

# Effectiveness of aerobic training on adverse symptoms related to chemotherapy during treatment: protocol of a randomized controlled trial with cost-effectiveness assessment.

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### Table of Contents

Original Manuscript	5
Supplementary Files	
S-PP	
Existing Peer-Review Reports from Funding Agencies (for protocols/proposals only)s	29
Existing Peer-Review Reports from Funding Agencies (for protocols/proposals only) 0	
Existing Peer-Review Reports from Funding Agencies (for protocols/proposals only) 0	
Existing Peer-Review Reports from Funding Agencies (for protocols/proposals only) 0	29
Existing Peer-Review Reports from Funding Agencies (for protocols/proposals only) 0	

Effectiveness of aerobic training on adverse symptoms related to chemotherapy during treatment: protocol of a randomized controlled trial with cost-effectiveness assessment.

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#### Abstract

**Background:** One of the strategies to prevent adverse effects resulting from chemotherapy treatment is to perform physical exercises during treatment. However, there is still no consensus on the best type and intensity of exercise, nor when it should be started. Most studies have been carried out in breast cancer patients, usually a few weeks after starting chemotherapy, on an outpatient basis, two to three times a week. The main differences of our study are: carrying out physical training in hospitalized patients to undergo a cycle of chemotherapy for cancer treatment, this training being carried out five times a week and not being restricted to a specific type of cancer.

**Objective:** To evaluate the effects of aerobic training on symptoms related to chemotherapy (nausea, vomiting, asthenia and sensation of weakness), fatigue, mobility, clinical complications and length of hospital stay of patients during the drug treatment cycle. The adverse effects of training aerobics and patient satisfaction with the proposed intervention. In addition to also evaluating the cost-effectiveness of this intervention.

**Methods:** This is a controlled and randomized trial with blinded evaluation that will include 94 hospitalized cancer patients for one or more cycles of chemotherapy. The intervention group will perform aerobic training during a cycle of chemotherapy. The control group will receive a booklet with guidelines for staying active during the hospitalization period. The groups will be compared using the Linear Mixed Model, regarding fatigue, mobility and chemotherapy-related symptoms before and after the intervention. The length of hospital stay will also be compared between groups using Kaplan-Meier survival analysis. The incidence of complications will be compared using the chi-square test. Cost-effectiveness and cost-utility analyzes will be performed for the impact of exercise and quality-adjusted life years (QALYs) through the EQ-5D3L21 quality of life trials. The implementation variables (acceptability, suitability and feasibility) will be evaluated by frequencies.

**Results:** In March 2023, the clinical trial registration was approved. Recruitment and data collection for the trial is ongoing, and the results of this study are likely to be published in late 2025.

**Conclusions:** Impact: Chemotherapy has side effects that negatively impact the quality of life of cancer patients. Aerobic exercise can reduce those side effects in a simple and inexpensive way. Oncology could be an expanded field of work for physical therapists if the intervention works Clinical Trial: RBR-6b4zwx3.

Acess: https://ensaiosclinicos.gov.br/rg/RBR-6b4zwx3

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# **Original Manuscript**

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**ABSTRACT** 

**Background:** One of the strategies to prevent adverse effects resulting from chemotherapy treatment

is to perform physical exercises during treatment. However, there is still no consensus on the best

type and intensity of exercise, nor when it should be started. Most studies have been carried out in

breast cancer patients, usually a few weeks after starting chemotherapy, on an outpatient basis, two

to three times a week. The main differences of our study are: carrying out physical training in

hospitalized patients to undergo a cycle of chemotherapy for cancer treatment, this training being

carried out five times a week and not being restricted to a specific type of cancer.

**Objectives:** To evaluate the effects of aerobic training on symptoms related to chemotherapy

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length of hospital stay of patients during the drug treatment cycle. The adverse effects of training

aerobics and patient satisfaction with the proposed intervention. In addition to also evaluating the

cost-effectiveness of this intervention. Methods: This is a controlled and randomized trial with

blinded evaluation that will include 94 hospitalized cancer patients for one or more cycles of

chemotherapy. The intervention group will perform aerobic training during a cycle of chemotherapy.

The control group will receive a booklet with guidelines for staying active during the hospitalization

period. The groups will be compared using the Linear Mixed Model, regarding fatigue, mobility and

chemotherapy-related symptoms before and after the intervention. The length of hospital stay will

also be compared between groups using Kaplan-Meier survival analysis. The incidence of

complications will be compared using the chi-square test. Cost-effectiveness and cost-utility analyzes

will be performed for the impact of exercise and quality-adjusted life years [QALYs] through the

EQ-5D3L21 quality of life trials. The implementation variables [acceptability, suitability and

feasibility] will be evaluated by frequencies.

**Results:** In March 2023, the clinical trial registration was approved. Recruitment and data collection

for the trial is ongoing, and the results of this study are likely to be published in late 2025.

**Conclusion:** Chemotherapy has side effects that negatively impact the quality of life of cancer

patients. Aerobic exercise can reduce those side effects in a simple and inexpensive way. Oncology

could be an expanded field of work for physical therapists if the intervention works.

Registred on the website Registro Brasileiro de Ensaios Clínicos (REBEC) (RBR-6b4zwx3).

**Key-words:** cancer; exercise; chemotherapy; economic evaluation.

Introduction

Cancer is already the biggest public health problem in the world. In Brazil, the estimate for the 2023-

2025 period is 704 thousand new cases of cancer per year (excluding cases of non-melanoma skin

cancer) [1]. One of the main forms of treatment for cancer is chemotherapy, which consists of a

systemic treatment, where the drug used aims to interfere with cell proliferation, targeting its DNA

or RNA and its metabolism [2]. The costs of cancer treatment in the United States already reach

US\$158 billion per year [3] and exceed R\$3.5 billion in Brazil [4]. The application of these resources

includes healthcare staff, medications used directly and indirectly in treatment, equipment and

hospitalization days.

Treatment with chemotherapy involves a series of side effects, including nausea, vomiting, diarrhea and febrile neutropenia, which are treated with supplementary medications to treat the disease, and such adverse effects have a major impact on patients' lives, as well as on adherence and compliance with the recommended dose of treatment and are also associated with an increase in the rate of hospitalization. At least one third of women undergoing adjuvant chemotherapy treatment for breast cancer are unable to complete the prescribed dose of treatment due to adverse effects, thus compromising the prognosis of the disease [5].

Physical exercise in cancer patients during chemotherapy has been tested in randomized trials [5-11] and appears to improve physical function, fatigue, symptom burden and quality of life of patients, in addition to inducing the non-reduction of chemotherapy doses. However, most studies are carried out on an outpatient basis, involve patients with breast cancer, with three weekly exercise sessions and evaluate fatigue as the primary outcome. There are still no clinical trials testing the effect of exercise in a hospital environment, in daily sessions (Monday to Friday), carried out during the chemotherapy cycle.

Therefore, our objective is to evaluate the effects of aerobic training on chemotherapy-related symptoms (nausea, vomiting, asthenia and sensation of weakness), fatigue, mobility, clinical complications and length of hospital stay in patients during the drug treatment cycle. Furthermore, also evaluate the adverse effects of aerobic training and patient satisfaction with the proposed intervention, implementation and the cost-effectiveness of this intervention.

Our hypothesis is that aerobic training will decrease chemotherapy-related symptoms, fatigue, clinical complications, and length of hospital stay, in addition to not increasing mobility. In addition, Furthermore, the proposed intervention will be cost-effective from the point of view of the patient and society due to the preservation of quality of life and lower health costs related to the treatment of

chemotherapy adverse effects.

#### **Methods**

This is the protocol for a randomized controlled trial with 2 parallel groups, 1:1 allocation and blind evaluation, which will be conducted in the Oncology Ward of the Instituto de Assistência Médica ao Servidor State Public, São Paulo-SP, Brazil, which will be conducted in the Oncology Ward of Hospital, conducted in accordance with the CONSORT Checklist (Consolidated Standards of Reporting Trials) [12] and registred on the website Registro Brasileiro de Ensaios Clínicos (REBEC) (RBR-6b4zwx3).

This study's protocol was approved by the Research Ethics Committees of the Universidade Cidade de São Paulo and Instituto de Assistência Médica ao Servidor (CAAE: 50436221.7.3001.5463). All participants will provide written informed consent before participating in this study. This will be collected and stored securely by one of the clinical data collection team members.

Patients over 18 years old diagnosed with cancer and hospitalized in the ward to undergo at least one cycle of chemotherapy will be eligible for this study. Patients without musculoskeletal, cognitive or clinical limitations that interfere with the proposed assessments and interventions will be included in the study, such as: heart disease (moderate to severe aortic or pulmonary stenosis, decompensated heart failure, advanced cardiac arrhythmias, myocarditis, unstable coronary insufficiency, for example), lung diseases (chronic obstructive pulmonary disease and/or decompensated asthma, for example), diabetes mellitus and decompensated systemic arterial hypertension and serum hemoglobin (Hb) < 8g/dL or hematocrit (Ht) < 25% or platelets < 30,000 mm [5, 13-15].

Patients who require transfer to the intensive care unit, or for any reason have chemotherapy treatment contraindicated or discontinued, will be excluded from the study.

During the protocol, all patient admitted to the Oncology Ward who is identified during the study period and meets the eligibility criteria will be invited to participate in the study by the

physiotherapist evaluating the study. This eligible patient will be informed about the objectives of the study and invited to sign the informed consent form. Next, the patient will be evaluated regarding anthropometric and clinical characteristics, fatigue, mobility and the occurrence, frequency, intensity and discomfort of the main adverse effects of chemotherapy. After the initial assessment, patients will be randomized into an intervention group, which will perform aerobic exercise sessions, and a control group, which will receive a booklet with guidelines (the same booklet will be given to patients in the intervention group). The next day, the intervention will begin. Aerobic training will be carried out from Monday to Friday, while the patient is hospitalized for the chemotherapy cycle in the Oncology Ward. Before carrying out the day's aerobic exercise session, the patient will be asked if they felt any type of discomfort that is related to the previous day's training (for example, muscle or joint pain in the lower limbs). If for any reason the patient has chemotherapy interrupted, the exercises will also be interrupted, and as soon as chemotherapy treatment is resumed, the exercise will also be resumed. The booklet will be given to the patient and explained by a trained physiotherapist. Patients will be re-evaluated on the day following the last day of the chemotherapy cycle regarding the occurrence, frequency, intensity and discomfort of adverse effects of treatment, fatigue, mobility and satisfaction with the proposed intervention.

After the study intervention period, patients who need it will receive routine physiotherapeutic care provided by the Physiotherapy team at the hospital. The incidence of clinical complications from chemotherapy and length of hospital stay will be outcomes evaluated until hospital discharge. All data will be collected by a blinded assessor. Additionally, data will be coded and entered into an Excel spreadsheet and will be double-checked before analysis. The visual representation of the study design is presented in Figure 1.

Immediately after baseline assessments and before starting the intervention, patients will be randomly allocated to one of two groups: intervention or control. The allocation will be conducted by a researcher who will not be involved in the selection, evaluation or intervention of patients and will

follow a randomization schedule generated by the website http://www.sealedenvelope.com, with a 1:1 allocation rate. The rooms in the ward accommodate 2 to 4 patients (beds), therefore, randomization will be carried out by group or cluster [16]. The rooms will be randomized, because, although the intervention is directed to one patient, it can affect another patient in the same room, contaminating those who should not receive the intervention, and reducing the estimated result [16]. The researcher responsible for randomization will place a written document inside a sealed opaque envelope which group (intervention or control) each room belongs to to ensure the confidential allocation of patients to the blinded evaluator [17]. Before starting the intervention, the physiotherapist responsible for the intervention will open the envelope in front of the patient and disclose which group the room in which the patient is admitted to corresponds to.

Due to the nature of the study, it will not be possible to blind the physiotherapist responsible for the intervention or the patients. However, the evaluator will be blinded to the groups (intervention and control). After the intervention and assessments, the physiotherapist responsible for the intervention will ask the blinded evaluator to which group (intervention or control) he believes each patient belonged to evaluate the evaluator's blinding.

First of all, a standardized printed form will be used which will include: personal data (name, age, sex, place of birth, contact telephone number, education, monthly family income, marital status, occupation) and anthropometric data (height and weight measured as recommended by the National Institute of Health, Heart, Lung and Blood) [18]; diagnosis of current illness; pre-existing illnesses; current or past smoking history; history of alcohol consumption and medications used; previous chemotherapy or radiotherapy; whether the current chemotherapy is neoadjuvant, adjuvant, treatment of choice or palliative and whether the patient is or was a practitioner of physical activity and how often he performed such activity.

The primary outcome will be assessed via frequency, intensity and discomfort caused by the main

adverse symptoms of chemotherapy (such as pain, nausea, dry mouth) will be assessed using the Memorial Symptom Assessment Scale, Brazilian version, (MSAS-BR) [19]. This scale consists of 32 symptoms that are scored by the patient according to their frequency and intensity (1-4 points, with 1 being less intensity and frequency) and the discomfort (0-4, zero being no discomfort) that this symptom caused him last week. This scale gives us a final index, which consists of the average of the three domains (frequency, severity and bother) and all items (TMSAS), in addition to four subscales: PSYCH which assesses psychological symptoms (with six items), PHYS H which assesses the most prevalent physical symptoms (with 12 items), PHYS L which assesses the less prevalent physical symptoms (with 14 items) and the Global Suffering Index (GDI) which contains four psychological and six physical symptoms [19,20]. This scale will be applied in the initial and final assessment by an evaluator blind to which group the patient belongs.

Other outcomes will be assessed, such as fatigue, level of patients' mobility, length of hospital stay, and clinical complications. The fatigue will be assessed using the Brief Fatigue Inventory (BFI), Brazilian version. This inventory consists of nine items that are rated from zero to ten on a visual numeric scale. The first question is a dichotomous question about whether the patient has felt tired or fatigued in the last seven days. Three items refer to the severity of fatigue at the time of assessment, the usual fatigue in the last 24 hours and the worst fatigue in the last 24 hours, where zero represents no fatigue and ten "the worst fatigue imaginable". The other six items refer to how fatigue interfered with different aspects of the patient's life in the last 24 hours, these items are: general activities, mood, ability to walk, work (including work outside and at home and daily tasks), relationships with other people and enjoying life, where zero means that it does not interfere and ten means that it interferes completely [21,22]. This inventory will be applied in the initial and final assessment, by an evaluator blind to which group the patient belongs to.

The level of mobility will be assessed using the De Morton Mobility Index (DEMMI). This scale is made up of 15 activities, where 11 of them are classified as zero or one (incapable or capable,

respectively) and four are classified as zero, one or two (incapable/partial/capable, respectively). Of the fifteen activities, three are performed in bed, three in a chair, four involve static balance, two involve walking and three involve dynamic balance. The scale was translated and validated in Brazilian-Portuguese [23,24] and ranges from a score of zero, which represents low mobility, to 100, which represents high mobility. This index will be applied by an evaluator who is blind to which group the patient belongs to, and will be applied in the initial and final assessment.

In addition, the total number of days of hospital stay, possible clinical complications (cardiac, pulmonary, infectious or neurological) arising from chemotherapy treatment, and the need for transfer to the intensive care unit, will be accessed through the medical record of the patient.

The adverse effects of aerobic training, such as muscle pain, will be collected in the form of a question, developed by the researchers themselves, which will be answered every day before starting a new aerobic exercise session. In this same sense, patient's subjective perception of satisfaction and discomfort in relation to the proposed protocol will also be assessed through 2 questions developed by the researchers themselves that will be answered on the day of the patient's final assessment. The patient's response to the questions will vary on a scale of 0 to 10. In the question about satisfaction with the treatment, 0 will indicate "complete dissatisfaction" and 10, "maximum satisfaction." When the question is about the discomfort of the treatment, 0 will indicate "no discomfort" and 10 will indicate "maximum discomfort."

At the end of the treatment, the acceptability, suitability and feasibility outcomes will be assessed using the Weiner scale [25], which was translated and adapted into Brazilian-Portuguese [26]. The answer options for all questions are: completely disagree (1 point), disagree (2 points), neither agree nor disagree (3 points), agree (4 points) and completely agree (5 points).

Acceptability is the perception among parties interested in implementing that a given treatment is pleasant or satisfactory. It will be evaluated by the satisfaction reported by the patient allocated to the

intervention group by answering the following questions: 1) "Physical exercise during chemotherapy treatment has my approval"; 2) "Physical exercise during chemotherapy treatment is attractive to me"; 3) "I enjoyed physical exercise during chemotherapy treatment"; and 4) "I recommend physical exercise during chemotherapy treatment".

As for suitability, it is the relevance or compatibility of the proposed innovation (treatment) for a given clinical practice environment. It will be evaluated by the following questions addressed to health professionals who care for patients included in this study, such as doctors, nurses and physiotherapists: 1) "Physical exercise during chemotherapy treatment seems appropriate"; 2) "Physical exercise during chemotherapy treatment seems appropriate"; 3) "Physical exercise during chemotherapy treatment seems applicable"; and 4) "Physical exercise during chemotherapy treatment seems to be a good option".

Feasibility is defined as the extent to which a new treatment can be implemented within a given environment. It will be evaluated by the following questions addressed to physiotherapists and patients included in this study: 1) "Physical exercise during chemotherapy treatment seems implementable"; 2) "Physical exercise during chemotherapy treatment seems possible to perform"; 3) "Physical exercise during chemotherapy treatment seems feasible"; and 4) "Physical exercise during chemotherapy treatment seems feasible"; and 4) "Physical exercise during chemotherapy treatment seems easy to use."

Economic evaluation will be carried out through monitoring during the hospitalization period [27]. The index year will refer to the year of data collection. The costs of the intervention used will be assumed through the estimated value of the analysis of the material used (oximeter, cycle ergometer), the booklets and the in-hospital physiotherapy session (using the reference fees from the Physiotherapy council table). The assessment of healthcare costs corresponds to the individual's costs to healthcare systems and the costs of lost productivity due to total days of hospitalization. This assessment will be carried out using cost information obtained at the hospital. The cost-effectiveness

analysis will be carried out by evaluating the effects of the intervention using the MSAS-BR16 questionnaire, while the cost-utility analysis will be measured by quality-adjusted life years (QALYs) using the quality-of-life questionnaire EQ-5D-3L [28]. Sensitivity analysis will test uncertainty in key parameters such as selection of cost weights and statistical variation in quality of life scores.

The patients allocated to the intervention group will participate in an aerobic training protocol, on a cycle ergometer, during the period in which they are hospitalized and undergoing the chemotherapy cycle. The training will be carried out with a daily session for 4 days lasting 40 minutes, while the chemotherapy cycle lasts. Exercise on the cycle ergometer will begin with a 5-minute warm-up, and will progress to 30 minutes of exercise at a speed corresponding to 40-60% of the heart rate reserve calculated by the Karvonen formula [29] ([220 - age] - [heart rate of rest \* % intensity] + resting heart rate), ending with 5 minutes of recovery. The objective will be to maintain the patient at a score of "12" for the perception of dyspnea/physical fatigue measured by the Borg scale [30] (a score that means that the patient's dyspnea/physical fatigue is above "relatively easy" and below "slightly tiring") during exercise on the cycle ergometer. The Borg scale presents a range of scores from: 6 (no effort) to 20 (maximum effort). Therefore, if the patient is considered fit by the physiotherapist, the speed on the cycle ergometer will be gradually increased until the patient reaches 60% of the heart rate reserve. Patients will have heart rate and peripheral oxygen saturation (Palmsat 2500 pulse oximeter, NONIN), dyspnea and physical fatigue (Borg scale) [27] and blood pressure (Premium aneroid sphygmomanometer and Littmann classic II stethoscope) recorded before, during and after each physical training protocol session. The session may be interrupted at any time if the patient presents signs or symptoms, such as dizziness, dyspnea, fatigue, nausea. If the patient requires any emergency assistance during the period in which they are undergoing physical training supervised by the study physiotherapist, the same physiotherapist will contact the medical team on duty, responsible for the patient in the Oncology Ward, to provide the necessary assistance to stabilize the

condition. patient. To assist in blinding the evaluator, the booklet entitled: "Why do I need to move when I am hospitalized" [31] will be given to patients in both groups. The cycle ergometer will always be removed from the patient's room after the training session to ensure blind evaluation.

The patients allocated in the control group will receive a booklet entitled: "Why do I need to move when I'm hospitalized", where through illustrations and short texts, patients are encouraged to spend more time in the chair, walk and go up and down stairs (with companion) [31]. This booklet will be delivered and explained by a trained physiotherapist and the participant will keep it for any questions and consultations.

The calculation to determine the sample size was carried out based on a previous randomized clinical trial that also compared the effect of aerobic training compared to usual care on the deleterious effects of chemotherapy in patients with breast cancer [11]. Our study was designed to detect a difference of  $2.7 \pm 4$  points in physical fatigue, in addition to a difference of  $6.2 \pm 7$  episodes of vomiting or nausea between the groups. A power of 80% and an alpha of 5% and a loss to follow-up of 15% of the sample were considered. A sample of 94 patients (47 patients in each group) was estimated.

After the data collection, all analyzes will be conducted following intention-to-treat principles and will be performed by a researcher who will not be involved in the study assessments and intervention.

For analyzing the effect of intervention, after the descriptive analysis and the Shapiro-Wilk normality test with visual analysis, the groups will be compared using the Linear Mixed Model, regarding fatigue, mobility and chemotherapy-related symptoms before and after the intervention. The length of hospital stay will also be compared between groups using Kaplan-Meier survival analysis. The chi-square test will be used to compare the clinical complications rates between groups. Descriptive analysis will be used to describe recruitment, completion and adherence rates and potential adverse

events. The significance level will be set at 5%. For all these analyses, IBM SPSS software, version 21.0 [IBM Corp, Armonk, New York] will be used.

For economic evaluation, the analysis will be performed using chemotherapy-related symptoms, fatigue and mobility as outcomes, and cost-utility analysis using QALYs. Missing data will be handled using Multiple Imputation by Chained Equations. Ten complete datasets will be created (efficiency loss <5%). Pooled estimates will be calculated according to Rubin's rules [32]. Average cost differences between groups will be calculated for total and disaggregated costs. Incremental cost-effectiveness and cost-utility rates will be calculated by dividing the difference in total costs by the difference in effects. Uncertainty surrounding cost differences and incremental cost-effectiveness and cost-utility ratios will be estimated using corrected and accelerated bootstrap techniques (5,000 replications). The latter will be presented graphically in cost-effectiveness plans [33]. Cost-effectiveness acceptability curves will be estimated to indicate the probability of interventions being cost-effective compared to each other at different willingness-to-pay values [34]. Sensitivity analyzes will be performed to assess the robustness of the results. The first sensitivity analysis will be performed from a healthcare perspective, and the second sensitivity analysis will be performed per protocol. The economic evaluation will be carried out using STATA [V.14, StataCorp, College Station, Texas, USA].

#### Results

In March 2023, the clinical trial registration was approved. Recruitment and data collection for the trial is ongoing, and the results of this study are likely to be published in late 2025.

#### Discussion

To our knowledge, this will be the first controlled trial with economic analysis that will be carried out testing the acute effect of aerobic exercise during patients undergoing a cycle of chemotherapy. However, based on previous studies conducted in the outpatient phase of cancer treatment [35], we

believe that aerobic training will be cost-effective and will cause a lower incidence of adverse effects from chemotherapy treatment, less fatigue, maintenance of mobility, shorter hospital stays and lower incidence of clinical complications when compared to the control group.

Despite the potential beneficial effects of physical exercise for cancer patients, a decline in activity level has been reported in this population [36]. This decline appears to have an impact on quality of life and lower performance in activities of daily living in women with breast cancer. A possible hypothesis for this decrease in physical exercise may be the relationship with psychosocial barriers in these patients [36].

Smith and colleagues conducted a study that aimed to assess exercise behavior, barriers, facilitators, and motivators for exercise participation and the different exercise support needs of cancer survivors living in a rural Canadian community and observed that the main barriers reported were cost, time, distance, transportation and side effects [37]. Still in the study described above, regarding facilitators, they were able to observe that patients report that access to the gym, access to equipment, social support, transportation, information regarding physical exercise are considered facilitators [37].

The Clinical Oncology Society of Australia (COSA) and Exercise and Sport Science Australia (ESSA) encourage healthcare professionals who work with cancer patients to seek to know more about the relationship between physical activity and cancer and understand how they must guide their patients to practice physical activity [38]. They also advise health professionals to refer patients to professionals who are more prepared and who better understand the practice of exercise in cancer patients.

In the study by Park and colleagues (2015), the authors analyzed the influence of doctors on their patients, where they had 162 people who overcame early-stage breast and colorectal cancer, and who completed primary and adjuvant treatment [39]. But only 80.7% (130 participants) of those included

in the study remained until the end. 3 groups were stratified, the first was the control group (here there were 59 participants), the second group was the exercise recommendation group from oncologists (here there were 53 participants) and the third group was the PA recommendation group from oncologists with exercise motivation package (here there were 50 participants). Participants were assessed at the beginning of the study and after 4 weeks [39].

In the motivation package they provided exercise DVDs, a pedometer, an exercise diary and a 15-minute physical education session. In the recommendation, the oncologists said: "Studies have shown that engaging in moderate PA more than 150 minutes per week could significantly reduce the recurrence of breast and colorectal cancer. Therefore, it is highly recommended that breast and colorectal cancer survivors participate in at least 150 minutes of moderate-level PA and twice-weekly strengthening exercises" [39].

We have seen in current literature the importance of understanding how much physical exercise can impact the treatment and quality of life of cancer patients undergoing chemotherapy treatment. Studies have shown that incorporating adequate and supervised exercise can help combat fatigue, improve physical fitness, reduce anxiety and depression, as well as help maintain functionality. However, it is important that the exercise program is individualized, taking into account the stage of the disease, the patient's age, needs and limitations. Supervision by specialized professionals is essential to ensure safety and effectiveness. In summary, physical exercise can be a valuable tool in managing symptoms and promoting well-being in cancer patients, complementing conventional treatments, providing both physical and emotional improvements during the cancer treatment journey.

**Conclusion:** Chemotherapy has side effects that negatively impact the quality of life of cancer patients. Aerobic exercise can reduce those side effects in a simple and inexpensive way. Oncology could be an expanded field of work for physical therapists if the intervention works.

#### Acknowledgments

The São Paulo Research Foundation (FAPESP) sponsors ACL (grants #2023/07735-8). The Brazilian Federal Agency for Suport and Evaluation of Graduate Education (CAPES) sponsors WLS. The study funders (FAPESP and CAPES) are public research foundations and do not have any influence on the study's results, including data collection; the management, analysis, and interpretation of data; or writing of the manuscript.

#### **Data Availability**

The data obtained in this study will be available from the corresponding author (ACL) upon reasonable request.

#### **Conflicts of Interest**

None declared.

#### **FIGURE**

#### DETERMINATION OF ELIGIBILITY OF PARTICIPANTS

**ASSESSMENT** 

ANTHROPOMETRIC AND CLINICAL CHARACTERISTICS, MSAS-BR, BFI AND DEMMI [N= 94]

RANDOM ALLOCATION [N= 94]

INTERVENTION GROUP [N= 47]

PATIENT RANDOMIZATION

CONTROL GROUP [N= 47]

MSAS-BR, BFI, DEMMI
AND PATIENT
SATISFACTION
I AND PATIENT
SATISFACTION

NEXT DAY AFTER LAST INTERVENTION

MSAS-BR, BFI, DEMMI AND PATIENT SATISFACTION

LENGTH OF HOSPITAL STAY AND CLINICAL COMPLICATIONS

UNTIL HOSPITAL DISCHARGE

LENGTH OF HOSPITAL STAY AND CLINICAL COMPLICATIONS

Figure 1: Clinical trial flowchart

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## **Supplementary Files**

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