

# BMJ Open 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

## STRENGTHS AND LIMITATIONS OF THIS STUDY

- ⇒ A strength of our study is the codesign of the intervention, underpinned by social cognitive theory and attention to implementation factors.
- ⇒ The study is an innovative multimodal approach to prehabilitation that utilises complementary therapies to support quality of life and facilitate exercise compliance, meeting the demand documented in the prehabilitation literature for multimodal approaches.
- ⇒ The study findings will be limited by the small sample size.
- ⇒ The study is conducted at a single hospital that supports the delivery of integrative oncology which underpins the intervention.
- ⇒ The women in this study are all receiving neoadjuvant therapy, but they will likely be a heterogeneous group in terms of the treatment they receive.

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.<sup>1,2</sup> 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.<sup>3–7</sup> Providing early supportive care prior to surgery (typically termed ‘prehabilitation’) may mitigate these side effects and improve quality of life.<sup>8</sup>

Most research to date on prehabilitation programmes has been undertaken in gastrointestinal and urological cancer,<sup>7 9 10</sup> but studies in women with breast cancer have increased in volume.<sup>8 11–13</sup> 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.<sup>14–17</sup>

Prehabilitation studies in cancer to date largely focus on exercise. Low muscle mass<sup>18</sup> and quality,<sup>19</sup> and high visceral adiposity<sup>20</sup> may predict poorer treatment tolerance and are associated with shorter disease-free survival after chemotherapy.<sup>21</sup> Patients undergoing systemic therapy for breast cancer, such as anthracycline chemotherapy and HER-2 targeted therapies, are also at risk of cancer therapy-related cardiac dysfunction.<sup>22</sup> These variables are all modifiable targets even with a limited programme of exercise.<sup>23</sup>

While exercise is an essential component of prehabilitation, participants have expressed a preference for multimodal interventions that include other supportive care interventions.<sup>8 24</sup> Psychosocial barriers and cancer-related side effects hinder the uptake of exercise in people with cancer.<sup>25</sup> 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.<sup>7 8 26–28</sup> 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.<sup>29–32</sup> 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.<sup>33</sup>

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.<sup>34</sup>

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<sup>35</sup> (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,<sup>36</sup> 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.<sup>37</sup>

### 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.<sup>38 39</sup> 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

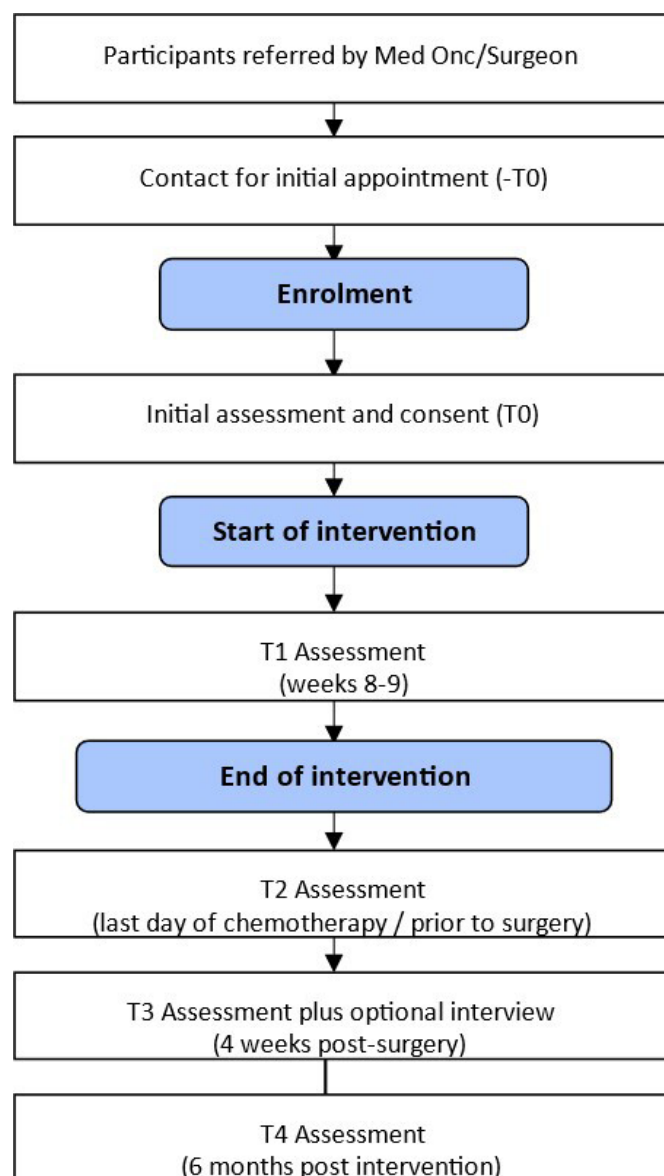
We will exclude women who are lactating, pregnant or of childbearing potential who are not willing to avoid becoming pregnant during the study; unable to give informed consent; who have completed more than two cycles of NACT at time of enrolment; or are unable to participate due to no computer at home 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.



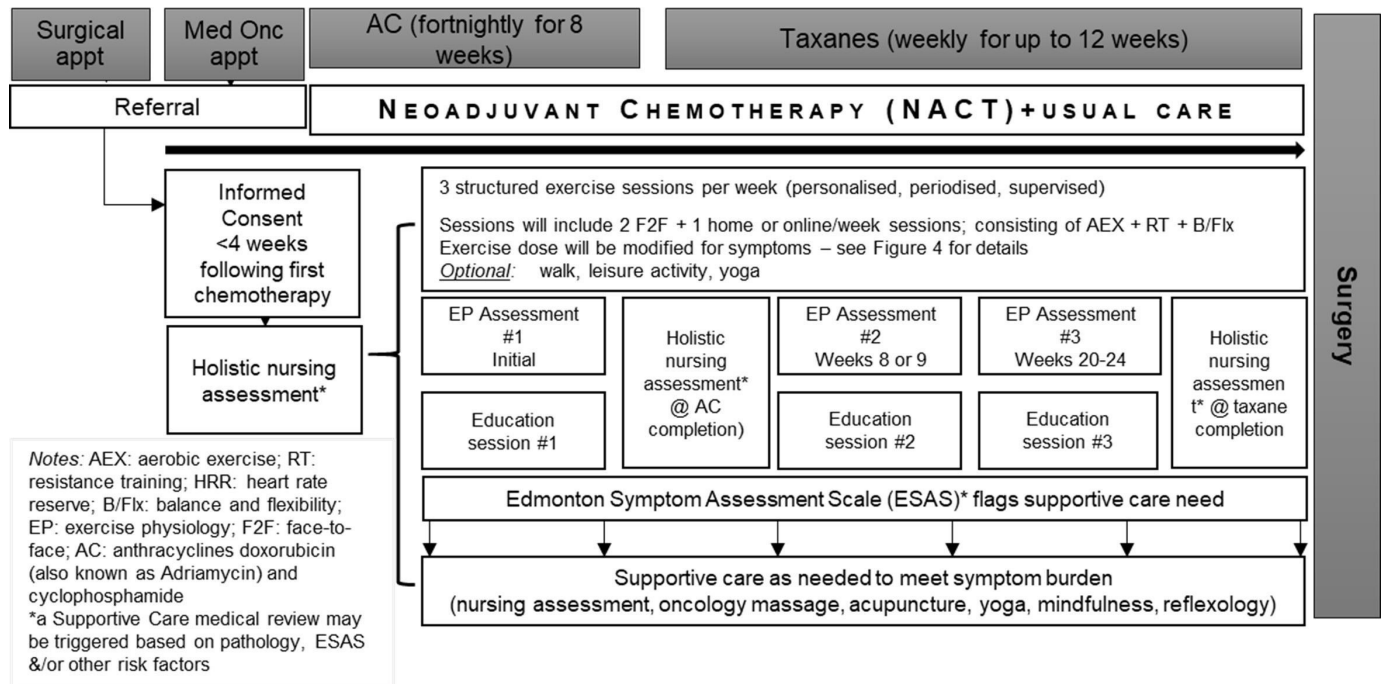
**Figure 1** Study flow chart.

### 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.<sup>40 41</sup> 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





**Figure 2** Study intervention.

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.<sup>42</sup> Self-efficacy, an important component of social cognitive theory, is recognised for its significant effect on patients' adaptation to their diagnosis and self-management.<sup>31 42</sup> 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.
- **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.<sup>43</sup> 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<sup>44</sup> 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.

Table 1 shows a suggested algorithm of integrative therapy referral options for symptom control to facilitate discussions on evidence-informed approaches.<sup>45 46</sup>

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

Symptom	Pain <sup>59</sup>	Fatigue	Insomnia	Anxiety <sup>60</sup>
Modality	Acupuncture Massage Mindfulness	Yoga <sup>61</sup> Acupuncture <sup>62</sup>	Yoga <sup>61</sup> Acupuncture <sup>63</sup>	Mindfulness Yoga Massage Reflexology
Symptom	Nausea and vomiting	Neuropathy	Dry mouth	Hot flashes
Modality	Acupuncture <sup>46</sup> Acupressure <sup>46</sup>	Acupuncture <sup>62</sup> Massage <sup>64</sup> Reflexology <sup>65</sup>	Acupuncture <sup>62</sup>	Acupuncture <sup>62</sup> Yoga <sup>66</sup>

► *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<sup>47</sup> supported with behavioural coaching models of HealthChange Australia methodology ([www.healthchange.com](http://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.<sup>48</sup> 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.<sup>49</sup>

► *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 ( $T_0$ ), mid-chemotherapy ( $T_1$ ), end of chemotherapy ( $T_2$ ), after surgery ( $T_3$ ), and at 6 months after completion of the study intervention ( $T_4$ ) ([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

Measure	Screening	Baseline*	During NACT	Post-NACT	Post- surgery	Follow-up
	-T <sub>0</sub>	T <sub>0</sub>	T <sub>1</sub>	T <sub>2</sub>	T <sub>3</sub>	T <sub>4</sub>
<b>Enrolment and Clinical Measures</b>						
Eligibility screen	✓					
Informed consent		✓				
Demographic data		✓				
NCCN Distress Thermometer		✓			✓	✓
Lymphoedema assessment		✓		✓	✓	✓
Standard Pathology (extracted from EMR): FBC, EUC, LFT, CMP and CRP					✓	✓
<b>Feasibility measures</b>						
Acceptability, AIM, IAM, FIM				✓		
Recruitment, completion and adherence rates		✓		✓		
Interviews & Focus Groups					✓	
<b>Patient Reported Outcome Measures</b>						
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		✓		✓		✓
<b>Costs</b>						
Program delivery costs (all interventions/ consultations)					✓	
UK Cancer Costs Questionnaire: Baseline questions (T0)		✓				
UK Cancer Costs Questionnaire: follow-up assessment					✓	✓
<b>Surgical, medical and biochemical outcomes</b>						
Medical record data (relative dose intensity)					✓	
Micronutrient assessment (Vitamin B12, zinc, Vitamin D, iron studies, folate)		✓		✓		✓

Continued

Table 2 Continued

Measure	Screening	Baseline*	During NACT	Post-NACT	Post- surgery	Follow-up
Cardio-metabolic markers (fasting glucose, HbA1c, fasting serum insulin, triglycerides, Chol, HDL, LDL, thyroid)		✓		✓		✓
Surgical record data					✓	
BREAST-Q (preoperative satisfaction module only)		✓				
BREAST-Q (postoperative satisfaction module only)						✓
Safety and adverse events						
Adverse events	Collected throughout the intervention					
*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.						

(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.<sup>50</sup> To measure self-efficacy, the Brief Cancer Behaviour Inventory (CBI-B) will be used.<sup>51</sup>

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'.<sup>52</sup>
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.<sup>53</sup>

Physical activity will be assessed using the Godin-Shephard Leisure-Time Physical Activity Questionnaire (GSLTPAQ).<sup>54</sup>

*Surgical outcomes* BREAST-Q (preoperative and post-operative satisfaction modules specific to planned and performed surgery): the BREAST-Q modules related to satisfaction will be used in this study.<sup>55</sup>

*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 B<sub>12</sub>.

*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, total 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, SpO<sub>2</sub> (Welch Allyn sphygmomanometer).<sup>56</sup>
- ii. 30s chair stand<sup>57</sup>
- iii. Single leg balance<sup>58</sup>
- iv. Pre-post exercise: fatigue, nausea, and pain using VAS 0–10.
- v. Upper and lower body strength (one repetition maximum: 1RM).
- vi. Grip strength: measures as the best of three scores SAEHAN Medical hydraulic hand dynamometer SH5001<sup>58</sup>

*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 (SpO<sub>2</sub>) 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.<sup>8</sup> 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; n attending education sessions; n referred to supportive care therapy / n 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 V.11) 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.

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**Contributors** All members (SJG, SKay, JL, SK, KK-A, JS, MG, ST, GH, SW, AM, CM, and SG) of the study team conceived and contributed to the planning of the study through a series of meetings. SJG, SG, KK-A, SKay, JL, and MG prepared the initial protocol draft for comment and contribution by all other team members. JC provided lived experience insight into the format, and content of the intervention. SJG made the first draft of the manuscript, figures, and tables. GH provided advice on statistical procedures and data analysis. SKay designed the exercise protocol. KK-A and JL planned the holistic nursing intervention. SG planned the surgical outcomes. All members contributed to revisions and approved the final protocol.

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### REFERENCES

- 1 Zdenkowski N, Butow P, Hutchings E, *et al*. A decision aid for women considering Neoadjuvant systemic therapy for operable invasive breast cancer: development and protocol of a phase II evaluation study (Anz1301 DOMINO). *JMIR Res Protoc* 2016;5:e88.
- 2 Patiniott PD, Wong GYM, Lam YH, *et al*. Neoadjuvant chemotherapy rates for breast cancer in Australia—are we there yet. *Ann Breast Surg* 2019;3:9.
- 3 Rossi C, Maggiore C, Rossi MM, *et al*. A model of an integrative approach to breast cancer patients. *Integr Cancer Ther* 2021;20:15347354211040826.
- 4 Beaver K, Williamson S, Briggs J. Exploring patient experiences of Neo-adjuvant chemotherapy for breast cancer. *Eur J Oncol Nurs* 2016;20:S1462-3889(15)30002-8:77–86.
- 5 Huehnchen P, van Kampen A, Boehmerle W, *et al*. Cognitive impairment after cytotoxic chemotherapy. *Neurooncol Pract* 2020;7:11–21.
- 6 Binkley JM, Harris SR, Levangie PK, *et al*. Patient perspectives on breast cancer treatment side effects and the prospective surveillance model for physical rehabilitation for women with breast cancer. *Cancer* 2012;118(8 Suppl):2207–16.

- 7 Faithfull S, Turner L, Poole K, *et al.* Prehabilitation for adults diagnosed with cancer: A systematic review of long-term physical function, nutrition and patient-reported outcomes. *Eur J Cancer Care (Engl)* 2019;28:e13023.
- 8 Toohey K, Hunter M, McKinnon K, *et al.* A systematic review of Multimodal Prehabilitation in breast cancer. *Breast Cancer Res Treat* 2023;197:1–37.
- 9 Bolshinsky V, Li MH-G, Ismail H, *et al.* Multimodal Prehabilitation programs as a bundle of care in gastrointestinal cancer surgery: A systematic review. *Diseases of the Colon & Rectum* 2018;61:124–38.
- 10 Briggs LG, Reitblat C, Bain PA, *et al.* Prehabilitation exercise before urologic cancer surgery: A systematic and Interdisciplinary review. *Eur Urol* 2022;81:S0302-2838(21)00353-5:157–67..
- 11 Brahmabhatt P, Sabiston CM, Lopez C, *et al.* Feasibility of Prehabilitation prior to breast cancer surgery: A mixed-methods study. *Front Oncol* 2020;10:571091:571091..
- 12 Baima J, Reynolds S-G, Edmiston K, *et al.* Teaching of independent exercises for Prehabilitation in breast cancer. *J Cancer Educ* 2017;32:252–6.
- 13 Wu F, Laza-Cagigas R, Pagarkar A, *et al.* The feasibility of Prehabilitation as part of the breast cancer treatment pathway. *PM R* 2021;13:1237–46.
- 14 Luoma M-L, Hakamies-Blomqvist L, Blomqvist C, *et al.* Experiences of breast cancer survivors participating in a tailored exercise intervention -A qualitative study. *Anticancer Res* 2014;34:1193–9.
- 15 Backman M, Browall M, Sundberg CJ, *et al.* Experiencing health - physical activity during adjuvant chemotherapy treatment for women with breast cancer. *Eur J Oncol Nurs* 2016;21:S1462-3889(15)30030-2:160–7..
- 16 Santa Mina D, van Rooijen SJ, Minnella EM, *et al.* Multiphasic Prehabilitation across the cancer continuum: A narrative review and conceptual framework. *Front Oncol* 2020;10:598425:598425..
- 17 Santa Mina D, Brahmabhatt P, Lopez C, *et al.* The case for Prehabilitation prior to breast cancer treatment. *PM R* 2017;9:S1934-1482(17)31200-5:S305–16..
- 18 Pin F, Couch ME, Bonetto A. Preservation of muscle mass as a strategy to reduce the toxic effects of cancer chemotherapy on body composition. *Curr Opin Support Palliat Care* 2018;12:420–6.
- 19 Aleixo GFR, Shachar SS, Nyrop KA, *et al.* Myosteatosis and prognosis in cancer: systematic review and meta-analysis. *Crit Rev Oncol Hematol* 2020;145:S1040-8428(19)30225-2:102839..
- 20 Cespedes Feliciano EM, Chen WY, Lee V, *et al.* Body composition, adherence to anthracycline and Taxane-based chemotherapy, and survival after Nonmetastatic breast cancer. *JAMA Oncol* 2020;6:264.
- 21 Wang W, Gao Y, Cui J. High visceral fat in female breast cancer patients correlates with the risk of progression after adjuvant chemotherapy. *Nutr Cancer* 2022;74:2038–48.
- 22 Lyon AR, López-Fernández T, Couch LS, *et al.* ESC guidelines on Cardio-oncology 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 Cardio-oncology of the European society of cardiology (ESC). *Eur Heart J* 2022;43:4229–361.
- 23 Ligibel JA, Dillon D, Giobbie-Hurder A, *et al.* Impact of a pre-operative exercise intervention on breast cancer proliferation and gene expression: results from the pre-operative health and body (Prehab) study. *Clin Cancer Res* 2019;25:5398–406.
- 24 Garssen B, Boomsma MF, Meezenbroek E de J, *et al.* Stress management training for breast cancer surgery patients. *Psychooncology* 2013;22:572–80.
- 25 Elshahat S, Treanor C, Donnelly M. Factors influencing physical activity participation among people living with or beyond cancer: a systematic Scoping review. *Int J Behav Nutr Phys Act* 2021;18:50.
- 26 Silver JK, Baima J. Cancer Prehabilitation: an opportunity to decrease treatment-related morbidity, increase cancer treatment options, and improve physical and psychological health outcomes. *Am J Phys Med Rehabil* 2013;92:715–27.
- 27 Tsimopoulou I, Pasquali S, Howard R, *et al.* Psychological Prehabilitation before cancer surgery: A systematic review. *Ann Surg Oncol* 2015;22:4117–23.
- 28 Moore J, Merchant Z, Rowlinson K, *et al.* Implementing a system-wide cancer Prehabilitation programme: the journey of greater Manchester's 'Prehab4Cancer'. *Eur J Surg Oncol* 2021;47(3 Pt A):S0748-7983(20)30438-8:524–32..
- 29 Liang S-Y, Chao T-C, Tseng L-M, *et al.* Symptom-management self-efficacy mediates the effects of symptom distress on the quality of life among Taiwanese oncology outpatients with breast cancer. *Cancer Nurs* 2016;39:67–73.
- 30 Zhang Y, Kwekkeboom K, Petrini M. Self-efficacy, and self-care behavior in patients with breast cancer undergoing chemotherapy in China. *Cancer Nurs* 2015;38:E19–26.
- 31 Lev EL, Daley KM, Conner NE, *et al.* An intervention to increase quality of life and self-care self-efficacy and decrease symptoms in breast cancer patients. *Sch Inq Nurs Pract* 2001;15:277–94.
- 32 White LL, Cohen MZ, Berger AM, *et al.* Perceived self-efficacy: a concept analysis for symptom management in patients with cancer. *Clin J Oncol Nurs* 2017;21:E272–9.
- 33 Buchanan DR, O'Mara AM, Kelaghan JW, *et al.* Quality-of-life assessment in the symptom management trials of the National Cancer Institute-supported community clinical oncology program. *J Clin Oncol* 2005;23:591–8.
- 34 Grimmett C, Bradbury K, Dalton SO, *et al.* The role of behavioral science in personalized Multimodal Prehabilitation in cancer. *Front Psychol* 2021;12:634223.
- 35 Chan A-W, Tetzlaff JM, Götzsche PC, *et al.* SPIRIT 2013 explanation and elaboration: guidance for protocols of clinical trials. *BMJ* 2013;346:e7586.
- 36 Weiner B, *et al.* Acceptability of intervention measure (AIM). In: *Intervention Appropriateness Measure (IAM), and Feasibility of Intervention Measure (FIM). Implementation Science*. 2017: 12.
- 37 Osborne RH, Elsworth GR, Whitfield K. The health education impact questionnaire (heiQ): an outcomes and evaluation measure for patient education and self-management interventions for people with chronic conditions. *Patient Education and Counseling* 2007;66:192–201.
- 38 Teresi JA, Yu X, Stewart AL, *et al.* Guidelines for designing and evaluating feasibility pilot studies. *Med Care* 2022;60:95–103.
- 39 Julious SA. Sample size of 12 per group rule of thumb for a pilot study. *Pharmaceutical Statistics* 2005;4:287–91. 10.1002/pst.185 Available: <https://onlinelibrary.wiley.com/toc/15391612/4/4>
- 40 Nguyen LT, Alexander K, Yates P. Psychoeducational intervention for symptom management of fatigue, pain, and sleep disturbance cluster among cancer patients: a pilot quasi-experimental study. *J Pain Symptom Manage* 2018;55:1459–72.
- 41 Silver JK, Baima J. Cancer Prehabilitation: an opportunity to decrease treatment-related morbidity, increase cancer treatment options, and improve physical and psychological health outcomes. *American Journal of Physical Medicine & Rehabilitation* 2013;92.
- 42 Bandura A. Self-efficacy: toward a unifying theory of behavioral change. *Psychol Rev* 1977;84:191–215.
- 43 Whitlock EP, Orleans CT, Pender N, *et al.* Evaluating primary care behavioral counseling interventions: an evidence-based approach. *Am J Prev Med* 2002;22:267–84.
- 44 NCCN. NCCN Clinical Practice Guidelines in Oncology: Distress management. . 2019Available: [http://www.nccn.org/professionals/physician\\_gls/distress.pdf](http://www.nccn.org/professionals/physician_gls/distress.pdf)
- 45 Latte-Naor S, Mao JJ. Putting integrative oncology into practice: concepts and approaches. *J Oncol Pract* 2019;15:7–14.
- 46 Lyman GH, Greenlee H, Bohlke K, *et al.* Integrative therapies during and after breast cancer treatment: ASCO endorsement of the SIO clinical practice guideline. *J Clin Oncol* 2018;36:2647–55.
- 47 Gale J, Skouteris H. Health coaching: facilitating health behavior change for chronic condition prevention and self-management, in applied topics in health psychology. *Wiley-Blackwell* 2013:15–28.
- 48 Henriksson A, Arving C, Johansson B, *et al.* Perceived barriers to and Facilitators of being physically active during adjuvant cancer treatment. *Patient Educ Couns* 2016;99:1220–6.
- 49 Depenbusch J, Haussmann A, Wiskemann J, *et al.* The relationship between exercise self-efficacy, intention, and structural barriers for physical activity after a cancer diagnosis. *Cancers* 2022;14:2480.
- 50 Brady MJ, Cella DF, Mo F, *et al.* Reliability and validity of the functional assessment of cancer therapy-breast quality-of-life instrument. *J Clin Oncol* 1997;15:974–86.
- 51 Heitzmann CA, Merluzzi TV, Jean-Pierre P, *et al.* Assessing Self-Efficacy for coping with cancer: development and Psychometric analysis of the brief version of the cancer behavior inventory (CBI-B). *Psychooncology* 2011;20:302–12.
- 52 Bruera E, Kuehn N, Miller MJ, *et al.* The Edmonton symptom assessment system (ESAS): a simple method for the assessment of palliative care patients. *J Palliat Care* 1991;7:6–9.
- 53 Cutillo A, O'Hea E, Person S, *et al.* The distress thermometer: cutoff points and clinical use. *Oncol Nurs Forum* 2017;44:329–36.
- 54 Amireault S, Godin G, Lacombe J, *et al.* The use of the Godin-Shepherd leisure-time physical activity questionnaire in oncology research: a systematic review. *BMC Med Res Methodol* 2015;15:60.
- 55 Pusic AL, Klassen AF, Scott AM, *et al.* Development of a new patient-reported outcome measure for breast surgery: the BREAST-Q. *Plast Reconstr Surg* 2009;124:345–53.

- 56 Society, B.H. Available: <https://bihsoc.org/resources/bp-measurement/measure-blood-pressure/>
- 57 Rikli RE, Jones CJ. Functional fitness normative scores for community-residing older adults, ages 60-94. *J Aging Phys Act* 1999;7:162-81.
- 58 Liguori G, A.C.o.S. Medicine. *ACSM's guidelines for exercise testing and prescription* 11th ed. 2021: Lippincott Williams & Wilkins,
- 59 Mao JJ, Ismaila N, Bao T, *et al.* Integrative medicine for pain management in oncology: society for integrative oncology-ASCO guideline. *J Clin Oncol* 2022;40:3998-4024.
- 60 Carlson LE, Ismaila N, Addington EL, *et al.* Integrative oncology care of symptoms of anxiety and depression in adults with cancer: society for integrative oncology-ASCO guideline. *J Clin Oncol* 2023;41:4562-91.
- 61 Mustian KM, Morrow GR, Carroll JK, *et al.* Integrative Nonpharmacologic behavioral interventions for the management of cancer-related fatigue. *Oncologist* 2007;12 Suppl 1:52-67.
- 62 Zia FZ, Olaku O, Bao T, *et al.* The National Cancer Institute's conference on Acupuncture for symptom management in oncology: state of the science, evidence, and research gaps. *J Natl Cancer Inst Monogr* 2017;2017:lgx005:52..
- 63 Mao JJ, Xie S, Duhamel K, *et al.* The effect of Acupuncture versus cognitive behavior therapy on insomnia in cancer survivors: A randomized clinical trial. *JCO* 2018;36:10001.
- 64 Menendez AG, Cobb R, Carvajal 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.
- 65 Ben-Horin I, Kahan P, Ryvo L, *et al.* Acupuncture and Reflexology for chemotherapy-induced peripheral neuropathy in breast cancer. *Integr Cancer Ther* 2017;16:258-62.
- 66 Cramer H, Rabsilber S, Lauche R, *et al.* Yoga and meditation for menopausal symptoms in breast cancer survivors—a randomized controlled trial. *Cancer* 2015;121:2175-84. 10.1002/cncr.29330 Available: <https://acsjournals.onlinelibrary.wiley.com/toc/10970142/121/13>