Trials

STUDY PROTOCOL

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Home-based patient-centered physical activity program for quality of life preservation during neoadjuvant chemotherapy in breast cancer: the AURORA randomized controlled trial protocol

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Abstract

Background Despite the known benefits of physical activity for women with breast cancer (BC), adherence to recommended guidelines remains low, especially during neo-adjuvant chemotherapy. The Aurora intervention presents a multidimensional approach to improve physical activity adherence, considering the patient's emotional and physical needs and barriers to physical activity. This protocol aims to evaluate Aurora's effects compared to standard care in BC patients.

Methods In this 9-week randomized controlled trial, 30 female BC patients under 70 years of age, undergoing neo-adjuvant chemotherapy in the Metropolitan Region of Chile, will be recruited. Participants will receive a standard online education class on the benefits of physical activity for BC patients, which includes general information on the importance of exercise during treatment, recommended physical activity guidelines, and tips for safely incorporating movement into daily routines. Afterward, participants will be randomly allocated in a 1:1 ratio to either the 9-week Aurora experimental program (Aurora experimental kit: branded box containing exercise equipment, designed logbook journal, hydration bottle, exercise leaflet, and arm volume measurement tape) or the Aurora control program (Aurora control kit: branded tote bag containing a blank notebook, hydration bottle, and exercise leaflet). The study will employ a mixed-methods approach to assess multidimensional treatment effects through baseline and post-intervention measurements. The primary outcome will be quality of life, which will be assessed using questionnaires and patient perceptions, with thematic analysis of patient-recorded journals and in-depth group interviews to evaluate emotional treatment effects. Secondary outcomes will include (1) functional capacity tests to measure adverse physical effects and (2) biological markers assessed through lipid profiling, inflammation biomarkers, and tumor progression.

Discussion Our conceptual hypothesis is that the Aurora intervention program will positively impact primary and secondary outcomes compared to the control group. Integrating the behavior change COM-B model and a patient-centered design facilitates tailoring interventions to BC patients' multidimensional needs and barriers.

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Additionally, we expect the Aurora program to promote more significant effects than standard care on physical activity adherence, intensity, and time.

Trial registration The study was registered at ClinicalTrials.gov, NCT06449417. Registered on May 28, 2024. Unique Protocol ID: 230126002. https://clinicaltrials.gov/study/NCT06449417.

Background and rationale {6a}

Breast cancer (BC) remains a significant global health concern, with 2.3 million women diagnosed and 685,000 deaths in 2020. In Chile, BC is the most common cancer among women and the leading cause of cancer-related deaths, with approximately 5331 new cases diagnosed in 2020 [1–3] and a 20% higher disease burden than the global rate (AVISA). Despite improved survival rates, BC treatment, particularly chemotherapy, is associated with adverse effects such as fatigue, loss of muscle mass, and peripheral neuropathy, which negatively impact health-related quality of life [4, 5].

Physical activity has been shown to improve survival and quality of life in BC patients by mitigating chemotherapy-related side effects and potentially reducing cancer recurrence risk [6, 7]. Despite these benefits, physical activity levels often decrease during chemotherapy, with only 13% of BC survivors in Chile engaging in sufficient physical activity [8, 9]. Although Chile's Ministry of Health guarantees essential cancer services, preventive physical therapy for BC patients is omitted, early and prospective models are limited [10, 11], and specialized facilities and professionals are lacking. These barriers highlight the need for feasible, accessible alternatives, such as home-based interventions, empowering patients to engage in physical activity within their environment.

Physical activity during chemotherapy offers a feasible approach to prevent or mitigate some of the adverse physical, biological, and emotional consequences of treatment [12]. By addressing these multidimensional effects, studying physical activity through a comprehensive approach may provide the evidence needed to overcome barriers to physical activity for BC patients.

Examining biomarkers that capture biological and physical responses related to treatment and physical activity is essential to understanding how physical activity impacts BC patients. Inflammation, a critical issue in BC, is reflected in elevated levels of interleukin-6 (IL-6), a key marker of pro-inflammatory activity. Studies have shown that physical activity can reduce IL-6 levels [13], potentially alleviating inflammation-related symptoms and improving overall health. Another relevant biomarker is linoleic acid—an omega-6 polyunsaturated fatty acid (PUFA) measured in red blood cell membranes (RBCm)—which has been linked to poor neo-adjuvant chemotherapy response [14]. Physical activity has also been shown to influence fatty acid metabolism in various tissues, including skeletal muscle, myocardium, and liver [15], and has improved plasma fatty acid composition in children, helping to preserve levels of PUFAs like linoleic acid [16]. These biomarkers remain underexplored in BC patients and could offer critical insights into how physical activity supports physical health and treatment efficacy.

In addition to physical barriers, BC patients undergoing chemotherapy often experience emotional challenges that limit physical activity engagement, such as fear of injury, uncertainty about performing exercises correctly, and a lack of motivation [17]. To effectively meet these complex needs, Aurora integrates a combined human centered design and behavior change approach that has been successful in various health interventions [18, 19]. However, this approach has not been explicitly applied to BC patients, nor has its multidimensional assessment been evaluated through a randomized controlled trial protocol [20]. The Aurora protocol aims to assess its effects on overall quality of life, functional capacity, and the biomarker linoleic acid, thereby providing critical insights into how physical activity can support treatment efficacy and enhance the well-being of women undergoing neoadjuvant chemotherapy.

Explanation for choice of comparators {6b}

The study uses an active control group with minimal intervention to account for potential attention effects and to ensure that any observed differences can be attributed to the Aurora intervention rather than the mere receipt of attention or materials. This design allows for a more rigorous evaluation of the Aurora program's unique impact on physical activity and the emotional and physical effects of treatment in BC patients undergoing neoadjuvant chemotherapy.

Objectives {7}

We aim to evaluate the effects of a 9-week Aurora multidimensional therapeutic intervention program compared to standard care on emotional, physical, and biological

outcomes in women undergoing neoadjuvant chemotherapy for BC in the Metropolitan Region of Chile.

Secondary objectives include evaluating the effects of the following:

- Overall quality of life through questionnaires, log book journal and group in-depth interviews.
- Functional capacity through aerobic capacity, arm volume, and upper and lower extremity strength.
- Biological markers through lipid profile, inflammation markers, and tumor progression.

Based on the intervention design and outcomes of interest, we hypothesize that the Aurora program will significantly improve the investigated outcomes compared to standard care. Additionally, we expect the Aurora intervention to positively impact participants' engagement with physical activity during neo-adjuvant chemotherapy, as measured by physical activity levels through intensity, time, and adherence.

Trial design {8}

The Aurora trial is a randomized clinical trial employing a 1:1 allocation ratio. It is designed as a superiority trial with two parallel groups (intervention and control), controlled by active intervention, and blinded to outcome assessors and data analysts. The study will follow a mixed-methods approach, incorporating quantitative and qualitative data collection and analysis over a 9-week intervention period.

Methods: participants, interventions, and outcomes

Study setting {9}

This study will be conducted at the Cancer Center of Pontificia Universidad Católica de Chile (UC | Chile), Hospital Red Salud UC Christus, Hospital Clínico UC San Carlos de Apoquindo, and Complejo Asistencial Dr. Sótero del Rio (CASR), all located in the Metropolitan Region of Chile. Participants will be recruited from these centers' outpatient clinics. The intervention will be home-based, with participants performing the exercises in their environments. However, functional capacity assessments will be conducted under the supervision of physical therapists, and blood draws will be taken either at the participants' respective centers, where they receive care or at their homes by health professionals.

Eligibility criteria {10}

The inclusion and exclusion criteria for participants are outlined as follows:

Inclusion criteria:

1. Women under 70 years old
2. Diagnosis of primary breast carcinoma
3. Indication for neoadjuvant chemotherapy
4. Access to a safe physical space for performing physical activity
5. Connection to the Internet
6. Access to an electronic device for video conferencing

Exclusion criteria:

1. Stage IV cancer (non-curative)
2. Medical contraindications to physical activity
3. Self-report of physical activity participation equivalent to the current governmental Physical Exercise Recommendation Guide
4. Body mass index lower than 18.5 kg/m^2 or greater than 40 $kg/m.^2$

Interventions

Intervention description {11a}

All participants will be asked to attend an online education session explaining physical activity's benefits. Guidelines for physical activity and exercises will be presented, including recommendations for planning exercise sessions. Safety tips for performing physical activity will also be provided, and the Aurora protocol will be introduced.

Active control group: control kit

The control group receives a kit containing essential basic monitoring and record-keeping items. This kit includes a hydration bottle, an arm volume measurement tape, a logbook journal with blank pages, and an electronic step count wristband. All items are packaged in an Aurora-branded tote bag. Participants are instructed to use these items as they see fit and to record their activities in the blank journal. The purpose of this kit is to provide a minimal intervention that allows for some level of self-monitoring without the structured exercise program of the Aurora intervention. Participants in the control group are encouraged to maintain their usual activities and routines throughout the study period. They receive weekly reminders via phone calls or text messages to confirm the number of exercise sessions executed every week, mirroring the follow-up provided to the intervention group. This approach ensures that differences observed between the groups can be attributed to the Aurora intervention rather than merely receiving attention or materials.

Exercise intervention group: Aurora kit

The Aurora intervention kit is provided to participants in the intervention group. This kit includes a resistance band, two 2 kg dumbbells, a proprioceptive therapeutic ball, an arm volume measurement tape, a hydration bottle, a leaflet with recommended exercises, an electronic step-count wristband, and a specially designed logbook journal. All items are contained in a plastic box branded with Aurora. During the 9-week intervention period, participants receive detailed instructions on using each item and guidance on what to document in the journal.

The logbook journal features a pre-cut envelope and pre-cut sheets on the final pages, allowing participants to dedicate their experience to another patient. Participants will keep the hydration bottle and journal, and the kit will be passed on with a new bottle, journal, and dedication letter for the next patient. The journal also provides instructions on replacing physical activity equipment with household materials.

Weekly reminders are provided via phone calls or text messages to support adherence and address any concerns.

Criteria for discontinuing or modifying allocated interventions {11b}

Participants may discontinue the intervention if as follows:

- They experience any adverse effects related to the exercise program
- Their oncologist recommends discontinuation due to changes in their medical condition
- They voluntarily choose to withdraw from the study

Modifications to the allocated interventions may be made if recommended by the participant's healthcare team or if the participant reports difficulties with specific exercises.

Strategies to improve adherence to interventions {11c}

- Weekly reminders via phone calls or text messages
- Regular check-ins to address any concerns or difficulties
- Encouragement to use the logbook journal for self-monitoring
- Provision of clear, illustrated instructions for exercises
- Flexibility in exercise scheduling to accommodate treatment-related fatigue

Relevant concomitant care permitted or prohibited during the trial {11d}

Participants will continue their standard neo-adjuvant chemotherapy and other prescribed treatments as directed by their oncology team. No specific concomitant care is forbidden, but participants are asked to inform the research team of any changes in their treatment regimen or additional therapies they undertake during the study period.

Provisions for post-trial care

After the trial, participants in the control group will be offered the opportunity to receive the Aurora intervention kit for 9 weeks. All participants will receive a summary of the study findings and recommendations for continuing physical activity based on the study outcomes.

Outcomes {12}

Primary outcome:

- Quality of life as measured by the EORTC QLQ-BR23 questionnaire

Secondary outcomes:

1. Functional capacity (aerobic capacity, arm volume, upper and lower extremity strength)
2. Biological markers (lipid profile, inflammation markers, tumor progression)
3. Physical activity levels (intensity, time, and adherence)

Participant timeline

Time schedule of enrolment, intervention assessments, and visits for participants {13}

Weeks 0–4: Recruitment, informed consent, online class, baseline assessments, kit delivery.
Weeks 4–13: 9-week intervention period.
Weeks 13–16: Post-intervention assessments, kit return, blood sampling, and group in-depth interviews (Fig. 1).

Sample size {14}

Based on previous data indicating that 13% of BC patients adhere to WHO physical activity recommendations in Chile [8], with a confidence of 95% and a margin of error

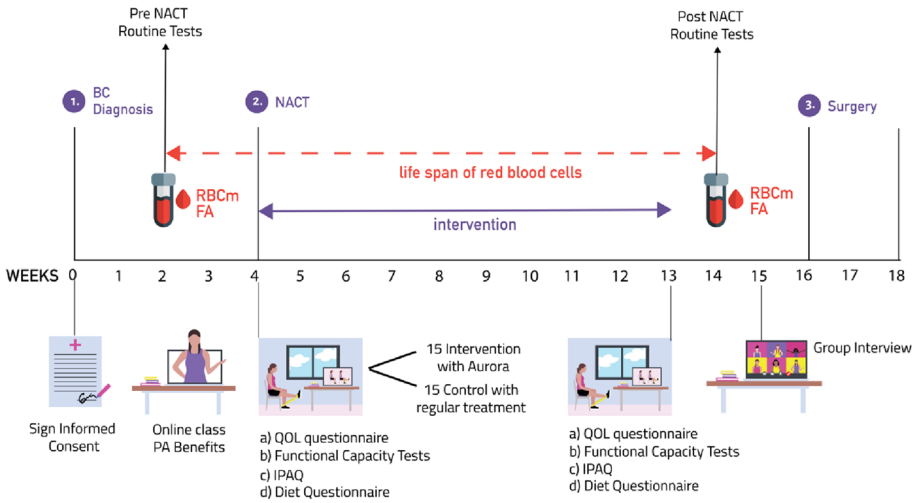

Fig. 1 Aurora participant timeline

of 5%, the study's sample size should be 12 patients in each group. Assuming a loss percentage of 20%, each group should include 15 patients. This number was considered both statistically adequate and operationally feasible within the study timeframe and resources.

Recruitment {15}

The recruitment period will begin in November 2024 and is expected to conclude by September 2025. Upon authorization from the heads of the Cancer Centers at Pontificia Universidad Católica de Chile (UC | Chile), Hospital Red Salud UC Christus, Hospital Clínico UC San Carlos de Apoquindo, and Complejo Asistencial Dr. Sótero del Rio, the principal investigator (DM) or a designated member of the research team distributes informational flyers containing a QR code in the waiting reception rooms of these centers. This QR code leads potential participants to an online survey that includes the informed consent document. The survey aims to collect both contact and health information and complete the Internation Physical Activity Questionnaire to assess eligibility based on predefined inclusion and exclusion criteria. The research team verifies enrollment and participation through WhatsApp or email to respect patient preferences. Subsequently, the research team coordinates with each participant to schedule a meeting in person or via video conference to provide detailed information about the study procedures, including potential risks and benefits, and address any questions. During this meeting, participants who agree to participate are asked to sign the informed consent form.

Methods: assignment of interventions

Allocation

Sequence generation {16a}

Given the constraints of the study in terms of time, ongoing recruitment, and availability of intervention kits, we will use minimization as the randomization strategy. This method is a form of adaptive randomization that considers each new participant's characteristics, such as age and cancer stage, which are determinant factors for physical activity adherence. Participants will be assigned to the intervention or control group in a way that best maintains balance across these prognostic factors. The minimization process will be conducted manually by a research team member who is not involved in participant recruitment or data collection. This individual will review the characteristics of the new participant and the current balance of the groups, then make an allocation decision that minimizes the imbalance between groups.

Concealment mechanism {16b}

To ensure allocation concealment, the minimization process will be conducted by a research team member who is not involved in participant recruitment or data collection. This individual will review the characteristics of each new participant and the current balance of the groups, then make an allocation decision that minimizes the imbalance between groups. The allocation decision will be communicated to the research coordinator, who will then inform the participants of their group assignment. The research team members responsible for conducting assessments and analyzing data will remain blinded to the group allocation throughout the study. To maintain the concealment, all participants will receive a kit, with the contents differing based on their

group assignment. The intervention group will receive the Aurora Experimental Kit, while the control group will receive the Aurora Control Kit. Both kits will be packaged similarly to prevent easy identification of group assignments.

Implementation {16c}

KR is the researcher responsible for the allocation sequence and assigning participants to interventions using the minimization method. DM is responsible for enrolling participants and conducting the 9-week intervention follow-up. DM is responsible for the delivery of kits and providing education to the participants.

Assignment of interventions: blinding

Who will be blinded {17a}

Due to the nature of the physical-activity intervention, participants cannot be blinded to their group assignment. However, several measures will minimize bias. Researchers responsible for collecting data from the quality of life questionnaires, functional-capacity tests, and biological samples will be blinded to participants' group allocation. The statisticians conducting the analyses will also remain unaware of group assignments. Treating oncologists and other healthcare professionals not involved in the study procedures will not be informed of participants' allocation.

All participants will receive a kit to maintain concealment, with the contents differing based on their group assignment. The intervention group will receive the Aurora Human Centered Design product system therapeutic intervention kit, while the control group will receive a kit with essential monitoring items. Both kits will be packaged similarly to prevent easy identification of group assignments. Participants will be instructed not to disclose their group assignment to the outcome assessors or healthcare providers. The research team members responsible for the weekly follow-ups and kit distribution will not be involved in outcome assessment or data analysis. These measures collectively aim to ensure the integrity of the study results by minimizing potential biases that could arise from knowledge of group assignments.

Procedure for unblinding if needed {17b}

While the study design aims to maintain blinding of outcome assessors and data analysts, there may be circumstances where unblinding becomes necessary for patient safety or ethical reasons. In such cases, the decision to unblind will be made by the principal investigator (DM) in consultation with the study's medical team. If unblinding is deemed necessary, it will be done to minimize the number of individuals who become aware of the treatment allocation. The reason for unblinding will be documented in the participant's study record and log. Only the medical personnel directly involved in the participant's care will be informed of the treatment allocation if possible. The study statistician and other team members involved in data collection and analysis will remain blinded unless necessary for data interpretation or participant safety. Any unblinding event will be reported to the Pontificia Universidad Católica de Chile Ethics Committee as part of the regular study updates. The impact of any unblinding on the study results will be discussed in the final study report and any resulting publications.

Methods: data collection and management

Data collection methods {18a}

After signing the informed consent form, each patient will be invited to participate in an online class on the benefits of physical activity and to view presentations on both the experimental and control Aurora kits. Study outcomes are assessed at two time points: baseline (weeks 0–4) and post-intervention (weeks 13–16). All randomized participants undergo outcome assessments, regardless of their adherence or completion status. After randomization, participants who withdraw from the study are still invited to complete the final evaluations, ensuring data inclusion in the intention-to-treat analysis.

Visit 1 (week 1): The Aurora kit is delivered to each participant's home.
Visit 2 (week 2): Blood sample collection.

- For patients from UC | Chile: 1 ml blood samples are collected during routine tests before and after neoadjuvant chemotherapy, coordinated with the participant's treatment schedule.
- For patients from Complejo Asistencial Dr. Sótero del Rio (CASR): A qualified phlebotomist conducts a home visit to obtain the blood sample, adhering to standard venipuncture protocols and maintaining proper sample handling procedures.

These blood samples are used to measure RBCm fatty acids, lipid profiles, and inflammation markers.

Session 1 (week 4 after neoadjuvant chemotherapy): Online synchronous session.

- Quality of life questionnaire (EORTC QLQ-BR23, completed without supervision)

- Physical activity levels questionnaire (Internation Physical Activity Questionnaire short form, completed without supervision)
- Functional capacity tests (supervised by a physical therapist):
  - Two-minute walk test
  - Elbow Flexion–Extension Test
  - 30 Seconds Sit-to-Stand Test
- Arm volume measurement (6 Measures Assessment of Arm Volume, supervised by a physical therapist)
- Dietary survey (online survey supervised by a nutritionist)

Session 2 (week 13): Online synchronous session following the same protocol as Session 1.
Visit 3: The Aurora kit is collected from each experimental participant's home. Logbook journals are scanned. Visit 4 (week 14): Post-intervention blood sample collection following the same protocol as Visit 2; Participants are instructed to avoid intense physical activity 72 h before the first evaluation session. Post-intervention evaluations occur within 72 h after the last week of the intervention. To ensure consistency, the same investigator applies each test at baseline and post-intervention time points. Outcome assessors are trained, and standardized procedures are followed for each assessment.
Session 3 (week 15): Online session for the intervention group, including a system design evaluation through in-depth interviews.

An additional qualitative assessment is conducted at the end of the intervention through thematic analysis of the Aurora logbook journal. Journals are scanned and anonymized for analysis and then returned to participants.

All data collection procedures adhere to standardized protocols to ensure consistency and reliability across all participants and time points.

Plans to promote participant retention and complete follow-up {18b}

Several strategies will be implemented to enhance participant retention and ensure complete follow-up:

Regular communication will be maintained with participants throughout the 9-week intervention period. Weekly reminders will be sent via phone calls or text messages to confirm the number of exercise sessions executed and address any concerns or questions. This consistent engagement aims to sustain motivation and provide ongoing support.
The Aurora logbook journal serves as a tool for self-monitoring and reflection, encouraging participants to track their progress and engage with the intervention. This personal investment in the process is expected to promote retention.
Regardless of their adherence or completion status, all participants will be invited to complete the final evaluations at the end of the intervention period. This approach ensures data inclusion in the intention-to-treat analysis and provides valuable insights even from those who may not have fully adhered to the protocol.
Participants in the control group will be offered the opportunity to receive the Aurora intervention for 9 weeks after the study concludes. This incentive may encourage retention and complete follow-up among control group participants.
Detailed records of any discontinuation or deviation from intervention protocols will be kept. Data from these participants will still be collected and analyzed to ensure a comprehensive and transparent analysis of study results.
The research team will maintain flexibility in scheduling follow-up assessments to accommodate participants' needs and minimize inconvenience.
At the end of the study, all participants will receive a summary of the study findings and recommendations for continuing physical activity based on the study outcomes. This gesture of appreciation and information sharing may encourage participants to complete all follow-up procedures.

Data management {19}

At the end of each assessment session, a designated researcher verifies the completeness and accuracy of collected data. Double data entry is performed for primary and secondary outcomes to minimize errors. Electronic data, including questionnaire responses and physical activity measurements from wrist pedometers, are automatically backed up.

Blood samples are labeled with unique identification codes and stored securely at the Nutrition Laboratory at Universidad de Chile.

Scanned Aurora logbook journals and anonymized interview transcripts are encrypted on the secure UC cloud server.

Original audio recordings are deleted after transcription and verification. Physical documents, such as signed consent forms, are stored in locked cabinets at the UC

research facility, the School of Design. All digital records will be password-protected and saved on a OneDrive UC cloud, with access restricted solely to the principal investigator. Data retention and sharing comply with institutional policies and applicable data protection regulations.

Statistical methods

Statistical methods for primary and secondary outcomes {20a}

We will use descriptive statistics, including mean, standard deviation, and frequency distributions, as appropriate. The Shapiro–Wilk test will be used to assess data normality. For the primary outcome (Quality of life measured by EORTC QLQ-BR23), paired *t*-tests or Wilcoxon signed-rank tests will compare within-group differences. In contrast, independent *t*-tests or Mann–Whitney *U* tests will analyze between-group differences. For secondary outcomes, repeated-measures ANOVA or mixed-effects models will analyze changes in physical activity levels over time. Chi-square tests will compare adherence rates between groups. Functional capacity tests and biological markers will be analyzed using paired and independent *t*-tests or non-parametric equivalents. Correlation coefficients will explore relationships between physical activity levels and other outcomes. Regression analysis will assess the predictive value of physical activity on dependent variables while controlling for potential confounders. Qualitative data from the Aurora logbook journal and interviews will undergo thematic analysis using the Qcamap online platform. A multiple-imputation strategy will handle missing data. Considering BC molecular subtypes, subgroup analyses will be conducted for pathological complete response and residual cancer burden results. All statistical analyses will be performed using R Studio, with significance set at $p \leq 0.05$. The statistician will be blinded to group allocation.

Measurement of the primary outcome

Quality of life

Quality of life is measured using the European Organization for Research and Treatment of Cancer (EORTC) QLQ-BR23 questionnaire, a validated instrument for assessing quality of life in Chilean BC patients [21]. The EORTC QLQ-BR23 is a 23-item questionnaire specifically tailored for BC patients. It comprises five multi-item scales that measure body image, sexual functioning, systemic therapy side effects, breast symptoms, and arm symptoms. Participants complete the online EORTC QLQ-BR23 questionnaire at two-time points: baseline (weeks 0–4) and post-intervention (weeks 13–16). The questionnaire is administered without supervision, allowing participants to complete it at their convenience within the specified timeframe. Responses are collected and stored securely in the study's database. The EORTC QLQ-BR23 is scored according to the EORTC scoring manual. Higher scores on the functional and global quality of life scales indicate better functioning and quality of life, while higher scores on the symptom scales represent higher symptomatology or problems. The change in quality of life scores from baseline to post-intervention is the primary measure of the Aurora intervention's effectiveness. Statistical analysis compares these changes between the intervention and control groups to determine the impact of the Aurora program on participants' quality of life.

Measurements of secondary outcomes

Physical activity levels

Physical activity levels will be assessed using three methods:

Physical activity intensity will be measured daily using wrist pedometers (Huawei Band 4) provided by the Oncology Physical Theraphy unit at Complejo Asistencial Dr. Sótero del Río. These devices will collect step count, active minutes, and heart rate data. Seven-day averages will be calculated for recorded steps and "active minutes" daily. Non-wear time will be identified when the device records less than 1000 daily steps, as per findings in cancer patients [22]. Participants will be provided with a replacement in case of device loss or failure. Data will be exported from the device's online platform at least once a week and organized appropriately. Missing values will be handled using a multiple-imputation statistical strategy [23].

Physical activity time will be evaluated using the International Physical Activity Questionnaire short form at baseline and the end of the intervention. The Internation Physical Activity Questionnaire is a valid and reliable instrument for assessing physical activity in various populations [24].

Physical activity adherence will be defined as compliance with exercise recommendations. The number of exercise sessions will be measured and reported weekly, and their compliance with the reported minimum of 3 weekly sessions for BC patients in Chile. The intervention group will record this information in their specially designed Aurora journal pages, while the control group will use blank pages. Weekly reminders will be sent by phone calls or text messages for participants to confirm the number of sessions executed every week.

Functional capacity

Functional capacity will be assessed through several tests conducted online under the supervision of a physical therapist:

Aerobic capacity will be assessed using a two-minute walk test [25]. This test evaluates walking capacity and is recommended for people with BC due to its good psychometric properties and ease of administration. Participants will be instructed to walk as far as they can in two minutes in a safe, open space at home. The distance covered will be estimated based on the number of laps completed in the designated area.

Arm volume will be quantified using the 6 Measures Assessment of Arm Volume [26]. This reliable method uses a tape measure to calculate the estimated arm volume and has been used in previous studies to assess arm volume in BC survivors. Participants will be guided to measure their arm circumference at six specific points, and these measurements will be used to calculate the estimated arm volume.

Upper extremity strength will be evaluated with the Elbow Flexion–Extension Test [27]. This test measures the isometric strength of the elbow flexors and extensors. Participants will be instructed to perform elbow flexions and extensions with a weight appropriate to their capacity, and the number of repetitions completed in a set time will be recorded.

Lower extremity strength will be measured with the 30 Seconds Sit-to-Stand Test [28]. This test is commonly used in geriatric and cancer rehabilitation to estimate functional fitness and lower body strength. Participants will be asked to stand up from a seated position and sit back down as many times as possible in 30 s, with the number of complete stand-sit cycles recorded. 115.

Biological markers

The biological consequences of BC and the impact of the Aurora intervention will be assessed through several markers:

- Lipid profile: LDL, HDL, and RBCm fatty acids will be measured. Blood samples (1 ml) are collected during routine tests before and after neoadjuvant chemotherapy. These samples are used to measure RBCm fatty acids, lipid profiles, and inflammation markers. The fatty acid profile of RBCm will be evaluated in phospholipids separated from total lipid extracts using thin-layer chromatography (TLC). Phospholipid spots will be removed from plates and analyzed following the method described by Ruiz-Gutiérrez et al. [29].
- Inflammation markers: C-reactive protein (CRP) and neutrophil to lymphocyte ratio will be assessed. The neutrophil and lymphocyte count ratio (NLR) will be obtained from a complete blood count at baseline before starting neo-adjuvant chemotherapy treatment and another before surgery at the end of the 9-week intervention. Data are reported in the patient's electronic medical records.
- Tumor progression: Residual cancer burden and pathological complete response will be evaluated. Residual cancer will be measured with the MD Anderson calculator following tumor removal surgery [30]. Pathological complete response is the absence of residual invasive disease in the breast tissue and axillary lymph nodes after neo-adjuvant chemotherapy [31]. A pathologist will examine tissue samples under a microscope to determine whether there are any remaining cancer cells. All biological markers will be assessed at baseline and the end of the 9-week intervention period.

Patient perceptions

Two methods will be assessed at the end of the intervention to understand Aurora's perception: a thematic analysis of the Aurora journals and a system design evaluation. The reflections recorded in the Aurora logbook journal will be transcribed, and an inductive thematic analysis of the data will be conducted following the COM-B constructs. The process will involve coding, with codes organized into themes and findings. These results will be presented and validated with participants to ensure resonance with the experiences and perceptions within the Aurora intervention. Triangulation will be implemented by integrating data from multiple sources, such as interviews, observations, relevant documents, and scientific research. This comprehensive approach ensures a robust and holistic understanding of the experiences and perceptions captured in the Aurora logbook journal.

For evaluating the design perception of Aurora, an adapted model based on the guidelines of Bush et al. for patient adherence to the use of new orthoses is proposed [32]. Four dimensions of analysis will be considered:

- Fit and function
- Style and aesthetics
- Material and manufacturing

- Emotional commitment and meaning

This evaluation will be conducted through online, in-depth, focused interview sessions with participants from the intervention group at the end of the last patient's cycle. Depending on the availability of participants, these sessions could be individual or group-based.

Methods for additional analysis {20b}

Socio-demographic and clinical characteristics

The study will collect socio-demographic data from participants' electronic clinical records, including age, education level, marital status, and employment status. Additionally, information on BC subtype and stage will be extracted from these records. A questionnaire administered before the intervention will gather information on reproductive history, menstrual characteristics, family history of BC, oral contraceptive use, hormone replacement therapy history, smoking habits, and alcohol consumption. Clinical data from medical records will include tumor histological type, tumor staging, hormone receptor status (estrogen and progesterone receptors), and HER-2 expression. This comprehensive socio-demographic and clinical data collection will allow for a more nuanced analysis of the intervention's effects across different patient subgroups and potentially identify factors that influence the intervention's effectiveness.

Methods in analysis to handle protocol non-adherence and any statistical methods to handle missing data {20c}

The study will employ an intention-to-treat analysis to handle protocol non-adherence, including all randomized participants in the analysis regardless of their adherence to the intervention. A multiple imputation approach will be used to find missing data. This method involves creating multiple plausible imputed datasets, analyzing each dataset separately, and then combining the results using Rubin's rules. Sensitivity analyses will be conducted to assess the impact of different missing data assumptions on the study results.

Methods: monitoring

Data monitoring

Composition of the coordinating center and trial steering committee {21a}

Given the low-risk nature of the intervention and the small sample size, a formal data monitoring committee is not required for this study. However, the principal investigator (DM) will oversee all aspects of the trial, maintaining regular communication with the co-investigators (KR and GN) and the research team. The principal investigator is responsible for training the team, providing ongoing support, and ensuring adherence to the study protocol.

Interim analyses {21b}

No interim analyses are planned for this study. The Aurora intervention is considered low-risk, and no anticipated issues would be detrimental to the participants or require premature interruption of the trial. The study will proceed as planned until its completion, with the final analysis conducted after all participants have completed the 9-week intervention period and the post-intervention assessments.

Adverse event reporting and harms {22}

Despite the low-risk nature of the intervention, any adverse events will be systematically collected and reported. During their weekly check-ins, participants will be instructed to report any unusual symptoms or concerns. The principal investigator will review all reported events and classify them according to severity, predictability, and potential relationship to the study procedures. Any serious adverse events will be promptly reported to the Ethics Committee of Pontificia Universidad Católica de Chile.

Frequency and plans for auditing trial conduct {23}

While formal auditing is not planned due to the study's small scale, the research team will meet monthly to review trial conduct, participant progress, and any issues that arise. These meetings will ensure adherence to the protocol and allow for the timely resolution of any concerns.

Ethics and dissemination

Research ethics approval {24}

The study received ethical approval from the Scientific and Ethics Committee of the Pontificia Universidad Católica de Chile (Approval ID #230,126,002).

Plans for communicating important protocol amendments to relevant parties {25}

Any amendments to the study protocol will be promptly communicated to the Ethics Committee of Pontificia Universidad Católica de Chile for approval. Once approved, all relevant parties, including study participants and involved healthcare providers, will be informed of the changes. The clinical trial registry will also be updated with the revised protocol.

Who will take informed consent? {26a}

During the recruitment process at the Cancer Center of Pontificia Universidad Católica de Chile (UC | Chile), Hospital Red Salud UC Christus, Hospital Clínico UC San Carlos de Apoquindo, and Complejo Asistencial Dr. Sótero del Rio, potential participants are provided with an informational flyer containing a QR code. This code leads to an online survey that includes the informed consent document. The principal investigator (DM) or a designated research team member will then contact interested participants to schedule a meeting, either in person or via video conference, to provide detailed information about the study procedures, including potential risks and benefits, and address any questions. During this meeting, participants who agree to participate will be asked to sign the informed consent form. The research team will ensure that participants comprehensively understand the study objectives and procedures before obtaining their signature on the informed consent document.

Additional consent provisions for collection and use of participant data and biological specimens {26b}

The informed consent process includes specific provisions for collecting and using participant data and biological specimens. Participants will be notified that blood samples (1 ml) will be collected at baseline and the end of the intervention as part of their routine tests before and after neoadjuvant chemotherapy. These samples will be used to measure red blood cell membrane fatty acids, lipid profile, and inflammation markers. They will be stored and analyzed at the Nutrition Laboratory at Universidad de Chile. Participants' socio-demographic information, BC subtype, and stage will be extracted from electronic clinical records. Qualitative data will be collected through interviews and the Aurora logbook journal. All data and biological specimens will be anonymized to protect participants' privacy and used solely for the purposes outlined in this study. Participants will be informed of their right to withdraw consent to use their data or biological specimens at any time. Any future use of the data or specimens for purposes beyond this study will require additional informed consent from the participants. Participants will be asked to provide explicit consent for these procedures as part of the overall informed consent process for the study.

Confidentiality {27}

All study-related information will be stored securely at the School of Design at UC. A unique code will identify participant data. Digital records will be password-protected and saved on a OneDrive UC cloud, with access restricted to the principal investigator. Physical documents will be stored in locked cabinets. Data will be retained for 5 years post-study completion. Only de-identified, aggregated data will be presented in any publications or presentations resulting from this research.

Declaration on interest {28)

All authors of this study, who are members of the research team, declare no financial or other competing interests related to the overall trial or any of the study sites.

Access to data {29}

Access to the final trial dataset will be restricted to the principal investigator (DM-B) and the co-investigator (KR). Data will be securely stored at the Centro del Cáncer UC in compliance with institutional data management policies. The data will be retained for 5 years after the completion of the study and will only be accessible to the research team for analysis. After this period, the data will be securely destroyed.

Dissemination policy

Dissemination plans {31a}

Upon completion of the study, we will implement a comprehensive dissemination plan to share our findings with a wide range of stakeholders. Each participant will receive a personalized report detailing their measurements and interpretations, presented in accessible language, along with general guidance on BC, overall health care, and physical activity recommendations. Study results will be disseminated to the general public through press releases and media outreach. Research articles will be submitted to peer-reviewed journals in the fields of oncology, physical therapy, and health design, and findings will be presented at relevant national and international scientific conferences. Results will be shared with healthcare providers through workshops and seminars at participating institutions, and a summary report will be prepared for relevant health authorities in Chile. Key findings and infographics will be shared on the study's website and social media channels, and we will collaborate with BC support groups and organizations to disseminate the results and potential benefits of the Aurora intervention. This multi-faceted approach ensures that the study's findings reach all relevant stakeholders and contribute to improving care for BC patients.

Plans to give access to the full protocol, participant-level data, and statistical code {31c}

Access to the full study protocol, participant-level data, and statistical code will be available from the corresponding author upon reasonable request.

	Enrolment	Allocation	Post-allocation		Close-out
TIMEPOINT	$-t_1$	t_0	t_1	t_{2-} t_9	t_{10}
ENROLMENT:					
Eligibility screen	X				
Informed consent	X				
Allocation		X			
INTERVENTIONS:					
Intervention Group: *Aurora Exercise Kit*			←	→	
Control: *Aurora Control Kit*			←	→	
ASSESSMENTS:					
Sociodemographic Data	X				
Anthropometric Data	X				
Clinical Data	X				
Quality of Life			X		X
Physical Activity			X	X	X
Assessment Questionnaire			X		X
Adherence			X	X	
Intensity			X		X
Functional Capacity			X	X	
Aerobic Capcity			X	X	
Arm Volume			X	X	
Upper Extremity Strength			X	X	
Lower Extremity Strength			X	X	
Biological Markers			X		X
Plasma Lipid Profile			X		X
ω-3/ω-6 fatty acids			X		X
Inflammatory markers			X		X
Tumor progression			X		X
Patient Perceptions					X
Diet Questionnaire			X		X

Fig. 2 SPIRIT figure Aurora

Discussion 506

The Aurora study aims to understand the effects of a home-based, unsupervised physical activity intervention on women undergoing neo-adjuvant chemotherapy for BC. As an unsupervised intervention, Aurora is designed to improve quality of life, physical capacity, and biological markers by providing tools and strategies tailored to these patients' physical and emotional needs. An innovative feature of Aurora is the peer dedication system, which provides through peers with an important source of social motivation and is expected to have positive effects on physical activity behavior [33, 34]. The intervention also uses behavioral prompts to help patients incorporate exercises into their routines. Many regular physical exercise programs that improve variables such as strength, endurance, and flexibility in BC patients have been reported, including activities supervised by rehabilitation professionals with expertise in oncology and physical activity sciences [35]. Aurora builds on successful elements observed in other unsupervised interventions that have demonstrated an impact on physical activity adherence, including the provision of exercise kits [36], written material [9], and a pedometer [37]. These components help patients overcome common barriers like fatigue, lack of motivation, and logistical constraints often limiting participation in traditional exercise programs [38].

Our 9-week intervention program is aligned with findings on daily ratings of the subjective automaticity of the behavior or habit strength, which show an asymptotic increase, with an initial acceleration that slows to a plateau after an average of 66 days [39]. From a clinical standpoint, studies involving 9-week physical activity intervention programs have shown significant effects on the health and quality of life of BC patients [40]. Additionally, a survey by Lally et al. revealed that a healthy habit repeated for 12 weeks can achieve a 95% level of automatization in individuals. However, the time required to reach automatization varies between 18 and 254 days [41]. The Aurora protocol combines aerobic and resistance training, which has proven effective in enhancing quality of life for BC survivors [42]. Specifically, aligning with findings on the positive impact of physical activity in various domains of quality of life, including physical function, emotional well-being, and daily life activities in a safe and hygienic home environment [43].

Functional capacity has been extensively studied worldwide, demonstrating how beneficial physical activity can be for BC patients [44–47], with an emphasis on how the physical activity programs may need to be adjusted for individual survivors based on their health status, treatments received, and expected disease progression [48, 49]. Also, interventions tailored explicitly to BC survivors show a more sustained impact on physical activity behavior [50, 51]. The Aurora program includes these considerations by offering personalized recommendations documented in the Aurora logbook journal, which assists patients in regulating their weekly physical activity program. This approach aims to achieve high adherence to exercise training with a flexible exercise prescription while maintaining alignment with established guidelines [52].

While numerous studies have demonstrated the benefits of physical activity on BC outcomes, the underlying biological mechanisms remain poorly understood, especially in the context of unsupervised, home-based interventions and its comprehensive evaluation on modulating immune and inflammatory mediators and affection on tumorigenic potential at the cellular level [53, 54]. The Aurora protocol presents a novel approach by examining RBCm fatty acid profiles, potentially guiding future personalized interventions and rehabilitation strategies [55]. Given that changes in fatty acid levels, including PUFAs, may be associated with the response to neo-adjuvant chemotherapy in non-metastatic patients [14]. RBCm levels can offer a more sensitive measure of long-term PUFA status than plasma levels [56].

Our mixed-methods approach, combining quantitative assessments of physical and biological outcomes with qualitative analysis of patient experiences, will provide a more comprehensive understanding of the intervention's impact [57]. Contributing with the growing emphasis on patient-centered care and the need to incorporate patients' perspectives in healthcare delivery and research, ensuring that research outcomes are relevant and meaningful to those receiving care [58].

Although previous studies have assessed some health-related outcomes following physical activity interventions in BC patients, more research is needed to fully elucidate the biological pathways involved in these benefits [59]. The Aurora protocol aims to address this gap by evaluating the impact of a home-based, patient-centered intervention on multiple dimensions of health, including physical capacity, quality of life, and biological markers. As the evidence is, Chile has only recently started to grow through the leading work of Ramírez et al. [8, 35]. Contributing to this area is essential to guide public policies by recognizing physical activity's clinical impact on patients.

One limitation of this study is its relatively small sample size, which may impact the statistical power and generalizability of the findings. The limited scope reflects the financial constraints of conducting research as part of a PhD thesis. Nonetheless, this study provides valuable preliminary evidence that can inform a larger-scale trial,

ultimately aiding in developing a more accessible intervention for BC patients across Chile and Latin America.

Another limitation is the study's confinement to the Metropolitan Region of Chile and a single healthcare system, which may restrict the generalizability to other healthcare contexts. However, the focus on the Chilean public healthcare system offers insights into implementing a patient-centered intervention like Aurora within resource-constrained environments. It highlights its potential to address the high burden of BC (Fig. 2).

Appendix

Informed Consent

LogBook Journal

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Authors' contributions
DM-B and KR conceived the study idea. DM-B took the lead in writing the manuscript. KR and VM contributed to the study methodology. All authors read and approved the final version of the manuscript.

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Data availability
The data will be available from the corresponding author upon reasonable request.

Declarations

Consent for publication
Not applicable. No identifying images or other personal or clinical details of participants are presented here or will be included in reports of the trial results. The participant information materials and informed consent form are available from the corresponding author upon request.

Competing interests
The authors declare that they have no competing interests.

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References

1. Kashyap D, Pal D, Sharma R, Garg VK, Goel N, Koundal D, et al. Global increase in breast cancer incidence: risk factors and preventive measures. BioMed Res Int. 2022;2022:9605439. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9038417/. Cited 2023 November 29.
2. Ormeño IA. Patología GES: Cáncer de mama y mamografías en Chile. Biblioteca del Congreso Nacional de Chile.
3. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, et al. Global Cancer Statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2021;71(3):209–49. Available from: https://onlinelibrary.wiley.com/doi/10.3322/caac.21660. Cited 2022 Nov 14.
4. Berger AM, Mitchell SA, Jacobsen PB, Pirl WF. Screening, evaluation, and management of cancer-related fatigue: ready for implementation to practice? CA Cancer J Clin. 2015;65(3):190–211.
5. Binotto M, Reinert T, Werutsky G, Zaffaroni F, Schwartsmann G. Health-related quality of life before and during chemotherapy in patients with early-stage breast cancer. 2020. Available from: http://ecancer.org/en/journal/article/1007-health-related-quality-of-life-before-and-during-chemotherapy-in-patients-with-early-stage-breast-cancer. Cited 2024 November 3.
6. Phillips SM, McAuley E. Physical activity and quality of life in breast cancer survivors: the role of self-efficacy and health status. Psychooncology. 2014;23(1):27–34. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4762278/. Cited 2024 Jan 16.
7. Kang H, Moon M. Effects of digital physical activity interventions for breast cancer patients and survivors: a systematic review and meta-analysis. Healthc Inform Res. 2023;29(4):352–66. Available from: http://e-hir.org/journal/view.php?doi=10.4258/hir.2023.29.4.352. Cited 2023 Dec 4.
8. Ramírez-Parada K, Courneya KS, Muñiz S, Sánchez C, Fernández-Verdejo R. Physical activity levels and preferences of patients with breast cancer receiving chemotherapy in Chile. Support Care Cancer. 2019;27(8):2941–7. Available from: https://doi.org/10.1007/s00520-018-4595-1. Cited 2023 Dec 21.
9. Rogers LQ, Courneya KS, Anton PM, Hopkins-Price P, Verhulst S, Vicari SK, et al. Effects of the BEAT Cancer physical activity behavior change intervention on physical activity, aerobic fitness, and quality of life in breast cancer survivors: a multicenter randomized controlled trial. Breast Cancer Res Treat. 2015;149(1):109–19.
10. Mella-Abarca W, Barraza-Sánchez V, Ramírez-Parada K. Telerehabilitation for people with breast cancer through the COVID-19 pandemic in Chile. ecancermedicalscience. 2020;14:1085. Available from: https://pmc.ncbi.nlm.nih.gov/articles/PMC7434512/. Cited 2024 November 3.
11. Ministerio de Salud De Chile. Listado de prestaciones especificas: Régimen de Garantías Explícitas en Salud. Ministerio de Salud de Chile. División de Prevención y Control de Enfermedades. 2016. Available from: https://diprece.minsal.cl/wrdprss_minsal/wp-content/uploads/2016/07/LEP_2016_RECTIFICATORIO.pdf. Cited 2024 Nov 3.
12. Análisis de tendencia de Mortalidad y Mortalidad Prematura-Años de vida Potencialmente Perdidos (AVPP) por Cáncer, 2000–2019. Ministerio de Salud de Chile. Departamento de Epidemiología.; 2023.
13. Jones SB, Thomas GA, Hesselsweet SD, Alvarez-Reeves M, Yu H, Irwin ML. Effect of exercise on markers of inflammation in breast cancer survivors: the yale exercise and survivorship study. Cancer Prev Res (Phila Pa). 2013;6(2):109–18. Available from: https://aacrjournals.org/cancerpreventionresearch/article/6/2/109/50067/Effect-of-Exercise-on-Markers-of-Inflammation-in. Cited 2023 Dec 19.
14. Valenzuela R. High linoleic acid levels in red blood cells predict a poor response to neoadjuvant chemotherapy in HER2-positive breast cancer patients (Paper under revision).
15. Hannukainen JC, Nuutila P, Ronald B, Kaprio J, Kujala UM, Janatuinen T, et al. Increased physical activity decreases hepatic free fatty acid uptake: a study in human monozygotic twins. J Physiol. 2007;578(Pt 1):347–58. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2075122/. Cited 2023 Dec 12.
16. Venäläinen TM, Viitasalo AM, Schwab US, Eloranta AM, Haapala EA, Jalkanen HP, et al. Effect of a 2-y dietary and physical activity intervention on plasma fatty acid composition and estimated desaturase and elongase activities in children: the Physical Activity and Nutrition in Children Study. Am J Clin Nutr. 2016;104(4):964–72. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0002916522046202. Cited 2023 Dec 12.
17. Physical exercise in Chilean breast cancer survivors: qualitative study of barriers, facilitators and preferences. 2024. Available from: https://www.medwave.cl/investigacion/estcualit/2963.html. Cited 2024 November 5.
18. Fuster M, Hipol S, Huang TT, Colón-Ramos U, Conaboy C, Abreu R, et al. Bridging implementation science and human-centered design:

developing tailored interventions for healthier eating in restaurants. Glob Implement Res Appl. 2024. Available from: https://doi.org/10.1007/s43477-024-00133-7. Cited 2024 October 24.
19. Voorheis P, Zhao A, Kuluski K, Pham Q, Scott T, Sztur P, et al. Integrating behavioral science and design thinking to develop mobile health interventions: systematic scoping review. JMIR MHealth UHealth. 2022;10(3):e35799. Available from: https://pmc.ncbi.nlm.nih.gov/articles/PMC8968622/. Cited 2024 November 5.
20. Bluethmann SM, Bartholomew LK, Murphy CC, Vernon SW. Use of theory in behavior change interventions: an analysis of programs to increase physical activity in posttreatment breast cancer survivors. Health Educ Behav Off Publ Soc Public Health Educ. 2016;44(2):245. Available from: https://pmc.ncbi.nlm.nih.gov/articles/PMC5503486/. Cited 2024 November 5.
21. Irarrázaval ME, Rodríguez PF, Fasce G, Silva FW, Waintrub H, Torres C, et al. Calidad de vida en cáncer de mama: validación del cuestionario BR23 en Chile. Rev Médica Chile. 2013;141(6):723–34. Available from: http://www.scielo.cl/scielo.php?script=sci_abstract&pid=S0034-98872013000600006&lng=es&nrm=iso&tlng=es. Cited 2024 Oct 25.
22. Hardcastle SJ, Jiménez-Castuera R, Maxwell-Smith C, Bulsara MK, Hince D. Fitbit wear-time and patterns of activity in cancer survivors throughout a physical activity intervention and follow-up: exploratory analysis from a randomised controlled trial. PLoS ONE. 2020;15(10):e0240967. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7571692/. Cited 2024 January 13.
23. Jakobsen JC, Gluud C, Wetterslev J, Winkel P. When and how should multiple imputation be used for handling missing data in randomised clinical trials–a practical guide with flowcharts. BMC Med Res Methodol. 2017;17(1):162. Available from: https://doi.org/10.1186/s12874-017-0442-1. Cited 2024 January 13.
24. Craig CL, Marshall AL, Sj??Str??M M, Bauman AE, Booth ML, Ainsworth BE, et al. International Physical Activity Questionnaire: 12-country reliability and validity: Med Sci Sports Exerc. 2003;35(8):1381–95. Available from: http://journals.lww.com/00005768-200308000-00020. Cited 2024 Jan 13.
25. Reinmann A, Koessler T, Bodmer A, Baud-Grasset A, Mentha G, Gligorov J, et al. Feasibility, criterion and construct convergent validity of the 2-minute walk test and the 10-meter walk test in an oncological context. Heliyon. 2023;9(11):e22180. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10692807/. Cited 2024 January 13.
26. Mastick J, Smoot BJ, Paul SM, Kober KM, Cooper BA, Madden LK, et al. Assessment of arm volume using a tape measure versus a 3D optical scanner in survivors with breast cancer-related lymphedema. Lymphat Res Biol. 2022;20(1):39–47. Available from: https://www.liebertpub.com/doi/10.1089/lrb.2020.0119. Cited 2023 Dec 22.
27. Kotte SHP, Viveen J, Koenraadt KLM, The B, Eygendaal D. Normative values of isometric elbow strength in healthy adults: a systematic review. Shoulder Elb. 2018;10(3):207–15. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5960876/. Cited 2024 Jan 12.
28. Díaz-Balboa E, González-Salvado V, Rodríguez-Romero B, Martínez-Monzonís A, Pedreira-Pérez M, Cuesta-Vargas AI, et al. Thirty-second sit-to-stand test as an alternative for estimating peak oxygen uptake and 6-min walking distance in women with breast cancer: a cross-sectional study. Support Care Cancer. 2022;30(10):8251–60. Available from: https://link.springer.com/10.1007/s00520-022-07268-z. Cited 2023 Dec 22.
29. Ruiz-Gutierrez V, Cert A, Rios JJ. Determination of phospholipid fatty acid and triacylglycerol composition of rat caecal mucosa. J Chromatogr. 1992;575(1):1–6.
30. MD Anderson Cancer Center. Residual cancer burden calculator. Available from: https://www3.mdanderson.org/app/medcalc/index.cfm?pagename=jsconvert3. Cited 2024 January 1.
31. Waljee JF, Newman LA. Neoadjuvant systemic therapy and the surgical management of breast cancer. Surg Clin North Am. 2007;87(2):399–415, ix.
32. Bush P, ten Hompel S. An integrated craft and design approach for wearable orthoses. Des Health. 2017;1(1):86–104. Available from: https://www.tandfonline.com/doi/full/10.1080/24735132.2017.1299439. Cited 2022 Nov 5.
33. Blosser JL, DePompei R. Preparing education professionals for meeting the needs of students with traumatic brain injury. J Head Trauma Rehabil. 1991;6(1):73. Available from: https://journals.lww.com/headtraumarehab/abstract/1991/03000/preparing_education_professionals_for_meeting_the.12.aspx. Cited 2024 Nov 26.
34. Ginis KAM, Nigg CR, Smith AL. Peer-delivered physical activity interventions: an overlooked opportunity for physical activity promotion. Transl Behav Med. 2013;3(4):434. Available from: https://pmc.ncbi.nlm.nih.gov/articles/PMC3830020/. Cited 2024 November 3.
35. Ramírez K, Acevedo F, Herrera ME, Ibáñez C, Sánchez C. Actividad física y cáncer de mama: un tratamiento dirigido. Rev Médica Chile. 2017;145(1):75–84. Available from: http://www.scielo.cl/scielo.php?script=sci_arttext&pid=S0034-98872017000100011&lng=en&nrm=iso&tlng=en. Cited 2022 Apr 8.
36. Mustian KM, Peppone L, Darling TV, Palesh O, Heckler CE, Morrow GR. A 4-week home-based aerobic and resistance exercise program during radiation therapy: a pilot randomized clinical trial. J Support Oncol. 2009;7(5):158–67.
37. Goldschmidt S, Schmidt ME, Steindorf K. Long-term effects of exercise interventions on physical activity in breast cancer patients: a systematic review and meta-analysis of randomized controlled trials. Support Care Cancer. 2023;31(2). Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9873715/. Cited 2024 January 17.
38. Brennan L, Sheill G, O'Neill L, O'Connor L, Smyth E, Guinan E. Physical therapists in oncology settings: experiences in delivering cancer rehabilitation services, barriers to care, and service development needs. Phys Ther. 2022;102(3):pzab287. Available from: https://academic.oup.com/ptj/article/doi/10.1093/ptj/pzab287/6515750. Cited 2023 December 18.
39. Lally P, Van Jaarsveld CHM, Potts HWW, Wardle J. How are habits formed: modelling habit formation in the real world. Eur J Soc Psychol. 2010;40(6):998–1009. Available from: https://onlinelibrary.wiley.com/doi/10.1002/ejsp.674. Cited 2023 Dec 27.
40. Campbell KL, Winters-Stone KM, Wiskemann J, May AM, Schwartz AL, Courneya KS, et al. Exercise guidelines for cancer survivors: consensus statement from international multidisciplinary roundtable. Med Sci Sports Exerc. 2019;51(11):2375–90. Available from: https://journals.lww.com/10.1249/MSS.0000000000002116. Cited 2023 Jan 30.
41. Lally P, van Jaarsveld CHM, Potts HWW, Wardle J. How are habits formed: modelling habit formation in the real world. Eur J Soc Psychol. 2010;40(6):998–1009. Available from: https://onlinelibrary.wiley.com/doi/10.1002/ejsp.674. Cited 2022 Nov 5.
42. Agussalim NQ, Ahmad M, Prihantono P, Usman AN, Rafiah S, Agustin DI. Physical activity and quality of life in breast cancer survivors. Breast Dis. 2024;43(1):161. Available from: https://pmc.ncbi.nlm.nih.gov/articles/PMC11191433/. Cited 2024 November 26.
43. Chen L, Peng P, Xu Z, Ding X. The effects of exercise on the quality of life of patients with breast cancer: a systematic review and meta-analysis based on the QLQ-C30 quality of life scale. Gland Surg. 2023;12(5):63350–650. Available from: https://gs.amegroups.org/article/view/114103. Cited 2024 Nov 26.
44. Stalsberg R, Bertheussen GF, Børset H, Thomsen SN, Husøy A, Flote VG, et al. Do breast cancer patients manage to participate in an outdoor, tailored, physical activity program during adjuvant breast cancer treatment, independent of health and socio-demographic characteristics? J Clin Med. 2022;11(3):843. Available from: https://www.mdpi.com/2077-0383/11/3/843. Cited 2022 November 6.
45. Campbell KL, Winters-Stone KM, Wiskemann J, May AM, Schwartz AL, Courneya KS, et al. Exercise guidelines for cancer survivors: consensus statement from international multidisciplinary roundtable. Med Sci Sports Exerc. 2019;51(11):2375–90.
46. Irwin ML, Smith AW, McTiernan A, Ballard-Barbash R, Cronin K, Gilliland FD, et al. Influence of pre- and postdiagnosis physical activity on mortality in breast cancer survivors: the health, eating, activity, and lifestyle study. J Clin Oncol. 2008;26(24):3958–64. Available from: https://ascopubs.org/doi/10.1200/JCO.2007.15.9822. Cited 2023 Dec 2.
47. Kim S, Ko YH, Song Y, Kang MJ, Lee H, Kim SH, et al. Development of an exercise adherence program for breast cancer survivors with cancer-related fatigue—an intervention mapping approach. Support Care Cancer. 2019;27(12):4745–52. Available from: http://link.springer.com/10.1007/s00520-019-04785-2. Cited 2022 Sep 29.
48. Marco Continente C, Luesma Bartolomé MJ, Santander Ballestín S. Influencia de la actividad física en la prevención, tratamiento antineoplásico y supervivencia de pacientes con cáncer de mama. Rev Senol Patol Mamar.

2021;34(4):220–35. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0214158220300748. Cited 2023 Dec 2.
49. Bourke L, Homer KE, Thaha MA, Steed L, Rosario DJ, Robb KA, et al. Interventions for promoting habitual exercise in people living with and beyond cancer. Cochrane Gynaecological, Neuro-oncology and Orphan Cancer Group, editor. Cochrane Database Syst Rev. 2013. Available from: https://doi.wiley.com/10.1002/14651858.CD010192.pub2. Cited 2023 December 4.
50. Bravo P, Dois A, Villarroel L, González-Agüero M, Fernández-González L, Sánchez C, et al. Factors influencing the implementation of shared decision-making in breast cancer care: protocol for a mixed-methods study. BMJ Open. 2023;13(7):e074111. Available from: https://bmjopen.bmj.com/lookup/doi/10.1136/bmjopen-2023-074111. Cited 2023 August 27.
51. Schmitz KH. Balancing lymphedema risk: exercise versus deconditioning for breast cancer survivors. Exerc Sport Sci Rev. 2010;38(1):17–24. Available from: https://journals.lww.com/00003677-201001000-00005. Cited 2022 Nov 29.
52. Kirkham AA, Bonsignore A, Bland KA, Mckenzie DC, Gelmon KA, Van Patten CL, et al. Exercise prescription and adherence for breast cancer: one size does not FITT all. Med Sci Sports Exerc. 2018;50(2):177. Available from: https://journals.lww.com/acsm-msse/fulltext/2018/02000/exercise_prescription_and_adherence_for_breast.1.aspx. Cited 2024 November 26.
53. Baldelli G, Natalucci V, Ferri Marini C, Sisti D, Annibalini G, Saltarelli R, et al. A home-based lifestyle intervention program reduces the tumorigenic potential of triple-negative breast cancer cells. Sci Rep. 2024;14(1):2409. Available from: https://www.nature.com/articles/s41598-024-52065-9. Cited 2024 November 26.
54. Xu Y, Rogers CJ. Physical activity and breast cancer prevention: possible role of immune mediators. Front Nutr. 2020;7. Available from: https://www.frontiersin.org/journals/nutrition/articles/10.3389/fnut.2020.557997/full. Cited 2024 November 26.
55. Invernizzi M, Lippi L, Folli A, Turco A, Zattoni L, Maconi A, et al. Integrating molecular biomarkers in breast cancer rehabilitation. What is the current evidence? A systematic review of randomized controlled trials. Front Mol Biosci. 2022;9. Available from: https://www.frontiersin.org/journals/molecular-biosciences/articles/10.3389/fmolb.2022.930361/full. Cited 2024 November 26.
56. Liu H, Wang F, Liu X, Xie Y, Xia H, Wang S, et al. Effects of marine-derived and plant-derived omega-3 polyunsaturated fatty acids on erythrocyte fatty acid composition in type 2 diabetic patients. Lipids Health Dis. 2022;21(1):20. Available from: https://doi.org/10.1186/s12944-022-01630-0. Cited 2024 Jan 18.
57. Regnault A, Willgoss T, Barbic S, On behalf of the International Society for Quality of Life Research (ISOQOL) Mixed Methods Special Interest Group (SIG). Towards the use of mixed methods inquiry as best practice in health outcomes research. J Patient-Rep Outcomes. 2018;2(1):19. Available from: https://doi.org/10.1186/s41687-018-0043-8. Cited 2024 Nov 26.
58. Edgman-Levitan S, Schoenbaum SC. Patient-centered care: achieving higher quality by designing care through the patient's eyes. Isr J Health Policy Res. 2021;10:21. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7934513/. Cited 2024 July 21.
59. García-Chico C, López-Ortiz S, Peñín-Grandes S, Pinto-Fraga J, Valenzuela PL, Emanuele E, et al. Physical exercise and the hallmarks of breast cancer: a narrative review. Cancers. 2023;15(1):324. Available from: https://pmc.ncbi.nlm.nih.gov/articles/PMC9818971/. Cited 2024 November 26.

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