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Feasibility and potential effects of breathing exercise for chronic pain management in breast cancer survivors: study protocol of a phase II randomised controlled trial

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ABSTRACT

Introduction Chronic pain is a common symptom significantly affecting the quality of life of breast cancer survivors. Despite the achievement of pharmacological interventions, the barriers associated with this approach such as inaccessibility, misuse and side effects drive research into effective non-pharmacological interventions to improve chronic pain management, quality of life, anxiety and depression. Breathing exercise (BE) can be a promising option, but research evidence is sparse. This pilot study aims to examine the feasibility and preliminary effect of using an evidence-based BE intervention for chronic pain management in breast cancer survivors.

Method and analysis This study will be a two-parallel-arm, open-labelled, phase II randomised controlled trial with 1:1 allocation. Seventy-two participants will be recruited from a tertiary hospital in China and randomly allocated to either a BE intervention group (n=36) or a control group (n=36). The participants in the intervention group will receive the usual care, a pain information booklet and a 4-week self-administered BE intervention; the participants in the control group will receive the usual care and the pain information booklet only. The assessment will be conducted at three time points: baseline (week 0), immediately after the intervention completion (week 5) and 4 weeks after the intervention completion (week 9). The primary outcomes will be the acceptability and feasibility assessment of the study protocol and methodological procedures. The secondary outcomes will be the effects of BE on pain, quality of life, anxiety and depression in breast cancer survivors. Descriptive statistics will be applied to present the primary outcomes and the Generalised Estimating Equation Model will be utilised to analyse the clinical outcomes.

Ethics and dissemination This study has received ethical approvals from the Human Research Ethics Committee at Charles Darwin University (H21089) and the Clinical Trial Ethics Committee at the Affiliated Hospital of Southwest Medical University (KY2022107). Findings from this study will be presented at academic conferences and submitted to peer-reviewed journals for publication.

Trial registration number ClinicalTrials.gov: NCT05257876.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ This study design follows the Medical Research Council Framework for Developing and Evaluating Complex Interventions.
⇒ This study will explore the feasibility and preliminary effects of an evidence-based breathing exercise (BE) protocol.
⇒ This study is a phase II randomised controlled trial, which will only contribute to a preliminary analysis of the effects of BE on chronic pain in breast cancer survivors.

INTRODUCTION

Chronic pain is one of the most common symptoms among breast cancer survivors. Almost three (74%) out of four breast cancer survivors experience chronic pain.[1] Chronic pain has been reported as the most significant problem leading to poor quality of life (QoL) in breast cancer survivors compared with other symptoms such as allodynia (48%), paraesthesia (63%) and phantom sensations (15%).[1] Chronic pain is defined as pain lasting more than 3 months either continuously or intermittently.[2] Pain can be caused by cancer itself, surgery, chemotherapy, radiotherapy and other treatments,[3–5] and pain may occur in the breast site, shoulder region, chest, axilla, arms, hands, feet or even the whole body.[1 6] A cancer survivor indicates a person living with cancer or has lived with cancer.[7] Breast cancer survivors with distant metastases are likely to experience more severe pain than those without metastases.[8 9] Despite the efforts made to prevent and manage chronic pain, chronic pain remains a major challenge affecting breast cancer survivors' physical functions and QoL.[1 10 11] Meanwhile, anxiety and depression as other common symptoms further impact the QoL of breast cancer survivors.[12 13]

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Research evidence has shown that chronic pain can cause a range of problems for breast cancer survivors such as disability, sleep disturbance, financial burden, unemployment and mental health disorders.[1 14–17]

Chronic pain management in cancer survivors has been best achieved through a patient-centred, multidisciplinary approach that includes pharmacological and non-pharmacological interventions.[18–21] Currently, pharmacological interventions lay the foundation for chronic pain management based on the WHO's 3-step pain management guideline.[22] Following this guideline, a great number of cancer survivors' pain can be well managed, but about one-third of cancer survivors experience insufficient pain management due to various reasons such as lack of access to opioid medications,[23] lack of pain management knowledge[24] or having side effects of the medications.[25] Therefore, the effects and feasibility of utilising non-pharmacological interventions as adjuvant treatments for chronic pain management for cancer survivors are worthy of further study.

Currently, a number of non-pharmacological interventions have gained popularity for chronic pain management in breast cancer survivors, such as acupuncture,[26] aerobic exercise[27] and cognitive behavioural therapy.[28] Despite the potential effects for chronic pain management, these approaches either need the patient to engage in moderate physical exercise,[27] or the involvement of skilled professionals and/or supervised practice,[26 28] which can be an additional burden to cancer survivors physically and financially.[29] Given that breast cancer survivors may experience other chronic health conditions and symptoms of fatigue and psychological distress,[30 31] an energy-saving, cost-effective and self-manageable practice could be more suitable for chronic pain management for breast cancer survivors.

Breathing exercise (BE) is a promising candidate of self-management intervention for chronic pain management. BE refers to breathing activities that change breathing depth and frequency to promote an individual's well-being.[32] There are two theories supporting its potential effect for pain relief. According to the fight-or-flight theory, unmanaged pain can activate sympathetic nervous system, which causes more pain; whereas BE can activate the parasympathetic nervous system, which can ease pain.[33 34] Moreover, the vagus nerve theory suggests that pain can be manipulated via BE techniques[35 36] through its systematic neurovisceral regulation ability.[35 37 38] The symptoms of stress, anxiety and depression that the cancer survivors often experience can also be managed through BE techniques.[39]

Existing research evidence suggests that BE can be a promising approach for pain management in cancer survivors.[40–46] However, the methodological flaws such as lack of allocation concealment and blinding of outcome assessments indicated a high bias in these study outcomes.[47] Most importantly, there is a lack of the consistence of BE techniques applied in these studies, which suggests a need for a well-defined BE intervention protocol to be tested for its efficacy.[47] All these highlight that a standardised evidence-based BE protocol is required to be tested in a rigorously designed randomised controlled trial (RCT) for its effect.

According to the Medical Research Council (MRC) framework, it is necessary to conduct a pilot trial before the main RCT to enhance its chance of success.[48] The proposed study follows the MRC framework for Developing and Evaluating Complex Interventions.[48] Findings of this study can be used to inform a future main RCT study design regarding calculating sample size, the feasibility planning and safety management of the BE intervention. Study findings may also benefit clinicians, researchers and healthcare policymakers in making decisions about non-pharmacological interventions for effective chronic pain management for breast cancer survivors.

The study protocol has been reported according to the Standard Protocol Items: Recommendations for Interventional Trial Checklist.[49] The intervention report in this paper is guided by the TiDier guidelines.[50]

Aims and objectives

This study aims to examine the feasibility of an evidence-based BE intervention protocol and its preliminary effects on chronic pain, QoL, depression and anxiety in breast cancer survivors through a phase II RCT, with the following specific objectives:

1. To pilot the methodological procedures of the RCT utilising the evidence-based BE intervention for chronic pain management in breast cancer survivors.
2. To demonstrate the eligibility rate, retention rate, recruitment rate, attrition rate and intervention completion rate.
3. To evaluate the acceptability and feasibility of the BE intervention and the selected study questionnaires.
4. To identify potential adverse events associated with the BE.
5. To examine the preliminary effects of the BE on chronic pain, QoL, depression and anxiety in breast cancer survivors.

Study design

This study will be a phase II, two-parallel-arm and open-labelled RCT. After the eligibility assessment, all consented participants will be allocated randomly into two parallel groups: the BE intervention group and the control group (wait list control), and the allocation ratio will be 1:1. This study will include a 4-week BE intervention and a follow-up 4 weeks after the intervention completion. The proposed study is expected to start on 1 January 2023 and end on 31 December 2023. The study's design and process are presented in figure 1. The schedule of participants enrolment, intervention and outcomes assessment is shown in table 1.

METHODS: PARTICIPANTS, INTERVENTION AND OUTCOMES

Study setting

This study will take place in a tertiary hospital, the Affiliated Hospital of Southwest Medical University, Luzhou, Sichuan, China. The hospital provides healthcare services

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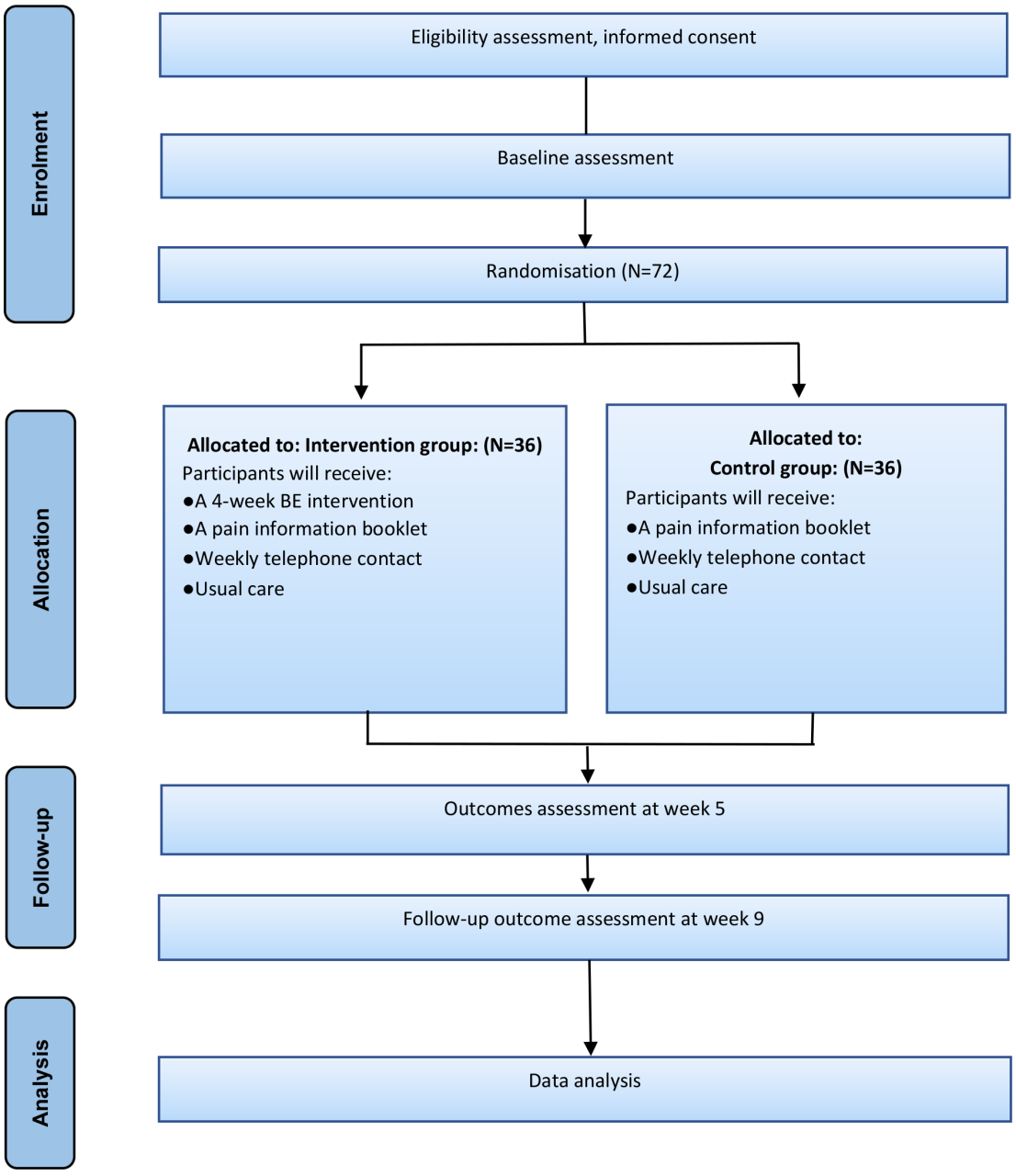

Figure 1 Consolidated Standards of Reporting Trials flow diagram shows the study process including participants enrolment, allocation, follow-up and data analysis. After the eligibility assessment and consent signed, baseline data collection will be conducted. Following that, participants will be randomised into intervention group or control group. Each group will have 36 participants. The only difference between intervention group and control group is that participants in the intervention group will receive breathing exercise training and self-administered BE practice for 4 weeks. After 4-week intervention, second round of data collection will be conducted in week 5 for outcomes assessment for participants in both groups. After 4 weeks of the intervention completion, in week 9, the third round of data collection as the follow-up outcomes assessment will be conducted. Once all data collection is completed, data analysis will be conducted.

to over 40 million local residents, with over 210 beds specialised for oncological patients, treating about 1500 patients with breast cancer per year.

Participants and sample size

Potential participants need to meet the inclusion criteria to be recruited: (1) female patients ≥18 years age; (2) has a confirmed diagnosis of breast cancer from stage I to IIIa; (3) has been experiencing pain since cancer diagnosis constantly or intermittently for ≥3 months, with the average pain intensity in the last 7 days on a numerical scale ≥4/10 ('0' means no pain and '10' means the worst pain); (4) has completed active anticancer treatment (such as surgery, chemotherapy, radiotherapy) for at least 3 months; (5) agrees to participate in the study and are willing to sign the informed consent and (6) can read and understand Mandarin Chinese.

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Table 1 The schedule of participants' enrolment, intervention and outcomes assessment

Study period	Enrolment (week 0)	Intervention (weeks 1–4)	After intervention (week 5)	Follow-up (week 9)
Enrolment				
Eligibility assessment	X			
Informed consent	X			
Demographic characteristics	X			
Allocation	X			
Intervention				
BE group		X		
Outcomes assessment				
Feasibility of recruitment and follow-up process	X	X	X	X
Feasibility of the questionnaires	X		X	X
Feasibility and acceptability of the intervention		X	X	
BPI	X		X	X
HADS	X		X	X
QOL-CSV	X		X	X
FACT-B	X		X	X
Safety measurement		X		

BE, breathing exercise; BPI, Brief Pain Inventory; FACT-B, Functional Assessment of Cancer Therapy Breast; HADS, Hospital Anxiety and Depression Scale; QOL-CSV, Quality of Life Cancer Survivors Version.

Potential participants who meet any of the following exclusion criteria will be excluded: (1) extremely weak and unable to perform the BE; (2) mentally incapable (ie, unable to follow the study instructions); (3) has scheduled treatment plan which may affect the pain experience, such as having a procedure or an operation; (4) receiving other non-pharmacological pain relief treatments, such as acupuncture, yoga, qigong, exercise programme and so on and (5) has any pre-existing chronic pain conditions prior to cancer diagnosis, such as arthritis, rheumatoid arthritis, chronic low back pain, migraines, trigeminal neuralgia, fibromyalgia, joint dysfunction, complex regional pain syndrome, endometriosis and so on. If the participants are unable to provide a detailed medical history, the information will be collected from their hospital medical records after they have signed the study consent form.

As the primary focus of this study is to assess the feasibility and acceptability of the RCT's methodological procedures, intervention protocol and questionnaires, a power-based sample size estimation was deemed unnecessary.[51] Having 30 participants per study group is considered reasonable and sufficient for estimation of between-group comparison and effect size in a pilot study.[52] Thus, the study aims to recruit 30 participants in each group. Considering a potential dropout rate of 20% during the pilot trial process,[53] therefore, the total sample size for this study will be 72, with 36 subjects in each group.

Recruitment and consent

The potential participants will be recruited from both the hospital outpatient clinics and inpatient oncological wards. When doctors and nurses are conducting ward rounds or making follow-up phone calls to the discharged oncological patients, they will talk to the patients about the study. Meanwhile, study flyers will be displayed in oncological wards and outpatient clinics to generate interest. Interested patients can approach the research assistants for more details. The participant information sheet, including the aim, activities and potential benefits and risks of the study will be given to the potential participants by the research assistants. Once potential participants' questions are answered and they meet the study inclusion criteria, they will need to sign the informed consent. The participant's right of withdrawing from the study at any time and without penalty will be clearly explained to the participant before the study commences.

Randomisation

In this study, all participants will be randomised after baseline assessments are completed. A web-based randomisation system will be utilised for participants randomisation (https://sealedenvelope.com/). The allocation ratio of this study will be 1:1. The randomisation sequence will

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be generated by using online software application of randomly permuted block sizes to reduce the predictability of group allocation and to balance the sample size in each study arm.

Concealment

To reduce the risk of selection bias, allocation concealment will be implemented. The randomisation sequence will be kept by a third person who will not be involved in any other parts of this study. After a participant is formally enrolled and the baseline data collection is completed, the research assistants will contact the third person for the allocation. No allocation sequence will be revealed before a participant is ready for randomisation.

Blinding

Given the visibility of the intervention to the participant, it is not possible to blind the participant to the intervention and blind to the intervention facilitator, so the study is designed as an open-labelled trial. This means that the participants will know their allocation to either the intervention or control group after their allocation. Data analysists will be blinded to group allocation and to the research assistants.

Study arms and intervention

This study will include two arms: the BE intervention group and the control group. All participants in the study will receive usual care as prescribed or advised by either their doctors or other healthcare professionals for ongoing care such as regular health checks, regular medications, usual diet, usual social activities and lifestyle. All participants will also receive a pain information booklet that has been developed based on the recommendations of relevant Clinical Practice Guidelines, International Association for the Study of Pain and relevant research evidence from peer-reviewed publications.[20–22 54–56] The pain information booklet provides brief and general information about pain management without containing any therapeutic components. Participants in the intervention group will receive an additional BE intervention.

Intervention description

Intervention group (BE + pain information booklet + usual care)

Participants allocated to the intervention group will receive BE training and a 4-week self-administered BE intervention. The BE intervention, using slow deep pursed lip breathing, is presented in online supplemental appendix 1 (details of the intervention protocol development and validation have been separately reported in a methodological paper).[57] The training for participants will be delivered face to face at the study hospital by the trained research assistant who is a registered nurse. Participants are required to practice BE 5 min per session, 3–5 sessions a day, for 4 weeks. During the study period, the research assistant will conduct weekly phone calls to participants to encourage them to practice their BE and also to collect information of any adverse events and changes in their pain management plans. Any new pain management interventions since the study commencement need to be recorded by the research assistant immediately. All participants will continue their usual care. They will also receive an information booklet about pain management.

Control group (the waiting list control group, pain information booklet + usual care)

Participants allocated to the control group will receive their usual care and the same pain information booklet as the intervention group. Equally, participants in the control group will also receive a weekly phone call to collect information of any changes in their pain management plans. On the completion of the RCT, participants in the control group will be offered the same BE training that the intervention group received.

Intervention adherence and monitoring

To encourage intervention adherence, a BE logbook specially designed for this study will be provided to participants in the intervention group to record their BE practice including frequency of practice, duration of each session, adverse events and corresponding actions. The research assistant will also make weekly phone calls to remind each participant to practice their BE and complete their logbooks. Meanwhile, challenges to practicing BE raised by participants will be collected by the research assistant, and appropriate strategies will be discussed at the regular research group meetings. Participants withdraw from the study will be investigated, and the reasons of withdrawal will be collected and analysed, which may be used for this study protocol modification. If a modification of study protocol is required, ethical approvals will be obtained from both the Charles Darwin University and the study hospital.

Intervention fidelity

In this study, the BE intervention has been developed according to the MRC Framework and based on the most appropriate research evidence through relevant theories, systematic reviews, research studies, practice recommendations and experts' consensus via a content validation study. The doctoral investigator will be leading the study conceptualisation and design, study coordination and facilitation, implementation and quality assurance, supported by two research assistants. To ensure the intervention protocol is carried out as designed, comprehensive training of the research assistants will be conducted according to the Research Assistant Training Manual that is specially designed for this study. After the training, the research assistants will be assessed by the doctoral investigator to ensure each research assistant has thoroughly understood the study design, aims, objectives, intervention and data collections. To ensure the participants' fidelity to the BE protocol, participants will be asked to perform a return demonstration of BE to the research assistant after the initial training to make sure they have mastered skills, and during the weekly phone

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call, the research assistant will also check if a participant has any questions regarding of practicing BE. In addition, as a supplement to the training, a short video of the intervention BE will be given to the participants in the intervention group for self-reference by the research assistant after the initial training. During the intervention period, regular research team meetings will be held to address any potential problems about the BE intervention protocol implementation.

Patient and public involvement

This study protocol development has not involved patients or public members at this stage. However, patients will be involved in the next stage of this multiphase research project for the refinement of the future study design.

Outcome measures

The study outcome measures will consist of baseline assessment, primary outcomes, and secondary outcomes.

Baseline assessment

A demographic form specially designed for this study will be utilised to collect the participants' sociodemographic data (T1, week 0) including gender, age, weight, height, religion, marital status, employment status, education level, sleep, financial condition, drinking and smoking history, and medical history including cancer diagnoses, treatment, comorbidities, pain history, pain relief medications and family history, and so on.

Primary outcomes: feasibility and acceptability

Feasibility of recruitment and follow-up process

The feasibility outcomes will be assessed with regard to (1) referral rate: the proportion of referrals sent by clinicians among all referrals from the inpatient and outpatient clinics; (2) recruitment rate: the proportion of participants who participated in the study from all eligible participants for this study; (3) retention rate: the proportion of participants who completed the whole study, from the beginning to the follow-up assessment; (4) dropout rate: the proportion of participants who withdraw or drop out after randomisation; (5) time taken to recruit enough participants for this study; and (6) feedback from the dropout participants and the reasons of dropping out of the study.

Feasibility of the questionnaires

The feasibility of the utilised questionnaires in the study will be measured by the calculating the proportion of missing values at both scale-level and item-level of the Brief Pain Inventory (BPI), Hospital Anxiety and Depression Scale (HADS), Quality of Life Cancer Survivors Version (QOL-CSV) and Functional Assessment Cancer Therapy-Breast (FACT-B) questionnaires at baseline (T1, week 0), after the intervention (T2, week 5) and at the follow-up (T3, week 9). Item-level missing values will be calculated as the percentages of the items that participants did not respond to; and scale-level missing values will be determined as the percentages of the questionnaires with at least one item with a missing value. The time to complete each questionnaire will also be measured based on participants' reports.

Feasibility, acceptability and safety of the intervention

The feasibility and acceptability of the study intervention will be assessed in terms of: (1) adherence rate: the percentage of the number of BE sessions performed by participants in the total number of BE sessions required; (2) the participants' feedback: data will be collected from feedback forms provided by participants in the intervention group; and (3) safety of the intervention: data will be collected from the participants' BE logbooks and supplemented by information collected during weekly telephone contact. The feasibility and acceptability of the intervention will be assessed during the intervention and immediately after 4 weeks of the BE intervention completion at T2.

Secondary outcomes: pain, QoL, anxiety and depression

A set of questionnaires will be utilised to measure the secondary outcomes including pain (BPI), QoL (QOL-CSV, FACT-B) and anxiety and depression (HADS).

Pain

The BPI is a multidimensional pain measurement tool specially designed for patients with cancer which has been tested with good validity and reliability in many languages.[58–61] The BPI short version measures pain intensity and its interference with life.[58] The Chinese version of BPI is available and has good psychometric properties when used in Chinese patients with breast cancer .[61]

Quality of life

The QOL-CSV and FACT-B will be employed to measure cancer survivors' QoL. The English version of QOL-CSV has showed excellent reliability and internal consistency[62] and has been validated in other languages.[63–65] The Chinese version of the QOL-CSV will be validated by the same research team prior to this study. The QOL-CSV contains 41 items covers four domains in physical, psychological, social and spiritual well-being, and each item is assessed based on a '0' (worst outcome) to '10' (best outcome) scale, higher numbers indicating better outcomes.[62] The FACT-B is designed for patients with breast cancer and has 37 items with a 5-point Likert scale ranging from 0 to 4, a higher score indicating better QoL.[62] A simplified Chinese version of the FACT-B is available with satisfactory psychometric properties in Chinese patients with breast cancer.[66]

Anxiety and depression

The HADS will be utilised to assess the participants' anxiety and depression. It contains 14 items consisting of two subscales: the anxiety subscale and the depression subscale, each containing 7 items.[67] The scale uses a 4-point Likert scale ranging from 0 to 3 with a high score indicating a more severe condition.[67] The Chinese version of the HADS has shown good psychometric properties

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in Chinese patients with cancer[68] and well accepted by Chinese patients with breast cancer.[69]

Data collection, management and analysis

Data collection

The participants' baseline information will be collected through the specially designed demographic data collection form at T1 (week 0) before randomisation. All the data about primary outcomes will be collected throughout the entire study process. All the data about secondary outcomes will be assessed at three time points: T1 (week 0), T2 (week 5) and T3 (week 9). The adverse events of BE intervention will be assessed, monitored and managed by a medical practitioner on the study site during the intervention period. Any severe events will be immediately reported by the principal investigator to the ethics committees of both the study hospital and Charles Darwin University. Questionnaires used for clinical outcome data collection will be conducted through face-to-face or telephone survey by research assistants. All the participants will be encouraged to complete the questionnaires by themselves. However, if a participant needs help to understand the questionnaire, or has a reading impairment, a neutral interpretation of the question will be provided by the research assistants.

Data management

All data collected will be kept securely. All hard copies of the data will be temporarily stored in a locked cabinet in the study hospital during study period of time and will be stored at Charles Darwin University once the study is finished. The electronic data will be stored at Charles Darwin University in a compressed folder with passcode protection. All the datasets will be double-checked against the original recording of the primary data to ensure data accuracy. Storage and disposal of research data will strictly follow the policies and regulations of the study hospital and the Charles Darwin University Research Data Management Guide.

Confidentiality

Information provided by participants will be used for scientific research only. After the baseline data collection, a series number will be assigned to each participant to replace their names and other important identifiers to maintain the confidentiality and anonymity. A file with serial numbers assigned to participants will be stored separately with passcode protection. In the future publication, only non-identifiable information will be presented.

Statistic methods

The SPSS V.26.0 will be used for statistical data analysis. Descriptive statistics will be utilised for primary outcomes description in terms of feasibility of recruitment and follow-up assessment, feasibility of the questionnaires and feasibility and acceptability of the intervention. For the secondary outcomes, the intention-to-treat principle will be applied to manage missing data. For demographic data, the χ^2 test or Fisher's exact test will be applied to examine the baseline comparison between the intervention group and the control group. An independent t-test or Mann-Whitney U test will be utilised to assess the continuous variables. For repeated multivariate analysis of the clinical outcomes (BPI, QOL-CSV, FACT-S and HADS), the Generalised Estimating Equation Model will be applied. The statistical significance will be set as $p<0.05$, and the substantive significance (effect size) will be measured by the standardised difference between two means as Cohen's d.[70]

Safety monitoring

During the study period, participants will be encouraged to report any side effects associated with the BE. A medical practitioner from the study site can be reached by the doctoral investigator at any time for instructions on managing adverse events. Any adverse events associated with BE will be recorded in the participant's exercise logbook and the investigator's adverse events record and managed by the onsite medical practitioner. During the study period, a medical practitioner from the study hospital will review all reported side effects daily to monitor the safety of the BE intervention. If a severe adverse event occurred, the principal investigator would immediately report the event to the ethics committees at both the university and the study hospital, and relevant medical treatment and care will be conducted as directed by the on-site medical practitioner.

DISCUSSION

Despite the increasing number of patients surviving breast cancer,[71] chronic pain remains a common and a distressing problem, dramatically affecting the breast cancer survivors' function status and QoL.[1 72 73] Pain management is a major challenge in breast cancer survivors, in part because many different factors can cause pain. The pathophysiology of chronic pain is complex and often it is hard to determine the exact causes. Pain may be associated with cancer treatments or can be a combination outcome of all factors associated with type of cancer, stage of cancer, means of surgery, previous pain experience, mental health condition, family history, comorbidity and so on.[74] Although pharmacological interventions play a significant role in chronic pain management for cancer survivors, non-pharmacological interventions working as the adjuvant treatment have gradually gained popularity for their potential pain reduction effects.[75–77] Among all the non-pharmacological interventions, BE can be a promising strategy for pain management in cancer survivors. This has been supported by a number of clinical studies.[40–46] However, very limited evidence is available about the effect of BE intervention on chronic pain in breast cancer survivors. The proposed study will provide some evidence on this topic.

There are some strengths in this study. First of all, this study design followed the MRC Framework and used a validated evidence-based BE intervention protocol, which

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filled the knowledge gap identified by a systematic review that existing studies were lack of rigorous methodological design and strong evidence supported intervention protocols.[47] Furthermore, this study focuses on chronic pain management. Needless to say, acute pain management is important; however, chronic pain management needs more attention given the big number of populations of cancer survivors and the profound negative impact on the survivors' long-term QoL.[1 78 79] Nevertheless, the majority of the existing studies on this topic focusing on acute pain management.[47] In addition, this study will assess the safety of the BE intervention, which was hardly assessed and reported in many other BE intervention studies.[47 80]

This study has some limitations. This study is a phase II RCT, and will only have a small sample size, so the outcomes of the study will not be able to provide a definite conclusion about the effect of the BE for chronic pain management in breast cancer survivors as it is lack of sufficient power. Therefore, a phase III RCT with a larger sample size will be required to confirm its effect in the future. Additionally, due to the visible nature of BE intervention, the study is 'open-label' in its design, so neither blinding between the BE instructor and participants, nor the BE intervention and participants, which may introduce detection bias. Besides, the follow-up period after completion of the BE intervention is only 4 weeks, which can be considered as a short term to assess the ongoing effect of the BE intervention.

In Brief, this is a rigorously designed phase II RCT, aiming to assess the study feasibility and methodological procedures of the study and examine the preliminary effects of using an evidence-based BE intervention protocol for managing chronic pain in breast cancer survivors. The findings from this study can be utilised to inform a future large-scale phase III RCT study design in sample size calculation, feasibility planning and intervention protocol refinement.

Ethics and dissemination

This study has received ethical approvals from the Human Research Ethics Committee at Charles Darwin University (H21089) and the Clinical Trial Ethics Committee at the Affiliated Hospital of Southwest Medical University (KY2022107). Findings from this study will be presented at academic conferences and submitted to peer-reviewed journals for publication.

Contributors HW conducted the study conception, study design and drafted the manuscript. J-YT contributed to the study conception, study design and manuscript revision. TW contributed to the study conception, study design and manuscript review. X-LL contributed to the study conception, study design and manuscript revision. DTB contributed to the study design and manuscript revision. S-LZ contributed to the study design and manuscript revision. H-QH contributed to the study site coordination, quality assurance strategies and manuscript revision. The final version of the manuscript has been approved by all authors including the authorship.

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