Feasibility study of a multimodal prehabilitation programme in women receiving neoadjuvant therapy for breast cancer in a major cancer hospital: a protocol

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ABSTRACT

Introduction Neoadjuvant therapy has become a standard treatment for patients with stage II/III HER2 positive and triple negative breast cancer, and in well-selected patients with locally advanced and borderline resectable high risk, luminal B breast cancer. Side effects of neoadjuvant therapy, such as fatigue, cardiotoxicity, neurotoxicity, anxiety, insomnia, vasomotor symptoms, gastrointestinal disturbance as well as a raft of immune-related adverse events, may impact treatment tolerance, long-term outcomes, and quality of life. Providing early supportive care prior to surgery (typically termed ‘prehabilitation’) may mitigate these side effects and improve quality of life. During our codesign of the intervention, consumers and healthcare professionals expressed desire for a programme that ‘packaged’ care, was easy to access, and was embedded in their care pathway. We hypothesise that a multimodal supportive care programme including exercise and complementary therapies, underpinned by behavioural change theory will improve self-efficacy, quality of life, readiness for surgery and any additional treatment for women with breast cancer. We seek to explore cardiometabolic, residual cancer burden and surgical outcomes, along with chemotherapy completion (relative dose intensity). This article describes the protocol for a feasibility study of a multimodal prehabilitation programme.

Methods and analysis This is a prospective, mixed-method, feasibility study of a multi-modal programme in a hospital setting for 20–30 women with breast cancer receiving neoadjuvant therapy. Primary outcomes are recruitment rate, retention rate, adherence and acceptability. Secondary outcomes include patient reported outcome measures (PROMs), surgical outcomes, length of stay, satisfaction with surgery, chemotherapy completion rates, changes in metabolic markers and adverse events. Interviews and focus groups to understand the experience with prehabilitation and different factors that may affect feasibility of the intervention. The output of this study will be a codesigned, evidence-informed intervention assessed for feasibility and acceptability by women with breast cancer and the healthcare professionals that care for them.

Ethics and dissemination The study received ethics approval from the St Vincents Hospital HREC (HREC/2021/ETH12198). Trial results will be communicated to participants, healthcare professionals, and the public via publication and conferences.

Trial registration number ACTRN12622000584730.

INTRODUCTION

Neoadjuvant therapy has become a standard treatment for patients with stage II/III HER2 positive and triple negative breast cancer, and in well-selected patients with locally advanced and borderline resectable high risk, luminal B breast cancer. Current rates of women receiving neoadjuvant therapy are increasing. Benefits of neoadjuvant therapy include downstaging to potentially allow less extensive surgery in the breast and/or axilla,
as well as permitting evaluation of response to guide the choice of adjuvant therapies and for prognostication. However, side effects include fatigue, cardiotoxicity, neurotoxicity, anxiety, insomnia, vasomotor symptoms, gastrointestinal disturbance as well as a raft of immune-related AEs, which may impact treatment tolerance, long-term outcomes and quality of life. Providing early supportive care prior to surgery (typically termed ‘prehabilitation’) may mitigate these side effects and improve quality of life.

Most research to date on prehabilitation programmes has been undertaken in gastrointestinal and urological cancer, but studies in women with breast cancer have increased in volume. These studies have demonstrated trends including a reduction in symptom burden, increased physical and mental well-being during cancer treatment, improvements in sleep patterns, positive impacts on mood, and reduced anxiety.

Prehabilitation studies in cancer to date largely focus on exercise. Low muscle mass and quality, and high visceral adiposity may predict poorer treatment tolerance and are associated with shorter disease-free survival after chemotherapy. Patients undergoing systemic therapy for breast cancer, such as anthracycline chemotherapy and HER2 targeted therapies, are also at risk of cancer therapy-related cardiac dysfunction. These variables are all modifiable targets even with a limited programme of exercise.

While exercise is an essential component of prehabilitation, participants have expressed a preference for multimodal interventions that include other supportive care interventions. Psychosocial barriers and cancer-related side effects hinder the uptake of exercise in people with cancer. The most effective prehabilitation programmes take a holistic, multimodal approach. These programmes may combine exercise with psychological and well-being support, fatigue management strategies, nutrition, lifestyle advice, supportive oncology symptom management, and complementary therapies. Comprehensive supportive care builds self-efficacy, reduces anxiety, prepares the patient for treatment and surgery, and facilitates post-treatment recovery.

Self-efficacy mediates symptom distress and quality of life in people with cancer, and aids compliance with cancer treatment. Self-efficacy is also an important correlate to exercising in women with breast cancer. Self-efficacy may also be moderated by the use of patient-reported outcome measures (PROMs) by imparting a sense of control and involvement to the participant during treatment.

We hypothesise that a multimodal supportive care programme incorporating PROMs and underpinned by behavioural change theory will improve self-efficacy and quality of life, readiness for surgery and any additional treatment for women with breast cancer.

We undertook a codesign approach to developing and investigating a prehabilitation programme. We engaged key stakeholders as members of the research team including consumers and healthcare professionals. A qualitative study was undertaken to explore consumers’ and healthcare professionals’ views about the content and format of the proposed programme along with perceived facilitators and barriers to conducting the programme. Findings indicated that consumers and healthcare professionals wanted a programme that ‘packaged’ care, was easy to access, and was embedded in their care pathway.

This article describes a protocol for a study investigating the feasibility of a multimodal prehabilitation programme in women with breast cancer receiving neoadjuvant therapy.

AIMS AND OBJECTIVES

This study aims to determine the feasibility of a multimodal early supportive care programme for women with breast cancer delivered during neoadjuvant therapy.

Study objectives

1. To assess the feasibility of the programme to women receiving neoadjuvant therapy for breast cancer, and measure recruitment, adherence, and retention.
2. To investigate the potential efficacy of the programme to maximise functioning, self-efficacy, and well-being during neoadjuvant treatment, at completion of treatment/prior to surgery, and at 6-month follow-up. We also sought to explore cardiometabolic, residual cancer burden (pCR), and surgical outcomes, along with chemotherapy completion (relative dose intensity, RDI).
3. To identify moderators that influence success (or failure) of the programme such as cost and engagement; and any strategies that may facilitate implementation.

METHODS AND ANALYSIS

Study design

This is a prospective, mixed-method, feasibility study combining qualitative and quantitative data collection and analysis. This protocol was written in accordance with the Consolidated Standard of Reporting Trials, and followed recommendations from the Standard Protocol Items: Recommendations for Interventional Trials Checklist (online supplemental file 1).

Setting

All participants recruited will be from a single site. All study-based procedures are conducted in the outpatient Supportive Care and Integrative Oncology department, which includes a gym, of a major cancer hospital located in Sydney, Australia. Interviews will be conducted using an online medium for participant convenience.

Feasibility

Feasibility will be assessed by recruitment rate, retention rate, and adherence to programme. We will also assess acceptability, appropriateness, and feasibility of the programme by administering three, validated short
outcome measures, the four-item Acceptability of Intervention Measure, the four-item Intervention Appropriateness Measure, the four-item Feasibility of Intervention Measure,36 and conducting interviews with participants and healthcare professionals engaged in the programme. The Health Education Questionnaire (HeiQ) will be used to assess the effects of health education programmes on self-management.37

**Sampling**

We aim to recruit between 20 and 30 women as a consecutive sample and determine the rate of recruitment per month. Sample size recommendations for feasibility studies vary but between 20 and 30 is considered adequate where there is no prior information on which to base a sample size.38 39 The hospital study site delivers neoadjuvant chemotherapy (NACT) to approximately seven women per month.

**Inclusion criteria**

Eligible patients for this study are women >18 years diagnosed with breast cancer who are identified as a patient for the NACT pathway by treating breast surgeon and/or medical oncologist, and is willing to provide consent, complete the written study assessments and understand instruction for the programme in English.

**Exclusion criteria**

We will exclude women who are lactating, pregnant or of childbearing potential who are not willing to avoid becoming pregnant during the study; unable to give informed consent; who have completed more than two cycles of NACT at time of enrolment; or are unable to participate due to no computer at home or device to teleconference. Contraindications to participation will be determined based on oncologist and exercise physiologist review using the Participation Activity Readiness Questionnaire (PAR-Q) and the Exercise and Sports Science Australia recommendations.

**Additional study participants**

We will also include interviews and/or focus groups with healthcare practitioners involved in the programme delivery.

**Recruitment**

Participants meeting the inclusion criteria are referred by the medical oncologist, breast surgeon, or nursing staff; or may self-refer by reading about the study on a flyer or poster with a QR code which includes screening criteria. Potential participants will be provided with the information and consent form and invited to attend an appointment to ask any further questions, and to enrol in the study if they are interested. Informed consent will be obtained by a member of the study team prior to enrolment (online supplemental file 2). The study commenced recruitment in 2023 and will be complete in mid-2024.

**Intervention**

The intervention combines a holistic nursing assessment, education, personalised exercise, PROMs, and selected evidence informed complementary therapies, along with a supportive care physician review when required for symptom management.

The intervention is based on a stepped care approach, where the severity of the symptoms, such as anxiety or neuropathy, along with the preferences of patients, are matched to the intensity and frequency of the intervention. The design builds on the emerging evidence in prehabilitation for a multimodal approach tailored to the individual.40 41 The intervention commences at enrolment and completes at the end of chemotherapy treatment, an estimated 20–24 weeks with a follow-up 6 months later (figure 1). Our holistic multimodal programme aims to address barriers such as side effects of treatment, through

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**Figure 1** Study flow chart.

<table>
<thead>
<tr>
<th>Participants referred by Med Onc/Surgeon</th>
</tr>
</thead>
<tbody>
<tr>
<td>Contact for initial appointment (-T0)</td>
</tr>
<tr>
<td>Enrolment</td>
</tr>
<tr>
<td>Initial assessment and consent (T0)</td>
</tr>
<tr>
<td><strong>Start of intervention</strong></td>
</tr>
<tr>
<td>T1 Assessment (weeks 8–9)</td>
</tr>
<tr>
<td><strong>End of intervention</strong></td>
</tr>
<tr>
<td>T2 Assessment (last day of chemotherapy / prior to surgery)</td>
</tr>
<tr>
<td>T3 Assessment plus optional interview (4 weeks post-surgery)</td>
</tr>
<tr>
<td>T4 Assessment (6 months post intervention)</td>
</tr>
</tbody>
</table>
the inclusion of acupuncture, yoga, massage, and other supportive care therapies.

The study intervention is guided by a social cognitive theory framework, particularly the construct of self-efficacy.\textsuperscript{42} Self-efficacy, an important component of social cognitive theory, is recognised for its significant effect on patients’ adaptation to their diagnosis and self-management.\textsuperscript{31} The study intervention has four components (figure 2):

1. Holistic nurse practitioner assessment, including a lymphoedema assessment and pathology
2. Personalised, periodised exercise programme
3. Education sessions focusing on nutrition, preparing for surgery, lymphoedema, and understanding yoga and mindfulness.
4. Supportive care therapies including mindfulness, yoga, acupuncture, massage and reflexology provided on an as needed basis and as needed supportive care medical assessment.

\textit{Holistic assessment}: a holistic assessment will be conducted by the nurse practitioner. The nursing component includes a discussion of patient goals—aiming to support those things that matter to the patient and their carers at the forefront. The framework for this component is based on the five A’s model of patient-centred care and self-management.\textsuperscript{45} The framework uses motivational interviewing and assesses readiness to change. The assessment involves:

- Lifestyle risk assessment diet and management including smoking status, alcohol consumption and comorbidities.
- Participants are asked to complete the National Comprehensive Cancer Network (NCCN) Distress Thermometer and Problem list\textsuperscript{44} to facilitate referral to resources and supportive care.
- Participants are asked to identify goals and readiness to change.
- Review of risk factors, blood results, micronutrient, and cardiac risk factors, and identification of concerns that would trigger a referral for supportive care medical assessment and referred to the supportive care multidisciplinary team.

The consultation also involves a discussion around treatment, lymphoedema, complementary therapies, and exercise. This will use an evidence-informed approach allowing the nurse practitioner to incorporate participants’ values and preferences along with their own clinical experience and current research evidence for therapeutic approaches (eg, medications or acupuncture for pain) to support a shared decision-making process for study participants and families.

\textbf{Table 1} shows a suggested algorithm of integrative therapy referral options for symptom control to facilitate discussions on evidence-informed approaches.\textsuperscript{45,46}

If the holistic nursing assessment identifies any concerns that cannot be addressed by the programme, then the participant will be referred for a supportive care medical assessment and/or presentation at the Supportive Care Multidisciplinary Team meeting. For example, if there are any abnormalities in the pathology such as metabolic risk factor abnormalities, vitamin D deficiency or other micronutrient deficiencies, complex symptoms, or baseline comorbidities, the patient will be referred to the Supportive Care Specialist.
Table 1  Evidence-based complementary therapy approaches for symptom control

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Pain</th>
<th>Fatigue</th>
<th>Insomnia</th>
<th>Anxiety</th>
</tr>
</thead>
<tbody>
<tr>
<td>Modality</td>
<td>Acupuncture</td>
<td>Yoga</td>
<td>Yoga</td>
<td>Yoga</td>
</tr>
<tr>
<td></td>
<td>Massage</td>
<td>Acupuncture</td>
<td>Acupuncture</td>
<td>Yoga</td>
</tr>
<tr>
<td></td>
<td>Mindfulness</td>
<td></td>
<td></td>
<td>Massage</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Reflexology</td>
</tr>
<tr>
<td>Nausea and vomiting</td>
<td>Acupuncture</td>
<td>Acupuncture</td>
<td>Acupuncture</td>
<td>Acupuncture</td>
</tr>
<tr>
<td></td>
<td>Acupressure</td>
<td>Reflexology</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- **Personalised, periodised exercise programme incorporating behavioural support:** the exercise intervention combines goal setting and planning, monitoring and feedback with social support and instruction (more detail is provided in online supplemental file 3). The intervention is adapted to severity of symptom burden, and is designed to:
  - maintain or minimise the decline in muscle mass, metabolic, cardiorespiratory and psychosocial health
  - improve or maintain balance
  - create self-efficacy in exercise behaviour

The plan includes a periodised model of aerobic, resistance, balance, and flexibility training supported with behavioural coaching models of HealthChange Australia methodology (www.healthchange.com). A key component is that training dose will be modified according to symptom burden aiming to encourage consistent exercise ‘behaviour’ and self-efficacy. If a participant faces barriers to exercise, social support will be provided as the scaffold for re-engagement when the participant is ready.

Face-to-face exercise in a dedicated space with experienced exercise physiologists and other women will provide social support, and address concerns regarding safety which can also be barriers. Our study also focuses on strengthening self-efficacy to help women become or remain sufficiently physically active, which has been shown to mitigate unfavourable structural conditions.

- **Education sessions:** three types of education sessions (40 min) will be offered to participants as a hybrid option (face-to-face or online). Education sessions are designed to use self-efficacy principles by providing opportunities to observe, experience, and practice behaviours such as mindfulness (performance accomplishments), to listen and see desired behaviours around healthy lifestyle. Nutrition and lifestyle modification, and impact on modifying cardiac and other risk factors will be included. Family members and carers will be encouraged to attend. The aim of these sessions is to improve participant’s knowledge and skills aimed to build self-management.

The sessions will involve a presentation and an opportunity to ask questions:
1. Using mindfulness and gentle yoga to manage stress
2. Healthy eating and lifestyle choices (to modify risk factors after cancer)
3. Preparing for surgery and understanding lymphoedema

- **Supportive care therapies:** participants will be offered additional supportive care therapies and/or medical review if symptom burden increases during treatment. The Edmonton Symptom Assessment Scale (ESAS) allows participants to rank the severity of their symptoms. The ESAS will trigger the option for the participant to choose to engage with a recommended supportive care therapy. This will follow the Screening pathway for additional supportive care—ESAS (online supplemental file 4). Supportive care therapies include oncology massage, acupuncture, reflexology, yoga, and mindfulness in addition to allied health such as psych-oncology.

The programme has several strengths. It is based on codesign with women who have lived experience and healthcare professionals engaged in providing hospital cancer care. The programme is underpinned by social cognitive theory and principles of self-efficacy. Taken together, the evidence demonstrating the value of proactively managing side effects of treatment, lifestyle risk factors, and the use of exercise in prevention and management of cardiometabolic and biopsychosocial health, signals an urgent priority for early intervention programmes in women with breast cancer.

**Outcome measures**

The primary outcome for the study is feasibility. This is measured by recruitment, completion and adherence rates, and acceptability (outlined in table 2). Secondary outcome measures include PROMs outlined in table 2, surgical outcomes, length of stay, satisfaction with surgery, RDI calculation, changes in metabolic markers and AEs.

Data will be captured for study participants across five timepoints: baseline (T₀), mid-chemotherapy (T₁), end of chemotherapy (T₂), after surgery (T₃), and at 6 months after completion of the study intervention (T₄) (table 2).

**Demographic data:** gender, date of birth (DOB), country of birth, language spoken at home, highest level of education attained, employment status, postcode.

**Anthropometric and body composition data:** weight, height, waist (waist-height ratio; BMI), fat free mass (kg); fat mass...
**Table 2**  Schedule of enrolment, interventions, and assessments

<table>
<thead>
<tr>
<th>Measure</th>
<th>Screening</th>
<th>Baseline*</th>
<th>During NACT</th>
<th>Post-NACT</th>
<th>Post- surgery</th>
<th>Follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>T₀</td>
<td>T₀</td>
<td>T₁</td>
<td>T₂</td>
<td>T₃</td>
<td>T₄</td>
</tr>
</tbody>
</table>

**Enrolment and Clinical Measures**

- Eligibility screen ✓
- Informed consent ✓
- Demographic data ✓
- NCCN Distress Thermometer ✓ ✓ ✓ ✓
- Lymphoedema assessment ✓ ✓ ✓ ✓
- Standard Pathology (extracted from EMR): FBC, EUC, LFT, CMP and CRP ✓ ✓ ✓

**Feasibility measures**

- Acceptability, AIM, IAM, FIM ✓
- Recruitment, completion and adherence rates ✓ ✓
- Interviews & Focus Groups ✓

**Patient Reported Outcome Measures**

- ESAS ✓ ✓ ✓ ✓ ✓ ✓
- FACT-B ✓ ✓ ✓ ✓ ✓
- Anthropometric and body composition data ✓ ✓
- Exercise physiology assessment & measures ✓ ✓ ✓
- Godin Leisure Time Activity Questionnaire ✓ ✓
- Programme satisfaction: HeiQ (Domain 9) ✓
- Self-efficacy: CBI-B ✓ ✓

**Costs**

- Program delivery costs (all interventions/consultations) ✓
- UK Cancer Costs Questionnaire: Baseline questions (T0) ✓
- UK Cancer Costs Questionnaire: follow-up assessment ✓ ✓

**Surgical, medical and biochemical outcomes**

- Medical record data (relative dose intensity) ✓
- Micronutrient assessment (Vitamin B12, zinc, Vitamin D, iron studies, folate) ✓ ✓ ✓

Continued
Surgical outcomes

**BREAST-Q** (preoperative satisfaction module only)

**BREAST-Q** (postoperative satisfaction module only)

**Safety and adverse events**

<table>
<thead>
<tr>
<th>Measure</th>
<th>Screening</th>
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</thead>
<tbody>
<tr>
<td>Cardio-metabolic markers (fasting glucose, HbA1c, fasting serum insulin, triglycerides, Chol, HDL, LDL, thyroid)</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
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<tr>
<td>Surgical record data</td>
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<tr>
<td>BREAST-Q (preoperative satisfaction module only)</td>
<td>✓</td>
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<td></td>
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<tr>
<td>BREAST-Q (postoperative satisfaction module only)</td>
<td>✓</td>
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</table>

*Baseline: Pre-NACT or <4 wks into NACT. NACT: neoadjuvant chemotherapy.

AIM, Acceptability of Intervention Measure; Assessments: ESAS, Edmonton Symptom Assessment Scale; CBI-B, Brief Cancer Behaviour Inventory; EMR, electronic medical record; FIM, Feasibility of Intervention Measure; HeiQ, Health Education Impact Questionnaire; IAM, Intervention Appropriateness Measure.

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Table 2 Continued

<table>
<thead>
<tr>
<th>Measure</th>
<th>Screening</th>
<th>Baseline*</th>
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</table>

**Safety and adverse events**

<table>
<thead>
<tr>
<th>Adverse events</th>
<th>Collected throughout the intervention</th>
</tr>
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</table>

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(kg); skeletal muscle mass (kg) using the SOZO bioelectrical spectroscopy.

**Patient-Reported Outcome Measures (PROMs):** to assess quality of life, the Functional Assessment of Cancer Therapy-Breast (FACT-B) will be used. This instrument is designed to measure five domains of health-related quality of life in women with breast cancer: physical, social, emotional, functional well-being as well as a breast-cancer subscale. To measure self-efficacy, the Brief Cancer Behaviour Inventory (CBI-B) will be used.

To guide the individualisation of the intervention and supportive care service referral, two outcome measures will be collected:

1. The ESAS will be used as a weekly audit of the intensity of patient’s symptoms. Patients rate 17 items including pain, activity, nausea, depression, anxiety, drowsiness, appetite, and sensation of well-being on a 10-point Likert scale, a score of 0 correlates with no symptom and 10 being ‘worst symptom’.

2. The NCCN Distress Thermometer and Problem list for Patients (NCCN DT) combines a distress thermometer (DT) and a problem list to identify sources of distress. Physical activity will be assessed using the Godin-Shephard Leisure-Time Physical Activity Questionnaire (GSLTPAQ).

**Surgical outcomes** BREAST-Q (preoperative and postoperative satisfaction modules specific to planned and performed surgery): the BREAST-Q modules related to satisfaction will be used in this study.

Pretreatment and post-treatment tumour characteristics and pathological data will be collected extracted from the study participant’s medical record.

Surgical complications will be extracted from the medical record.

Quality measures will be extracted from the participant’s electronic medical record (EMR): length of stay, surgical complications, unplanned hospital visits or readmissions, Common Terminology Criteria for Adverse Events (CTCAE), RDI calculation (planned and actual). RDI calculation RDI is calculated as actual/planned. Reasons for dose reduction will be recorded. Change in metabolic and micronutrient pathology: fasting serum insulin, HBA1C, cholesterol, high-density lipoprotein, low-density lipoprotein, triglycerides, vitamin D, zinc, iron studies, and B12.

**Physical and functional measures:** outcome measures for exercise during the programme will be calculated as follows:

**Aerobic exercise training**

Prescribed and completed duration (time in minutes) will be recorded for each exercise modality (eg, treadmill, cycle/arm/rowing ergometer). The sum will provide the total session aerobic duration. Intensity will be recorded as average exercise heart rate (HR) and time in the prescribed HR zone.

The aerobic exercise relative dose (AE x RDI) will be calculated as the actual/prescribed, that is, duration (minutes), average HR (beats per minute), and time (minutes) in a HR zone that is tolerated at each session relative to prescribed.

**Resistance training**

Prescribed and completed training volume (repetitions x sets x training load in kilograms) will be calculated for each individual exercise. The sum will provide the total session volume.

Resistance training exercise relative dose (RTE xRDI) will be calculated as the total actual/prescribed, that is, volume completed relative to total prescribed cumulative dose volume.
Attendance/adherence rate reflects behaviour, but E x RDI represents the actual dose of the exercise stimulus. Dose adjustments will be reported with the reason, for example, fatigue, shortness of breath, elevated or irregular HR. Dose interruptions will be reported with the reason, for example, holiday, family, treatment, and/or non-treatment health.

Additional measures will be taken as follows to guide the individualisation of the intervention:

i. Blood pressure (BP), HR, $\text{SpO}_2$ (Welch Allyn sphygmomanometer).56
ii. 30 s chair stand57
iii. Single leg balance58
iv. Pre-post exercise: fatigue, nausea, and pain using VAS 0–10.
v. Upper and lower body strength (one repetition maximum: 1RM).
vii. Grip strength: measures as the best of three scores SAEHAN Medical hydraulic hand dynamometer SH500158

Cost: The UK Cancer Costs questionnaire (V2) will be used to capture the resources used by participants. This tool is specifically designed to be used within an observational study, without duplicating standard data collection on case report forms. Societal costs are also captured including participant’s out-of-pocket costs, costs incurred by carers and time taken off work.

Safety considerations

Clinic protocols for exercise include recording oxygen saturation ($\text{SpO}_2$), HR via pulse oximeter and manual pulse palpation (to detect arrhythmias), BP in assessment, before and after exercise to identify hypertension and hypotension and dysregulated response to exercise. All study related and non-study related AEs will be collected and reported. An AE or adverse reaction is defined to be any event or experience which compromises the ethical acceptability of the protocol. There are no drugs or devices being tested in this study.

QUALITATIVE DATA

The purpose of the qualitative part of the study is to understand the experience with prehabilitation and different factors that affected feasibility of the intervention (eg, challenges to participation and preference aspects of the intervention delivery). Interviews with participants will seek to explore the feasibility of the programme and cover content, complexity, comfort, delivery, and credibility. To further understand intervention design and viability, as well as the perceived value of prehabilitation, we will also interview healthcare professionals involved in the delivery of the programme. Consolidated Framework for Implementation Research (CFIR) and Reach, Effectiveness, Adoption, Implementation, and Maintenance (RE-AIM) constructs have been incorporated in the interview guide (online supplemental file 5).

Theoretical saturation will guide sample size for this study. Data collection and data analysis will occur concurrently in order to determine its saturation. The intention is to recruit at least six women with breast cancer who participate in the study and at least six healthcare professionals who are engaged in the delivery of the programme to ensure saturation will occur.

DATA COLLECTION, DATA ANALYSIS, AND DISSEMINATION OF RESULTS

The output of this study will be a codesigned, evidence informed intervention assessed for feasibility and acceptability by women with breast cancer, and the healthcare professionals that care for them. The results of this study will provide an insight into the appropriateness of a multimodal prehabilitation programme for women receiving chemotherapy for breast cancer. This will guide future research to understand the contribution of the effect of a single intervention compared with a multimodal intervention, on clinical, physical, and psychological outcomes identified as a research gap in a systematic review of prehabilitation and breast cancer.8 The study will also provide an indication of the short-term effects of a multimodal programme on a range of patient-reported outcomes, cardiometabolic, and surgical outcomes.

The data analysis for the feasibility objectives will be descriptive.

1. Recruitment rate: number of enrolments per week of active recruitment, percentage conversion to enrolment measured as n enrolled/n of enquiries, and n enrolled/n potentially eligible. Retention rate: recruitment rate will be deemed feasible if 60% of potential participants are recruited and retention rate is >75%.
2. Adherence to programme: % exercise sessions attended or completed/ % expected; % attending education sessions; % referred to supportive care therapists/ % attending supportive care therapy at end of programme. Adherence will be deemed feasible if women attend >70% of planned sessions.
3. Reporting of the number of serious AEs experienced by participants
4. Reporting of the primary endpoints: quality of life outcome (FACT-B) and self-efficacy (CBI-B).

For all outcome measures, descriptive statistics will be used, at all-time points measured. Continuous variables, including PROMs, will be summarised either as mean (SE) or median (range), as appropriate. Changes from baseline will be similarly reported. Categorical variables such as surgical complications will be tabulated.

Data will be collected from participants who deviate from the protocol, and reasons for deviation and any discontinuation recorded. Missing data will be addressed by using last observation carried forward methods.

Data will be sourced from the hospital EMR (Meditech and Powerchart), and surgeon records. All study visit data will be recorded and stored in REDCap. Participant registration will be recorded in a locked excel spreadsheet.
stored on the secure hospital server. The spreadsheet will be destroyed at the end of the study. Only deidentified data will be uploaded to and analysed in R Studio. A data management plan has been developed to support the study. As this is a small, non-blinded single-centre study, a data management committee is not being convened.

**Qualitative analysis**

Interviews will be recorded using ZOOM Cloud and transcribed verbatim using TRINT. Transcripts will be deidentified and assigned an identification number as part of the e-consent process to ensure anonymity. Transcripts will be read line by line, independently by a minimum of two researchers and coded using open coding (ie, the codes emerged from the data) with the NVivo (QSR International V11) software. A thematic approach driven by grounded theory will underpin the data analysis. Codes will be categorised and discussed until consensus is reached on themes. Transcripts will be reread to selectively search for data related to the identified themes. A final list of themes including a main theme and subtheme will be formulated, and transcripts will be reread to ensure comprehensive analysis.

Trial results will be communicated to participants, healthcare professionals, and the public via publication and conferences.

The qualitative components of the study will inform an understanding of the implementation framework, as well as providing an understanding of the level of satisfaction with the programme.

**Patient and public involvement statement**

The protocol intervention and study were codesigned through focus groups and interviews with women with breast cancer who had lived experience of undergoing chemotherapy to reflect their preferences, experience, and priorities. We also interviewed healthcare professionals involved in the delivery of care for women undergoing chemotherapy. The study team includes a consumer representative—a woman with breast cancer who has had chemotherapy, who has been consulted at key timepoints in the study. Patients will not be involved in the recruitment to the study.

**Ethics and dissemination**

The study received ethics approval from the St Vincents Hospital HREC (HREC/2021/ETH12198). Trial results will be communicated to participants, healthcare professionals, and the public via publication and conferences.

**REFERENCES**


Lyon AR, López-Fernández T, Couch LS, et al. ESC guidelines on Cancer-endoxyology developed in collaboration with the European hematology Association (EHA), the European society for Therapeutic Radiology and oncology (ESTRO) and the International Cardio-oncology society (IC-OS) developed by the task force on Cardi-oncology of the European society of cardiology (ESC). *Eur Heart J* 2022;43:4229–361.:


Lyon AR, Lopez-Fernandez T, Couch LS, et al. ESC guidelines on Cancer-endoxyology developed in collaboration with the European hematology Association (EHA), the European society for Therapeutic Radiology and oncology (ESTRO) and the International Cardio-oncology society (IC-OS) developed by the task force on Cardi-oncology of the European society of cardiology (ESC). *Eur Heart J* 2022;43:4229–361.:


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64 Menendez AG, Cobb R, Carvalal AR, et al. Effectiveness of massage therapy (MT) as a treatment strategy and preventive modality for chemotherapy-induced peripheral neuropathy (CIPN) symptoms. JCO 2016;34:193.


Reporting checklist for protocol of a clinical trial.

Based on the SPIRIT guidelines.

**Instructions to authors**

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

Your article may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please write "n/a" and provide a short explanation.

Upload your completed checklist as an extra file when you submit to a journal.

In your methods section, say that you used the SPIRIT Reporting guidelines, and cite them as:


<table>
<thead>
<tr>
<th>Reporting Item</th>
<th>Page Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Administrative information</td>
<td></td>
</tr>
<tr>
<td>Title</td>
<td>#1</td>
</tr>
<tr>
<td>Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym</td>
<td>1</td>
</tr>
<tr>
<td>Trial registration</td>
<td>#2a</td>
</tr>
<tr>
<td>Trial identifier and registry name. If not yet registered, name of intended registry</td>
<td>6</td>
</tr>
<tr>
<td>Trial registration: data set</td>
<td>#2b</td>
</tr>
<tr>
<td>All items from the World Health Organization Trial Registration Data Set</td>
<td>6</td>
</tr>
<tr>
<td>Protocol version</td>
<td>#3</td>
</tr>
<tr>
<td>Date and version identifier</td>
<td>6</td>
</tr>
<tr>
<td>Funding</td>
<td>#4</td>
</tr>
<tr>
<td>Sources and types of financial, material, and other support</td>
<td>16</td>
</tr>
<tr>
<td>Roles and responsibilities: contributorship</td>
<td>#5a</td>
</tr>
<tr>
<td>Names, affiliations, and roles of protocol contributors</td>
<td>1 and 16</td>
</tr>
<tr>
<td>Roles and responsibilities: sponsor contact information</td>
<td>#5b</td>
</tr>
<tr>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>Roles and responsibilities: sponsor and funder</td>
<td>#5c</td>
</tr>
<tr>
<td>Roles and responsibilities: committees</td>
<td>#5d</td>
</tr>
</tbody>
</table>

**Introduction**

| Background and rationale | #6a | Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention | 4-5 |
| Background and rationale: choice of comparators | #6b | Explanation for choice of comparators | n/a |

| Objectives | #7 | Specific objectives or hypotheses | 5 |
| Trial design | #8 | Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, non-inferiority, exploratory) | 6 |

**Methods:**
Participants, interventions, and outcomes
<table>
<thead>
<tr>
<th>Study setting</th>
<th>#9</th>
<th>Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained</th>
<th>6</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eligibility criteria</td>
<td>#10</td>
<td>Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)</td>
<td>6-7</td>
</tr>
<tr>
<td>Interventions:</td>
<td></td>
<td><strong>description</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td>#11a</td>
<td>Interventions for each group with sufficient detail to allow replication, including how and when they will be administered</td>
<td>7-10</td>
</tr>
<tr>
<td></td>
<td>#11b</td>
<td>Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving / worsening disease)</td>
<td>7-10</td>
</tr>
<tr>
<td></td>
<td>#11c</td>
<td>Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return; laboratory tests)</td>
<td>7-10</td>
</tr>
<tr>
<td></td>
<td>#11d</td>
<td>Relevant concomitant care and interventions that are permitted or prohibited during the trial</td>
<td>7-10</td>
</tr>
<tr>
<td>Outcomes</td>
<td>#12</td>
<td>Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended</td>
<td>10-14</td>
</tr>
<tr>
<td>Participant timeline</td>
<td>#13</td>
<td>Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)</td>
<td>Fig 1; Table 2</td>
</tr>
<tr>
<td>Sample size</td>
<td>#14</td>
<td>Estimated number of participants needed to achieve study objectives and how it was</td>
<td>6; 14</td>
</tr>
</tbody>
</table>
determined, including clinical and statistical assumptions supporting any sample size calculations.

**Recruitment**

| #15 | Strategies for achieving adequate participant enrolment to reach target sample size |

**Methods:**

**Assignment of interventions (for controlled trials)**

| #16a | Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions |
| #16b | Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned |
| #16c | Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions |

**Blinding (masking):**

| #17a | Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how |
| #17b | If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial |
### Data collection plan

**#18a** Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol

**#18b** Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols

### Data management

**#19** Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol

### Statistics: outcomes

**#20a** Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol

### Statistics: additional analyses

**#20b** Methods for any additional analyses (eg, subgroup and adjusted analyses)

### Statistics: analysis population and missing data

**#20c** Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)

### Methods: Monitoring

### Data monitoring: formal committee

**#21a** Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to
where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed

<table>
<thead>
<tr>
<th>Data monitoring: interim analysis</th>
<th>#21b</th>
<th>Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial</th>
<th>n/a</th>
</tr>
</thead>
<tbody>
<tr>
<td>Harms</td>
<td>#22</td>
<td>Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct</td>
<td>15-16</td>
</tr>
<tr>
<td>Auditing</td>
<td>#23</td>
<td>Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor</td>
<td>n/a</td>
</tr>
</tbody>
</table>

**Ethics and dissemination**

<p>| Research ethics approval         | #24  | Plans for seeking research ethics committee / institutional review board (REC / IRB) approval | 6    |
| Protocol amendments             | #25  | Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC / IRBs, trial participants, trial registries, journals, regulators) | n/a  |
| Consent or assent               | #26a | Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32) | 7    |
| Consent or assent: ancillary studies | #26b | Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable | n/a  |
| Confidentiality                 | #27  | How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial | 15-16|</p>
<table>
<thead>
<tr>
<th>Section</th>
<th>#</th>
<th>Description</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Declaration of interests</td>
<td>#28</td>
<td>Financial and other competing interests for principal investigators for the overall trial and each study site</td>
<td>16</td>
</tr>
<tr>
<td>Data access</td>
<td>#29</td>
<td>Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators</td>
<td>17</td>
</tr>
<tr>
<td>Ancillary and post trial care</td>
<td>#30</td>
<td>Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation</td>
<td>n/a</td>
</tr>
<tr>
<td>Dissemination policy: trial results</td>
<td>#31a</td>
<td>Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions</td>
<td>16</td>
</tr>
<tr>
<td>Dissemination policy: authorship</td>
<td>#31b</td>
<td>Authorship eligibility guidelines and any intended use of professional writers</td>
<td>n/a</td>
</tr>
<tr>
<td>Dissemination policy: reproducible research</td>
<td>#31c</td>
<td>Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code</td>
<td>n/a</td>
</tr>
</tbody>
</table>

**Appendices**

<table>
<thead>
<tr>
<th>Section</th>
<th>#</th>
<th>Description</th>
<th>Supplemental Material 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Informed consent materials</td>
<td>#32</td>
<td>Model consent form and other related documentation given to participants and authorised surrogates</td>
<td></td>
</tr>
<tr>
<td>Biological specimens</td>
<td>#33</td>
<td>Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable</td>
<td>n/a</td>
</tr>
</tbody>
</table>

The SPIRIT Explanation and Elaboration paper is distributed under the terms of the Creative Commons Attribution License CC-BY-NC. This checklist was completed on 24. September 2023 using https://www.goodreports.org/, a tool made by the EQUATOR Network in collaboration with Penelope.ai
Participant Information Sheet/Consent Form

Title
PREhabilitation and Supportive Care in Oncology Treatment of Breast Cancer (PROactive-B): a feasibility study of women with Breast cancer receiving neoadjuvant chemotherapy

Short Title
PROactive-B: PREhabilitation and Supportive Care for Women with Breast Cancer

Protocol Number
Version 1.0

Project Sponsor
Chris O’Brien Lifehouse

Coordinating Principal Investigator/Principal Investigator
Dr Suzanne Grant

Coinvestigators
A/Prof Judith Lacey, Dr Susannah Graham, Kim Kerinn-Ayres, Dr Cindy Mak, Dr Sanjeev Kumar, Dr Shelley Kay, Dr Ash Malalasekera, Dr Sara Wahlroos, Dr Jane Cockburn, Maria Gonzalez Sandra Templeton, Prof Gillian Heller

Location
Chris O’Brien Lifehouse

Part 1 What does my participation involve?

1 Introduction

You are invited to take part in an early supportive care multimodal program and research study that aims to provide interventions that may improve your wellbeing and cancer treatment experience. This program will be evaluated for its feasibility and acceptability and provided to you free of charge. You have been invited to participate in this program and study because you have been diagnosed with breast cancer and are undergoing neoadjuvant chemotherapy.

Early supportive care at diagnosis and during treatment aims to proactively treat side effects, mitigate post-treatment symptoms and empower people diagnosed with cancer with self-management strategies that may improve recovery and post-treatment outcomes.

The aim of this study is to investigate the feasibility of a multimodal prehabilitation program to address side effects of treatment, maximise quality of life and wellbeing during and after treatment and prepare you for your surgery. The program includes a holistic nursing +/- medical assessment, exercise tailored to you, education on healthy lifestyle, nutrition and pre-surgery care, lymphoedema early assessment and education, along with surveillance for side effects from treatment and optional complementary therapies to help with these. The program will be delivered at the Chris O’Brien Lifehouse Comprehensive Cancer Hospital.

This Participant Information Sheet (PIS) will tell you what is involved in the study and help you decide if you wish to take part. Please read this information carefully. If there is anything you do not understand or if you feel you need more information about anything, please ask. Before you make a decision, please feel free to talk things over with a relative, a friend or your doctor.
2 What does participation in this research involve?

You will be asked if you agree to a member of the research team to contact you for a screening session.

Screening
Before you decide to participate in this research study, we need to ensure it is OK for you to take part. You will be asked to take part in a screening session with a member of the research team, to be conducted in person or over the phone.

Intervention
If you are eligible for the study, you will be invited to undertake a program consisting of four components: holistic assessment, exercise program, education and self-care, and supportive care therapies (these may include mindfulness, yoga, acupuncture, massage and reflexology). The program will be delivered in a tailored fashion to suit your needs and preferences. We will use a combination of face-to-face and online sessions. The program will run for the period from when you are enrolled until the completion of your neoadjuvant chemotherapy. This will vary from person to person but may be up to 24 weeks.

Additional costs
There are no additional costs associated with participating in this research project, nor will you be paid for your participation. The intervention will occur alongside your usual medical care.

3 What do I have to do?

The initial screening session will take approximately 10 minutes and will involve you being asked questions about your physical and mental health.

When you enrol in the study, you will be asked to attend:

1. a holistic nursing assessment which will aim to understand any concerns and goals you may have or need addressing, and tailor the services and support to you as part of the program. Some additional blood tests will be requested to understand any health risk factors and any micronutrient deficiencies you may have. These can be done at the same time as your usual blood tests for chemotherapy treatment and will be taken in the morning after a 12 hour fast. You may be referred to the Supportive Care and Integrative Oncology specialist at Chris O'Brien Lifehouse who will recommend how best to address any abnormalities or complex symptoms or medical issues.

2. an exercise physiology assessment which will guide what exercise protocol is best for you. The exercise program will be adapted to meet your needs and ability. You will be recommended three exercise sessions per week during your treatment. These sessions will be a combination of face-to-face and online (using ZOOM) sessions. These sessions will be supervised by the exercise physiologist at the hospital gym and will usually be offered as part of a group session. You will be asked what combination of online/face-to-face sessions you would prefer.

3. a baseline assessment of lymphoedema and receive personalised education and information based on your risk assessment of developing lymphoedema related to your diagnosis and proposed treatment.

4. three education sessions throughout your treatment. These will be offered either online or face-to-face in a group setting. If you wish, you may invite a family member,
friend or carer to attend these sessions with you. The sessions will involve a presentation and an opportunity to ask questions:

i) using mindfulness and gentle yoga to manage stress during treatment and surgery

ii) healthy lifestyle and nutrition

iii) preparing for surgery and understanding lymphoedema risk

Throughout the program, each time you attend for chemotherapy you will be asked to complete a short questionnaire on an iPAD to rate any symptoms you may be experiencing on a scale of 1 to 10. This will done using a questionnaire called the Edmonton Symptom Assessment Scale (known as the ESAS). If you rate symptoms above 4, one of the study team may contact you by phone or when you are at the hospital for chemotherapy or an exercise session to discuss any further supportive care you may need. Supportive care therapies include oncology massage, acupuncture, reflexology, yoga and mindfulness.

Questionnaires and assessment measures

We will ask you to complete online questionnaires and face to face assessment measures related to your health as part of the study. These will be required at five timepoints during the study period. The following table provides a summary of the time we estimate that these appointments and assessments will take. We will aim to make these appointments at time that is convenient to you, either using ZOOM/phone or when you may be attending the hospital for other appointments.

<table>
<thead>
<tr>
<th>Enrolment</th>
<th>During chemotherapy</th>
<th>At completion of chemotherapy</th>
<th>After Surgery</th>
<th>Follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>An initial appointment will be made to enrol in the study and complete the initial assessments.</td>
<td>An appointment between weeks 6-8</td>
<td>An appointment will be made before your surgery</td>
<td>An appointment will be made &lt; 2 weeks into any scheduled radiotherapy</td>
<td>An appointment will be made for a date 6 months from when you completed chemotherapy</td>
</tr>
</tbody>
</table>
| Questionnaires (x4)  
(15 mins) | ESAS questionnaire  
(2 mins) | Questionnaires (x4)  
(15 mins) | Questionnaires (x3)  
(12 mins) | Questionnaires (x5)  
(18 mins) |
| Exercise physiology assessment  
(60 mins) | Exercise physiology assessment  
(60 mins) | Exercise physiology assessment  
(60 mins) | Exercise physiology assessment  
(60 mins) | |
| Blood test | Blood test | Blood test | Blood test | |
| Holistic nursing assessment  
Lymphoedema baseline measures  
(45 mins) | Optional: attend an interview (20 mins) or focus group (60 mins).  
Lymphoedema baseline measures  
(45 mins) | Holistic nursing assessment  
Lymphoedema baseline measures  
(45 mins) | Holistic nursing assessment  
Lymphoedema baseline measures  
(45 mins) | |

Bloods will be collected at three timepoints during the study period; enrolment, at completion of chemotherapy and at follow up. In addition to standard blood pathology testing, we will also be analysing micronutrient and cardio-metabolic markers. Completing this analysis will require us to take between 6-23mLs of additional blood.

Medical records and surgical data

Some data from your medical records at Chris O’Brien Lifehouse will be collected as part of the study. This will include demographic information, diagnostic and pathology data, data on any other conditions or diseases you may have. We will also request a copy of your surgical report from your surgeon as part of our study.

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

MASTER Participant Information Sheet, Version 1, 07/01/2022

Chris O’Brien Lifehouse SITE SPECIFIC Participant Information Sheet Version 1, 07/01/22
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 Chris O'Brien Lifehouse.

5 What are the possible benefits of taking part?

We cannot guarantee or promise that you will receive any benefits from this research; however, possible benefits may include alleviation of cancer treatment side effects, quality of life, coping and outcomes of surgery.

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

All therapies described in the study are currently part of standard supportive care and integrative oncology at Chris O'Brien Lifehouse. Standard hospital procedures will be followed should you present with pathology values out of range, or as unwell or become unwell during treatment or any study activities.

The risks associated with this study are minimal. All therapists delivering the sessions (exercise, yoga, mindfulness, massage, acupuncture, reflexology) have experience working with people with cancer and are credentialed as treating health practitioners at Chris O'Brien Lifehouse. Each consultation will begin with an interview to understand any changes in symptoms you may be experiencing. Screening to determine readiness to undertake physical activity will be conducted prior to commencing the exercise program.

If any symptoms do develop after consent and during the trial, you will be instructed to contact a member of the research team in addition to your usual healthcare provider. An adverse events record form will be used to record any unexpected signs, symptoms or feelings of distress or discomfort during the trial period. All reported adverse events that occur between consent and the last visit for the study will be recorded in detail.

7 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 choose to withdraw, any information that you have supplied will remain confidential. You can also advise if you consent for the use of your data, up and until your withdrawal from the study. If you do not give consent, your information and data will be securely disposed of in accordance with the Australian privacy and other relevant laws.

8 What will happen to information about me?

Please be assured that only the researchers will have access to the data you provide. You will be assigned a code that will replace identifying information in your data. Coded information collected about you will be kept for future use for research studies currently unknown and may be shared with National and International research collaborators however ethical approval will be obtained prior to their use.

All web-based information transmission is encrypted. This study will collect data in Research Electronic Data Capture (REDCap) and Qualtrics. REDCap was developed specifically to meet
HIPAA-Security guidelines. REDCap is maintained according to Chris O'Brien Lifehouse guidelines. The data will be stored on a secure a fire-wall protected server within RedCAP under the license of Chris O'Brien Lifehouse. All data transmitted to the Qualtrics platform are encrypted using the industry standard TLS protocol and stored in a Chris O'Brien Lifehouse managed server in Sydney, Australia. Access is restricted to the Research team named on the Ethics approval. We will store all information collected for this study securely and destroy it 15 years after the results are published in accordance with hospital policy and the Australian Code for the Responsible Conduct of Research.

Coded information collected about you will be kept for future use for research studies currently unknown and may be shared with National and International research collaborators however ethical approval will be obtained prior to their use.

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 the participant cannot be identified, except with your permission.

9 Ethics Approval and Complaints

This study has been approved by the St Vincent’s Human Research Ethics Committee. The Approval number is 2021/ETH12198.

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:

<table>
<thead>
<tr>
<th>Reviewing HREC name</th>
<th>St Vincent’s Hospital HREC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Position</td>
<td>Research Officer</td>
</tr>
<tr>
<td>Telephone</td>
<td>02 8382 4960</td>
</tr>
<tr>
<td>Email</td>
<td><a href="mailto:SVHS.Research@svha.org.au">SVHS.Research@svha.org.au</a></td>
</tr>
</tbody>
</table>

Reviewing HREC approving this research and Research Officer details

| Local Research Office (contact the Chris O’Brien Lifehouse Research Governance Officer) |
|----------------------------------------|----------------------------------------|
| Name                                   | Research Governance Officer            |
| Position                               | Research Governance Officer            |
| Telephone                              | 02 8514 0410                           |
| Email                                  | ResearchGovernance@lh.org.au           |
Consent Form

Title
Better health outcomes during neoadjuvant breast cancer treatment with an early supportive care program: a feasibility study

Short Title
A feasibility study for an Early Supportive Care Program

Protocol Number
Version 1.0

Project Sponsor
Chris O'Brien Lifehouse

Coordinating Principal Investigator/
Dr Suzanne Grant

Coinvestigators
A/Prof Judith Lacey, Dr Susannah Graham, Kim Kerin-Ayres, Dr Cindy Mak, Dr Sanjeev Kumar, Dr Shelley Kay, Dr Ash Malalasekera, Dr Sara Wahlroos, Jane Cockburn, Maria Gonzalez Sandra Templeton, Prof Gillian Heller

Location
Chris O'Brien Lifehouse

I hereby consent to participate in the above-named research project.

I acknowledge that:
- I have read the participant information sheet (or where appropriate, have had it read to me) and have been given the opportunity to discuss the information and my involvement in the project with the researcher/s
- The procedures required for the project and the time involved have been explained to me, and any questions I have about the project have been answered to my satisfaction.
- I have been made aware of the procedures involved in the study, including any known or expected inconvenience, risk, discomfort or potential side effect and of their implications as far as they are currently known by the researchers.
- I freely choose to participate in this study and understand that I can withdraw at any time.
- The research study is strictly confidential.

I consent to:

☐ Participating in this research project as described (providing demographic information; allowing access to Chris O'Brien Lifehouse medical records; attending consultations, assessments and therapy sessions; completing self-report assessment measures)

☐ Participating in an interview for focus group with a research team member following the program, and it being audio-recorded (optional)

☐ Being contacted by phone during the study by members of the research team as needed

☐ My surgeon providing my surgical report to the research team

☐ I understand that my coded data may be used for future research (only after ethics committee approval is received) and I agree to this

I hereby agree to participate in this research study.
Participant Name: ____________________________________________
Participant signature: ____________________________________________
Date: __________________________________________________________
Form for Withdrawal of Participation

**Title**
Better health outcomes during neoadjuvant breast cancer treatment with an early supportive care program: a feasibility study

**Short Title**
A feasibility study for an Early Supportive Care Program

**Protocol Number**
Version 1.0

**Project Sponsor**
Chris O'Brien Lifehouse

**Coordinating Principal Investigator/Co-Investigator(s)**
Dr Suzanne Grant
A/Prof Judith Lacey, Dr Susannah Graham, Kim Kerinn-Ayres, Dr Cindy Mak, Dr Sanjeev Kumar, Dr Shelley Kay, Dr Ash Malalasekera, Dr Sara Wahlroos, Jane Cockburn, Maria Gonzalez Sandra Templeton, Gillian Heller

**Location**
Chris O'Brien Lifehouse

**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 Chris O'Brien Lifehouse.

Name of Participant (please print) ____________________________________________________________________________
Signature ____________________________________________________________________________ Date ____________________________________________________________________________

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

**Declaration by Study Doctor/Senior Researcher†**
I have given a verbal explanation of the implications of withdrawal from the research project and I believe that the participant has understood that explanation.

Name of Study Doctor/Senior Researcher† (please print) ____________________________________________________________________________
Signature ____________________________________________________________________________ Date ____________________________________________________________________________

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

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

MASTER Participant Information Sheet, Version 1, 22/11/2021
Chris O’Brien Lifehouse SITE SPECIFIC Participant Information Sheet Version 1, 22/11/2021
Supplemental material: Study Intervention – exercise component

The exercise intervention will be aligned with treatment schedules recommending 2 x face-to-face multi-modal exercise sessions (60 minutes) with an additional online or home session. However, options are included to accommodate individual needs and treatment-related side effects:

- 2 clinic supervised group exercise + 1 home (or online group)
- 1 clinic + 1 online group + 1 home program
- 1 clinic + 2 home + 1 support phone call
- COVID contingency (already in operation): 2 online group + 1 home program

**Resistance training:** Resistance training in clinic typically consists of at least six exercises targeting the large muscle groups using pin loaded and cable equipment: leg press, knee extension, knee flexion, lat pulldown, seated row, chest press (depending on personal comfort) as well as optional biceps and triceps. Rate of perceived exertion (RPE: 15 – 18/20) will be used in session after the first set to determine training load progression. Leisure-time physical activity, yoga or stretching will be encouraged.

**Aerobic exercise (AEX):** Aerobic exercise in clinic includes one or more self-selected modes of treadmill, upright or recumbent cycle, rowing ergometer, arm ergometer or stepping. This can be continuous or intermittent.

Initial introduction: Continuous or intermittent starting @ 50 to 59 % of Heart Rate Reserve (recently measured resting heart rate or perceived exertion) and progressing to continuous or intervals @ 60 to 65 % of Heart Rate Reserve Progressed each week by 5% from previous cycle week 2.

**Exercise intervention sessions**

Example:

- Warm up: continuous 5 minutes, intervals 15 to 25 minutes of high:low of 15:45 seconds, 30:30 seconds or 30: 90 seconds depending on the individual symptoms and/or motivation
- Resistance + aerobic circuit (lat pulldown + step ups x 3)
- Conclusion: Progressive balance and flexibility according to individual ability.

Support for exercise behaviour will occur in usual clinic communication while reviewing training documents. For those choosing more home-based exercise, a weekly phone call will follow up to identify enablers or barriers to participation in relation to symptom burden.

Template example for 2 week AC cycle:

<table>
<thead>
<tr>
<th>Week 1</th>
<th>2/week</th>
<th>1/week</th>
<th>Option</th>
</tr>
</thead>
<tbody>
<tr>
<td>AEX RT B/Flx</td>
<td>15-20m @ 50-55% HRR 2 x 5 reps @ 70-80% 1RM 10 minutes</td>
<td>Online circuit theraband/dumbbells Home program</td>
<td>Leisure activity Yoga</td>
</tr>
</tbody>
</table>

Week 2 2/week session day before or day of Tx
Template example of weekly taxane cycle

<table>
<thead>
<tr>
<th>Day 4</th>
<th>Day 6</th>
<th>Infusion day</th>
</tr>
</thead>
<tbody>
<tr>
<td>Online theraband/dumbbell circuit or Home program</td>
<td>AEX: 15-20m @ 50-55% HRR RT: 2 x 5 reps @ 70-80% 1RM B/Fix: 10 minutes</td>
<td>AEX: 20-25m @60-70% HRR/Intervals RT: 6 x 5 reps @70-80% 1RM B/Fix: 10 minutes</td>
</tr>
</tbody>
</table>

Modification of exercise intervention according to symptom severity

Day of treatment or day before chemotherapy (end week 2): higher intensity or interval variations are options.

 symptom severity

exercise dose

 exercise dose

 symptom severity
Supplemental material

51: Screening pathway for additional supportive care – ESAS

Participants complete an ESAS at each chemotherapy visit. Participant ESAS scores will be reviewed weekly by a member of the study team. If a member of the study team identifies an ESAS score in the following range they will be contacted by phone and offered one of the treatments and/or referrals to a health professional listed below.

<table>
<thead>
<tr>
<th>SYMPTOM</th>
<th>ESAS Score 4-6</th>
<th>ESAS Score 7-10</th>
</tr>
</thead>
<tbody>
<tr>
<td>PAIN</td>
<td>Self-management / acupuncture / nursing +/- medical review</td>
<td>Medical review</td>
</tr>
<tr>
<td>FATIGUE &amp; DROWSINESS</td>
<td>Yoga/touch/acupuncture</td>
<td>Nursing +/- medical</td>
</tr>
<tr>
<td>NAUSEA</td>
<td>acupuncture /Medical</td>
<td>Medical</td>
</tr>
<tr>
<td>DEPRESSION</td>
<td>Offer referral to psych-oncology</td>
<td>Referral to psych oncology</td>
</tr>
<tr>
<td></td>
<td>Mindfulness/yoga/touch</td>
<td></td>
</tr>
<tr>
<td>ANXIETY</td>
<td>Offer referral to psych oncology</td>
<td>Referral to psych oncology</td>
</tr>
<tr>
<td></td>
<td>Mind body/yoga/touch</td>
<td></td>
</tr>
<tr>
<td>SHORTNESS OF BREATH</td>
<td>Refer to medical oncology</td>
<td>Refer to medical oncology</td>
</tr>
<tr>
<td>APPETITE</td>
<td>Nursing +/- medical . Dietitian if weight changes associated</td>
<td>Medical</td>
</tr>
<tr>
<td>SLEEP</td>
<td>Can-sleep resource</td>
<td>Medical +/- psych onc</td>
</tr>
<tr>
<td></td>
<td>Touch/acupuncture/mind-body</td>
<td></td>
</tr>
<tr>
<td>FEELING OF WELLBEING</td>
<td>Massage/reflexology</td>
<td></td>
</tr>
<tr>
<td>FINANCIAL DISTRESS</td>
<td>Offer referral to social work</td>
<td>Referral to social work</td>
</tr>
<tr>
<td>SADNESS</td>
<td>Offer referral to psych oncology</td>
<td>Referral to psych oncology</td>
</tr>
<tr>
<td>VOMITING</td>
<td>Medical review</td>
<td>Medical review</td>
</tr>
<tr>
<td>NUMBNESS/TINGLING</td>
<td>Acupuncture/reflexology</td>
<td>Medical review</td>
</tr>
<tr>
<td>DRY MOUTH</td>
<td>Education/self-management</td>
<td>nursing +/- medical</td>
</tr>
<tr>
<td>MEMORY</td>
<td>Yoga/mindfulness/brain training/nursing</td>
<td>Nursing +/- medical</td>
</tr>
<tr>
<td>DISTRESS</td>
<td>Yoga, mindfulness, touch</td>
<td>Referral to psych oncology</td>
</tr>
<tr>
<td>HOT FLUSHES</td>
<td>Acupuncture</td>
<td>Medical review</td>
</tr>
</tbody>
</table>
**S2: Interview guide**

The following questions will be used as a guide for the healthcare professionals (HCPs) and patients who consent to an interview or focus group.

<table>
<thead>
<tr>
<th>CFIR Code</th>
<th>Item Source</th>
<th>Question</th>
<th>Respondent</th>
</tr>
</thead>
</table>
| Knowledge & beliefs about: | Implementation Climate | What did you think of the program?  
Is there a strong need for this program?  
Do you think others see a need for the program? | All        |
| Relative Priority | | | |
| Need | | | |
| Tension for Change | | | |
| Knowledge & beliefs about: | Implementation Climate | In a healthcare setting, influential stakeholders may include influential and well-respected clinicians, where as in an education setting, this may include influential and well-respected teachers or educators.  
To what extent does implementing this program align with the hospital goals and priorities? What level of endorsement or support have you seen or heard from other HCPs? | HCPs only |
| Relative Priority; Leadership | | | |
| Engagement Process | Process | Were all the appropriate voices at the table from the start for setting up this intervention? Are there any voices you feel are missing? | HCPs only |
| Outer setting Complexity | Process | How well do you think the program will meet the needs of the patients served by the hospital?  
In what ways will the program meet their needs?  
E.g. improved access to services? Help with self-management?  
What barriers will the individuals served at the hospital face to participating in the intervention?  
Have you elicited information from participants regarding their experiences with the program?  
- What are their perceptions of the intervention?  
- Can you describe what kind of specific information you have heard?  
Have you heard stories about the experiences of participants with the intervention? Can you describe a specific story? | HCPs only |
<table>
<thead>
<tr>
<th>Complexity Process</th>
<th>Complexity Process</th>
<th>Knowledge &amp; beliefs about Complexity/ Cost Process</th>
<th>Intervention Source Adapability Intervention Characteristics</th>
<th>Trial-ability</th>
<th>Stakeholders Implementation Strategy</th>
<th>Structural Characteristics Process</th>
<th>All</th>
<th>All</th>
<th>All</th>
<th>Patients only</th>
<th>HCPs &amp; participants only</th>
<th>HCPs only</th>
</tr>
</thead>
<tbody>
<tr>
<td>Which factors do you feel were the most critical to address early on (i.e., would threaten success/derail the project if not addressed?)</td>
<td>Were there factors or costs that weren’t considered at the time, that you wish had been prioritized in hindsight?</td>
<td>What do you think are the core components of the program that must be retained?</td>
<td>What did you think about the assessments and measures that were collected?</td>
<td>What was your communication with your/other HCPs around the program? Any resistance?</td>
<td>What kinds of infrastructure changes were necessary to accommodate the program? Changes in scope of practice? Changes in formal policies? Changes in information systems or electronic records systems? Other?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Supplemental material 4: Focus group and interview guide

The following questions will be used as a guide for the healthcare professionals (HCPs) and study participants who consent to an interview or focus group. CFIR and RE-AIM constructs have been incorporated into the interview guide.

<table>
<thead>
<tr>
<th>CFIR Code</th>
<th>Item Source</th>
<th>Question</th>
<th>Respondent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Knowledge &amp; beliefs about:</td>
<td>Implementation Climate</td>
<td>What did you think of the program?</td>
<td>All</td>
</tr>
<tr>
<td>Relative Priority</td>
<td></td>
<td>Is there a strong need for this program?</td>
<td></td>
</tr>
<tr>
<td>Need</td>
<td></td>
<td>Do you think others see a need for the program?</td>
<td></td>
</tr>
<tr>
<td>Tension for Change</td>
<td></td>
<td>In a healthcare setting, influential stakeholders may include influential and well-respected clinicians, where as in an education setting, this may include influential and well-respected teachers or educators.</td>
<td>HCPs only</td>
</tr>
<tr>
<td></td>
<td></td>
<td>To what extent does implementing this program align with COBLH goals and priorities? What level of endorsement or support have you seen or heard from other HCPs?</td>
<td></td>
</tr>
<tr>
<td>Engaging</td>
<td>Process</td>
<td>Were all the appropriate voices at the table from the start for setting up this intervention? Are there any voices you feel are missing?</td>
<td>HCPs only</td>
</tr>
<tr>
<td>Outer setting Complexity</td>
<td>Process</td>
<td>How well do you think the program will meet the needs of the patients served by COBLH?</td>
<td>HCPs only</td>
</tr>
<tr>
<td></td>
<td></td>
<td>In what ways will the program meet their needs? E.g. improved access to services? Help with self-management?</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>What barriers will the individuals served at COBLH face to participating in the intervention?</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Have you elicited information from participants regarding their experiences with the program?</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>- What are their perceptions of the intervention?</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Can you describe what kind of specific information you have heard?</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Have you heard stories about the experiences of participants with the intervention? Can you describe a specific story?</td>
<td></td>
</tr>
<tr>
<td>Complexity</td>
<td>Process</td>
<td>Which factors do you feel were the most critical to address early on (i.e., would threaten success/derail the project if not addressed?)</td>
<td>All</td>
</tr>
<tr>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>Knowledge &amp; beliefs about Complexity/Cost</td>
<td>Process</td>
<td>Were there factors or costs that weren’t considered at the time, that you wish you had prioritized in hindsight?</td>
<td>All</td>
</tr>
<tr>
<td>Intervention Source</td>
<td>Intervention Characteristics</td>
<td>What do you think are the core components of the program that must be retained?</td>
<td>All</td>
</tr>
<tr>
<td>Adaptable</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trial-ability</td>
<td></td>
<td>What did you think about the assessments and measures that were collected?</td>
<td>Patients only</td>
</tr>
<tr>
<td>Stakeholders</td>
<td>Implementation Strategy</td>
<td>What was your communication with other HCPs around the program? Any resistance?</td>
<td>HCPs only</td>
</tr>
<tr>
<td>Structural Characteristics</td>
<td>Process</td>
<td>What kinds of infrastructure changes were necessary to accommodate the program? Changes in scope of practice? Changes in formal policies? Changes in information systems or electronic records systems? Other?</td>
<td>HCPs only</td>
</tr>
</tbody>
</table>