, body compositions, and blood pressure). Independent T-test will be used to compare means for continuous data and the Pearson Chi square will be used for testing the difference in distribution of a categorical variable at baseline [93].

Repeated measures analysis of variance (ANOVA) will be used to compare physical activity volume by step count, psychological health and the QoL of participants at 3 times (T1 to T3) between 2 groups [94]. This statistic will also be used to compare biomarkers at 3 time between 2 groups.

Linear-mixed models will be used to identify the relationship between physical activity volume by step counting and mental health (DASS-21), QoL (FACT-B), self-regulation (BREQ2) and self-efficacy at T1, T2 and T3; the relationship between activity volume by step counting and biomarker changes at T1,T2, and T3.

We will apply the concept of intention to treat analysis to prevent selection bias. We will manage missing data and try to include all data in the final analysis. Imputation method with predicted values such as observed or predicted means will be used to handle missing data. We will report the numbers of withdrawal and drop-out with their reasons [95].

9. Storage of Blood and Tissue Samples

9.1. Details of where samples will be stored, and the type of consent for future use of samples

Approximately 10 ml of blood will be collected via a venipuncture for biological assays at T1, T2 and T3 for both groups. Whole blood will be collected into a tube containing anticoagulant and centrifuged immediately after collection or on the same day approximately 7 h later.

Plasma samples will be stored at -20º to -80º C up to one year prior to analysis for biomarker-related adiposity assay at WCHRE or Werribee campus laboratories. The sample will not be affected by up to 3 freeze/thaw cycles. Plasma concentration of adiponectin, leptin, IGF, TNFα and CRP will be measured.

Isolation of peripheral blood mononuclear cells by density gradient configuration using Ficoll-Paque will be used for immune cell functions. PBMCs will be stored in refrigerator not longer than one day and then used flow cytometry to assess the composition of the isolated PBMC populations.

10. Data Security & Handling

10.1. Details of where records will be kept & How long will they be stored

The patient's personal information and health history which are necessary for this research study must be protected for their privacy and confidentiality [96]. All data of participants should be recorded adequately and stored in databank with secure format and password protection for the verification of research results and discussion amongst the research team members. Agreements involving data ownership and storage will be done between Western health and Victoria University. This study has planned to hold clinical trials research data for 15 years or more based on circumstances [76]. It is possible to keep files of hard copy and saved on a computer disk in a research office at Sunshine hospital. A locked filing cabinet and a computer for research data can only be accessed by agreed members of the research team. More specifically, the researchers will have a backup or reserved storage [76]. For destruction of the data, hard copy will be shredded by hospital and university office's shredder. Digital information will be destroyed by deleting or overwriting the files.

10.2. Confidentiality and Security

According to the protection of participants' privacy, personal, health related data and clinical outcomes will be kept and reported in coded or reversibly anonymised technique. Re-identifiable information will be used for data management (name will be removed and replaced by a code which can be re-identified for relating the different data sets and data verification) [76]. This research will only obtain personal data and health history from medical records at some points only, especially for participant identification and recruitment process. It is possible

that reversible anonymous data and key-codes can solve this problem. Furthermore, our researcher team will set up a data management system for holding the key code [97]. Identifiable data will only be used for the process of data collection from participants and medical records as well as the process of integration of re-identified data using linkage keys [77]. Firstly, the name of participants will be indicated in all data collecting documents. This identifiable data will be recorded in hard copies and kept in locked cabinet by a data custodian. Raw data from data collecting documents will be extracted and transformed into electronic database by creation of linkage keys and removal of identifiers (using participants' code). The data custodian will hold this key codes (key-coded data set) in electronic file in a computer with password protection. Then re-identified data will be transferred to data analytics team [77]. Identifiable data can be shared only between research term for data verification and linkage of different data sets [77]. Primary investigator will share about individual blood test (immune function and adiposity) and any individual research results to participants during follow-up time. Overall research outcomes will be shared to all participants after research completion prior to research result publication by community meeting at Western health or the finding newsletter by mailing [98].

10.3. Ancillary data

Information given by participants such as MI will be recorded in audio-tape and kept in re-identifiable data [76]. This record will be held in the safe and secure storage at research office of Sunshine hospital [76].

11. Appendix

List of Attachments included:

Document Name	Version Number	Date (e.g., 18 January 2012)
2018.339 Project protocol	8	20 April 2020
2018.339 PICF	3	16 April 2019
2018.339 Victorian specific module	2	1 February 2019
2018.339 Biomarkers record form	1	3 September 2018
2018.339 Daily step count record form	3	31 March 2019
2018.339 FACT-B	1	16 November 2007
2018.339 Mental Health_DASS_21	1	3 September 2018
2018.339 Exercise self-regulation_BREQ2	2	2004
2018.339 Exercise barrier and task self- efficacy	1	2006
2018.339 Motivational interviewing dialogue _face to face	2	1 February 2019
2018.339 Motivational interviewing dialog_phone call	1	1 February 2019

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4. Wolin, K.Y., et al., *Implementing the exercise guidelines for cancer survivors.* The journal of supportive oncology, 2012. **10**(5): p. 171.
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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 Sara Jorgensen, Professor Vasso Apostolopoulos, Ms Anne O'Connor, Professor Remco Polman, Emeritus Professor Lily Stojanovska, Ms Supa Pudkasam
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.

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 Sara Jorgensen
Position	Breast care nurse, Specialist nurse manager, Breast cancer service clinic, Western Health
Telephone	0466449397
Email	Sara.Jorgensen@wh.org

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 Sara Jorgensen, Professor Vasso Apostolopoulos, Ms Anne O'Connor, Professor Remco Polman, Emeritus Professor Lily Stojanovska, Ms Supa Pudkasam
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 <u>unable</u> to read the information and consent form

Witness to the informed consent process

Name (please print) _____

Signature _____ Date _____

* Witness is <u>not</u> to be the investigator, a member of the study team or their delegate. In the event that an interpreter is used, the interpreter may <u>not</u> act as a witness to the consent process.

Witness must be 18 years or older.

<u>Declaration by Study Doctor/Senior Researcher</u>†

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 Sara Jorgensen, Professor Vasso Apostolopoulos, Ms Anne O'Connor, Professor Remco Polman, Emeritus Professor Lily Stojanovska, Ms Supa Pudkasam
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 _____

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.

Breast cancer survivors are invited for a research study

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

The study aims to find out the advantages of 12 weeks self-directed physical activity combined with motivational interviewing on (i) mental health, (ii) quality of life (QoL) and (iii) immunity in breast cancer survivors.

We would like to invite breast cancer survivors within 3 years of diagnosis and at least 6 months after breast cancer treatments. You may be undergoing hormonal treatments and/or Herceptin treatment.

What is involved in the study?

- 24 weeks total in the study project
- 24 week-self-directed physical activity program wearing a step count tracker
- Motivational interviewing (MI); 1 x face-to-face and 3 x by phone call, over 12 weeks
- 3 times answering of 4 questionnaires
- 3 times blood sampling

There will be 2 groups in the study, both groups wear the step count tracker (Fitbit alta HR)**.**

- ***One group will have immediate Motivational interviewing.***
- ***Other group will have delayed Motivational interviewing.***

The project has been approved by the Melbourne Health Human Research Ethics Committee.

To find out more about this research, please contact;

Ms Supa Pudkasam
PhD candidate, Victoria University
Phone 0432400308
Email: Supa.pudkasam@live.vu.edu.au

Ms Sara Jorgensen
Western Health, Australia
Phone: 0466449397
Email:Sara.Jorgensen@wh.org.au

Date

Dear, breast cancer survivors

The PAPHIO study

We are a team of researchers at Western Health and Victoria University interested in the advantages of physical activity or exercise on mental health, quality of life and body's immune system in breast cancer survivors. We would like to invite you to participate in our study.

This study aims to assess the short-term benefits of 24 weeks self-directed (your own decision and management) physical activity combined with counselling for physical activity motivation) on mental health, quality of life (QoL), and the body's immune function in breast cancer survivors.

We would like to encourage you to participate in self-directed physical activity. We are inviting all female breast cancer survivors who are within 3 years of disease diagnosis and at least 6 months after breast surgery, chemotherapy or radiotherapy and over the age of 18. Women receiving hormone therapy or Herceptin are eligible to apply.
If you take part in this study, you will participate in this study for 24 weeks. We will randomly allocate you into either an immediate intervention group (group-1) or a delayed intervention group (group-2).

All participants will provide limited personal information about their treatment and will complete 4 questionnaires regarding quality of life and attitudes to exercise, plus have a blood test looking at the body's immune function and inflammatory markers. All of the participants will receive a step tracker and be shown how to use this and record its' data.

Half the participants will then meet face to face with a health coach to explore and plan their exercise goals, and will receive 3 follow up short 10-15 minute phone calls form the coach to provide ongoing support, tips and motivation. After 12 weeks they will continue to collect data from their step tracker but will not have any coaching. The rest of the participants will record their activity for 12 weeks and after that meet face to face with the health coach, have the same telephone contact and will continue to record their activity. The initial questionnaires will be repeated at 12 weeks and at 24 weeks for both groups, and blood tests will also be repeated at this time.

We look forward to speaking with you in greater details regarding the study.

Yours sincerely,
On behalf of the PAPHIO study team

DASS 21

NAME _____ Code (for researcher only) _____ Date_____

Please read each statement and tick a number 0, 1, 2 or 3 which indicates how much the statement applied to you **over the past week**. There are no right or wrong answers. Do not spend too much time on any statement.

The rating scale is as follows:

0 Did not apply to me at all

1 Applied to me to some degree, or some of the time

2 Applied to me to a considerable degree or a good part of time

3 Applied to me very much or most of the time

Items	Statement	0	1	2	3
1 (s)	I found it hard to wind down				
2 (a)	I was aware of dryness of my mouth				
3 (d)	I couldn't seem to experience any positive feeling at all				
4 (a)	I experienced breathing difficulty (e.g. excessively rapid breathing, breathlessness in the absence of physical exertion)				
5 (d)	I found it difficult to work up the initiative to do things				
6 (s)	I tended to over-react to situations				
7 (a)	I experienced trembling (e.g. in the hands)				
8 (s)	I felt that I was using a lot of nervous energy				
9 (a)	I was worried about situations in which I might panic and make a fool of myself				
10 (d)	I felt that I had nothing to look forward to				
11 (s)	I found myself getting agitated				
12 (s)	I found it difficult to relax				
13 (d)	I felt down-hearted and blue				
14 (s)	I was intolerant of anything that kept me from getting on with what I was doing				

15 (a)	I felt I was close to panic				
Items	**Statement**	**0**	**1**	**2**	**3**
16 (d)	I was unable to become enthusiastic about anything				
17 (d)	I felt I wasn't worth much as a person				
18 (s)	I felt that I was rather touchy				
19 (a)	I was aware of the action of my heart in the absence of physical exertion (e.g. sense of heart rate increase, heart missing a beat)				
20 (a)	I felt scared without any good reason				
21 (d)	I felt that life was meaningless				

Arabic DASS21

اسم:_____ التاريخ:_____

اقرأ كل من النصوص التالية ثم ضع دائرة حول الرقم ٠،١،٢ أو ٣ الذي يبين درجة انطباق هذا الشعور عليك في الأسبوع الماضي. لا يوجد إجابات صحيحة أو خاطئة. لا تقضي وقتاً طويلاً في أي منها.

استعمل التقديرات التالية:

٠ لا ينطبق عليّ بتاتاً

١ ينطبق عليّ بعض الشيء أو قليلاً من الأوقات

٢ ينطبق عليّ بدرجة ملحوظة أو بعض الأوقات

٣ ينطبق عليّ كثيراً جداً، أو معظم الأوقات

١	وجدت صعوبة في الاسترخاء والراحة	٠	١	٢	٣
٢	شعرت بجفاف في حلقي	٠	١	٢	٣
٣	لم يبدو لي أن بإمكاني الإحساس بمشاعر إيجابية على الإطلاق	٠	١	٢	٣
٤	شعرت بصعوبة في التنفس (شدة التنفس السريع، اللهثان بدون القيام بمجهود جسدي مثلاً)	٠	١	٢	٣
٥	وجدت صعوبة في أخذ المبادرة بعمل الأشياء	٠	١	٢	٣
٦	كنت أميل إلى ردة فعل مفرطة للظروف والأحداث	٠	١	٢	٣
٧	شعرت برجفة (باليدين مثلاُ)	٠	١	٢	٣
٨	شعرت بأنني أستهلك الكثير في الطاقة العصبية (شعرت بأنني أستهلك الكثير من قدرتي على تحمل التوتر العصبي)	٠	١	٢	٣
٩	كنت خائفاً من مواقف قد أفقد فيها السيطرة على أعصابي واسبب إحراجاً لنفسي	٠	١	٢	٣
١٠	شعرت بأن ليس لدي أي شيء أتطلع إليه	٠	١	٢	٣
١١	شعرت بأنني مضطرب ومنزعج	٠	١	٢	٣
١٢	أجد صعوبة في الاسترخاء	٠	١	٢	٣
١٣	شعرت بالحزن والغم	٠	١	٢	٣
١٤	كنت لا أستطع تحمل أي شيء يحول بيني وبين ما أرغب في القيام به	٠	١	٢	٣
١٥	شعرت بأنني على وشك الوقوع في حالة من الرعب المفاجئ بدون سبب	٠	١	٢	٣
١٦	فقدت الشعور بالحماس لأي شيء	٠	١	٢	٣
١٧	شعرت بأن قيمتي قليلة كشخص	٠	١	٢	٣
١٨	شعرت بأنني أميل إلى الغيظ بسرعة	٠	١	٢	٣
١٩	شعرت بضربات قلبي بدون مجهود جسدي (زيادة في معدل الدقات، أو غياب دقة قلب، مثلاً)	٠	١	٢	٣
٢٠	شعرت بالخوف بدون أي سبب وجيه	٠	١	٢	٣
٢١	شعرت بأن الحياة ليس لها معنى	٠	١	٢	٣

DASS21

姓名：　　日期：

填表說明：

請小心閱讀以下每一個句子，並在其右方圈上一數字，表示「過往一個星期」如何適用於你。答案並無對錯之分。請不要花太多時間在某一句子上。

評估量表：

0 = 不適用
1 = 頗適用，或間中適用
2 = 很適用，或經常適用
3 = 最適用，或常常適用

1	我覺得很難讓自己安靜下來	0	1	2	3
2	我感到口乾	0	1	2	3
3	我好像不能再有任何愉快、舒暢的感覺	0	1	2	3
4	我感到呼吸困難（例如不是做運動時也感到氣促或透不過氣來）	0	1	2	3
5	我感到很難自動去開始工作	0	1	2	3
6	我對事情往往作出過敏反應	0	1	2	3
7	我感到顫抖（例如手震）	0	1	2	3
8	我覺得自己消耗很多精神	0	1	2	3
9	我憂慮一些令自己恐慌或出醜的場合	0	1	2	3
10	我覺得自己對將來沒有甚麼可盼望	0	1	2	3
11	我感到忐忑不安	0	1	2	3
12	我感到很難放鬆自己	0	1	2	3
13	我感到憂鬱沮喪	0	1	2	3
14	我無法容忍任何阻礙我繼續工作的事情	0	1	2	3
15	我感到快要恐慌了	0	1	2	3
16	我對任何事也不能熱衷	0	1	2	3
17	我覺得自己不怎麼配做人	0	1	2	3
18	我發覺自己很容易被觸怒	0	1	2	3
19	我察覺自己在沒有明顯的體力勞動時，也感到心律不正常	0	1	2	3
20	我無緣無故地感到害怕	0	1	2	3
21	我感到生命毫無意義	0	1	2	3

Moussa, M.T., Lovibond, P.F. & Laube, R. (2001). *Psychometric properties of a Chinese version of the short Depression Anxiety Stress Scales (DASS21)*. Report for New South Wales Transcultural Mental Health Centre, Cumberland Hospital, Sydney.

Hindi अवसाद, चिंता एवं तनाव मापनी (लघु संस्करण)

कृपया प्रत्येक कथन को ध्यान पूर्वक पढ़े । पिछले एक सप्ताह मे यह कथन आपके ऊपर किस हद तक लागू होते हैं इसका निर्धारण उनके सामने बने, खाली स्थानों में से सबसे उपयुक्त मे सही का चिन्ह लगाकर करें । प्रश्नों का कोई सही या गलत उत्तर नहीं हैं यह केवल आपके पिछले अनुभव जानने के लिए है कृपया उत्तर देने मे जयादा समय न लगायें ।

बिलकुल नहीं = ० कुछ हद तक = १ काफी ज्यादा = २ पूरी तरह से = ३

क्र.	कथन	०	१	२	३
१	धीरे धीरे कार्य क्षमता में क्षीणता / कमी ने मुझे परेशान किया था।				
२	मुझे पता है कि मेरा मुँह सूख जाता था।				
३	मैं कोई सकारात्मक भाव अनुभव नहीं कर सका।				
४	मैंने साँस लेने में तकलीफ महसूस की (जैसे कि सामान्य से तेज साँस लेना, शारीरिक श्रम के बिना भी साँस का फूलना महसूस किया)।				
५	किसी भी कार्य की शुरुआत करने में मुझे दिक्कत होती है।				
६	मैंने परिस्थितियों को जरुरत से ज्यादा प्रतिक्रिया दी।				
७	मैंने कम्पन महसूस किया (जैसे- हांथो में)।				
८	मैंने ऐसा महसूस किया कि मैं कई बार कुछ ज्यादा ही घबरा जाता हूँ ।				
९	मैं उस परिस्थिति के बारे में बहुत चिंतित था, जिसमे मैं बहुत बेचैन हो गया था और मैंने बेवकूफी की।				
१०	मैंने अपने आपको ग्लानित/ दोषी महसूस किया ।				
११	मैंने अपने आपको बहुत घबराया हुआ महसूस किया।				
१२	मैंने विश्राम करना मुश्किल पाया।				
१३	मैंने अपने आपको उदास और दुखी महसूस किया ।				
१४	किसी विशेष उपक्रम या व्यवस्था द्वारा मेरे कार्यो पर नजर रखी जाये यह मुझे बर्दाश्त नहीं है।				
१५	मैंने आतंकित महसूस किया था।				
१६	किसी भी कार्य को करने के लिए मैं अपने आपको उत्साहित कर पाने में असमर्थ पता था।				
१७	मैंने महसूस किया कि मैं ज्यादा योग्य व्यक्ति नहीं था।				
१८	मैंने महसूस किया कि मैं ज्यादा भावुक हो गया था।				
१९	शारीरिक परिश्रम के बिना भी मैं अपने दिल की धड़कनों को महसूस करता था (जैसे- तेज गति से धड़कना या कभी रुक जाना)।				
२०	मैंने बिना किसी कारण के डर महसूस किया ।				
२१	मुझे लगा कि जीवन सार्थक नहीं था।				

Vietnam DASS 21

(BẢNG ĐO LƯỜNG MỨC ĐỘ ƯU SẦU, LO SỢ, CĂNG THẲNG TINH THẦN)

Tên:…… Ngày:……/……/……..

Xin vui lòng đọc từng câu và khoanh tròn số 0, 1, 2, hay 3 để chỉ định xem câu nào thích hợp với những gì đã xảy ra cho mình trong tuần lễ vừa qua. Không có câu trả lời nào đúng hay sai. Không nên mất quá nhiều giờ để lựa chọn.

Cách phân loại như sau :

0 Điều nầy hoàn toàn không xảy ra cho Tôi
1 Xảy ra cho tôi một phần nào, hay thỉnh thoảng
2 Thường xảy ra cho Tôi, hay nhiều lần
3 Rất thường xảy ra, hay hầu hết lúc nào cũng có

	D	A	S
1. Tôi nhận thấy khó mà nghỉ ngơi..... 0 1 2 3			.....
2. Tôi thấy mình bị khô miệng..... 0 1 2 3		.....	
3. Tôi không thấy có một cảm giác lạc quan nào cả 0 1 2 3	.....		
4. Tôi bị khó thở (thở nhanh, khó thở mà không do làm việc mệt)..... 0 1 2 3		.....	
5. Tôi thấy khó mà bắt tay vào làm công việc..... 0 1 2 3	.....		
6. Tôi đã phản ứng cách quá lố khi có những sự việc xãy ra..... 0 1 2 3			.....
7. Tay tôi bị run..... 0 1 2 3		.....	
8. Tôi thấy mình đã dùng quá nhiều năng lực vào việc lo lắng 0 1 2 3			.....
9. Tôi lo mình đến những nơi mà tôi có thể bị hốt hoảng và tự làm mất mặt.. 0 1 2 3		.....	
10. Tôi thấy tương lai mình chả có gì để mong chờ cả 0 1 2 3	.....		
11. Tôi thấy bồn chồn 0 1 2 3			.....
12. Tôi thấy khó mà thư giãn 0 1 2 3			.....
13. Tôi thấy mình xuống tinh thần và buồn rầu 0 1 2 3	.....		
14. Tôi thấy thiếu kiên nhẫn với những điều cản trở việc tôi đang làm 0 1 2 3			.....
15. Tôi thấy mình gần như bị hốt hoảng..... 0 1 2 3		.....	
16. Tôi không thấy hăng hái để làm bất cứ chuyện gì..... 0 1 2 3	.....		
17. Tôi thấy mình là người kém giá trị..... 0 1 2 3	.....		
18. Tôi thấy mình rất dễ nhạy cảm..... 0 1 2 3			.....
19. Tôi thấy tim mình đập nhanh, đập hụt nhịp mà không do làm việc mệt... 0 1 2 3		.....	
20. Tôi cảm thấy sợ vô cớ..... 0 1 2 3		.....	
21. Tôi cảm thấy cuộc sống mình không có ý nghĩa..... 0 1 2 3	.....		
Tổng cộng số điểm			
Tổng cộng số điểm sau khi nhân cho 2			

This version was translated and reviewed by the Vietnamese Committee on Anxiety/Panic Attack in Sydney (April 2003).
Contact person: Tung_Pham@wsahs.nsw.gov.au

Filipino DASS 2 1	*Name:*	*Date:*

Basahin ang mga talata at bilugan ang mga numero na nagpapahayag ng mga nararamdaman mo o nangyayari sayo sa mga nakalipas na lingo. Walang tama o maling sagot. Iwasang pagtuunan ng maraming oras ang bawat talata.

Panuto:

0 Hindi nangyayari / nagaganap sa akin
1 Paminsanminsan nangyayari / nagaganap sa akin 2 Pangkaraniwang nangyayri / nagaganap sa akin 3 Madalas na nangyayari / nagaganap sa akin.

1 Nahihirapan akong tumimo 0 1 2 3 2 Batid ko ang panunuyo ng aking bibig 0 1 2 3

3 Hindi ko man lang maranasan ang makaramdam ng mabuti 0 1 2 3

4 Nakakaranas ako ng hirap na paghinga (hal. Sobrang bilis ng paghinga, 0 1 2 3 kawalan ng hininga kung hindi aapuhin ito)

5 Nahihirapan akong magkusa na gumawa 0 1 2 3

6 Masyado akong nagiging intimidida sa mga situasyon 0 1 2 3 7 Nakaranas ako ng panginginig (hal. Sa kamay) 0 1 2 3

8 Naramdaman ko na masyado akong gumagamit ng aking nevous energy 0 1 2 3

9 Nangangamba ako sa mga situasyong kung saan maari akong matuliro at 0 1 2 3 makagawa nang hindi matino

10 Nararamdaman ko na wala naman akong inaasahan 0 1 2 3 11 Nakita ko na lang ang sarili na masaya 0 1 2 3 12 Nahihirapan akong magrelaks / mamahinga 0 1 2 3 13 Naramadaman kong maging mapagkumbaba at matamlay. 0 1 2 3 14 Hindi ko pinapansin ang bagay na nakakahadlang sa aking ginagawa 0 1 2 3

15 Naramdaman kong muntik na akong matuliro 0 1 2 3

16 Hindi ko nagagawang maging magilas / aktibo sa kahit anong bagay 0 1 2 3

17 Naramdaman kong wala akong kwenta 0 1 2 3

18 Naramdaman kong sa halip ay nagiging mapangkupkop ako 0 1 2 3

19 Batid ko ang galaw ng aking puso kahit hindi ako kumikilos (hal. Pagbilis ng 0 1 2 3 pintig, pagkawala ng pintig ng puso)

20 Natatakot ako ng walang kadahilanan 0 1 2 3 21 Naramdaman kong walang kahulugan ang buhay 0 1 2 3

Dr. AnnaLiza H. Sta. Ana.

โครงการวิจัยอัลแทร์ **Thai แบบฟอร์ม DASS-21**

หมายเลขประจำตัวผู้ป่วย: ☐☐☐☐☐☐☐ **ชื่อย่อ :** ☐☐☐☐ วันเดือนปีเกิด **:** ☐☐-☐☐☐-☐☐☐☐ วัน เดือน ปี (ตัวอย่างเช่น: 01-JAN-2007)	**วันที่:** ☐☐-☐☐☐-2 0☐☐ วัน เดือน ปี (ตัวอย่างเช่น: 01-JAN-2007) **สัปดาห์:** ☐ 0 ☐ 48 ☐ 96 (จงวงกลมระยะเวลาที่ท่านเข้าร่วมในการวิจัย)	

โปรดอ่านข้อความแต่ละข้อและวงกลมหมายเลข 0, 1, 2 หรือ 3 ที่ระบุข้อความได้ตรงกับท่านมากสุด*ในช่วงสัปดาห์ที่ผ่านมา* ทั้งนี้ ไม่มีคำตอบที่ถูกหรือคำตอบที่ผิด ท่านไม่ควรใช้เวลามากนักในแต่ละข้อความ

เกณฑ์การประเมินมีดังนี้:

0 ไม่ตรงกับข้าพเจ้าเลย

1 ตรงกับข้าพเจ้าบ้าง หรือเกิดขึ้นเป็นบางครั้ง

2 ตรงกับข้าพเจ้า หรือเกิดขึ้นบ่อย

3 ตรงกับข้าพเจ้ามาก หรือเกิดขึ้นบ่อยมากที่สุด

1	ข้าพเจ้ารู้สึกว่ายากที่จะผ่อนคลายอารมณ์	0	1	2	3
2	ข้าพเจ้าทราบว่าข้าพเจ้ามีอาการปากแห้ง	0	1	2	3
3	ข้าพเจ้ารู้สึกไม่ดีขึ้นเลย	0	1	2	3
4	ข้าพเจ้ามีอาการหายใจลำบาก (เช่น มีอาการหายใจเร็วขึ้นผิดปกติ มีอาการหายใจไม่ออกแม้ว่าจะไม่ได้ออกแรง)	0	1	2	3
5	ข้าพเจ้ารู้สึกทำกิจกรรมด้วยตนเองได้ค่อนข้างลำบาก	0	1	2	3
6	ข้าพเจ้าเริ่มมีปฏิกิริยาตอบสนองต่อสิ่งต่าง ๆ มากเกินไป	0	1	2	3
7	ข้าพเจ้ามีอาการสั่น (เช่น ที่มือทั้งสองข้าง)	0	1	2	3
8	ข้าพเจ้ารู้สึกว่าข้าพเจ้าวิตกกังวลมาก	0	1	2	3
9	ข้าพเจ้ารู้สึกกังวลกับเหตุการณ์ที่อาจทำให้ข้าพเจ้ารู้สึกตื่นกลัวและกระทำสิ่งใดโดยมิได้คิด	0	1	2	3
10	ข้าพเจ้ารู้สึกว่าข้าพเจ้าไม่มีเป้าหมาย	0	1	2	3
11	ข้าพเจ้าเริ่มรู้สึกว่าข้าพเจ้ามีอาการกระวนกระวายใจ	0	1	2	3
12	ข้าพเจ้ารู้สึกไม่ผ่อนคลาย	0	1	2	3

13	ข้าพเจ้ารู้สึกจิตใจเหงาหงอยและเศร้าซึม	0	1	2	3
14	ข้าพเจ้าทนไม่ได้กับภาวะใดก็ตามที่ทำให้ข้าพเจ้าไม่สามารถทำอะไรต่อจากที่ข้าพเจ้ากำลังกระทำอยู่	0	1	2	3
15	ข้าพเจ้ารู้สึกว่าข้าพเจ้ามีอาการคล้ายกับอาการหวั่นวิตก	0	1	2	3
16	ข้าพเจ้าไม่รู้สึกกระตือรือร้นต่อสิ่งใด	0	1	2	3
17	ข้าพเจ้ารู้สึกเป็นคนไม่มีคุณค่า	0	1	2	3
18	ข้าพเจ้ารู้สึกว่าข้าพเจ้าค่อนข้างมีอารมณ์ฉุนเฉียวง่าย	0	1	2	3
19	ข้าพเจ้ารับรู้ถึงการทำงานของหัวใจของข้าพเจ้าในตอนที่ข้าพเจ้าไม่ได้ออกแรง (เช่น รู้สึกถึงการเต้นของหัวใจเพิ่มขึ้น การหยุดเต้นของหัวใจ)	0	1	2	3
20	ข้าพเจ้ารู้สึกกลัวโดยไม่มีเหตุผลใด ๆ	0	1	2	3
21	ข้าพเจ้ารู้สึกว่าชีวิตไม่มีความหมาย	0	1	2	3

DASS21

Greek translation and Adaptation

George N. Lyrakos and Chrysa Arvaniti *Όνομα :* *Ημερομηνία:*

Παρακαλώ διαβάστε κάθε δήλωση και κυκλώστε έναν αριθμό 0 ..1 ..2 ή 3 που προσδιορίζει πόσο η δήλωση σας αντιπροσώπευσε *κατά τη διάρκεια της προηγούμενης εβδομάδας*. Δεν υπάρχει καμία σωστή ή λανθασμένη απάντηση. Μην ξοδέψετε πάρα πολύ χρόνο σε οποιαδήποτε δήλωση.

Βαθμολογήστε σύμφωνα με την ακόλουθη κλίμακα:

0 Δεν ίσχυσε καθόλου για μένα
1 Ίσχυε για μένα σε έναν ορισμένο βαθμό, ή για μικρό χρονικό διάστημα.
2 Ίσχυε για μένα σε έναν ιδιαίτερο βαθμό, ή για μεγάλο χρονικό διάστημα.
3 Ίσχυε για μένα πάρα πολύ, ή τις περισσότερες φορές.

1	Δεν μπορούσα να ηρεμήσω τον εαυτό μου	0	1	2	3
2	Ένιωθα ότι το στόμα μου ήταν ξηρό	0	1	2	3
3	Δεν μπορούσα να βιώσω κανένα θετικό συναίσθημα	0	1	2	3
4	Δυσκολευόμουν ν' ανασάνω (π.χ., υπερβολικά γρήγορη αναπνοή, κόψιμο της ανάσας μου χωρίς να έχω κάνει σωματική προσπάθεια)	0	1	2	3
5	Μου φάνηκε δύσκολο να αναλάβω την πρωτοβουλία να κάνω κάποια πράγματα	0	1	2	3
6	Είχα την τάση να αντιδρώ υπερβολικά στις καταστάσεις που αντιμετώπιζα	0	1	2	3
7	Αισθάνθηκα τρεμούλα (πχ στα χέρια)	0	1	2	3
8	Αισθανόμουν συχνά νευρικότητα	0	1	2	3
9	Ανησυχούσα για τις καταστάσεις στις οποίες θα μπορούσα να πανικοβληθώ και να φανώ ανόητος στους άλλους	0	1	2	3
10	Ένιωσα ότι δεν είχα τίποτα να προσμένω με ενδιαφέρον	0	1	2	3
11	Βρήκα τον εαυτό μου να νιώθει ενοχλημένος	0	1	2	3
12	Μου ήταν δύσκολο να χαλαρώσω	0	1	2	3
13	Ένιωθα μελαγχολικός και απογοητευμένος	0	1	2	3
14	Δεν μπορούσα να ανεχτώ οτιδήποτε με κρατούσε από το να συνεχίσω με αυτό που έκανα	0	1	2	3
15	Ένιωσα πολύ κοντά στον πανικό	0	1	2	3
16	Τίποτα δεν μπορούσε να με κάνει να νιώσω ενθουσιασμό	0	1	2	3
17	Ένιωσα ότι δεν άξιζα πολύ ως άτομο	0	1	2	3
18	Ένιωσα ότι ήμουν αρκετά ευερέθιστος	0	1	2	3
19	Αισθανόμουν την καρδιά μου να χτυπάει χωρίς να έχει προηγηθεί σωματική άσκηση (ταχυπαλμία, αρρυθμία)	0	1	2	3
20	Ένιωσα φοβισμένος χωρίς να υπάρχει λόγος	0	1	2	3
21	Ένιωσα πως η ζωή δεν είχε νόημα	0	1	2	3

DASS21

Nome: *Data:*

Per favore legga ogni frase e cerchi un numero 0, 1, 2 o 3 che indichi quanto la frase le si addice considerando gli ultimi giorni. Non ci sono risposte giuste o sbagliate. Non impieghi troppo tempo per ogni frase.

L'indice della scala è:

0 Non mi si addice per niente
1 Si addice a me per alcuni aspetti, o a volte
2 Si addice a me per alcuni aspetti, o per buona parte delle volte
3 Si addice molto a me, o per la maggior parte delle volte

1	Ho trovato difficile calmarmi	0	1	2	3
2	Ero consapevole della secchezza della mia bocca	0	1	2	3
3	Non riuscivo a provare per niente un sentimento positivo	0	1	2	3
4	Ho provato difficoltà di respirazione (come: respiro eccessivamente rapido, mancanza del respiro anche in assenza di sforzo fisico)	0	1	2	3
5	Ho trovato difficile farmi venire iniziative per fare qualcosa	0	1	2	3
6	Ho avuto la tendenza a reagire eccessivamente a certe situazioni	0	1	2	3
7	Mi è capitato di tremare (specie alle mani)	0	1	2	3
8	Sentivo che ero troppo nervoso	0	1	2	3
9	Mi sono preoccupato a proposito di certe situazioni nelle quali potevo andare in panico o fare la figura dello stupido	0	1	2	3
10	Sentivo che non avevo voglia di fare niente	0	1	2	3
11	Mi sentivo agitato	0	1	2	3
12	Trovavo difficile rilassarmi	0	1	2	3
13	Mi sentivo abbattuto e malinconico	0	1	2	3
14	Ero intollerante verso tutto quello che mi tratteneva da quello che stavo facendo	0	1	2	3
15	Sentivo che ero vicino ad andare in panico	0	1	2	3
16	Non ero in grado di entusiasmarmi per niente	0	1	2	3
17	Mi sono sentita una persona di poco valore	0	1	2	3
18	Sentivo di essere piuttosto permaloso	0	1	2	3
19	Ero consapevole dell'azione del mio cuore in assenza di sforzo fisico (come: senso di aumento del ritmo cardiaco, cuore che manca un battito)	0	1	2	3
20	Mi spaventavo senza alcuna ragione	0	1	2	3
21	Sentivo che la vita era senza significato	0	1	2	3

DASS-21 Scoring Instructions

The DASS-21 should not be used to replace a face to face clinical interview. If you are experiencing significant emotional difficulties you should contact your GP for a referral to a qualified professional.

Depression, Anxiety and Stress Scale - 21 Items (DASS-21)

The Depression, Anxiety and Stress Scale - 21 Items (DASS-21) is a set of three self-report scales designed to measure the emotional states of depression, anxiety and stress.

Each of the three DASS-21 scales contains 7 items, divided into subscales with similar content. The depression scale assesses dysphoria, hopelessness, devaluation of life, self-deprecation, lack of interest / involvement, anhedonia and inertia. The anxiety scale assesses autonomic arousal, skeletal muscle effects, situational anxiety, and subjective experience of anxious affect. The stress scale is sensitive to levels of chronic non-specific arousal. It assesses difficulty relaxing, nervous arousal, and being easily upset / agitated, irritable / over-reactive and impatient. Scores for depression, anxiety and stress are calculated by summing the scores for the relevant items.

The DASS-21 is based on a dimensional rather than a categorical conception of psychological disorder. The assumption on which the DASS-21 development was based (and which was confirmed by the research data) is that the differences between the depression, anxiety and the stress experienced by normal subjects and clinical populations are essentially differences of degree. The DASS-21 therefore has no direct implications for the allocation of patients to discrete diagnostic categories postulated in classificatory systems such as the DSM and ICD.

Recommended cut-off scores for conventional severity labels (normal, moderate, severe) are as follows:

NB Scores on the DASS-21 will need to be multiplied by 2 to calculate the final score.

	Depression	Anxiety	Stress
Normal	0-9	0-7	0-14
Mild	10-13	8-9	15-18
Moderate	14-20	10-14	19-25
Severe	21-27	15-19	26-33
Extremely Severe	28+	20+	34+

Lovibond, S.H. & Lovibond, P.F. (1995). Manual for the Depression Anxiety & Stress Scales. (2nd Ed.)Sydney: Psychology Foundation.

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											
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.

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
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

QUESTIONARIO SULLE MOTIVAZIONI NELL'ESERICIZIO FISICO (BREQ-2) **Italiano**

PERCHE' TI DEDICHI ALL'ESERCIZIO FISICO?

Siamo interessati a capire le ragioni delle persone che decidono di pratica e non praticare esercizio fisico. Usando la scala sotto riportata, le chiediamo di indicare quanto è vera ogni affermazione per lei. Le ricordiamo che non ci sono risposte giusto o sbagliate e domande ingannevoli. Vogliamo semplicemente conoscere come lei personalmente vive l'esercizio fisico. Le sue risposte saranno mantenute riservate e usate solo per scopi di ricerca.

	LA SUA MOTIVAZIONE A PRATICARE ESERCIZIO FISICO	Per niente vero per me		Talvolta vero per me		Molto vero per me
1.	Faccio esercizio fisico perchè altre persone dicono che dovrei farlo	0	1	2	3	4
2.	Mi sento in colpa quando non faccio esercizio fisico	0	1	2	3	4
3.	Apprezzo i benefici dell'esercizio fisico	0	1	2	3	4
4.	Faccio esercizio fisico perché è divertente	0	1	2	3	4
5.	Non vedo perché dovrei fare esercizio fisico	0	1	2	3	4
6.	Faccio esercizio fisico perché i miai amici/famiglia/partner mi dicono che dovrei farlo	0	1	2	3	4
7.	Mi sento in imbarazzo quando perdo un allenamento	0	1	2	3	4
8.	E' importante per me fare esercizio fisico regolarmente	0	1	2	3	4
9.	Non vedo perché dovrei preoccuparmi di fare esercizio fisico	0	1	2	3	4
10.	Mi piacciono i miei allenamenti	0	1	2	3	4
11.	Faccio esercizio fisico perché gli altri non saranno contenti di me se non lo faccio	0	1	2	3	4
12.	Non vedo la ragione di fare esercizio fisico	0	1	2	3	4
13.	Mi sento incapace quando non faccio esercizio fisico da un pò	0	1	2	3	4
14.	Penso che sia importante fare lo sforzo di praticare esercizio fisico regolarmente	0	1	2	3	4
15.	Trovo l'esercizio fisico un'attività piacevole	0	1	2	3	4
16.	Mi sento "pressato" dagli amici/familiari a praticare esercizio fisico	0	1	2	3	4
17.	Divento inquieto se non faccio esercizio fisico regolarmente	0	1	2	3	4
18.	Traggo piacere e soddisfazione dal fare esercizio fisico	0	1	2	3	4
19.	Penso che l'esercizio fisico sia una perdita di tempo	0	1	2	3	4

Translation by Prof. Luca Pietrantoni and Isaac Ruiz Alfaro (2011)

EXERCISE REGULATIONS QUESTIONNAIRE (BREQ-2 norsk) **Norwegian**

Alder _____ år **Kjønn: Mann Kvinne (sett ring rundt)**

HVA ER GRUNNEN TIL AT DU TRENER?

Vi er interesserte i å finne ut underliggende grunner for hvorfor personer er delaktige eller ikke i fysisk aktivitet og trening. Ved å bruke skalaen under, vennligst marker i hvilken grad påstandene stemmer for deg. Vennligst legg merke til at det ikke finnes noen rette eller gale svar, og det er heller ingen lurespørsmål. Vi ønsker kun å vite dine personlige følelser rundt trening. Dine svar vil bli holdt konfidensielt og kun brukt i forbindelse med vår undersøkelse.

		Ikke sant for meg		Delvis sant for meg		Veldig sant for meg
1.	Jeg trenger fordi andre sier jeg skal	0	1	2	3	4
2.	Jeg får dårlig samvittighet når jeg ikke trener	0	1	2	3	4
3.	Jeg verdsetter fordelene av trening	0	1	2	3	4
4.	Jeg trener fordi det er gøy	0	1	2	3	4
5.	Jeg skjønner ikke hvorfor jeg skulle måtte trene	0	1	2	3	4
6.	Jeg deltar i trening fordi venner/familie/partner mener jeg bør	0	1	2	3	4
7.	Jeg skammer meg når jeg går glipp av en treningsøkt	0	1	2	3	4
8.	Det er viktig for meg å trene regelmessig	0	1	2	3	4
9.	Jeg skjønner ikke hvorfor jeg skal bry meg om å trene	0	1	2	3	4
10.	Jeg liker treningsøktene mine	0	1	2	3	4
11.	Jeg trener fordi andre ikke vil være fornøyd med meg om jeg ikke gjør det	0	1	2	3	4
12.	Jeg ser ikke noe poeng i å trene	0	1	2	3	4

13.	Jeg føler meg mislykket om jeg ikke har fått trent på en stund	0	1	2	3	4
14.	Jeg mener det er viktig å gjøre en innsats for å trene regelmessig	0	1	2	3	4
15.	Trening er for meg lystbetont	0	1	2	3	4
16.	Jeg føler press fra familie/venner om å trene	0	1	2	3	4
17.	Jeg blir rastløs om jeg ikke trener regelmessig	0	1	2	3	4
18.	Jeg får glede og tilfredstillelse av å delta i trening	0	1	2	3	4
19.	Jeg mener trening er bortkastet tid	0	1	2	3	4

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EXERCISE REGULATIONS QUESTIONNAIRE (BREQ-2)

Age: _____ years **Sex: male female (please circle)**

WHY DO YOU ENGAGE IN EXERCISE?

We are interested in the reasons underlying peoples' decisions to engage, or not engage in physical exercise. Using the scale below, please indicate to what extent each of the following items is true for you. Please note that there are no right or wrong answers and no trick questions. We simply want to know how you personally feel about exercise. Your responses 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

Thank you for taking part in our research

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April 2000

BREQ-2 – Versão Portuguesa

(Palmeira, A., Teixeira, P. Silva, M. & Markland, D., 2007)

Estamos interessados nas razões fundamentais das pessoas na decisão de se envolverem ou não envolverem no exercício físico. Usando a escala abaixo, por favor indique qual o nível mais verdadeiro para si. Relembramos que não há respostas certas ou erradas nem perguntas traiçoeiras. Queremos apenas saber como é que se sente em relação ao exercício.

Porque é que faz exercício?

Não é verdade para mim		Algumas vezes é verdade para mim		Muitas vezes é verdade para mim
0	1	2	3	4

1. Faço exercício porque outras pessoas dizem que devo fazer 0 1 2 3 4
2. Sinto-me culpado/a quando não faço exercício 0 1 2 3 4
3. Dou valor aos benefícios/vantagens do exercício 0 1 2 3 4
4. Faço exercício porque é divertido 0 1 2 3 4
5. Não vejo porque é que tenho de fazer exercício 0 1 2 3 4
6. Participo no exercício porque os meus amigos/família dizem que devo fazer 0 1 2 3 4
7. Sinto-me envergonhado/a quando falto a uma sessão de exercício 0 1 2 3 4
8. É importante para mim fazer exercício regularmente 0 1 2 3 4
9. Não percebo porque é que tenho de fazer exercício 0 1 2 3 4
10. Gosto das minhas sessões de exercício 0 1 2 3 4
11. Faço exercício porque os outros vão ficar insatisfeitos comigo se não fizer 0 1 2 3 4
12. Não percebo o objectivo de fazer exercício 0 1 2 3 4
13. Sinto-me fracassado/a quando não faço exercício durante algum tempo 0 1 2 3 4
14. Penso que é importante fazer um esforço por fazer exercício regularmente 0 1 2 3 4
15. Acho o exercício uma actividade agradável 0 1 2 3 4
16. Sinto-me pressionado/a pela minha família e amigos para fazer exercício 0 1 2 3 4
17. Sinto-me ansioso/a se não fizer exercício regularmente 0 1 2 3 4
18. Fico bem disposto e satisfeito por praticar exercício 0 1 2 3 4
19. Penso que o exercício é uma perda de tempo 0 1 2 3 4

Escala de regulación de la conducta en el ejercicio físico (BREQ-2) Markland y Tobin (2004). **Spanish**

	Yo hago ejercicio...	Totalmente en desacuerdo	Algo en desacuerdo	Neutro	Algo de acuerdo	Totalmente de acuerdo
1	Porque los demás me dicen que debo hacerlo	❶	❷	❸	❹	❺
2	Porque me siento culpable cuando no practico	❶	❷	❸	❹	❺
3	Porque valoro los beneficios que tiene el ejercicio físico	❶	❷	❸	❹	❺
4	Porque creo que el ejercicio es divertido	❶	❷	❸	❹	❺
5	No veo por qué tengo que hacer ejercicio	❶	❷	❸	❹	❺
6	Porque mis amigos/familia/pareja me dicen que debo hacerlo	❶	❷	❸	❹	❺
7	Porque no me siento bien conmigo mismo si falto a la sesión	❶	❷	❸	❹	❺
8	Porque para mí es importante hacer ejercicio regularmente	❶	❷	❸	❹	❺
9	No veo por qué debo molestarme en hacer ejercicio	❶	❷	❸	❹	❺
10	Porque disfruto con las sesiones prácticas	❶	❷	❸	❹	❺
11	Para complacer a otras personas	❶	❷	❸	❹	❺
12	No veo el sentido de hacer ejercicio	❶	❷	❸	❹	❺
13	Porque siento que he fallado cuando no he realizado un rato de ejercicio	❶	❷	❸	❹	❺
14	Porque pienso que es importante hacer el esfuerzo de ejercitarse regularmente	❶	❷	❸	❹	❺
15	Porque encuentro el ejercicio una actividad agradable	❶	❷	❸	❹	❺
16	Porque me siento bajo la presión de mis amigos/familia para realizar ejercicio	❶	❷	❸	❹	❺
17	Porque me pongo nervioso si no hago ejercicio regularmente	❶	❷	❸	❹	❺
18	Porque me resulta placentero y satisfactorio el hacer ejercicio	❶	❷	❸	❹	❺
19	Pienso que hacer ejercicio es una pérdida de tiempo	❶	❷	❸	❹	❺

Regulación intrínseca: 4, 10, 15, 18
Regulación identificada: 3, 8, 14, 17
Regulación introyectada: 2, 7, 13,
Regulación externa: 1, 6, 11, 16
Desmotivación: 5, 9, 12, 19

Moreno, J. A., Cervelló, E. M., y Martínez, A. (2007). Measuring self-determination motivation in a physical fitness setting: validation of the Behavioral Regulation in Exercise Questionnaire-2 (BREQ-2) in a Spanish sample. *The Journal of Sport Medicine and Physical Fitness, 47*(3), 366-378.

中文版運動行為調節問卷 Traditional Chinese

年齡：_____歲

性別：男性 / 女性 (請圈選)

為什麼你要從事運動呢？

對於民眾決定從事或不從事運動這件事情，其原因令我們感到非常有興趣。藉由下面的量表，請在每一個選項中，選出最適合你的描述。本問卷並沒有標準答案，因此每個選項並沒有對錯，也沒有陷阱題存在。我們只是單純的想了解您對於運動的個人觀感。本份問卷的內容將會被保密，且僅會應用在我們研究目的上。

		完全不適合我		有時適合我		非常適合我
1	我會運動，是因為別人認為我應該運動	0	1	2	3	4
2	我不運動時會有罪惡感	0	1	2	3	4
3	我重視運動帶來的益處	0	1	2	3	4
4	我運動是因為運動很有趣	0	1	2	3	4
5	我不認為我應該要運動	0	1	2	3	4
6	我去運動，是因為我的朋友 /家人 / 伴侶 說我應該要運動	0	1	2	3	4
7	當我缺席了一次運動，我會感到羞愧	0	1	2	3	4

8	對我而言規律運動是很重要的	0	1	2	3	4
9	我實在不認為為什麼要運動	0	1	2	3	4
10	我非常喜歡我的運動	0	1	2	3	4
11	我去運動是因為如果我不運動，別人會感到不高興	0	1	2	3	4
12	我不覺得運動有什麼重要性	0	1	2	3	4
13	當一段時間沒運動，我會覺得自己像個失敗的人	0	1	2	3	4
14	我認為努力地維持規律運動是很重要的	0	1	2	3	4
15	我覺得運動是個充滿樂趣的事情	0	1	2	3	4
16	我感受到來自朋友或家人的壓力，促使我去運動	0	1	2	3	4
17	我如果不規律運動會感到煩躁不安	0	1	2	3	4
18	我從參與運動中，獲得快樂和滿足	0	1	2	3	4
19	我認為運動是浪費時間的行為	0	1	2	3	4

FACT-B (Version 4)

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
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

	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

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

FACT- B (Version 4) Vietnam

Sau đây là những điều mà người đồng bệnh với quý vị cho là quan trọng. **Xin khoanh tròn hoặc đánh dấu một con số cho mỗi hàng để cho biết câu trả lời nào áp dụng cho quý vị trong 7 ngày qua.**

	TÌNH TRẠNG SỨC KHỎE	**Hoàn toàn không**	**Chút ít**	**Đôi chút**	**Khá nhiều**	**Rất nhiều**
GP1	Tôi thiếu năng lượng sống	0	1	2	3	4
GP2	Tôi bị buồn nôn	0	1	2	3	4
GP3	Vì tình trạng thân thể của tôi, tôi khó đáp ứng các nhu cầu trong gia đình tôi	0	1	2	3	4
GP4	Tôi bị đau nhức	0	1	2	3	4
GP5	Các phản ứng phụ của việc điều trị làm tôi bị khó chịu.	0	1	2	3	4
GP6	Tôi cảm thấy bệnh	0	1	2	3	4
GP7	Tôi bắt buộc phải nằm nghỉ trên giường	0	1	2	3	4

	TÌNH TRẠNG GIAO TIẾP VỚI GIA ĐÌNH/XÃ HỘI	**Hoàn toàn không**	**Chút ít**	**Đôi chút**	**Khá nhiều**	**Rất nhiều**
GS1	Tôi cảm thấy gần gũi với bạn bè	0	1	2	3	4
GS2	Tôi được gia đình nâng đỡ tinh thần	0	1	2	3	4
GS3	Tôi được bạn bè trợ giúp	0	1	2	3	4
GS4	Gia đình tôi chấp nhận bệnh của tôi	0	1	2	3	4
GS5	Tôi hài lòng với những giao tiếp trong gia đình về bệnh của tôi	0	1	2	3	4
GS6	Tôi cảm thấy gần gũi với bạn đời của tôi (hay người giúp đỡ chính của tôi)	0	1	2	3	4
Q1	*Bất kể mức độ hoạt động tình dục hiện nay của quý vị như thế nào, xin hãy cứ trả lời câu hỏi sau đây. Nếu quý vị không muốn trả lời, xin hãy đánh dấu vào ô này ☐ rồi chuyển tiếp sang phần sau.*					
GS7	Tôi vừa ý với cuộc sống tình dục của tôi	0	1	2	3	4

FACT- B (Version 4)

Xin khoanh tròn hoặc đánh dấu một con số cho mỗi hàng để cho biết câu trả lời nào áp dụng cho quý vị trong <u>7 ngày qua</u>.

	TÌNH TRẠNG TINH THẦN	**Hoàn toàn không**	**Chút ít**	**Đôi chút**	**Khá nhiều**	**Rất nhiều**
GE1	Tôi cảm thấy buồn	0	1	2	3	4
GE2	Tôi hài lòng với cách mà tôi đang thích nghi với bệnh của mình	0	1	2	3	4
GE3	Tôi mất dần hy vọng trong việc chống chọi lại bệnh của tôi	0	1	2	3	4
GE4	Tôi cảm thấy hồi hộp	0	1	2	3	4
GE5	Tôi lo lắng về cái chết	0	1	2	3	4
GE6	Tôi lo lắng rằng tình trạng của tôi sẽ trầm trọng thêm	0	1	2	3	4

	TÌNH TRẠNG CHỨC NĂNG	**Hoàn toàn không**	**Chút ít**	**Đôi chút**	**Khá nhiều**	**Rất nhiều**
GF1	Tôi có khả năng làm việc (kể cả việc ở nhà)	0	1	2	3	4
GF2	Công việc của tôi (kể cả việc ở nhà) đem lại sự hài lòng vui thích	0	1	2	3	4
GF3	Tôi có thể vui sống	0	1	2	3	4
GF4	Tôi đã chấp nhận bệnh của mình	0	1	2	3	4
GF5	Tôi ngủ ngon giấc	0	1	2	3	4
GF6	Hiện tại tôi vui thích những gì tôi thường làm để giải trí	0	1	2	3	4
GF7	Tôi hài lòng với chất lượng cuộc sống hiện tại của tôi	0	1	2	3	4

FACT- B (Version 4)

Xin khoanh tròn hoặc đánh dấu một con số cho mỗi hàng để cho biết câu trả lời nào áp dụng cho quý vị trong 7 ngày qua.

	NHỮNG MỐI QUAN TÂM KHÁC	Hoàn toàn không	Chút ít	Đôi chút	Khá nhiều	Rất nhiều
B1	Tôi hay bị thở dốc	0	1	2	3	4
B2	Tôi hay để ý và chú trọng về cách ăn mặc của tôi	0	1	2	3	4
B3	Một hoặc cả hai cánh tay của tôi bị sưng hoặc đau	0	1	2	3	4
B4	Tôi cảm thấy tôi vẫn còn hấp dẫn	0	1	2	3	4
B5	Tôi thấy khó chịu vì bị rụng tóc	0	1	2	3	4
B6	Tôi lo lắng là những người khác trong gia đình tôi cũng sẽ bị bệnh như tôi một ngày nào đó	0	1	2	3	4
B7	Tôi lo tâm trạng căng thẳng có ảnh hưởng đến bệnh tình của tôi	0	1	2	3	4
B8	Tôi thấy khó chịu vì cân lượng thay đổi	0	1	2	3	4
B9	Tôi có thể cảm thấy mình là một phụ nữ	0	1	2	3	4
P2	Tôi cảm thấy đau ở một số nơi trên cơ thể	0	1	2	3	4

FACT-B (Version 4.0) Arabic

هذه قائمة بالعبارات التي ذكر أشخاص بنفس علتك أنها مهمة بالنسبة لهم. **من فضلك ضع دائرة أو علامة على رقم واحد في كل سطر لبيان مدى انطباق إجابتك على حالتك في <u>الأيام السبعة الأخيرة</u>.**

	الكفاءة الجسمانية	**ليس على الإطلاق**	**مرات قليلة**	**نوعاً ما**	**غالبا**	**كثيرا جدا**
GP1	أشعر بالوهن.....	0	1	2	3	4
GP2	أشعر بالغثيان (إحساس بالقئ).....	0	1	2	3	4
GP3	بسبب حالتي الصحية – لدي صعوبة في تلبية احتياجات أسرتي.....	0	1	2	3	4
GP4	أشعر بألم	0	1	2	3	4
GP5	أشعر بالضيق من الآثار الجانبية للعلاج.....	0	1	2	3	4
GP6	أشعر أنني عليل (مريض)	0	1	2	3	4
GP7	أنا مضطر لملازمة الفراش.....	0	1	2	3	4

	الكفاءة الاجتماعية و الأسرية	**ليس على الإطلاق**	**مرات قليلة**	**نوعاً ما**	**غالبا**	**كثيرا جدا**
GS1	أشعر أنني قريب من أصدقائي	0	1	2	3	4
GS2	أحظى بتعاطف أسرتي.....	0	1	2	3	4
GS3	أجد كل الدعم من أصدقائي	0	1	2	3	4
GS4	لقد تقبلت أسرتي حالتي الصحية	0	1	2	3	4
GS5	أنا راض عن الكيفية التي تتعامل بها أسرتي مع مرضي.....	0	1	2	3	4
GS6	أشعر بالقرب من زوجي / زوجتي (أو الشخص الذي يمثل لي الدعم الرئيسي)	0	1	2	3	4
Q1	**بغض النظر عن حالتك الجنسية حاليا، من فضلك أجب عن هذا السؤال. إذا كنت لا ترغب في الإجابة من فضلك ضع علامة في هذا المربع ☐ ثم انتقل إلى السؤال التالي:**					
GS7	أنا راض عن حياتي الجنسية.....	0	1	2	3	4

FACT-B (Version 4.0)

من فضلك ضع دائرة أو علامة على رقم واحد في كل سطر لبيان مدى انطباق إجابتك على حالتك في الأيام السبعة الأخيرة.

	الكفاءة العاطفـــية	**ليس على الإطلاق**	**مرات قليلة**	**نوعاً ما**	**غالبا**	**كثيرا جدا**
GE1	أشعر بالحزن	0	1	2	3	4
GE2	أنا راض عن تقبلي لحالتي الصحية	0	1	2	3	4
GE3	أفتقد الأمل في مقاومتي لمرضي.....	0	1	2	3	4
GE4	أشعر بالعصبية	0	1	2	3	4
GE5	أنا قلق من الموت	0	1	2	3	4
GE6	أخاف أن تسوء حالتي.....	0	1	2	3	4

	الكفاءة الوظيفيـــــة	**ليس على الإطلاق**	**مرات قليلة**	**نوعاً ما**	**غالبا**	**كثيرا جدا**
GF1	أنا قادر على العمل (بما في ذلك العمل في المنزل).	0	1	2	3	4
GF2	عملي (بما في ذلك عملي في المنزل) يرضيني.....	0	1	2	3	4
GF3	أنا قادر على الاستمتاع بالحياة	0	1	2	3	4
GF4	لقد تقبلت مرضي.....	0	1	2	3	4
GF5	أنام جيدا.....	0	1	2	3	4
GF6	أستمتع بالأشياء التي أقوم بها للترفيه.....	0	1	2	3	4
GF7	أنا راض عن طبيعة حياتي الآن	0	1	2	3	4

FACT-B (Version 4.0)

من فضلك ضع دائرة أو علامة على رقم واحد في كل سطر لبيان مدى انطباق إجابتك على حالتك في <u>الأيام السبعة الأخيرة</u>.

	اهتمامات إضافية	**ليس على الإطلاق**	**مرات قليلة**	**نوعاً ما**	**غالبا**	**كثيرا جدا**
B1	أعاني من نوبات ضيق تنفس.....	0	1	2	3	4
B2	أشعر بحرج بسبب ملابسي.....	0	1	2	3	4
B3	أحد ذراعيّ أو كلاهما متورم أو حساس للغاية.....	0	1	2	3	4
B4	أشعر أنني جذاب/جذابة جنسياً	0	1	2	3	4
B5	يضايقني سقوط شعري.....	0	1	2	3	4
B6	أشعر بالقلق من احتمال أن يصاب أفراد آخرون من أسرتي يوماً ما بنفس المرض الذي لدي.....	0	1	2	3	4
B7	أشعر بالقلق من تأثير التوتر على مرضي.....	0	1	2	3	4
B8	يزعجني التغير في الوزن.....	0	1	2	3	4
B9	أنا قادرة على الشعور بأني امرأة.....	0	1	2	3	4
P2	هناك أجزاء معينة من جسمي أشعر فيها بألم	0	1	2	3	4

FACT-B (Version 4) **Greek**

Θα βρείτε παρακάτω έναν κατάλογο από προτάσεις που άλλοι, με την ίδια νόσο όπως εσείς, θεωρούν σημαντικές. **Παρακαλούμε βάλτε σε κύκλο ή σημειώστε έναν αριθμό ανά γραμμή για να υποδείξετε την απάντησή σας όσον αφορά τις τελευταίες 7 ημέρες.**

	ΠΡΟΣΩΠΙΚΗ ΦΥΣΙΚΗ ΚΑΤΑΣΤΑΣΗ	**καθόλου**	**λίγο**	**κάπως**	**πολύ**	**πάρα πολύ**
GP1	Μου λείπει ζωντάνια	0	1	2	3	4
GP2	Έχω ναυτία	0	1	2	3	4
GP3	Εξαιτίας της φυσικής μου κατάστασης, έχω πρόβλημα στο να ανταποκριθώ στις ανάγκες της οικογένειάς μου	0	1	2	3	4
GP4	Έχω πόνους	0	1	2	3	4
GP5	Ενοχλούμαι από τις παρενέργειες της θεραπείας μου	0	1	2	3	4
GP6	Νιώθω άρρωστος/η	0	1	2	3	4
GP7	Αναγκάζομαι να μένω στο κρεβάτι	0	1	2	3	4

	ΚΟΙΝΩΝΙΚΗ/ΟΙΚΟΓΕΝΕΙΑΚΗ ΚΑΤΑΣΤΑΣΗ	**καθόλου**	**λίγο**	**κάπως**	**πολύ**	**πάρα πολύ**
GS1	Νιώθω κοντά στους φίλους μου	0	1	2	3	4
GS2	Η οικογένειά μου μού προσφέρει συναισθηματική συμπαράσταση	0	1	2	3	4
GS3	Υποστηρίζομαι από τους φίλους μου	0	1	2	3	4
GS4	Η οικογένειά μου έχει αποδεχθεί την ασθένειά μου	0	1	2	3	4
GS5	Είμαι ικανοποιημένος/η με την επικοινωνία που έχω με την οικογένειά μου όσον αφορά την ασθένειά μου.	0	1	2	3	4
GS6	Αισθάνομαι κοντά στον/στη σύντροφό μου (ή στο άτομο που κυρίως μου συμπαραστέκεται)	0	1	2	3	4
Q1	*Ανεξάρτητα από το επίπεδο της σημερινής σας σεξουαλικής δραστηριότητας, παρακαλούμε απαντήστε στην ακόλουθη ερώτηση. Εάν προτιμάτε να μην την απαντήσετε, σημειώστε με Χ το κουτάκι αυτό □ και συνεχίστε στην επόμενη ενότητα.*					
GS7	Είμαι ικανοποιημένος/η με τη σεξουαλική μου ζωή	0	1	2	3	4

FACT-B (Version 4)

Παρακαλούμε βάλτε σε κύκλο ή σημειώστε έναν αριθμό ανά γραμμή για να υποδείξετε την απάντησή σας όσον αφορά τις <u>τελευταίες 7 ημέρες</u>.

	<u>ΣΥΝΑΙΣΘΗΜΑΤΙΚΗ ΚΑΤΑΣΤΑΣΗ</u>	**καθόλου**	**λίγο**	**κάπως**	**πολύ**	**πάρα πολύ**
GE1	Αισθάνομαι θλίψη	0	1	2	3	4
GE2	Είμαι ικανοποιημένος/η με τον τρόπο που αντιμετωπίζω την ασθένειά μου	0	1	2	3	4
GE3	Χάνω τις ελπίδες μου στη μάχη με την ασθένειά μου	0	1	2	3	4
GE4	Αισθάνομαι νευρικότητα	0	1	2	3	4
GE5	Ανησυχώ ότι θα πεθάνω	0	1	2	3	4
GE6	Ανησυχώ ότι η κατάστασή μου θα χειροτερέψει	0	1	2	3	4

	<u>ΓΕΝΙΚΗ ΙΚΑΝΟΤΗΤΑ ΛΕΙΤΟΥΡΓΙΚΟΤΗΤΑΣ</u>	**καθόλου**	**λίγο**	**κάπως**	**πολύ**	**πάρα πολύ**
GF1	Είμαι σε θέση να εργαστώ (συμπεριλάβετε την εργασία στο σπίτι)	0	1	2	3	4
GF2	Η εργασία μου (συμπεριλάβετε την εργασία στο σπίτι) με ικανοποιεί.	0	1	2	3	4
GF3	Μπορώ και χαίρομαι τη ζωή μου	0	1	2	3	4
GF4	Αποδέχομαι την ασθένειά μου	0	1	2	3	4
GF5	Κοιμάμαι καλά	0	1	2	3	4
GF6	Απολαμβάνω αυτά που συνήθως κάνω για διασκέδαση/αναψυχή	0	1	2	3	4
GF7	Είμαι ικανοποιημένος/η με την ποιότητα ζωής μου αυτή τη στιγμή	0	1	2	3	4

FACT-B (Version 4)

Παρακαλούμε βάλτε σε κύκλο ή σημειώστε έναν αριθμό ανά γραμμή για να υποδείξετε την απάντησή σας όσον αφορά τις <u>τελευταίες 7 ημέρες</u>.

	<u>ΠΡΟΣΘΕΤΕΣ ΑΝΗΣΥΧΙΕΣ</u>	**καθόλου**	**λίγο**	**κάπως**	**πολύ**	**πάρα πολύ**
B1	Λαχανιάζω	0	1	2	3	4
B2	Με πειράζει το πώς ντύνομαι	0	1	2	3	4
B3	Το ένα μου χέρι ή και τα δύο έχουν πρηστεί ή είναι ευαίσθητα	0	1	2	3	4
B4	Νιώθω σεξουαλικά ελκυστική	0	1	2	3	4
B5	Ενοχλούμαι που χάνω τα μαλλιά μου	0	1	2	3	4
B6	Ανησυχώ μήπως και άλλα μέλη της οικογένειας μου αποκτήσουν κάποια ημέρα την ίδια ασθένεια	0	1	2	3	4
B7	Ανησυχώ για την επίδραση του άγχους στην ασθένειά μου	0	1	2	3	4
B8	Ενοχλούμαι που αλλάζει το βάρος μου	0	1	2	3	4
B9	Μπορώ να αισθανθώ γυναίκα	0	1	2	3	4
P2	Αισθάνομαι πόνο σε ορισμένα σημεία του σώματός μου	0	1	2	3	4

FACT-B (Versione 4) Italian

Sotto abbiamo elencato delle affermazioni ritenute importanti da persone con la sua stessa malattia. **La preghiamo di cerchiare o contrassegnare un solo numero per riga per indicare la sua risposta in riferimento agli <u>ultimi 7 giorni</u>.**

	BENESSERE FISICO	**Per niente**	**Un po'**	**Abba-stanza**	**Molto**	**Moltis-simo**
GP1	Mi manca l'energia	0	1	2	3	4
GP2	Ho nausea	0	1	2	3	4
GP3	Ho difficoltà ad occuparmi delle necessità della mia famiglia a causa delle mie condizioni fisiche	0	1	2	3	4
GP4	Ho dolori	0	1	2	3	4
GP5	Mi danno fastidio gli effetti collaterali della cura	0	1	2	3	4
GP6	Mi sento male	0	1	2	3	4
GP7	Sono costretto/a a trascorrere del tempo a letto	0	1	2	3	4

	BENESSERE SOCIALE/FAMILIARE	**Per niente**	**Un po'**	**Abba-stanza**	**Molto**	**Moltis-simo**
GS1	Mi sento vicino/a ai miei amici	0	1	2	3	4
GS2	La mia famiglia mi sostiene moralmente	0	1	2	3	4
GS3	Ho appoggio morale dai miei amici	0	1	2	3	4
GS4	La mia famiglia ha accettato la mia malattia	0	1	2	3	4
GS5	Sono soddisfatto/a della comunicazione nella mia famiglia a proposito della mia malattia	0	1	2	3	4
GS6	Mi sento vicino/a al mio compagno/alla mia compagna (o alla persona che mi offre il maggiore appoggio)	0	1	2	3	4
Q1	*Indipendentemente dalla Sua attività sessuale, La preghiamo di rispondere alla seguente domanda. Se preferisce non rispondere, barri questa casella* ☐ *e passi alla prossima sezione.*					
GS7	Sono soddisfatto/a della mia attività sessuale	0	1	2	3	4

FACT-B (Versione 4)

La preghiamo di cerchiare o contrassegnare un solo numero per riga per indicare la sua risposta in riferimento agli <u>ultimi 7 giorni</u>.

	BENESSERE EMOTIVO	**Per niente**	**Un po'**	**Abba-stanza**	**Molto**	**Moltis-simo**
GE1	Mi sento triste	0	1	2	3	4
GE2	Sono soddisfatto/a di come sto affrontando la mia malattia	0	1	2	3	4
GE3	Sto perdendo la speranza nella lotta contro la mia malattia	0	1	2	3	4
GE4	Sono nervoso/a	0	1	2	3	4
GE5	Mi preoccupo al pensiero della morte	0	1	2	3	4
GE6	Mi preoccupo che le mie condizioni possano peggiorare	0	1	2	3	4

	BENESSERE FUNZIONALE	**Per niente**	**Un po'**	**Abba-stanza**	**Molto**	**Moltis-simo**
GF1	Sono in grado di lavorare (si intende anche il lavoro a casa)	0	1	2	3	4
GF2	Il mio lavoro (si intende anche il lavoro a casa) mi gratifica	0	1	2	3	4
GF3	Riesco a godermi la vita	0	1	2	3	4
GF4	Ho accettato la mia malattia	0	1	2	3	4
GF5	Dormo bene	0	1	2	3	4
GF6	Provo ancora piacere nel dedicarmi ad attività di tempo libero	0	1	2	3	4
GF7	Al momento, sono soddisfatto/a della qualità della mia vita	0	1	2	3	4

FACT-B (Versione 4)

La preghiamo di cerchiare o contrassegnare un solo numero per riga per indicare la sua risposta in riferimento agli <u>ultimi 7 giorni</u>.

	ULTERIORI PROBLEMI	**Per niente**	**Un po'**	**Abba-stanza**	**Molto**	**Moltis-simo**
B1	Ho problemi a respirare	0	1	2	3	4
B2	Il modo di vestirmi mi crea disagio	0	1	2	3	4
B3	Mi sento un braccio o le braccia gonfie o doloranti	0	1	2	3	4
B4	Mi sento attraente dal punto di vista sessuale	0	1	2	3	4
B5	Mi dà fastidio la perdita di capelli	0	1	2	3	4
B6	Ho paura che un altro membro della mia famiglia possa un giorno soffrire della mia stessa malattia	0	1	2	3	4
B7	Mi preoccupo degli effetti che lo stress può avere sulla mia malattia	0	1	2	3	4
B8	I cambiamenti del mio peso mi danno fastidio	0	1	2	3	4
B9	Riesco a sentirmi donna	0	1	2	3	4
P2	In certe zone del corpo sento dolore	0	1	2	3	4

FACT-B (Versi 4) Malay

Di bawah ini ialah senarai kenyataan yang dianggap penting oleh orang lain yang menghidap penyakit yang sama seperti anda. **Bulatkan atau tandakan satu nombor bagi setiap baris untuk menunjukkan respons anda berkenaan dengan 7 hari yang lepas.**

	KESIHATAN FIZIKAL	**Tidak benar**	**Sedikit benar**	**Agak benar**	**Hampir benar**	**Amat benar**
GP1	Saya mengalami kekurangan tenaga	0	1	2	3	4
GP2	Saya berasa loya	0	1	2	3	4
GP3	Keadaan fizikal saya membuatkan saya menghadapi masalah untuk memenuhi keperluan keluarga saya	0	1	2	3	4
GP4	Saya mengalami kesakitan fizikal	0	1	2	3	4
GP5	Saya terganggu oleh kesan sampingan rawatan	0	1	2	3	4
GP6	Saya berasa tidak sihat	0	1	2	3	4
GP7	Saya terpaksa berehat atas katil	0	1	2	3	4

	KEADAAN SOSIAL/KELUARGA	**Tidak benar**	**Sedikit benar**	**Agak benar**	**Hampir benar**	**Amat benar**
GS1	Saya rasa rapat dengan kawan-kawan saya.	0	1	2	3	4
GS2	Saya mendapat sokongan emosi daripada keluarga saya	0	1	2	3	4
GS3	Saya mendapat sokongan daripada kawan-kawan saya.	0	1	2	3	4
GS4	Keluarga saya telah menerima hakikat penyakit saya	0	1	2	3	4
GS5	Saya berpuas hati dengan perhubungan oleh keluarga tentang penyakit saya.	0	1	2	3	4
GS6	Saya rasa rapat dengan pasangan saya (atau orang yang menjadi penyokong utama saya)	0	1	2	3	4
Q1	*Tanpa mengambil kira tahap aktiviti seks anda pada masa ini, sila jawab soalan berikut. Jika anda memilih untuk tidak menjawabnya, sila tandakan ✓ pada petak ini ☐ dan terus ke seksyen berikutnya.*					
GS7	Saya berpuas hati dengan kehidupan seksual saya	0	1	2	3	4

FACT-B (Versi 4)

Bulatkan atau tandakan satu nombor bagi setiap baris untuk menunjukkan respons anda berkenaan dengan 7 hari yang lepas.

	KEADAAN EMOSI	**Tidak benar**	**Sedikit benar**	**Agak benar**	**Hampir benar**	**Amat benar**
GE1	Saya rasa sedih	0	1	2	3	4
GE2	Saya berpuas hati dengan bagaimana cara saya menghadapi penyakit saya	0	1	2	3	4
GE3	Saya semakin putus harapan untuk melawan penyakit saya	0	1	2	3	4
GE4	Saya rasa gelisah	0	1	2	3	4
GE5	Saya risau tentang kematian	0	1	2	3	4
GE6	Saya risau yang keadaan saya akan bertambah teruk	0	1	2	3	4

	KEADAAN FUNGSI DIRI	**Tidak benar**	**Sedikit benar**	**Agak benar**	**Hampir benar**	**Amat benar**
GF1	Saya berupaya bekerja (termasuk kerja di rumah)	0	1	2	3	4
GF2	Pekerjaan saya (termasuk kerja di rumah) amat memuaskan	0	1	2	3	4
GF3	Saya berupaya menikmati kehidupan	0	1	2	3	4
GF4	Saya telah menerima hakikat penyakit saya	0	1	2	3	4
GF5	Saya tidur lena	0	1	2	3	4
GF6	Saya menikmati perkara-perkara yang lazim saya buat untuk bersuka-suka	0	1	2	3	4
GF7	Saya berpuas hati dengan kualiti kehidupan saya kini	0	1	2	3	4

FACT-B (Versi 4)

Bulatkan atau tandakan satu nombor bagi setiap baris untuk menunjukkan respons anda berkenaan dengan 7 hari yang lepas.

	PERSOALAN TAMBAHAN	**Tidak benar**	**Sedikit benar**	**Agak benar**	**Hampir benar**	**Amat benar**
B1	Saya mengalami sesak nafas	0	1	2	3	4
B2	Saya resah sebab saya rasa orang lain memerhatikan cara saya berpakaian.....	0	1	2	3	4
B3	Salah satu atau kedua-dua lengan saya bengkak atau sensitif apabila disentuh	0	1	2	3	4
B4	Saya berasa menarik dari segi seksual	0	1	2	3	4
B5	Saya terganggu oleh keguguran rambut.	0	1	2	3	4
B6	Saya bimbang ahli keluarga saya yang lain suatu hari nanti mungkin mendapat penyakit yang sama seperti saya.....	0	1	2	3	4
B7	Saya risau tentang kesan stres pada penyakit saya.....	0	1	2	3	4
B8	Saya terganggu oleh perubahan berat badan	0	1	2	3	4
B9	Saya boleh merasa kewanitaan saya.....	0	1	2	3	4
P2	Ada bahagian-bahagian tertentu badan saya di mana saya mengalami kesakitan.....	0	1	2	3	4

FACT-B（第四版）Simplified Chinese

以下是一些与您患有同样疾病的人所认为重要的陈述。**请在每行圈选或标出一个数字来表明适用于您过去7天情况的回答。**

	生 理 状 况	一点也不	有一点	有些	相当	非常
GP1	我精神不好	0	1	2	3	4
GP2	我感到恶心	0	1	2	3	4
GP3	因为我身体不好，我满足家庭的需要有困难	0	1	2	3	4
GP4	我感到疼痛	0	1	2	3	4
GP5	治疗的副作用使我感到烦恼	0	1	2	3	4
GP6	我觉得病了	0	1	2	3	4
GP7	我因病被迫要卧床休息	0	1	2	3	4

	社 会 / 家 庭 状 况	一点也不	有一点	有些	相当	非常
GS1	我和朋友们很亲近	0	1	2	3	4
GS2	我在感情上得到家人的支持	0	1	2	3	4
GS3	我得到朋友的支持	0	1	2	3	4
GS4	我的家人已能正视我患病这一事实	0	1	2	3	4
GS5	我满意家人间对我疾病的沟通方式	0	1	2	3	4
GS6	我与自己的配偶（或给我主要支持的人）很亲近 ...	0	1	2	3	4
Q1	*不管你近期的性生活的程度，请回答下面的问题* *如果你不愿回答，请在这里注明 □，然后回答下一组问题*					
GS7	我对自己的性生活感到满意	0	1	2	3	4

FACT-B（第四版）

请在每行圈选或标出一个数字来表明适用于您过去7天情况的回答。

	情 感 状 况	一点也不	有一点	有些	相当	非常
GE1	我感到悲伤	0	1	2	3	4
GE2	我满意自己处理疾病的方式	0	1	2	3	4
GE3	在与疾病的抗争中，我越来越感到失望	0	1	2	3	4
GE4	我感到紧张	0	1	2	3	4
GE5	我担心我可能会去世	0	1	2	3	4
GE6	我担心自己的病情会恶化	0	1	2	3	4

	功 能 状 况	一点也不	有一点	有些	相当	非常
GF1	我能够工作（包括在家里工作）	0	1	2	3	4
GF2	我的工作（包括在家的工作）令我有成就感	0	1	2	3	4
GF3	我能够享受生活	0	1	2	3	4
GF4	我已能面对自己的疾病	0	1	2	3	4
GF5	我睡得很好	0	1	2	3	4
GF6	我在享受我常做的娱乐活动	0	1	2	3	4
GF7	我对现在的生活质量感到满意	0	1	2	3	4

FACT-B（第四版）

请在每行圈选或标出一个数字来表明适用于您过去7天情况的回答。

	附 加 关 注	一点也不	有一点	有些	相当	非常
B1	我一直感到呼吸急促	0	1	2	3	4
B2	我在意自己的衣着	0	1	2	3	4
B3	我的一只胳膊或两只胳膊发肿，或一碰就疼	0	1	2	3	4
B4	我感到自己在性方面有吸引力	0	1	2	3	4
B5	脱发使我烦恼	0	1	2	3	4
B6	我担心家里其他人有一天会得和我一样的病	0	1	2	3	4
B7	我担心紧张对我的疾病造成的影响	0	1	2	3	4
B8	体重的变化使我烦恼	0	1	2	3	4
B9	我能够感到自己像个女人	0	1	2	3	4
P2	我身体的某些部位感到疼痛	0	1	2	3	4

FACT-B (Version 4) Tagalog

Sa ibaba ay isang listahan ng mga pahayag na galing sa mga ibang taong may sakit na tulad ng sakit mo na inaakala nilang mahalaga. **Mangyaring bilugan o markahan ang isang numero para sa bawat linya para ipakita ang inyong sagot na naaangkop para sa <u>nakaraang 7 araw</u>.**

	<u>KAGALINGAN NG KATAWAN</u>	**Hindi kailan-man**	**Kaunti**	**Medyo**	**Medyo marami**	**Lubos na marami**
GP1	Kulang ako sa enerhiya	0	1	2	3	4
GP2	Pakiramdam ko na ako ay nasusuka	0	1	2	3	4
GP3	Dahil sa kalagayan ng aking katawan, nahihirapan ako na maibigay ang mga pangangailangan ng aking pamilya	0	1	2	3	4
GP4	Mayroon akong kirot	0	1	2	3	4
GP5	Nahihirapan ako dahil sa mga di-hangad na epekto ng paggamot	0	1	2	3	4
GP6	Masama ang aking pakiramdam	0	1	2	3	4
GP7	Ako ay napipilitang manatili sa aking higaan	0	1	2	3	4

	<u>KAGALINGAN NG PANLIPUNAN AT NG PAMILYA</u>	**Hindi kailan-man**	**Kaunti**	**Medyo**	**Medyo marami**	**Lubos na marami**
GS1	Pakiramdam ko na malapit ako sa aking mga kaibigan	0	1	2	3	4
GS2	Binibigyan ako ng aking pamilya ng emosyonal na suporta	0	1	2	3	4
GS3	Sinusuportahan ako ng aking mga kaibigan	0	1	2	3	4
GS4	Tanggap na ng aking pamilya ang aking sakit	0	1	2	3	4
GS5	Kontento ako sa pakikipagusap-usapan ng aking pamilya tungkol sa aking sakit	0	1	2	3	4
GS6	Pakiramdam ko na malapit ako sa aking kapareha (o sa taong pangunahing sumusuporta sa akin)	0	1	2	3	4
Q1	*Pakisagot po lamang ang sumusunod na tanong kahit anuman ang kalagayan ng inyong kaugnayang sekswal sa ngayon. Kung hindi po ninyo ninanais na sagutin ito, lagyan ng tsek ang kahong ito* ☐ *at magpatuloy sa susunod na bahagi.*					
GS7	Kontento ako sa aking buhay seksuwal	0	1	2	3	4

FACT-B (Version 4)

Mangyaring bilugan o markahan ang isang numero para sa bawat linya para ipakita ang inyong sagot na naaangkop para sa <u>nakaraang 7 araw</u>.

	<u>KAGALINGANG PANGDAMDAMIN</u>	**Hindi kailan-man**	**Kaunti**	**Medyo**	**Medyo marami**	**Lubos na marami**
GE1	Malungkot ako	0	1	2	3	4
GE2	Kontento ako sa kung papaano ko kinakaya ang aking sakit	0	1	2	3	4
GE3	Nawawalan na ako ng pag-asa sa paglaban sa aking sakit	0	1	2	3	4
GE4	Ninenerbiyos ako	0	1	2	3	4
GE5	Nag-aalala ako tungkol sa kamatayan	0	1	2	3	4
GE6	Nag-aalala ako na lulubha ang aking kalagayan	0	1	2	3	4

	<u>KAGALINGAN SA PANGARAW-ARAW NA KAKAYAHAN NG PAGGAWA</u>	**Hindi kailan-man**	**Kaunti**	**Medyo**	**Medyo marami**	**Lubos na marami**
GF1	Ako ay nakakapagtrabaho (kabilang ang trabaho sa bahay)	0	1	2	3	4
GF2	Ang aking trabaho (kabilang ang trabaho sa bahay) ay nagbibigay kasiyahan sa akin	0	1	2	3	4
GF3	Kinasisiyahan ko ang aking buhay	0	1	2	3	4
GF4	Tanggap ko na ang aking sakit	0	1	2	3	4
GF5	Nakakatulog ako nang mabuti	0	1	2	3	4
GF6	Kinasisiyahan ko ang mga bagay na aking kalimitang pinaglilibangan	0	1	2	3	4
GF7	Kontento ako sa kalidad ng buhay ko sa kasalukuyan	0	1	2	3	4

FACT-B (Version 4)

Mangyaring bilugan o markahan ang isang numero para sa bawat linya para ipakita ang inyong sagot na naaangkop para sa <u>nakaraang 7 araw</u>.

	KARAGDAGANG PINAG-AALALAHANAN	**Hindi kailan-man**	**Kaunti**	**Medyo**	**Medyo marami**	**Lubos na marami**
B1	Nangangapos ang aking hininga	0	1	2	3	4
B2	Nag-aalala ako sa aking pananamit	0	1	2	3	4
B3	Ang isa o pareho sa aking mga braso ay namamaga o masakit kapag hinipo	0	1	2	3	4
B4	Sa pakiramdam ko ay seksi ako	0	1	2	3	4
B5	Nahihirapan ako dahil sa pagkalagas ng buhok	0	1	2	3	4
B6	Nag-aalala ako na balang araw ang ibang miyembro ng aking pamilya ay magkakaroon ng kasakitan na tulad ko	0	1	2	3	4
B7	Nag-aalala ako tungkol sa epekto ng stress sa sakit ko.....	0	1	2	3	4
B8	Nababahala ako sa pagbabago ng aking timbang	0	1	2	3	4
B9	Nagagawa kong madama na ako ay babae	0	1	2	3	4
P2	May mga bahagi ng aking katawan na kung saan ako'y nakararamdam ng pananakit	0	1	2	3	4

FACT-B（第四版）Traditional Chinese

以下是那些跟您有同樣疾病的人所認為重要的一些陳述。**請在每一行圈出或標出一個數字，以表達適用於您過去7天的回答。**

	生理健全狀況	一點也不	有一點	有些	相當	非常
GP1	我精神不好	0	1	2	3	4
GP2	我有反胃噁心的情形	0	1	2	3	4
GP3	因為我的身體狀況，我有困難達到家人的需求	0	1	2	3	4
GP4	我有疼痛	0	1	2	3	4
GP5	我對治療的副作用感到困擾	0	1	2	3	4
GP6	我覺得身體不適	0	1	2	3	4
GP7	我因病被迫要臥床休息	0	1	2	3	4

	社交/家庭健全狀況	一點也不	有一點	有些	相當	非常
GS1	我覺得與我的朋友親近	0	1	2	3	4
GS2	我從我家人獲得情緒上的支持	0	1	2	3	4
GS3	我從我朋友獲得支持	0	1	2	3	4
GS4	我家人已接受我的疾病	0	1	2	3	4
GS5	我滿意家人之間對我疾病的溝通方式	0	1	2	3	4
GS6	我覺得與我的伴侶（或我主要支持者）親近	0	1	2	3	4
Q1	*不管你近期的性生活的程度，請回答下面的問題。* *如果你不願回答，請在這裡註明 □ 然後跳到下一部分。*					
GS7	我對我的性生活感到滿意	0	1	2	3	4

FACT-B（第四版）

請在每一行圈出或標出一個數字，以表達適用於您過去7天的回答。

	情緒健全狀況	一點也不	有一點	有些	相當	非常
GE1	我感到悲傷	0	1	2	3	4
GE2	我滿意自己處理疾病的方式	0	1	2	3	4
GE3	我逐漸失去對抗我的疾病的希望	0	1	2	3	4
GE4	我覺得緊張	0	1	2	3	4
GE5	我擔心死亡	0	1	2	3	4
GE6	我擔心我的狀況會惡化	0	1	2	3	4

	功能健全狀況	一點也不	有一點	有些	相當	非常
GF1	我能夠工作（包括在家的工作）	0	1	2	3	4
GF2	我滿意我的工作（包括在家的工作）	0	1	2	3	4
GF3	我能夠享受生活	0	1	2	3	4
GF4	我已接受我的疾病	0	1	2	3	4
GF5	我睡得好	0	1	2	3	4
GF6	我依然享受我以前常做的有趣的事	0	1	2	3	4
GF7	我滿足我現在的生活品質	0	1	2	3	4

FACT-B（第四版）

請在每一行圈出或標出一個數字，以表達適用於您過去7天的回答。

	附加關注事項	一點也不	有一點	有些	相當	非常
B1	我呼吸時曾有氣不足	0	1	2	3	4
B2	我在意自己的衣服穿著	0	1	2	3	4
B3	我有一側或兩側的手臂腫脹或疼痛	0	1	2	3	4
B4	我覺得自己是性感的	0	1	2	3	4
B5	我對掉頭髮感到困擾	0	1	2	3	4
B6	我擔心其他家人也會得到跟我同樣的疾病	0	1	2	3	4
B7	我擔心壓力會影響到我的疾病	0	1	2	3	4
B8	我對體重的改變感到困擾	0	1	2	3	4
B9	我能夠覺得自己像個女人	0	1	2	3	4
P2	我感到身體的某些部位有疼痛的症狀	0	1	2	3	4

FACT-B (Version 4) Thai

ข้อความต่างๆ ด้านล่างนี้คือสิ่งที่ผู้ป่วยโรคเดียวกับท่านกล่าวว่ามีความสำคัญ **ขอให้ท่านพิจารณาว่าข้อความแต่ละข้อตรงกับสถานการณ์ของท่านในช่วง 7 วันที่ผ่านมาหรือไม่ อย่างไร จากนั้น วงกลมหรือทำเครื่องหมายที่ตัวเลขเพียงตัวเดียวต่อหนึ่งบรรทัด เพื่อระบุคำตอบของท่าน**

ความผาสุกด้านร่างกาย

		ไม่เลย	เล็กน้อย	ปานกลาง	ค่อนข้างมาก	มากที่สุด
GP 1	ข้าพเจ้ารู้สึกหมดเรี่ยวแรง	0	1	2	3	4
GP 2	ข้าพเจ้ามีอาการคลื่นไส้	0	1	2	3	4
GP 3	เนื่องจากสภาพร่างกายที่เป็นอยู่ขณะนี้ ทำให้ข้าพเจ้ามีปัญหาในการดูแลรับภาระต่างๆในครอบครัว	0	1	2	3	4
GP 4	ข้าพเจ้ามีอาการปวด	0	1	2	3	4
GP 5	ข้าพเจ้ารำคาญต่อผลข้างเคียงที่เกิดจากการรักษา	0	1	2	3	4
GP 6	ข้าพเจ้ารู้สึกไม่สบาย	0	1	2	3	4
GP 7	ข้าพเจ้าจำต้องใช้เวลาส่วนใหญ่นอนอยู่บนเตียง	0	1	2	3	4

ความผาสุกด้านสังคม/ ครอบครัว

		ไม่เลย	เล็กน้อย	ปานกลาง	ค่อนข้างมาก	มากที่สุด
GS 1	ข้าพเจ้ารู้สึกใกล้ชิดสนิทสนมกับเพื่อนๆ	0	1	2	3	4
GS 2	ข้าพเจ้าได้รับกำลังใจจากครอบครัว	0	1	2	3	4
GS 3	ข้าพเจ้าได้รับการดูแลช่วยเหลือจากเพื่อนๆ	0	1	2	3	4
GS 4	คนในครอบครัวยอมรับการเจ็บป่วยของข้าพเจ้า	0	1	2	3	4
GS 5	ข้าพเจ้าพอใจกับการสื่อสารภายในครอบครัว เช่น การพูดคุย การแสดงความเห็นอกเห็นใจ เกี่ยวกับการเจ็บป่วยของข้าพเจ้า	0	1	2	3	4
GS 6	ข้าพเจ้ารู้สึกใกล้ชิดกับคู่ครอง (หรือคนสำคัญที่คอยให้กำลังใจ)	0	1	2	3	4
Q1	*ไม่ว่าในปัจจุบันท่านจะมีเพศสัมพันธ์มากน้อยเพียงใดก็ตาม กรุณาตอบคำถามต่อไปนี้ หากท่านไม่ต้องการตอบคำถามในส่วนนี้ กรุณากาเครื่องหมาย X ลงในช่องนี้* ☐ *แล้วข้ามไปทำข้อต่อไป*					
GS 7	ข้าพเจ้าพึงพอใจกับชีวิตทางเพศของตนเอง (ไม่ว่าขณะนี้จะมีเพศสัมพันธ์หรือไม่ก็ตาม)	0	1	2	3	4

FACT-B (Version 4)

ขอให้ท่านพิจารณาว่าข้อความแต่ละข้อตรงกับสถานการณ์ของท่านใน<u>ช่วง 7 วันที่ผ่านมา</u>หรือไม่ อย่างไร จากนั้น วงกลมหรือทำเครื่องหมายที่ตัวเลขเพียงตัวเดียวต่อหนึ่งบรรทัด เพื่อระบุคำตอบของท่าน

	<u>ความผาสุกด้านอารมณ์ จิตใจ</u>	**ไม่เลย**	**เล็กน้อย**	**ปานกลาง**	**ค่อนข้างมาก**	**มากที่สุด**
GE 1	ข้าพเจ้ารู้สึกเศร้าใจ	0	1	2	3	4
GE 2	ข้าพเจ้ารู้สึกพอใจกับวิธีที่ข้าพเจ้าปรับตัวกับการเจ็บป่วยของตนเอง.....	0	1	2	3	4
GE 3	ข้าพเจ้ารู้สึกหมดหวังในการต่อสู้กับการเจ็บป่วย	0	1	2	3	4
GE 4	ข้าพเจ้ารู้สึกกระวนกระวายใจ.....	0	1	2	3	4
GE 5	ข้าพเจ้ากังวลเกี่ยวกับความตาย	0	1	2	3	4
GE 6	ข้าพเจ้ากังวลว่าอาการจะแย่ลง.....	0	1	2	3	4

	<u>ความผาสุกด้านการปฏิบัติกิจกรรม</u>	**ไม่เลย**	**เล็กน้อย**	**ปานกลาง**	**ค่อนข้างมาก**	**มากที่สุด**
GF 1	ข้าพเจ้าสามารถทำงานทั่วไปได้ (รวมถึงงานบ้าน).....	0	1	2	3	4
GF 2	ข้าพเจ้าพึงพอใจในผลสำเร็จของงาน (รวมถึงงานบ้าน) .	0	1	2	3	4
GF 3	ข้าพเจ้ายังมีชีวิตที่สนุกสนานได้.....	0	1	2	3	4
GF 4	ข้าพเจ้ายอมรับการเจ็บป่วยที่เป็นอยู่ได้	0	1	2	3	4
GF 5	ข้าพเจ้านอนหลับสนิทดี	0	1	2	3	4
GF 6	ข้าพเจ้ายังคงสนุกสนานเหมือนเดิมกับสิ่งที่เคยทำเพื่อ ความสำราญ	0	1	2	3	4
GF 7	ข้าพเจ้าพึงพอใจกับคุณภาพชีวิตของตนเองในขณะนี้	0	1	2	3	4

FACT-B (Version 4)

ขอให้ท่านพิจารณาว่าข้อความแต่ละข้อตรงกับสถานการณ์ของท่านใน<u>ช่วง 7 วันที่ผ่านมา</u>หรือไม่ อย่างไรจากนั้น วงกลมหรือทำเครื่องหมายที่ตัวเลขเพียงตัวเดียวต่อหนึ่งบรรทัด เพื่อระบุคำตอบของท่าน

	<u>ด้านอื่นๆ เพิ่มเติม</u>	**ไม่เลย**	**เล็กน้อย**	**ปานกลาง**	**ค่อนข้างมาก**	**มากที่สุด**
B1	ข้าพเจ้าหายใจไม่เต็มอิ่ม.....	0	1	2	3	4
B2	ข้าพเจ้าขาดความมั่นใจในการแต่งกาย.....	0	1	2	3	4
B3	แขนข้างใดข้างหนึ่งหรือทั้งสองข้างของข้าพเจ้าบวมหรือตึงเจ็บ.....	0	1	2	3	4
B4	ข้าพเจ้ารู้สึกมีเสน่ห์เป็นที่ดึงดูดใจทางเพศ.....	0	1	2	3	4
B5	ฉันรำคาญเรื่องผมร่วง	0	1	2	3	4
B6	ข้าพเจ้ากังวลใจว่าสักวันหนึ่งสมาชิกในครอบครัวจะป่วยเป็นโรคเช่นเดียวกับข้าพเจ้า.....	0	1	2	3	4
B7	ข้าพเจ้ากังวลว่าความเครียดจะมีผลต่อการเจ็บป่วยของตัวเอง	0	1	2	3	4
B8	ข้าพเจ้าไม่สบายใจที่น้ำหนักตัวเปลี่ยนไป.....	0	1	2	3	4
B9	ข้าพเจ้ารู้สึกว่ายังเป็นผู้หญิงเหมือนกับหญิงอื่นโดยทั่วไป.....	0	1	2	3	4
P2	ข้าพเจ้ารู้สึกเจ็บปวดที่บางส่วนของร่างกายของข้าพเจ้า.....	0	1	2	3	4

Chapter 6

Chapter 6

Overall Discussion

Chapter preface:

This chapter discusses the overall research findings

including practical implications, the limitations of the study and

future research recommendations

Chapter 6

Overall discussion

In this PhD thesis, entitled "Physical activity motivation and self-directed physical activity in female breast cancer survivors" the findings from the systematic review with meta-analysis, the development of the clinical trial protocol, ethics approvals and all the paperwork required for its completion, and the pilot outcomes of the clinical trial, are presented.

Physical activity (PA) behaviour and PA motivation strategies were investigated, particularly step tracker and motivational interviewing (MI) for self-directed PA in breast cancer survivors. The research data shown limitation in the feasibility of a clinical trial on 12 weeks self-directed physical activity applying a pedometer and MI in breast cancer survivors; as participant recruitment and adequate clinical trial implementation were affected by the COVID-19 pandemic in 2020. In addition, the research has shown new evidence through a systematic review and meta-analysis regarding positive effects of these two motivational strategies (pedometer and MI) for adherence to self-directed PA in breast cancer survivors.

1. The findings from the pilot study of the clinical trial

The feasibility of this pilot study was limited by ~~the~~ low recruitment rate of participants over 11 months between February and December 2020. Even though the clinical trial was impacted by the COVID-19 outbreak, the study was able to continue albeit with a low recruitment rate throughout 2020. The recruitment rate was low at the rate of 1.5 participants per month compared to previous randomized-controlled trials (RCTs) in which the average recruitment rate was 4 participants per month, with time frames ranging between 6 and 14 months [1].

The retention rate of the study was high at 82.35 % over the 12-week period which was similar to previous RCT studies [2, 3]. High retention rate is possibly due to the willingness to engage self-directed physical activity of the most participants. In this study, the pedometer was found to be practical for everyday use among participants who were female breast cancer survivors. Most of the participants (94.12%) were able to operate the pedometer and were able to synchronize it with the Fibit application on their smartphone or computer. Only one participant who was in older adulthood (63 years old) withdrew the study as she was not willing to try out the pedometer which technological matter is likely an obstacle [4].

The current study showed that the average daily steps at baseline of participants across the two groups was 8,457.84 + 3,596.09 which was similar to a previously reported study [3]. The average of baseline daily steps in breast caner survivors was 7,400 steps per day [5]. Daily steps were not significantly different between groups and did not significantly change from baseline. While non-significant, the daily steps taken by both groups did appear to increase overall, with the non-significant outcome likely due to the small numbers [6]. Moreover, some participants declared their physical activity limitation due to lockdown restriction in Melbourne over the year 2020 (DIG1, DIG2 and DIG4). Two participants informed the researchers that they would not go out for exercise if it was too cold (IIG4 and IIG 8). There was evidence that lockdown and cold weather could be barriers to exercise [7,8]. This pilot study was not able to show an improvement in quality of life (QoL); the score of the Functional Assessment of Cancer Therapy Breast (FACT-B) and subscale, psychological health; the score of Depression Anxiety and Stress Scale-21 items (DASS-21), exercise self-regulation; the score of Behavioral Regulation in Exercise Questionnaire-2 (BREQ2), exercise barrier and task self-efficacy (the percent confidence for exercise) by the effect of MI in the intervention group and time. Unlike in previous studies, breast cancer survivors who met PA recommendations for malignant disease had higher levels of emotional well-being, likely due to the low sample size [9].

2. The findings from the systematic review and meta-analysis

The systematic review and meta-analysis determined whether step tracker (pedometer) and MI are effective motivation strategies to improve adherence in self-directed physical activity in breast cancer survivors. The meta-analysis showed that PA adherence was reported through various measurement scales including weekly intensity of PA (metabolic equivalent of task; MET), weekly minutes of moderate to vigorous physical activity (MVPA), daily steps, the numbers of participant who met PA goals and percentage of participants who met PA recommendations or % PA adherence. The study showed that pedometer combined with another motivation based on behavioral change theory such as Social Cognitive Theory (SCT), Theory of Planned Behaviour (TPB), and the Transtheoretical Model (TTM) can provide small to moderate effects on steps count and MVPA duration when compared to a control condition such as receiving standard PA recommendation or usual care of breast cancer patients. Likewise, PA with motivation strategies had positive effects on the number of participants who meet PA recommendation (odds ratio= 2.66, 95% CI 1.34, 5.27).

The study concluded that the improvements in PA adherence were mostly consistent across subgroups of PA motivation strategies, even though a variation among trials was detected.

3. The Limitations of the study

There were a few limitations in this study. One was the small sample size. The absences of the positive effect on PA adherence, QoL and psychological health in breast cancer survivors may result from the limitation of recruitment process during the outbreak of COVID-19 leading to a small sample size in the pilot study. There were significant challenges in the execution of the clinical trial to deal with the barrier of breast cancer survivors in order to adhere to the self-directed PA such as weather, family issues and work-life balance. These challenges were exaggerated by the COVID-19 pandemic, which significantly contributed to the small sample size. The pilot study may have some potential risks of bias such as the limited generalisation of participants and type 1 error results because most of recruited participants lived in Melbourne, Australia and they were willing to participate the self-directed physical activity program. Additionally, the study could not blind participants and outcome assessment because of our study design and human research ethics issue.

We did not analyse immune biomakers of participants while we were conducting the pilot study. It would be costly effective to analyse a large number of plasma samples when we use an assay kit.

Furthermore, the significant heterogeneity of the studies included in the systematic review and meta-analysis was the major limitation. The included trials in the review all showed unavoidable issues with blinding participants and exposing the trials to risks of bias.

4. Future research recommendations

This study recommends that it is worthy for the assessment of PA adherence in self-directed PA among breast cancer survivors. Future studies to identify optimal behavior change strategies to improve PA adherence in breast cancer survivors should be conducted. Additionally, the results of the study recommends further studies into validation of PA adherence measurement methods in self-directed physical activity programs.

Larger sample size of participants is recommended. In fact, this study will continue by the investigators as a larger randomized controlled with 2x2 crossover design study as described under the PAPHIO Study Protocol. The immunological assay will be conducted when the study can meet the target numbers of participant. The study will further adjust the recruitment strategy to achieve the sufficient number of participants.

5. Practical implication

The thesis has affirmed that PA motivation strategies encouraging self-monitoring through a step tracker and MI intervention were able to promote physical activity adherence in breast cancer survivors, as a result of the positive findings in the meta-analysis. Even though the daily steps did not change by the effect of intervention and time, the pilot study did show acceptable feasibility of self-directed physical activity by the usage of Fitbit for self-monitoring in breast cancer survivors. Likewise, MI via telehealth (video zoom or equivalent, and phone calls) during the lockdown period was successful in enhancing the participants' attitude towards self-directed PA with step trackers and in helping them decide their daily step goal.

6. Conclusion

Step tracker or pedometer combined with counselling, print material or MI according to behavior change theory, contributed consistent positive effects on adherence to self-directed PA among breast cancer survivors. It is practicable to apply self-directed PA by the use of a pedometer for self-monitoring and MI in breast cancer survivors. The study in this thesis showed limited efficacy of the intervention by time on PA adherence (by daily step count), psychological health and QoL in breast cancer survivors which is likely due to the small sample size by the impact of COVID-19 in 2020. Future studies will assess the efficacy of PA motivation for female breast cancer survivors with larger sample size (n=64 as in the study protocol).

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Independent chapter

Independent chapter

The Journey of the PAPHIO study

The long process of Human Research Ethics Approval and the Impact of COVID-19 on the study

Chapter preface:

This summary describes the journey and issues I encountered during my PhD caused by delays in Human Research Ethics approval, followed by the impact COVID-19 had on my research in 2020.

Independent chapter

The Journey of the PAPHIO study

The long process for Human Research Ethics and Impact of COVID-19 on the study

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1. Introduction

I would like to describe my experience of the journey to achieving human research ethics approval for my study, as it was one of the major components of my PhD. Together with the members of the research team a great deal of time and effort over the last 3 years were invested until the project; **P**hysical activity **A**dherence, **P**sychological **H**ealth and **I**mmunological **O**utcomes (PAPHIO Study) in breast cancer survivors, received approval from Melbourne Health Human Research Ethics Committee (HREC), Australia on 29 April 2019. The project was then authorized to be undertaken at Western Health, by the Office for Research, Western Health, Melbourne, Australia on 4 December 2019. On 23 January 2020 the project began recruitment of participants. After one month the project was impacted by the COVID-19 outbreak, with clinical studies in Melbourne halted, and the city entering lockdown from March-October 2020.

I hope that my experience and the long process encountered for obtaining human research ethics for the study would aid in future postgraduate candidates to obtain ethics either prior to starting their candidature or, understand the in dept process required and to ensure it is completed and approved in a timely manner. In addition, a number of mitigation strategies were used to deal with the impact that COVID-19 pandemic had on my research study.

2. Process of Human Research Ethics Approval

At the end of 2016, my supervisors and I had an initial meeting with our colleagues from Western Health, Sunshine Hospital VIC Australia and IPC Health (The Improving and Promoting Community Health), Altona Meadows VIC Australia, to assess the feasibility of a proposed study on the effect of self-directed physical activity on health and well-being of women with breast cancer. Western Health was able to provide participant recruitment, facilities including a clinical study site, and pathology lab. IPC Health were

able to assist with participant recruitment. Following 6 months of coursework and a successful candidature presentation in May 2017, I began writing a human research ethics application. My research ethics journey started at that point.

According to the Department of Health, State Government of Victoria, the clinical trial was considered as a high-risk project due to the acquisition of blood samples from each participant. Additionally, two approvals were required to begin the study. The first was the Human Research Ethics Application (HREA) to approve the study protocol, and the second, a Site Specific Assessment (SSA) to conduct the research study at Western Health facilities. The project was an investigator-initiated, single site study, with one research team and 7 investigators. The principal investigator of the study was a Breast Cancer Surgeon and Head of the Breast Cancer Unit at Western Health. The other 6 associate investigators were a breast care nurse from Western Health, a breast cancer support nurse from IPC health, my three supervisors (Professor Vasso Apostolopoulos, Professor Lily Stojanovska and Professor Remco Polman) and myself. Victoria University was the study sponsor and developed the study protocol. I myself undertook the coordination of the project with the offices for research at Melbourne Health and Western Health under the supervision of both the principal investigator and my supervisory team.

It took eighteen months (from mid-2017 and the end of 2018) to complete HREA in the newly developed Ethics Review Manager (ERM) platform and submit to Melbourne Health Human Research Ethics Committee (HREC). The process was particularly long, due to the many documents relating to the project that were required to be completed. The most important document was the research protocol, outlining the design of the study, its procedures and outcomes. After submission, it took another month to receive peer reviews and for amendments to be made according to the feedback received. Additionally, a number of other documents were submitted to the human research ethics committee, including the participant informed consent form, materials for participant recruitment (poster advertisement and letter of invitation) as well as assessment tools and questionnaires. All documents were prepared according to the requirements of the National statement on ethical conduct in human research by the National Health and Medical Research Council. Submission to the HREC was on 29 October 2018.

The feedback from the HREC was a significant challenge with 33 points of comments including suggested edits for the appropriateness of some documents such as the

participant informed consent form, advertising poster and letter of invitation. However, the committee made note of their appreciated the team members, calling it an impressive effort. The most significant concern of the HREC was regarding the research design, so in response we changed the design from a single armed pre-post study to a randomisation trial with a 2 x 2 crossover design. The revisions took an additional 3 months with resubmission in January 2019. Following this, we received further minor requests for alterations, with final approval received on 29 April 2019.

3. Site Specific Assessment Approval

The second approval required was the Site-Specific Assessment (SSA). This is a project authorization to conduct research at Western Health facilities, which despite human research ethics approval granted, this took an additional 8 months. This involved, (i) clinical site (breast cancer care unit) approval by the Director of surgery; (ii) pathology approval for participant blood collection through Dorevitch Pathology (on site at Western Health; taking one month for approval); (iii) honorary researcher appointments for myself and for the motivational interviewing counsellor who would conduct motivational interviewing for participants (taking an additional month for approvals due to requirements for health clearance and police checks); and (iv) research collaboration agreements between Western Health and Victoria University (taking another month). This was submitted in August 2019 with the project authorized on 4 December 2019. The overall process of Human Research Ethics approval is illustrated in Figure 1. We were unable to start recruitment until January 2020, as visiting schedules of potential participants at the breast cancer clinic were unavailable until after the Christmas and new year holiday period.

4. Participant Recruitment

On 23 January 2020, I introduced the project to the research team at a multidisciplinary team meeting at Western Health (Sunshine hospital) marking the start of the recruitment phase of the project. The first participant was enrolled on 30 January 2020.

The project was registered with the Australian and New Zealand Clinical Trial Registry (ANZCTR) on 13 September 2019 with the registration number ACTRN

12619001271190; a requirement for all clinical trials. The clinical trial is publicly posted on the ANZCTR website.

5. COVID-19 pandemic

Within a month of starting the recruitment process, the global outbreak of COVID-19 began with the situation accelerating in mid-March 2020. By this time, we had recruited 5 participants. Victoria declared a state of emergency on 16 March 2020 with Australia closing its borders on 20 March 2020. Western Health announced all existing clinical research was to be paused if participants were likely to be affected by the pandemic. Therefore, participant recruitment at the clinical site was stopped. At that time, Victoria University also announced limitation to access research laboratories which impacted participants' blood processing and testing. Melbourne was in stage-4 lockdown until October 2020.

5.1. Changes to Recruitment

The feasibility of the study, given the challenges of continuing participant recruitment during the restricted period was assessed to identify a way forward. Western Health introduced Telehealth to their breast cancer patients and this gave us the opportunity to identify potential participants during these consultations. As a result, amendments to the human ethics protocol for alternative recruitment methods to include telehealth, email and social media were required, and were submitted to HREC. At this point, IPC Health Altona Meadows was added as another recruitment site. Approval for the trial amendments was received in June 2020. Participant recruitment resumed via video calls and zoom meetings, and the motivational interviewing was moved to online rather than face-to-face.

In June 2020, five additional participants were recruited through the newly approved methods. However, at this point, Melbourne was impacted by a second wave of COVID-19 and in July 2020, there was a second stage-4 lockdown in the State of Victoria. The designated 'hot spot' areas in Melbourne which were mostly affected by the second wave were the western suburbs of Melbourne, in particular, Sunshine and Werribee. As these were also the sites of participant recruitment (Sunshine campus) and blood processing (Werribee campus). It was difficult to continue the project during the period of

restrictions, and so between July and October 2020, recruitment was very low. However, an additional six participants were able to be recruited. Unfortunately, the stage-4 lockdown restrictions were a barrier for participation in the study, with some declaring that they were too busy with their households or not available to join.

I was extremely impressed with, and grateful to the participants. They were very kind in trying circumstances, and enthusiastic for improving their physical activity. They sacrificed their time for testing at the hospital, undertook questionnaires and attended motivational interviewing for exercise via zoom meetings. Although we could not achieve the target recruitment of 64 participants, I am proud that my project could help breast cancer survivors becoming determined individuals again.

6. Progress reports to Human Research Ethics Committee

Approved projects are required to submit annual reports to Melbourne Health HREC and the office for research at Western Health until the project is concluded. The first submission was on the one-year anniversary of research ethics approval in March 2020. I reported on the project initiation, how many participants had been recruited and how the project was responding to the impact of COVID-19.

I have learned a lot from the process of applying for ethics approval. Developing the project protocol, and its review from the University panel and HREC gave me significant insight into research methodology. Additionally, the comments from the HREC enabled me to further understand how clinical trials should be conducted for vulnerable people in the real word. The timeline of my HREC application is illustrated in Figure 2.

I was fortunate to have had good support from my supervisors, particularly my principal supervisor Professor Vasso Apostolopoulos, who contributed significantly to the project's initiation and collaboration. Vasso introduced me to colleagues from Western Health and IPC Health as well as facilitating all requirements of research ethics and implementation. During the COVID-19 restrictions, she supported me in finding solutions for participant recruitment and ensured the project continued.

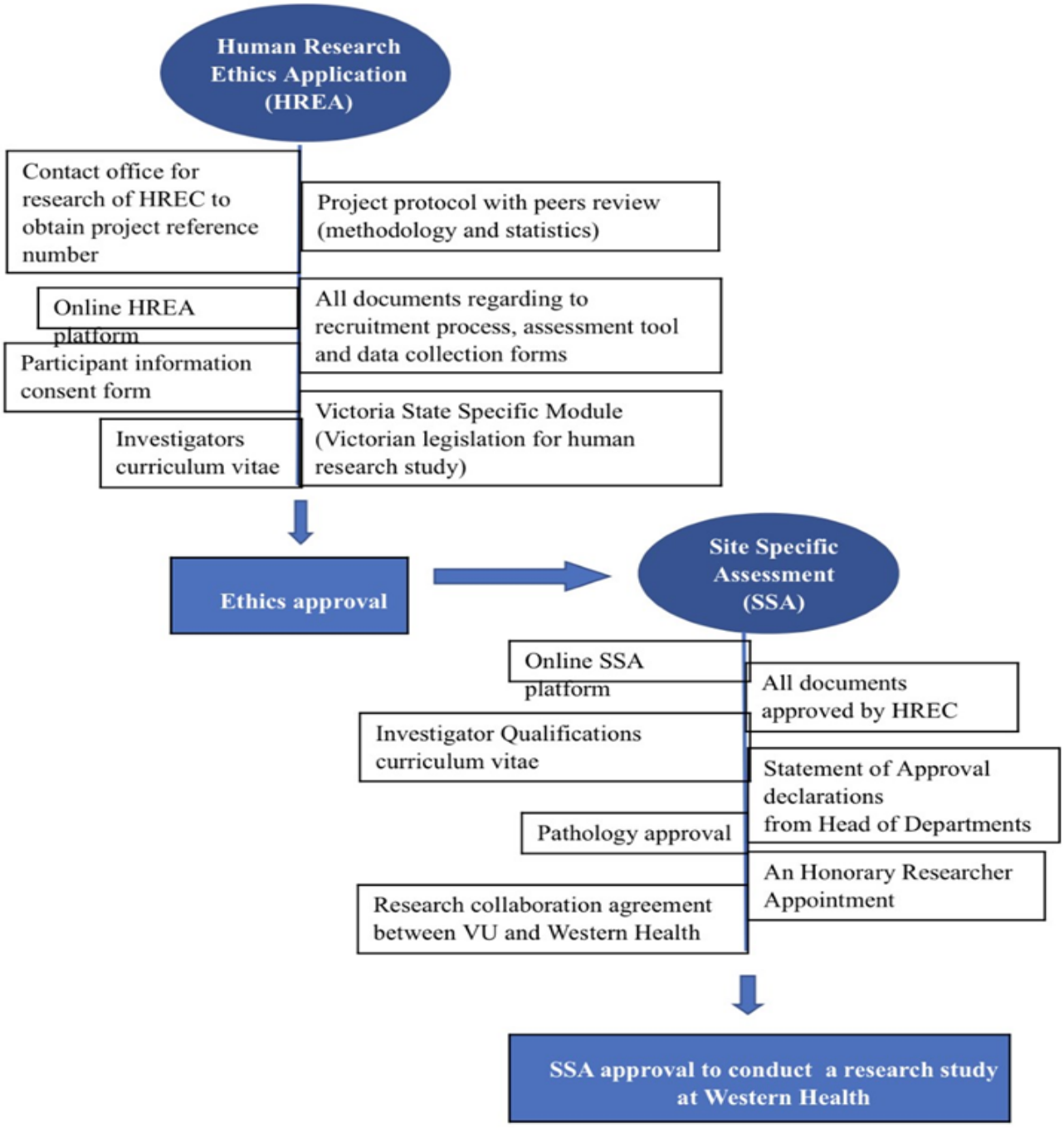

Figure 1. The process of Human Research Ethics Applications for the PAPHIO clinical trial conducted at Western Health and Victoria University, Melbourne VIC, Australia

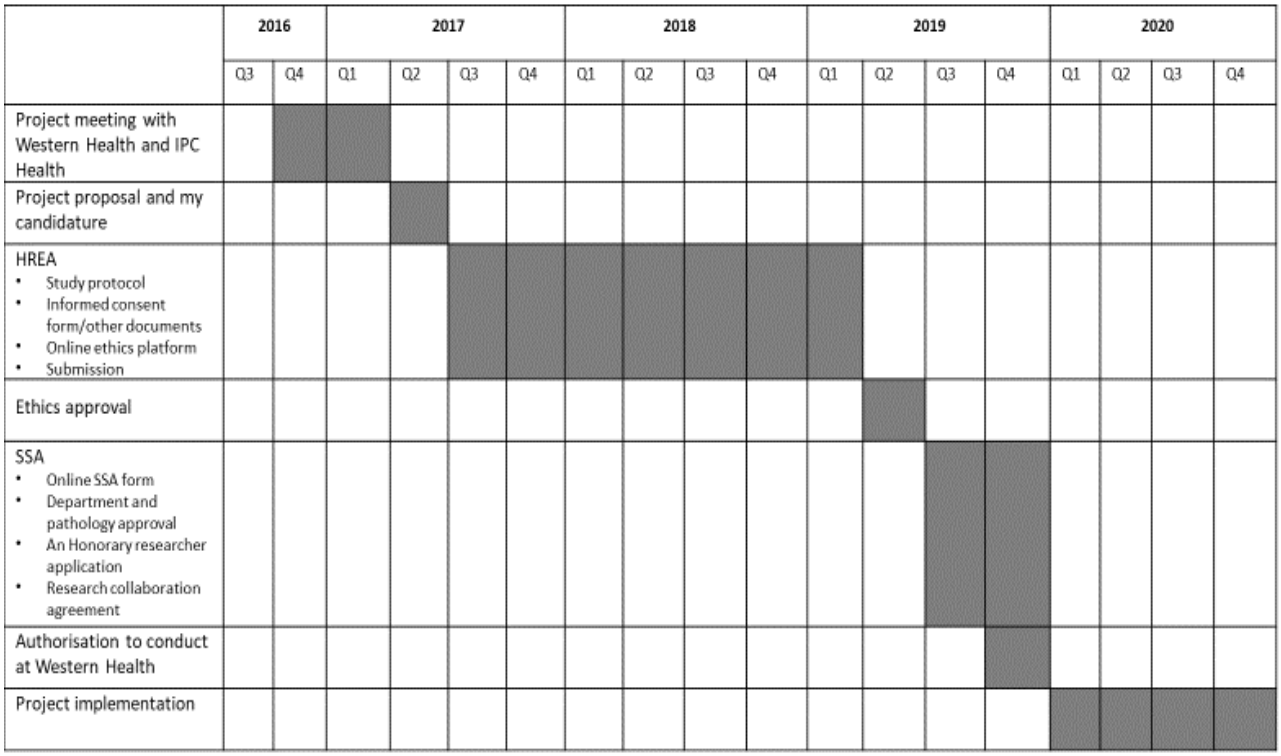

Figure 2. The timeline of the PAPHIO Study ethics application

7. Mitigation strategies for coping with research during COVID-19 pandemic

I would also like to describe the mitigation strategies for coping with my research study during the pandemic crisis. The entire world was affected and stressed by the pandemic. I was anxious when I first heard the announcement from the Victorian State Government and Western Health regarding the halt to clinical trials, and the University announcement of the limitations of human research conduct and laboratory access. I had never considered that this kind of problem would happen in the last year of my PhD candidature; particularly at a time when participant recruitment had just started. The prolonged ethics application was a large part of my thesis and then my research challenge was intensified by COVID-19. I was concerned by the extension of my candidature, study leave, tuition fee payments and my general financial situation. I cannot deny I was very stressed, and indeed I was concerned that I would have ongoing mental health problems.

7.1. In god I trust

I was calmed by praying to God to empower me in dealing with my uncertainty and helping me to move my research forward. I was encouraged by my peers in the church community in Melbourne. Since COVID-19 our church conducted weekly online prayer rooms and all members have been praying with our faith, hope and love for one other. I have trusted in God to anoint me with the spirit of encouragement to finish my thesis on time. Therefore, I leave all my burdens into his guidance. Thank you God.

7.2. Support

I had a wide range of support structures around me. Importantly, understanding and support from my parents cheered me up and kept my research going.

Identification of risks in research is very important. Seeking help through consultation with my supervisors and helpful individuals is the best solution. I appreciated all the support from my supervisors; Professor Vasso Apostolopoulos and Professor Lily Stojanovska during the final year of my candidature. Their suggestions and support of my six-month candidature extension due to the delayed ethics process and COVID-19, helped me tremendously to relieve my tension.

The University also supported me in my request of tuition fee waivers from the Institute for Health and Sport. I sincerely appreciated Professor John Price, the Deputy Director Research Training of the Institute for Health and Sport for providing me with two semesters of tuition fee waivers.

I also requested a 7 month study leave extension from Assumption University; my workplace and sponsor in Thailand at the beginning of 2020 as I estimated that I would be unable to finish my data collection by May 2020; the end of the study leave in my contract. I received a recommended letter from my supervisors and my Institute leader in Thailand; Assistant Professor Dr Nanthaphan Chinlumprasert, the former Dean of Nursing Science Faculty, Assumption University supporting me for the extension. Assumption University approved the request and I was able to stay longer in Melbourne for my data collection until December 2020.

Although I could not complete data collection from the 64 participants as indicated in the study protocol, I am reporting a pilot study for the feasibility of the research in my thesis. I wish to see the project completed in the near future. I hope the project can achieve its

target recruitment when the COVID-19 situation in the country is improved. In this regard, I am excited that a new Master's Student (Ms Katherine Harkin) has now enrolled and will continue with the project.