Programa de treinamento físico à distância para pessoas com câncer de mama ou próstata: um estudo de viabilidade

TESE DE DOUTORADO

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Só quando a última árvore for derrubada, o último peixe for morto e o último rio for poluído é que o homem perceberá que não pode comer dinheiro.

Provérbio Indígena

RESUMO

Os números de casos de câncer têm aumentado mundialmente, sendo uma das maiores causas de morte. No Brasil, os cânceres de mama e próstata estão entre os mais frequentes na população. Apesar das recomendações, a adesão a exercícios físicos durante o tratamento é baixa, devido a barreiras como a falta de acesso a serviços especializados. Programas tradicionais são geralmente supervisionados em centros de saúde, o que limita a participação de muitos pacientes. Barreiras adicionais incluem dificuldades econômicas, efeitos do tratamento e preocupações estéticas, impactando a participação em exercícios supervisionados. Considerando as incertezas sobre a participação de pacientes com câncer em programas remotos de exercício físico, este estudo investiga a viabilidade de uma intervenção de atividade física durante o tratamento de câncer de mama e próstata. Através de um delineamento de estudo de viabilidade, testamos um modelo de intervenção acessível e voltado para a participação remota, permitindo que os participantes realizassem o treinamento proposto em suas casas ou em locais de sua escolha, sem supervisão direta de profissionais. Os desfechos estudados incluem a aderência à intervenção, eventos adversos, índices de fadiga e qualidade de vida, força de preensão manual e distância percorrida no teste de caminhada de seis minutos. Além disso, com o intuito de envolver os participantes na decisão sobre um futuro ensaio clínico, realizamos discussões em grupos focais. Este trabalho está dividido em três partes: uma introdução geral ao tema com revisão de literatura, seguida por dois artigos específicos. O primeiro trata do artigo de protocolo do estudo, publicado previamente, e o segundo aborda os dados de recrutamento e a intervenção em si, contendo os resultados de aderência, eventos adversos, escores de fadiga e qualidade de vida, avaliações funcionais e *feedback* dos pacientes ao término do estudo.

Palavras chave: atividade física, exercício físico, câncer, viabilidade, câncer de mama, *home based*, *feedback*.

ABSTRACT

Cancer cases have been increasing worldwide, becoming one of the leading causes of death. In Brazil, breast and prostate cancers are among the most frequent in the population. Despite recommendations, adherence to physical exercise during treatment is low due to barriers such as lack of access to specialized services. Traditional programs are generally supervised in health centers, limiting the participation of many patients. Additional barriers include economic difficulties, treatment side effects, and aesthetic concerns, impacting participation in supervised exercise. Considering the uncertainties about the participation of cancer patients in remote exercise programs, this study investigates the feasibility of a physical activity intervention during breast and prostate cancer treatment. Using a feasibility study design, we tested an accessible intervention model aimed at remote participation, allowing participants to perform the proposed training at home or in locations of their choice, without direct supervision from professionals. The outcomes studied include adherence to the intervention, adverse events, fatigue levels, quality of life, handgrip strength, and distance covered in the six-minute walk test. Additionally, to engage participants in the decision-making for a future clinical trial, we conducted focus group discussions. This work is divided into three parts: a general introduction to the topic with a literature review, followed by two specific articles. The first discusses the study's protocol, and the second approaches the recruitment data and from the trial itself including adherence, adverse events, fatigue scores and quality of life, functional assessments and patient feedback at the end of the study.

Key words: physical activity, exercise, cancer, feasibility, breast cancer, home-based, patient feedback.

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LISTA DE ABREVIATURAS E SIGLAS

6MW	Six-minute walk test
BENEFIT CA	The home-based exercise for breast and prostate cancer patients during treatment: a feasibility trial" (BENEFIT CA trial)
CAPES	Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (Coordination for the Improvement of Higher Education Personnel)
COVID-19	Coronavirus Disease 2019
CONSORT	Consolidated Standards of Reporting Trials
ESF	Family Health Strategy
FACT-G	Functional Assessment of Cancer Therapy-General
FACT-B	Functional Assessment Cancer Therapy Breast
FACT-P	Functional Assessment Cancer Therapy Prostate
FAPERGS	Fundação de Amparo à Pesquisa do Estado do Rio Grande do Sul
FIPE	Fundo de Incentivo à Pesquisa
GEE	General Estimating Equations
HCPA	Hospital de Clínicas de Porto Alegre
HDI	Human Development Index
INCA	National Institute of Cancer
IPAQ	International Physical Activity Questionnaire
IRB	Institutional Review Board
ITT	Intention-to-treat analysis
LOCF	Last observation carried forward
OSF	Open Science Framework
PA	Physical activity
REDCap	Research Electronic Data Capture
RCT	Randomized controlled trial
SEER	Surveillance, Epidemiology and End Results
SPIRIT	Standard Protocol Items: Recommendations for Interventional Trials
SWAT	Study within a trial
UFRGS	Universidade Federal Do Rio Grande Do Sul, Porto Alegre, RS, Brazil
WHO	World Health Organization

SUMÁRIO

INTRODUÇÃO

O câncer é caracterizado pela divisão celular desordenada, podendo atingir um ou mais tecidos. Essa proliferação tende a ser agressiva e fora de controle, dando início a tumores em uma ou várias partes do corpo humano [1]. Os diversos tipos de câncer advém das diferentes células do corpo, como por exemplo, o carcinoma, que provém de células epiteliais, e o sarcoma, proveniente de células do tecido conjuntivo. Outra característica importante dessa doença é a capacidade e a velocidade com a qual pode se espalhar e se multiplicar, invadindo outros tecidos, fenômeno conhecido como metástase [1]. Diversos tipos de câncer têm incidência crescente e a doença representa uma das principais causas de morte prematura em nível global [2,3].

Para o Brasil, a estimativa para cada ano do triênio de 2023 a 2025 aponta que ocorrerão 704 mil casos novos de câncer, 483 mil se excluídos os casos de câncer de pele não melanoma, sendo este o mais incidente, com 220 mil casos novos (31,3%), seguido pelos cânceres de mama, com 74 mil (10,5%); próstata, com 72 mil (10,2%); cólon e reto, com 46 mil (6,5%); pulmão, com 32 mil (4,6%); e estômago, com 21 mil (3,1%) casos novos. Estima-se que os tipos de câncer mais frequentes em homens serão os de pele não melanoma, próstata, cólon e reto, pulmão, estômago e cavidade oral. Nas mulheres, os cânceres de pele não melanoma, mama, cólon e reto, colo do útero, pulmão e tireoide figurarão entre os principais [4].

Para pacientes já diagnosticados com câncer, os tratamentos disponíveis baseiam-se em cirurgia, quimioterapia, radioterapia, terapias hormonais e terapias alvo [5–7]. Além dos tratamentos cirúrgicos e farmacológicos convencionais, existe uma literatura crescente acerca dos benefícios para a população com câncer com o uso de outras abordagens, como a prática de atividade física e exercício físico [8–13]. O exercício físico está associado com a prevenção, melhora dos efeitos colaterais do tratamento, potencialização das respostas ao tratamento, assim como está relacionado a redução nas taxas de recorrência e mortalidade [8,12,14]. As evidências apontam que o exercício físico é seguro para a população com câncer [11] e proporciona inúmeros benefícios já citados. No entanto, ainda há uma baixa procura e manutenção de níveis desejados de atividade física nesta população

quando comparada com outras doenças crônicas, nas quais a prática de exercício físico é muito mais explorada [12]. Dentre potenciais motivos da aderência subótima a um programa de treinamento podem listar falta de incentivo por parte da equipe médica [6,8,15–17], desconhecimento por parte do paciente [8,16,17], e métodos de pesquisa com baixo foco em implementação das intervenções em diferentes contextos aos quais os pacientes estão expostos [12,15].

Em estudos clínicos, os modelos usualmente consistem no deslocamento do paciente ao local de treinamento para acompanhamento/supervisão. Tal formato de intervenção possui benefícios bem documentados para a população em questão [8,12]. Porém, uma parcela significativa dos pacientes com câncer não possui acesso a serviços especializados e, mesmo quando estes possuem, os serviços podem não disponibilizar programas de atividade física como parte do esquema terapêutico ou pós-terapêutico. Outras barreiras de acesso referem-se às dificuldades associadas à condição econômica, transtornos gerados pelo tratamento (como a imunossupressão, deixando os pacientes mais vulneráveis a doenças oportunistas) e fatores estéticos que podem influenciar no engajamento em um programa de exercício físico acompanhado [8,12].

Levando em consideração o cenário da doença, é importante identificar outros modelos de práticas de atividade física que possam ser ofertados a um maior número de pacientes. A maioria dos estudos têm foco em ensaios clínicos altamente controlados, o que pode limitar a translação do conhecimento para políticas de cuidado para os pacientes com câncer [18]. Considerando os fatores dificultantes já citados, o estilo de treinamento físico com orientação à distância (home based) poderia ser uma alternativa para que pessoas com câncer tenham maior aderência aos programas de atividade física. Estudos que utilizaram acompanhamento à distância para pessoas com câncer encontraram efeitos benéficos diversos, tais como redução de níveis de fadiga, incremento da capacidade funcional e cardiorrespiratória [8,12,19–21]. Além disso, as evidências ressaltam a importância do acompanhamento ao longo do estudo, como uso de telefonemas, e-mails e mensagens de texto ou voz que sejam direcionadas e individualizadas para cada paciente, o que auxilia na motivação, aderência e continuidade ao treinamento físico [8,19,22].

Modelos de acompanhamento à distância podem facilitar que pacientes com câncer mantenham atividade física, aproveitando seus benefícios mesmo em

condições subótimas. A pandemia de COVID-19 acelerou a adoção de tecnologias para consultas e acompanhamentos remotos, reduzindo custos e barreiras para pacientes e pesquisadores. No entanto, na urgência em promover o cuidado por telefone, via online ou outras formas de acompanhamento remoto, salienta-se a necessidade de atenção aos indicadores de aceitação e engajamento por parte dos participantes [23].

Portanto, o objetivo deste estudo foi abordar a amplificação da atividade física na população em tratamento para câncer de mama e próstata. Buscamos testar um modelo de intervenção de baixo custo, pragmático e orientado ao envolvimento de um maior número de pacientes. A proposta desse modelo foi de ofertar que os participantes realizassem o treinamento proposto em suas residências ou em outro local de sua escolha, sem supervisão direta da equipe de pesquisa ou assistencial.

Assim, esta pesquisa foi delineada como um estudo de viabilidade para reduzir incertezas metodológicas antes da potencial implementação de um ensaio clínico randomizado de fase 3 com uso de treinamento físico à distância. O estudo visou caracterizar o nível de aderência dos participantes e identificar barreiras e facilitadores à intervenção. Neste contexto, Investigamos desfechos de saúde cardiovascular e neuromuscular pela sua importância nas atividades diárias e qualidade de vida dos pacientes com câncer. Além disso, conduzimos grupos focais a fim de promover o engajamento dos participantes na discussão sobre atividade física e suas experiências antes e durante o estudo.

Este trabalho se divide em três partes: uma introdução geral ao tema com revisão de literatura, seguida por dois artigos específicos. O primeiro trata do protocolo do estudo e o segundo aborda dados de recrutamento e os resultados da intervenção em si com os resultados de aderência, eventos adversos, escores de fadiga e qualidade de vida, avaliações funcionais e feedback dos pacientes ao término do estudo.

REVISÃO DE LITERATURA

Atividade física/exercício físico e a prevenção do câncer

O câncer é causado por inúmeros fatores que incluem elementos inalteráveis, como mutações genéticas, porém, também é influenciado por fatores ambientais e hábitos de vida, os quais são modificáveis [24]. Fatores relacionados ao estilo de vida têm sido associados com o surgimento de diversos tipos de cânceres e causas preveníveis de morte [24], os quais salienta-se a associação de proteção entre prática de atividade física e a incidência de câncer [25,26]. Ainda que muitas das evidências sejam derivadas de estudos observacionais e que os mecanismos do exercício físico para a prevenção do câncer devam ser melhor estabelecidos, considera-se que o exercício físico possa reduzir o risco de desenvolvimento de câncer de modo direto ou indireto, via cascatas biológicas inter-relacionadas [8,14]. Em uma revisão de 45 estudos epidemiológicos [27] demonstrou-se que níveis mais elevados de atividade física estão associados a menores riscos de desenvolvimento de cânceres, incluindo os de bexiga, cólon, mama, endométrio, adenocarcinoma esofágico, rins e gástrico. Essa associação revelou reduções no risco relativo situadas na faixa de 10 a 20%, destacando a importância da atividade física na prevenção destas neoplasias.

Atividade física/exercício físico durante os principais tratamentos primários do câncer

A maioria dos pacientes é tratada para o câncer com o uso de cirurgia de remoção de algum tecido, quimioterapia e/ou radioterapia, além de outros tratamentos farmacológicos. As evidências sugerem que o exercício físico pode aumentar a eficácia de tratamentos anti câncer usuais, bem como atenuar os sintomas e efeitos adversos do tratamento (como fadiga, caquexia, sintomas depressivos e comprometimento cognitivo). Ainda, o exercício físico pode incrementar a sobrevida e a qualidade de vida de pacientes com câncer [24].

Cirurgia

Muitos pacientes passam por procedimento cirúrgico para retirada de tecido tumoral. A cirurgia é utilizada para prevenir, diagnosticar, determinar o estágio e tratar o câncer, geralmente aliviando problemas relacionados à doença. Muitas vezes, a remoção de tecido pode afetar a mobilidade, força e a elasticidade da

articulação, pele e tecido neuromuscular envolvido, levando a perdas funcionais que podem ser, mesmo que não em sua totalidade, mas parcialmente revertidas e com a prática de exercícios físicos [28–30].

Quimioterapia

O uso da quimioterapia é frequente em grande parte dos cânceres, incluindo os de mama ou próstata. Este método emprega agentes como alcaloides, antimetabólitos, anti-tumorais, antibióticos, inibidores mitóticos e corticosteróides. Esses medicamentos são utilizados para interromper a proliferação de células cancerígenas. Os efeitos adversos ao tratamento quimioterápico podem incluir ganho de peso [5,12], supressão imunológica aguda ou sustentada [31], cardiotoxicidade [8] e danos pulmonares [9]. Para as mulheres, existe também a possibilidade de amenorreia ou menopausa prematura [6]. Ainda, há chances de ocorrer o desenvolvimento de neuropatias periféricas advindas do tratamento, com possíveis interferências no equilíbrio e efeitos cognitivos deletérios a curto e longo prazo [31].

Apesar de servir no suporte de vida de muitos pacientes, a quimioterapia provoca efeitos adversos tais como a fadiga, perda da massa magra e óssea, e redução de capacidade funcional, além de potencial influência em aspectos psicológicos e cognitivos [32,33]. A prática de exercícios físicos durante a quimioterapia é benéfica para contornar alguns dos efeitos negativos do tratamento. Os efeitos são constatados tanto a partir de exercícios de força, os quais promovem ganhos ou manutenção de massa e força muscular, quanto por exercícios aeróbicos, cujos benefícios ocorrem por ganho ou manutenção nos níveis de capacidade cardiorrespiratória. Assim, ambas as intervenções contribuem para benefícios associados à fadiga [7,34,35], aspectos cognitivos [36,37], sintomas depressivos [28,38] e massa óssea [28,39].

Radioterapia

A radioterapia é um tratamento muito comum entre os(as) pacientes com câncer de mama e próstata, utilizando radiações ionizantes, como raios-X, para danificar ou destruir as células cancerígenas. Esse tratamento é projetado para direcionar as radiações de forma precisa às áreas afetadas, buscando minimizar os danos às células normais circundantes [40,41]. Além dos benefícios já

documentados na literatura, a mesma possui efeitos adversos, assim como a quimioterapia, muitos desses efeitos relacionados dependem da dosagem aplicada, da área atingida, se há cirurgia realizada no local e de tratamento concomitante com quimioterapia [5]. Muitas vezes, órgãos que não estão no escopo para tratamento são afetados, podendo gerar danos nesses tecidos. Exemplos desses efeitos colaterais podem ser problemas pulmonares [5,9], linfedemas [10], toxicidade cardíaca [42], assim como danos gastrointestinais [31] e imunossupressão sustentada [43]. Com relação à eficácia do tratamento farmacológico, seja quimioterapia ou radioterapia, a prática de exercício físico durante os tratamentos parece influenciar o microambiente do tumor através de ação antioxidativa [26], facilitando o aporte do tratamento farmacológico e a eficácia do mesmo nas células cancerígenas [24,26], podendo, ainda, reduzir o tamanho do tumor [13,26] e o seu crescimento, em diferentes tipos de câncer e em todas as etapas do desenvolvimento do tumor [13].

A prática de exercícios físicos durante a radioterapia reduz seus efeitos negativos, seja diretamente por preservar massa magra e óssea, ou indiretamente por estimular a independência funcional [7,8,12]. Ainda, os(as) pacientes em tratamento do câncer têm seu sistema imunológico debilitado, e a prática de exercícios incrementa o sistema imunológico do(a) paciente com câncer [44,45].

Terapias alvo

Outro tratamento ainda não tão frequente são as terapias alvo, que são um tipo de tratamento com medicamentos desenvolvidos para ação mais direcionada nas células cancerígenas [46]. As células cancerígenas são tipicamente diferentes de seus genes das células normais, de modo que, quando uma célula contém certas mudanças nos seus genes, a mesma passa a se comportar de maneira diferente. Mesmo entre pessoas diferentes com o mesmo tipo de câncer, as células cancerígenas podem ter diferentes mutações genéticas, fazendo com que as especificidades genéticas do câncer de uma pessoa sejam diferentes das demais. Ainda, as pesquisas mostram que o ambiente celular das células cancerígenas com relação ao início, o crescimento e proliferação celular nem sempre é o mesmo, pois, em alguns casos, alguns tipos de câncer fazem com que certas proteínas ou enzimas enviem determinadas sinalizações à célula cancerígena, para que a mesma cresça e se multiplique [46].

O desenvolvimento de medicamentos que podem ser direcionados a proteínas específicas possibilita bloquear os sinais que fazem com que as células cancerígenas cresçam, ou então estimular a apoptose celular [46]. Por tratar-se de um tratamento mais recente e ainda em desenvolvimento, diversos pacientes que estão sob este tipo de tratamento ainda precisam de cirurgia, quimioterapia, radioterapia e/ou bloqueio hormonal.

Imunoterapia

Outra abordagem de tratamento é a imunoterapia, um tratamento que utiliza determinadas partes do sistema imunológico para combater algumas doenças, como o câncer [47]. Este tratamento pode ser feito estimulando as defesas naturais do organismo para que o mesmo consiga identificar e combater células cancerígenas. Nas últimas décadas, a pesquisa e o tratamento nesta área têm crescido substancialmente, de modo que novos meios de se interagir com o sistema imunológico vêm sendo identificados em ampla escala. Um dos tipos mais comuns é o uso de inibidores de checkpoint, que ajudam o organismo a intensificar a defesa imune, com maior ação sobre as células cancerígenas [47].

Atividade física/exercício físico durante a hormonioterapia/bloqueio hormonal

As terapias hormonais (bloqueio hormonal) para mulheres em tratamento do câncer de mama incluem antiestrógenos e inibidores de aromatase, bem como procedimentos cirúrgicos (ooforectomia). Esses procedimentos têm efeitos similares aos da menopausa, causando os mesmo desconfortos associados, tais como ondas de calor, fadiga, perda de massa óssea, dores articulares, ganhos de peso e mudanças de humor [6,8]. Para os homens em tratamento do câncer de próstata, a terapia hormonal anti androgênica pode causar obesidade e síndrome metabólica [23,51,52], juntamente com perdas importantes de massa óssea [28,52], massa magra e força muscular [7,28,52].

Tanto para mulheres quanto para homens em tratamento com bloqueio hormonal, a prática de exercícios físicos promove aumento da capacidade aeróbica [7,28,53], a força e a massa muscular [7,28,39] e massa óssea [28,39], que são pontos chaves para a manutenção da independência funcional, por exemplo, principalmente em pacientes idosos [12,54]. O exercício físico também auxilia no controle do peso, que em si pode representar o aparecimento de outras doenças,

como diabetes, cuja a prática de exercício físico é fundamental, no manejo da síndrome metabólica, na melhora de sintomas e questões psicológicas, como a depressão [28,38], e também tem se mostrado benéfico para melhora de dores articulares advindas dos tratamentos e da fadiga e qualidade de vida como um todo [7,34,35].

Ainda, sínteses de evidências têm indicado que pacientes que praticam exercício físico reduzem as chances de reincidência ou de surgimento de novos cânceres [14,21], além de reduzir a mortalidade em geral [8,12,42]. Um estudo [55] que acompanhou por aproximadamente 9 anos pacientes com câncer de mama, mostrou que aquelas que atingiram os níveis recomendados de atividade física semanal tiveram uma redução de 23% no risco de doenças e eventos cardiovasculares em comparação àquelas que não atingiram os níveis recomendados. Ser fisicamente ativo é uma das atitudes mais importantes que pessoas de todas as idades, independente de suas habilidades, podem fazer para prevenir, auxiliar no tratamento e na sobrevivência ao câncer [53].

Usualmente, os modelos consistem no paciente deslocar-se ao local de treinamento e receber acompanhamento/supervisão. Tal formato de intervenção é amplamente utilizado e possui benefícios bem documentados. Porém, uma grande parcela dos pacientes com câncer não possui acesso a serviços especializados e, mesmo quando estes possuem, os serviços podem não disponibilizar programas de atividade física como parte do esquema terapêutico ou pós-terapêutico. Outros aspectos na dificuldade de acesso referem-se às dificuldades associadas à condição econômica, transtornos gerados pelo tratamento e fatores estéticos que podem influenciar no engajamento em um programa de exercício físico acompanhado [8,12].

Embora o presente estudo não tenha sido originalmente concebido dentro do cenário, a pandemia COVID-19 teve e ainda tem efeitos significativos nas vidas de pacientes com câncer. Apesar das recomendações da Organização Mundial da Saúde (OMS) para manter os níveis de movimento e atividade física mais elevados, é de se esperar que esses níveis tenham tido quedas em diversas populações, e a população com câncer não seria diferente [56]. Em um estudo recente [57] com mais de 1.8 milhões de participantes, foi visto que os indivíduos vivendo com câncer tinham um aumento de 60% de chance/probabilidade ter um teste positivo de COVID-19 ou hospitalização por COVID-19, com riscos maiores para aqueles mais

velhos ou recebendo terapia anticâncer [23]. Pacientes com câncer, tanto em tratamento quanto após tratamento, são imunossuprimidos e, no contexto da última pandemia e de outros eventos similares de saúde pública, são mais vulneráveis para contrair a doença [58] e ter maior risco de morte, efeitos adversos graves e internações relativos à mesma [58] e ter maior risco de morte, efeitos adversos graves e internações relativos à mesma [59], pois, além de efeitos relacionados ao câncer em si e ao tratamento, muitos pacientes sofrem de outras doenças ou comorbidades, como sobrepeso, obesidade, hipertensão, diabetes e etc, o que agrava o quadro para aqueles que venham a contagiar-se [58,60]. Dados de um estudo do Rio Grande do Sul (COORTE PAMPA) reforçam a importância da manutenção da prática de atividade física em populações com doenças crônicas, mesmo durante a pandemia, o que evidencia que indivíduos com doenças crônicas não transmissíveis que se mantiveram fisicamente ativos durante os períodos iniciais da pandemia (junho e julho de 2020), reduziram em 15% a probabilidade de perceber pior controle da doença e da sua condição de saúde [61].

Levando em consideração todo o cenário de doença, tratamento e a recente pandemia, seria interessante utilizar outros modelos de treinamento físico que possam abranger diferentes populações e alcançar um maior número de pacientes, para que os mesmos possam desfrutar dos benefícios do exercício físico. A maioria dos estudos têm foco em ensaios clínicos altamente controlados, porém, uma minoria desta pesquisa é traduzida em políticas de cuidado para os pacientes com câncer [18]. O estilo de treinamento físico home based poderia ser uma alternativa para que pessoas com câncer possam se exercitar. A proposta deste modelo de treinamento é fazer com que os participantes realizem o treinamento físico proposto em suas residências ou em outro local que preferirem, sem acompanhamento direto do pesquisador/ treinador. Estudos que utilizaram esse modelo de acompanhamento à distância, com pessoas com câncer, encontraram efeitos benéficos diversos, como redução de níveis de fadiga, incremento da capacidade funcional e cardiorrespiratória, por exemplo [8,12,19,21].

Com um modelo de acompanhamento à distância, cujo objetivo é fazer com que mais pacientes possam se beneficiar da prática, pacientes com câncer poderiam atingir bons níveis de atividade física, de maneira relativamente mais fácil e, mesmo que, em alguns casos, as condições para a realização do exercício físico não sejam as ideais, desfrutar dos seus benefícios. A pandemia fez com que

tivéssemos uma rápida implementação tecnológica, a qual permite contato seguro e com custos reduzidos para os pacientes e pesquisadores. Após o período pandêmico, os modelos de trabalho sofreram muitas mudanças, de modo que os modelos e métodos de atendimento físico também têm se mostrado mais versáteis, incorporando alguns elementos de acompanhamento remoto ou novas formas de atendimento. No entanto, na urgência em promover o cuidado por telefone, via online ou outras formas de acompanhamento remoto, foi dada pouca atenção para a promoção do engajamento dos pacientes, no que tange analisar se estes modelos são viáveis e aceitos por parte dos pacientes [23].

Portanto, o presente estudo aborda o problema de pesquisa relacionado à amplificação de acesso da atividade física para a população em tratamento do câncer de mama e câncer de próstata. Neste sentido, buscou-se testar um modelo de intervenção de baixo custo, pragmático e voltado ao aumento do volume de pacientes envolvidos. A proposta deste modelo foi de fazer com que os participantes realizassem o treinamento proposto em suas residências ou em outro local de suas preferências, sem acompanhamento direto do(a) pesquisador(a)/treinador(a). Estudos que utilizaram esse modelo em pessoas com câncer usaram estratégias de retenção que incluíram telefonemas e envio de mensagens individualizadas e planejadas, a fim de facilitar e motivar a continuidade no treinamento físico à distância [8,19,22].

Sendo assim, esta tese consiste de um estudo de viabilidade (*feasibility trial*) para a avaliação inicial de um modelo de treinamento à distância, o qual pretendemos futuramente testar em um ensaio clínico randomizado fase 3. O presente projeto buscou caracterizar o nível de aderência por parte dos participantes e a contabilização de eventos adversos (relacionados ou não ao presente estudo), além de ter aprofundado o conhecimento sobre possíveis barreiras e facilitadores para esta intervenção. Como forma de exploração de desfechos de interesse em um potencial ensaio clínico futuro, propusemos a avaliação de desfechos de saúde cardiovascular e neuromuscular, visto que os mesmos já terem demonstrado importância em atividades do dia a dia e qualidade de vida dos pacientes com câncer.

OBJETIVOS

Os objetivos deste estudo se caracterizam da seguinte maneira:

Objetivo geral

Avaliar a viabilidade de uma intervenção baseada em um programa de treinamento físico combinado, à distância (*home based*), aliado a conteúdos educativos relacionados à saúde no câncer (conteúdo via telefone e mensagem de texto).

Objetivos específicos

Artigo 1

Artigo de protocolo do estudo, que relata sobre os processos e procedimentos do estudo, relatando também acerca do manejo, backup e compartilhamento de dados.

Descrever as taxas de recrutamento de participantes para o ensaio clínico, considerando fatores como métodos de recrutamento, características individuais e dados clínicos.

Artigo 2

Descrever as taxas e os métodos de recrutamento de participantes para o estudo, avaliar os níveis de aderência e contabilização de eventos adversos, além de avaliar o perfil antropométrico (IMC e circunferência abdominal), desempenho em variáveis funcionais (preensão manual e teste de caminhada de seis minutos) e escores de qualidade de vida e fadiga, bem como as magnitudes de variação, via questionário, antes e após 12 semanas de um programa de treinamento físico combinado à distância (*home based*) em pacientes com câncer de próstata e mama.

HIPÓTESES

O presente projeto buscou um levantamento formal sobre a viabilidade para formulação de um ensaio clínico fase 3, sem hipóteses definidas nesta fase. Salienta-se que a formulação de hipóteses de efetividade ou eficácia não são recomendadas em estudos de viabilidade [62].

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Artigo 1

The “home-based exercise for breast and prostate cancer patients during treatment—a feasibility trial” (BENEFIT CA trial): rationale and methodological protocol

Pilot and Feasibility Studies

STUDY PROTOCOL

Open Access

The "home-based exercise for breast and prostate cancer patients during treatment—a feasibility trial" (BENEFIT CA trial): rationale and methodological protocol

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Abstract

Background Physical activity has been shown to benefit patients undergoing adjuvant cancer therapy. Although exercise interventions may be applied in several settings, most trials have focused on specialized facilities for their interventions. While these approaches benefit the access for individuals living near exercise centers, it hampers the assessment of real-world effectiveness. Therefore, evaluating the feasibility and implementation of home-based models of exercise training, especially in low-to-middle-income settings, may inform future physical activity trials and programs. In this article, we present the protocol for the BENEFIT CA trial, which aims to assess the implementation of a remote exercise intervention for patients with breast cancer or prostate cancer, primarily quantifying adherence to an exercise program.

Methods This is a 12-week study, utilizing a non-randomized, single-arm design to assess the feasibility of a home-based exercise training. The intervention is remotely guided, and participants also receive an educational component about cancer and exercise. The study aims to recruit 40 patients diagnosed with breast cancer and 40 patients diagnosed with prostate cancer, all of whom undergoing active hormonal treatment. The primary outcome is the level of adherence, indicated as the proportion of performed exercise episodes. Secondary outcomes include recruitment rates, fatigue, quality of life, and functional capacity. Adverse events will be monitored throughout the study. Because this is a feasibility trial, the statistical analysis plan is based on descriptive statistics, which encompasses an intention-to-treat analysis and a plan for handling missing data.

Discussion This is a low-cost feasibility study to orient the design of a wide-range, pragmatic phase 3 trial based on remote exercise intervention. With this study, we aim to better understand the adherence and implementation strategies regarding home-based exercise for the proposed population and, in the near future, move forward to a randomized clinical trial. In addition, this trial may contribute to engage patients with cancer in exercise programs throughout their treatment and beyond.

Trial registration This trial has been approved by the Hospital de Clínicas de Porto Alegre Ethics Committee/IRB (48,869,621.9.0000.5327), and it is registered at Clinicaltrials.gov (NCT05258526), registered on February 25, 2022, prior to the beginning of the study.

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Keywords Feasibility, Home-based, Physical activity, Exercise, Cancer

Background

There is a growing body of evidence indicating physical exercise plays a protective role against several types of cancer [1, 2], with a recent development of a Brazilian physical activity guide regarding recommendations to prevent and manage cancer [3]. Moreover, beyond the association with reduced risk of different types of cancer, exercise has been indicated during and after cancer treatment to improve overall fitness as well as to counterbalance side effects from pharmacological and surgical treatments [4, 5]. In addition, emerging studies have been exploring the potential association between physical activity and a reduced risk of breast cancer recurrence [4–6], further highlighting the potential benefits of an active lifestyle for individuals with cancer.

Numerous studies have investigated the relationship between cancer and exercise [1, 2, 6, 7], examining its impact before, during, and after treatment. Notably, the majority of these trials have been conducted in high-income countries, using supervised, face-to-face interventions [8–10]. However, many face-to-face programs rarely translate into public-wide implementation, since they are not designed to amplify the exercise strategies outside the training facilities [11–13]. Other difficulties to attend exercise sessions are associated with economic status, treatment side effects, and aesthetic factors that may influence the engagement in a face-to-face exercise program [4, 14]. To address this issue, other formats for exercise could be investigated as alternatives to amplify physical activity (PA) opportunities for the cancer population undergoing active treatment. With a remote follow-up, patients with cancer may achieve good levels of physical activity in an easier way and, even if the conditions are not ideal, enjoy the benefits of exercise training. The COVID-19 pandemic has prompted a rapid upsurge in the application of technology, providing a safe and affordable means of contact for patients and researchers. Nevertheless, the urgency to promote online care using smartphones and other remote ways should not reduce the attention to the promotion of patient engagement. With this in mind, it is important to analyze if these models are well accepted and feasible for patients with cancer [15].

Therefore, this study addresses the amplification of PA for individuals with cancer undergoing active treatment for breast or prostate cancer. In this regard, we seek to test a low-cost, pragmatic intervention designed to increase the number of patients involved in exercise programs. The study consists of a feasibility trial for the reduction in methodological uncertainties regarding the implementation of the home-based strategy, which will be potentially tested in a future phase-three randomized trial. This study intends to characterize the participant's level of adherence, as well as deepen the knowledge of possible barriers and facilitators for this type of intervention.

The main objective of this study is to evaluate the feasibility of a home-based exercise combined training by measuring adherence rates. The intervention includes educational contents related to health and cancer, which will be delivered through telephone, text messages, or email. The secondary objectives are to (1) evaluate the quality of life and fatigue levels, as well as their magnitude variations, through validated questionnaires, before and after a 12-week home-based combined training, with a remotely guided follow-up, and (2) assess the effects of 12-week home-based combined training on functional capacity, measured by 6-min walk test and hand grip strength. This study, being a feasibility trial, does not entail a formal hypothesis to be tested.

Methods

This single-arm feasibility trial was approved by Hospital de Clínicas de Porto Alegre (Ethics Committee/IRB: 48869621900005327) in the year of 2022. The trial will substantiate the decision regarding the design of a phase-three randomized clinical trial with remote approaches and clinical outcomes for cancer. This study, therefore, focuses on trial recruitment and patient acceptability, considering the disease and treatment aspects that may influence adherence to the proposed intervention. To qualify a possible future trial, this study might be used to facilitate public and patient involvement [16, 17].

Sample size calculation

Because this is a feasibility study, the study may preclude formal sample size calculation. Therefore, we predefined a total sample target of 80 participants, resulting in 40 patients for each cancer type (breast and prostate cancer). Assuming a potential dropout rate of 50%, we could anticipate that at least 20 participants for each cancer would complete the study.

Outcomes

The study's primary outcome is the participants' level of adherence to the planned exercise episodes. This outcome is measured by the cumulative number of times participants self-report engaging in the exercise program

from a total of 36 sessions prescribed in the program. This outcome is measured through weekly assessments carried out by phone call or text message. The cumulative number of self-reported engagement in sessions will be converted to percentages.

This study also addresses variables that may be relevant to methodological feasibility, participant safety, and potential direct effects of the exercise program, as follows:

1. Participate recruitment and engagement: this includes the number of participants selected and consenting to participate in the study, how participants were recruited, and participant attrition. This variable is assessed from the first contact with a potential individual with breast or prostate cancer until a decision regarding eligibility and study participation is reached [18].
2. Adverse events: the study team conducts weekly checks by phone call with participants to identify any potential adverse events, such as physical injury or mental/emotional issues.
3. Fatigue and quality of life: these variables are assessed using the Functional Assessment of Cancer Therapy Questionnaire [19]. The questionnaire comprises specific items that capture various aspects of fatigue and quality of life, and these items are combined to generate standardized values. The questionnaire is used in a pre-/post-text format in order to identify change throughout the study.
4. Functional capacity: a pre-/post-format is used to determine any changes in participants' functional capacity. These tests are conducted in person to measure participants' performance on the 6-min walk test and the hand-grip test.

Open feedback from participants

At the conclusion of the study, participants will be invited to participate in a focus group, wherein discussion questions pertaining to the study's intervention and outcomes will be used. The mode of conducting the focus group, either in-person or virtually, will be determined based on the availability and preferences of the participants.

Additional measures

To analyze the participants' initial PA levels, we will utilize the International Physical Activity Questionnaire (IPAQ), which will be administered at the beginning of the study. In addition, height, body weight, and abdominal circumference will be measured in-person, in a pre-/post-format. Lymphedema control circumferences will be measured in a pre-/post-format for female participants, regardless of their history of lymphedema. This measurement aims to provide participants with information about the limits of PA following surgery.

Study procedures

This study accounts for eligibility screening and recruitment, participant consent, initial evaluations, intervention, final evaluations, and hearing for open feedback, as stated in the figure below (Fig. 1). Moreover, we have developed this protocol in accordance with the Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) guidelines [20] and have incorporated the CONSORT 2010 statement: extension to randomized pilot and feasibility trials [21], whenever applicable. Figure 2 shows the SPIRIT timetable.

Eligibility screening and recruitment

To assess the eligibility of prospective individuals, a comprehensive screening plan was developed and is publicly available at the following link: (https://osf.io/n7g5p). The plan is detailed and thoroughly explained. This screening plan is uniformly employed for all potential participants, regardless of how they are recruited to the study. The study uses three methods of recruitment, which are as follows:

1. Referral from the hospital lists: this method involves obtaining patient lists from the oncology and urology clinics at the Hospital de Clínicas de Porto Alegre, Brazil. The lists include patients currently receiving treatment at the hospital.
2. Referral from professionals: In this approach, patients who appear to meet the eligibility criteria for the study are referred by healthcare professionals, such as oncologists, who have treated patients in their offices. These professionals identify patients who could potentially participate in the study and refer them to the study recruiting team.
3. Open advertisement: use of media, such as newspapers and social media (Instagram and Whatsapp) for propagation of the study.

Nevertheless, because of recruitment rates from the initial weeks of the project, we already have put to use the open advertisement.

Inclusion criteria

The following are the breast cancer patients' inclusion criteria:

(a) Age equal or superior to 18 years old.
(b) Living in the city of Porto Alegre or Porto Alegre Metropolitan Region.

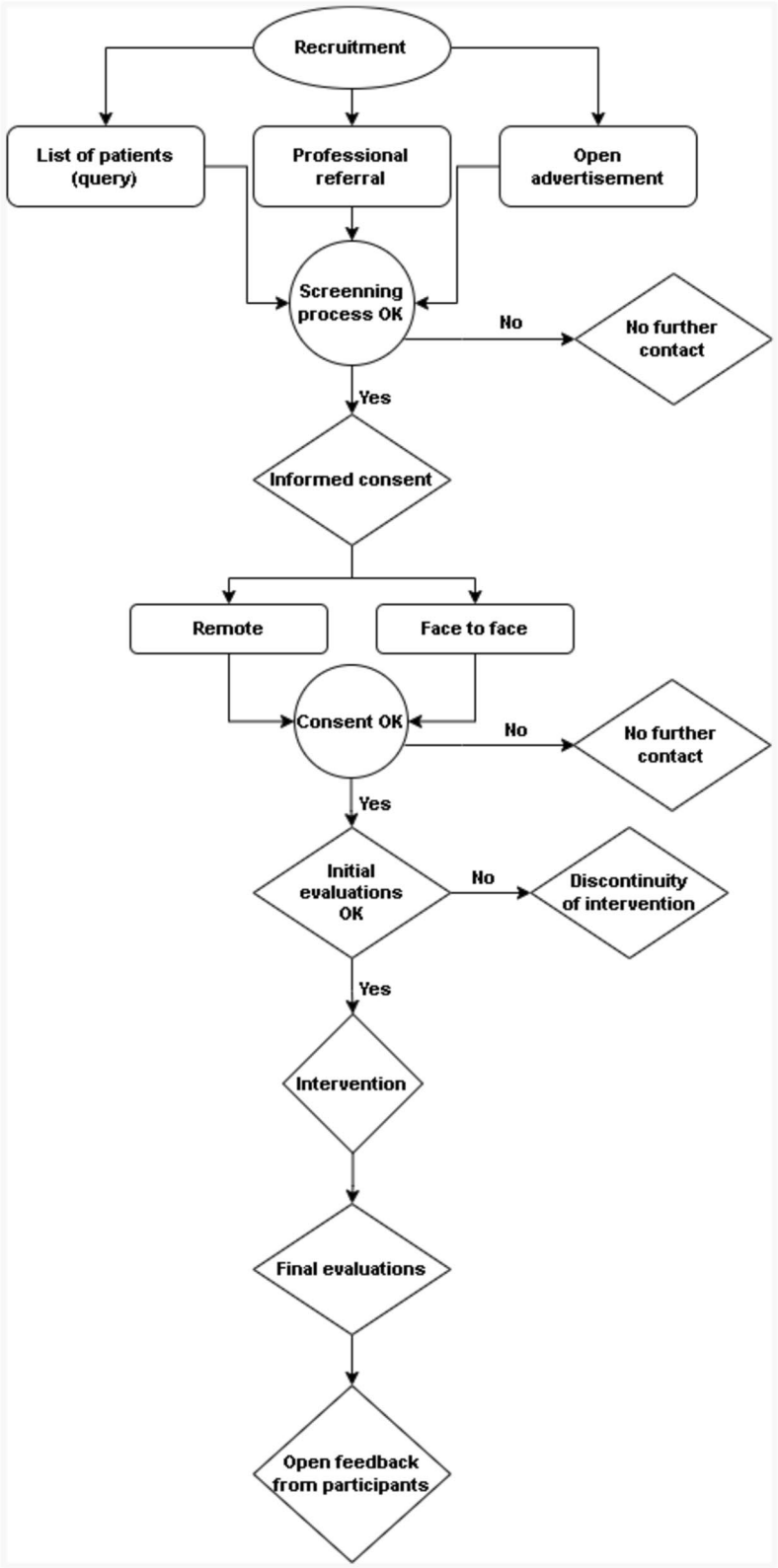

Fig. 1 Study flow diagram

STUDY PERIOD					
		Exercise training			Close out
TIMEPOINT	**Screening**	**Baseline**	**Week 1**	**Week 12**	**Qualitative Evaluation**
ENROLMENT:					
Eligibility screen	X				
Informed Consent	X				
INTERVENTIONS:					
Intervention: Exercise			←	→	
ASSESSMENTS:					
Baseline variables		X			
Follow-up variables				X	
Feasibility variables			←	→	
Open feedback from participants					X

Fig. 2 Study timetable with a specific period. SPIRIT figure regarding the study's phases

(c) Diagnosis of breast cancer stages 0 to III.
(d) Undergoing hormonal treatment/manipulation isolated or combined with other methods.
(e) Initiation of hormonal treatment/manipulation (such as anti-estrogen therapy) isolated or combined to others within the 3 months before enrolment and continued treatment at the beginning of the trial.
(f) Planning for consistent use of the hormone manipulation treatment throughout the intervention period.
(g) Ability to independently perform PA, including walking without assistance and engaging in daily chores such as standing up and sitting down a chair. This capability is verified during the initial contact by phone and in-person during the initial assessments.
(h) Not regularly practicing physical exercise (more than once a week) for the past 3 months.
(i) In case the patient has undergone some surgical procedure, they must have medical clearance for exercise training before participating in the study.

The following are the prostate cancer patients' inclusion criteria:

(a) Age equal or superior to 18 years old.
(b) Living in Porto Alegre or Porto Alegre Metropolitan Region.
(c) Localized prostate cancer diagnosis.
(d) Having initiated the hormonal treatment/manipulation (such as anti-androgen therapy) isolated or combined to others in the 3 months prior to the study enrollment and being under this treatment at the beginning of the trial.
(e) Ensure consistent and planned administration of hormonal therapy/manipulation throughout the entire intervention period.
(f) Ability to perform PA on their own, such as being able to walk without assistance and perform daily chores, such as standing up and sitting down a chair. This is verified during the initial contact by phone and in-person, during the initial evaluations.
(g) Not regularly practicing physical exercise (more than once a week) for the past 3 months.

(h) In case the patient has undergone some surgical procedure, they must have medical clearance for exercise training before participating in the study.

Exclusion criteria

The following are the exclusion criteria:

(a) Patients presenting metastatic disease or active loco-regional prior to their enrollment.
(b) Inability to understand the terms and study conditions, language, hearing and cognition difficulties, or any major psychiatric issues or hindrances.
(c) Simultaneous participation or a family member in the same household, already engaged in the study.
(d) Moving plans or a trip that causes an absence greater than 2 weeks throughout the study length.
(e) Medical history of cardiovascular disease (with the exception of hypertension under the use of medication) or severe cardiopulmonary disease, such as history of heart attack, revascularization procedures, deep venous thrombosis, cerebrovascular accident, or pulmonary embolism in the past 12 months.
(f) Chronic pulmonary disease requiring use of oxygen or corticosteroid therapy.
(g) Kidney disease with use or about to initiate dialysis, or yet, on the waitlist for a kidney transplant.
(h) Severe nausea, anorexia, or any other condition that does not allow the performance of exercise;
(i) Presentation of a medical report stating any contraindications or medical conditions that are incompatible with exercise training.

Patient consent

The patient consent is set by the reading, clarifications, and agreement of the informed consent form (https://osf.io/f24dn). This study utilizes two consent form procedures: a remote form, sent by email for the patient to read and decide his/her consent to participate in the study, and a printed form, which the patient signs during the face-to-face meeting, as requested by the local IRB. In addition, the consent form has two consenting parts: one related to consent to participate in the study and another related to data sharing in an anonymized approach, in a public repository. For example, if the patient, by any reason, cannot go to the hospital facilities to take part in the evaluations, the research team can visit the patient at his/her home.

Initial evaluations

Health, demographic, fatigue, quality of life, and physical activity questionnaires

All the questionnaires are answered (after the completion of the informed consent form). To note, sanitary recommendations set by the WHO [22] have been followed, in case of in-person contact.

The measurements of fatigue and quality of life scores are achieved through answering of specific scales for each sex: women will answer the *Functional Assessment Cancer Therapy Breast* (FACT-B) questionnaire, on its Portuguese version, whereas men will answer the *Functional Assessment Cancer Therapy Prostate* (FACT-P) questionnaire, on its Portuguese version. Such questionnaires are derived from the questionnaire *Functional Assessment of Cancer Therapy—General* (FACT-G), which is also being applied to the participants. The FACT-B and FACT-P comprise the instrument FACT-G and the domain "Additional Worries," composed by 10 and 12 questions regarding specifically to symptoms and issues from breast and prostate cancer, respectively. In total, we have 37 and 39 questions divided into 5 domains (physical well-being, social/family, emotionally, functionally, and additional worries). Each answer may vary from 0 (worst state of health) to 4 (best state of health).

PA is measured through the IPAQ, in its long version, in Portuguese. This instrument has 5 domains (PA at work, PA as a means of transportation, home chores, recreational activities, sport, leisure, and sitting time), totalling 27 items.

Six-minute walk test (6 MW)

The 6-min walk test 6 MW assesses an individual functional capacity to continuous walking for 6 min at a steady pace, aiming to cover the highest distance in meters. This procedure is held in a flat environment, 25 m wide, with visual markers placed every 3 m. The subjective effort is measured by the Borg scale at the beginning and at the end of the test. Standard stimuli are given to each individual at every minute of the test [23].

Handgrip test

The handgrip strength is assessed by manual dynamometry in both hands. The test consists of 3 attempts in each hand, with a minute apart from each attempt. The individual stands, with elbows flexed in a 90° angle and performs the maximum possible strength for 4 s. The highest value is chosen as the result of the test [24].

Anthropometric profile

To characterize the anthropometric profile, body mass (kg), height (cm), and abdominal circumference (cm)

are measured, following the standards from the International Society for Advances in Kinanthropometry (ISAK). Besides this, there are measures of lymphedema control for patients with breast cancer, with measurements at four circumference points: metacarpophalangeal joint, fist, 10 cm away from the lateral epicondyle and 12 cm in proximity to the lateral epicondyle regarding the superior limbs from each female patient, in a pre-/post-format. Differences larger than 2 cm at any point represent a statistical difference and, therefore, a lymphedema [25].

Training simulation

The research team provides training simulations of the exercises when the participants visit the laboratory or receive at-home visits. In addition, participants receive virtual or printed material as a visual aid for their workouts. The research team records the technical aspects (e.g., movement specificities) regarding the exercise performance so that these may be approached, if needed, in the follow-up telephone calls.

Intervention, contacts, and adverse events

The trial intervention was designed taking into account three major aims: (1) to offer a pragmatic intervention that could be adaptable for the public health system and scaled up depending upon the available setting for exercise training, (2) to implement an exercise program jointly to an educational component, and (3) to implement the intervention as remotely as possible so that the intervention could reduce accessibility and mobility barriers to exercise.

Both breast and prostate cancer patients receive, prior to the beginning of the trial, the same instructions to exercise at their homes, parks, or other places they feel comfortable, three times a week, at hours and days of their choice. Telephone calls, text messaging, and e-mail are conducted to follow up the patients' progression and their health status, to record possible issues, and to motivate them to continue exercising (all material is available at https://osf.io/3zcfn/).

During the weekly contact with the participant, adverse events that may have occurred are accounted for. Events or issues throughout the study length (e.g., sickness, fall, neuromuscular injury) are computed as adverse events, being classified according to their severity (mild, moderate, severe), predictability (expected or unexpected), and potential relation with study procedures (definitely related, possibly related, or unrelated).

Final evaluations

Aside from the participant's informed consent, the health and demographic questionnaires and the PA levels, fatigue and quality of life questionnaires, and anthropometric and functional capacity evaluations will be carried out again, during up to two visits to the laboratory or participants' home.

Statistical considerations

We will primarily follow intention-to-treat principles, therefore accounting for all participants in analyses, regardless of their level of adherence. One participant will be considered to be entered in analysis (analysis set) after completing baseline assessments. If the participant withdraws before the completion of baseline assessments, he/she will be presented in the flowchart but will be considered a loss before the intervention's allocation.

Statistical data treatment will be mostly by descriptive statistics, through means or medians for discrete and continuous variables, and frequencies (absolute and relative) for categorical variables, with their respective precision measures (ranges or 95% confidence interval). The Shapiro–Wilk test will be carried out to assess whether the main continuous outcomes follow a normal distribution.

We will use general estimating equations (GEE) to compare means over time (pre-post-assessments). For categorical variables, we will use the McNemar test, comparing data regarding the pre- and post-intervention moments.

Regarding missing data, we will employ different strategies for different variables. For the quality of life and fatigue scores, the last observation carried forward (LOCF) imputation method will be used. For the training sessions, a missed value will be considered as a non-attendance, since the trial accounts for multiple forms of contact that can verify if the participant performed or not the session.

Criterion to move forward to a phase 3 randomized controlled trial

The primary criterion for advancing to a randomized controlled trial (RCT) is based on the weekly adherence to the exercise sessions by at least 40% of our sample. To determine adherence, we defined a threshold of one or more exercise sessions per week for a minimum of 8 weeks, irrespective of the completion or non-completion of the intended exercise protocol. Consequently, if we have a total of 40 patients, and at least 16 of them consistently perform the exercise program more than once per week over 8 weeks, they will be classified as adherent, even if they did not fully complete the proposed exercises or if a session is partially incomplete.

In case the progression criterion is reached, other aspects such as adverse events, recruitment performance, overall satisfaction, and patient engagement will be considered to design a future trial.

Ethical and safety issues

A brief guideline was developed for patients to observe themselves at the moment of engaging in exercise (material available at: https://osf.io/xjgfh). In addition, there are some safety criteria observed during the study's achievement, such as:

- During the health questionnaire, the evaluations or the intervention, in case of any disorder, cardiopulmonary, and/or important neuromuscular dysfunction, there will be performed an additional analysis, along with the medical staff, to determine the continuity or not of the patient in the study.
- For any intercurrence that needs medical care, the researchers will immediately contact the emergency health centers from the surrounding regions.
- Absolute medical contraindications to patient participation in the study: recent modification in the rest electrocardiogram (ECG) indication of myocardial ischemia or other acute event (< 2 days), myocarditis or acute pericarditis, and systemic acute infection.
- Assessing medical eligibility and identifying contraindications for continued study participation: severe episode of hypertension (systolic blood pressure (SBP) > 200 mmHg or diastolic blood pressure (DBP) > 100 mmHg), tachydysrhythmia or bradyarrhythmia, hypertrophic cardiomyopathy, high degree atrium-ventricular blockage, decompensated metabolic disease, and chronic infectious disease.

The research team clarifies the participants that they can drop out the study at any time, for any reason they judge relevant. If a participant has a contraindication to exercise at a particular moment, this decision will be respected and the intervention will be discontinued. In addition, if there is any harm related to the intervention, or the occurrence of a major adverse event, the research team will provide assistance in a face-to-face or remote manner, contacting emergency and facilitating as much as possible the aspects related to the participant's safety.

Data management and dissemination

The handling, identification, and storage of generated and collected data, along with procedures regarding the data monitoring process, are described in our publicly available Data Management Plan (DMP; https://osf.io/8725a). According to the FAIR principles, this plan foresees the use of a standardized dictionary (NCI Thesaurus) for available variables, which seeks to increase tracking, interoperability, and possibility of research data. All the media materials used in this study have been made available for reuse throughout open platforms, such as Open Science Framework (OSF).

Ancillary, post-trial care, and harm from trial participation

All participants will receive results from the assessment carried out during the study, with available information that may assist their cancer treatment and overall healthcare. However, due to the feasibility nature of the trial and non-pharmacological intervention, no formal post-trial care (e.g., continuation of exercise prescription) is planned to be provided. However, at the end of the feasibility trial, the patients will be called out to participate in a focus group to discuss their views and choices of outcomes of this and future trials.

Discussion

This feasibility trial seeks to better understand and evaluate the home-based exercise training model, its implementation, and its acceptance by patients with breast or prostate cancer undergoing treatment. Since several clinical and contextual reasons may preclude patients from attending exercise training facilities, considering exercise at home could be beneficial and more inclusive for patients undergoing cancer treatment.

Although our intervention inevitably carries some risks, such as possible discomfort during the workouts, injuries related to exercise, excessive fatigue, muscle soreness, or others, we underscore that our aims include monitoring any adverse events. This contributes to characterizing potential harms induced by exercise training and tailor programs that may reduce or better handle such issues. Additionally, the use of web-based technology, through the use of phone messaging, may impair the intervention delivery for some participants. In this regard, we also offer conventional (phone or paper based) contacts and evaluations formats.

We anticipate that the motivation to exercise could be lower in remote intervention when compared with face-to-face approaches. Therefore, accounting for this potential scenario, the feasibility design allows us to "fail fast," without the spending of major resources, especially reducing the burden for trial participants. Alternatively, in a best case scenario, in which we detect moderate to high adherence to the proposed intervention, we can proceed with necessary adjustments and expand this investigation to a confirmatory trial, with substantial public and participant involvement. Based on a flexible approach to contact patients, adequate contact frequency, and open channels for discussions and support, it is reasonable to expect this research program is well positioned to move forward.

In summary, this pragmatic, low-cost feasibility trial seeks to test a model to distribute exercise interventions

more widely to people with breast or prostate cancer. Although exercise training has been consistently shown to benefit patients under active cancer treatment, reducing fatigue, improving neuromuscular status, and increasing quality of life [4, 5, 14, 26, 27], research oriented to a public health setting is needed to tailor interventions in a more equitable way, leaving no patients behind regarding their opportunities to engage in PA.

Trial status

By the moment of the submission of the present protocol, 10 women and 3 men have been recruited and engaged in intervention.

Registration

This trial has been approved by the Hospital de Clínicas de Porto Alegre Ethics Committee/IRB (48869621900005327), and it is registered at Clinicaltrials.gov (NCT05258526), registered on February 25, 2022, prior to the beginning of the study.

Protocol version

This manuscript is in its first version, dated as of May 25th, 2023.

Abbreviations

CAPES	Coordenação de Aperfeiçoamento de Pessoal de Nível Superior
DMP	Data Management Plan
DBP	Diastolic blood pressure
ECG	Electrocardiogram
FACT-G	Functional Assessment of Cancer Therapy-General
FACT-B	Functional Assessment Cancer Therapy Breast
FACT-P	Functional Assessment Cancer Therapy Prostate
FAIR	Findable-Accessible-Interoperable-Reusable-principles of data sharing and management
FAPERGS	Fundação de Amparo à Pesquisa do Estado do Rio Grande do Sul (Research Support Foundation of the State of Rio Grande do Sul)
FIPE	Fundo de Incentivo à Pesquisa
GEE	General estimating equations
HCPA	Hospital de Clínicas de Porto Alegre-City Hospital at Porto Alegre
IPAQ	International Physical Activity Questionnaire
IRB	Institutional Review Board
ITT	Intention-to-treat analysis
LOCF	Last observation carried forward
OSF	Open Science Framework
PA	Physical activity
RCT	Randomized controlled trial
SBP	Systolic blood pressure
SPIRIT	Standard Protocol Items: Recommendations for Interventional Trials
WHO	World Health Organization

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We would like to thank the thesis committee from this PhD project, which pointed out considerations to make this study more feasible. In addition, we thank the research participants in advance.

Protocol amendments

Any modifications to the protocol, which may impact relevant changes to study procedures (such as changes in eligibility criteria, assessments, information on risk/benefit) or to administrative routine, require a formal amendment to the protocol. These modifications should be approved by the ethics Committee/IRB prior to their implementation. So far, we are preparing the first amendment, which has some changes that do not impact the intervention itself or the main outcome.

Authors' contributions

LXNS, JSL, ACI, FDM, LOF, LASC, TSA, and DU contributed to the original draft preparation, reviewing, editing, and critical review. During the intervention, LXNS, JSL, FDM, and LOF will be involved in patient's recruitment. LXNS and JSL will be involved in remote informed consent procedures and remote evaluations. LXNS and FDM will be involved in face-to-face evaluations. ACI will be involved in data's organization and conference. LXNS, FDM, LASC, and TSA will be involved in patient's communication and data dissemination. DU will oversee all the study procedures. All authors have read and approved the manuscript.

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Availability of data and materials

Supplementary data and study materials are at the project's OSF page, available at https://osf.io/3zcfn/.

Declarations

Ethics approval and consent to participate

This trial has been approved by Hospital de Clínicas de Porto Alegre Ethics Committee/IRB (48869621900005327), and it is registered at ClinicalTrials.gov (NCT05258526), prior to the beginning of the study. The informed consent forms (remote and face-to-face) include the study's objectives, description of the testing procedures, explanation about the intervention, the potential risks and benefits involved in the study, the costs to the participants and information on anonymized data sharing. The investigator in charge of providing study clarifications and seeking the participant's ethical consent should send the remote informed consent form in advance, allowing the patient sufficient time to read, ask questions and decide to participate or not in the trial. If the patient does not agree or does not have a literacy in e-mailing, text messaging, and other forms of remote contact, by the time of the face-to-face interaction with the research team, there will be given enough time for the patient to read and ask questions, deciding whether or not to participate in the trial. It is important to notice that, if for the patients who have agreed to the remote consent form, at the time for the face-to-face evaluations, a paper signed consent form should be obtained. Once a patient decides to participate, a signed and personally dated informed consent is obtained from the patient before any trial-related procedure. A copy of the consent form is given to the participant (electronic and paper), and these procedures are documented in the patient's record.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests. The funders had no role in the design of the study at any stage.

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Publisher's Note

Article 2

Recruitment rates, adverse events, adherence, quality of life, functional outcomes levels and focus group findings from the BENEFIT CA trial.

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Abstract

Despite evidence supporting the safety and benefits of exercise for cancer patients, there remains a limited adoption of physical activity as a non-pharmacological intervention. This study aimed to describe recruitment strategies, willingness to engage and adherence to a 12-week physical activity program for breast and prostate cancer patients through a low-cost, pragmatic, and unsupervised intervention model. A total of 482 individuals were contacted (54.9% females; 45.1% males). Of these, 180 people were fully screened and 21 individuals consented to participate (3 men and 18 women), with the vast majority being of white patients. We used descriptive statistics and general estimating equations to assess pre-post intervention changes. Despite suboptimal recruitment rates, we reached the progression criterion to feasibility in order to move forward to a phase three randomized controlled trial in breast cancer patients. For the prostate cancer patients, no target recruitment rate was reached for the predefined eligibility criteria. Importantly, 85.7% of the patients met our adherence criteria for the intervention. For the women, 53% of the sessions included in the 12-week training program were performed as planned, without reducing any prescribed exercise set or walking time. There were no adverse events related to the intervention. In addition, the results showed either a maintenance in body weight, fatigue and quality of life scores and handgrip strength or an improvement in abdominal circumference and the distance in the six minute walk distance test. Focus group discussions highlighted diverse barriers throughout the cancer journey, with unanimous patient interest in a trial

duration of at least one year. We highlight the importance of diversifying our patient sample and the need to rethink eligibility criteria to reach other ethnic and socio demographic groups.

Keywords: breast cancer, exercise training, telehealth, recruitment.

Introduction

Cancer, a leading global cause of death, accounted for nearly 10 million fatalities in 2020, approximately one in six deaths, and, accounting for the most prevalent types, we have breast, lung, colon, rectum, and prostate cancers, with one-third of these deaths attributed to factors like tobacco use, high body mass index, alcohol consumption, low fruit and vegetable intake, and insufficient physical activity [1]. In the triennium spanning from 2023 to 2025, Brazil is anticipated to witness 704,000 new cancer cases per year (483,000 excluding non-melanoma skin cancer), with breast (10.5%), prostate (10.2%), colorectal (6.5%), lung (4.6%), and stomach (3.1%) cancers projected to lead the rankings in terms of prevalence [3]. In the context of cancer treatment, exercise is associated with preventing, managing treatment side effects, enhancing treatment responses, and reducing recurrence and mortality rates [2–6]. In Brazil's 2019 National Health Survey, 34.2% of adult men and 34.2% of adult women met the recommended levels of physical activity (PA) during their leisure time [7]. Regarding insufficient PA levels, 47.5% of women and 32.1% of men were classified as insufficiently active when considering physical activity during leisure time, work, and commuting [7].

Despite this, there is a paucity of studies on cancer survivors in low and middle-income countries, including Brazil. Data from the 2013 National Health Survey indicated that 31.6% of cancer survivors in Brazil did not achieve at least 150 minutes of physical activity per week [8]. Comparable studies in North America and Europe reveal that the majority of cancer survivors fail to meet recommended physical activity levels, with adherence ranging from 17% to 47% [9].

According to the National Institute of Cancer (INCA), in 2018, the federal direct healthcare costs related to cancer were approximately US$ 1.6 billion. Within this total, US$ 631 million were attributed to cancers associated with insufficient leisure-time physical activity. The highest costs among these activity-related cancers were observed in breast cancer (US$ 366 million), followed by colorectal cancer (US$ 245 million) and endometrial cancer (US$ 20 million). The costs associated with cancers linked to insufficient leisure-time physical activity were notably higher in women (US$ 507 million) compared to men (US$ 123 million) [10]. In the year 2040, it is projected that approximately US$ 3.4 billion in federal direct healthcare costs in Brazil will be allocated to addressing cancer. Within this total, an estimated US$ 1.5

billion is expected to be attributed to costs associated with cancers linked to insufficient physical activity [10].

Despite evidence pointing to the safety and numerous benefits of exercise for the cancer population [5,11,12] there is still a low uptake of physical activity in comparison to other chronic diseases. Barriers such as disease burden, lack of knowledge, lack of encouragement from the medical team, patient unawareness, economic constraints, and self-esteem and self-image issues [2,13–16]. Common models involve supervised training sessions, but many cancer patients lack access to such specialized services [2,3]. Within this scenario, alternative physical training models are suggested to encompass diverse populations and reach more patients. The COVID-19 pandemic accelerated technological advancements, enabling safe and cost-effective remote contact between patients and researchers; however, in the rush to implement remote care, little attention has been given to promoting patient engagement and assessing the viability and acceptance of these remote models [17].

The study aimed to improve physical activity in breast and prostate cancer patients through a low-cost, unsupervised intervention, emphasizing adherence, and evaluating health outcomes. It included comprehensive remote home-based training and focused on patient engagement through discussions, revealing insights into experiences. The primary goal was to assess adherence, identify adverse events, and evaluate the program's impact on functional variables, fatigue and quality of life.

Physical exercise has proven effective in improving both physical and psychological aspects associated with cancer treatment [2]. Since 2003, Courneya has emphasized the benefits of aerobic, strength, or combined training for women undergoing or post-treatment for breast cancer, positively impacting functional capacity, weight control, fatigue, and overall quality of life [2]. Exercise also mitigates treatment-related toxic effects, such as cardiotoxicity, by enhancing cardiorespiratory capacity, reducing lean mass loss, and minimizing abdominal fat gain. Similar benefits have been observed in men undergoing prostate cancer treatment, improving quality of life, reducing fatigue, and controlling weight [3,18]. Exercise addresses post-cancer challenges like increased body fat and muscle mass reduction, while also lowering the risks of cardiovascular and metabolic diseases,

reducing overall mortality rates, and decreasing the risk of cancer recurrence or new cancers [2,19–21] [4,22].

Methods

Study design

This single-arm feasibility trial was approved by Hospital de Clínicas de Porto Alegre (Ethics Committee/IRB: 48869621900005327) in the year of 2021 and adhered to the principles outlined in the World Medical Association Declaration of Helsinki. This trial substantiates the decision regarding the design of a phase three randomized clinical trial with remote approaches and clinical outcomes for cancer. This study, therefore, focused on trial recruitment and patient acceptability, considering the disease and treatment aspects that may influence adherence to the proposed intervention. To qualify a possible future trial, this study might be used to facilitate public and patient involvement [23,24]. In addition, this trial accounts for a data management plan, available at https://osf.io/8725a the published protocol for this trial can be found at: BENEFIT CA protocol. After the study protocol was published, we made one modification concerning the Consent Form. The form did not include a specified term regarding the focus group discussions. While the document provided explanations regarding the dynamics, we believed it could be better elucidated and clarified for the patients. Therefore, we performed an amendment to the Consent Form, incorporating an additional paragraph.

Study procedures

This study accounts for eligibility screening and recruitment, participant consent, initial evaluations, intervention, final evaluations, and hearing for open feedback. Moreover, we have developed this protocol in accordance with the Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) guidelines [25] and have incorporated the CONSORT extension to randomized pilot and feasibility trials [26], whenever applicable. While we had the option to collect data outside the Hospital's facilities, it ultimately proved unnecessary. All face-to-face procedures were conducted exclusively at the Hospital. Study data were collected and managed using REDCap electronic data capture tools hosted at Hospital de Clínicas de Porto Alegre [27,28] REDCap (Research Electronic Data Capture) is a secure, web-based software platform designed to support data capture for research

studies, providing 1) an intuitive interface for validated data capture; 2) audit trails for tracking data manipulation and export procedures; 3) automated export procedures for seamless data downloads to common statistical packages; and 4) procedures for data integration and interoperability with external sources.

Outcomes

The study's primary outcome was the participants' level of adherence to the planned exercise episodes. This outcome was measured by the cumulative number of times participants self-report engaging in the exercise program from a total of 36 sessions prescribed in the program. This outcome was measured through weekly assessments carried out by phone call or text message. This study also addressed other variables that may be relevant to methodological feasibility, participant safety, and potential direct effects of the exercise program, such as:

- patient recruitment and engagement in our trial, that includes the number of participants selected and consenting to participate in the study, how participants were recruited, and participant attrition [29];
- adverse events weekly checked by phone calls and messages with participants to identify any potential adverse events, such as physical injury or mental/emotional issues;
- functional capacity was used to determine any changes in participants' functional capacity. These tests were conducted in person to measure participants' performance on the 6-min walk test and the hand-grip test, in a pre-/post-format in order to determine any changes in participants' functional capacity;
- fatigue and quality of life were assessed using the Functional Assessment of Cancer Therapy Questionnaire [30]. The questionnaire comprises specific items that capture various aspects of fatigue and quality of life, and these items are combined to generate standardized values. The questionnaire is used in a pre-/post-text format in order to identify change throughout the study.

Open feedback from participants

Upon completion of the study, we extended invitations to participants for active involvement in a focused group discussion. This session aimed to delve into questions related to the study's intervention and outcomes. Opting for an in-person format, given the resolution of the pandemic scenario, we anticipated that this choice would foster more profound and spontaneous discussions, thereby enriching the overall dialogue.

Additional measures

Height, body weight, and abdominal circumference were measured in-person, in a pre-/ post-format. Lymphedema control circumferences were also measured in a pre-/post-format for female participants, regardless of their history of lymphedema.

Sample size

Because it is a feasibility trial, the study may preclude formal sample size calculation. However, we predefined a total sample target of 80 participants, resulting in 40 patients for each cancer type (breast and prostate cancer). Assuming a potential dropout rate of 50%, we could anticipate that at least 20 participants for each cancer would complete the trial.

Eligibility criteria

Inclusion criteria for both breast and prostate cancer patients

(a) Age equal or superior to 18 years old.

(b) Living in the city of Porto Alegre or Porto Alegre Metropolitan Region.

(c) Diagnosis of breast cancer stages 0 to III

(d) Undergoing hormonal treatment/manipulation isolated or combined with other methods.

(e) Initiation of hormonal treatment/manipulation (such as anti-estrogen therapy) isolated or combined to others within the 3 months before enrolment and continued treatment at the beginning of the trial.

(f) Planning for consistent use of the hormone manipulation treatment throughout the intervention period.

(g) Ability to independently perform PA, including walking without assistance and engaging in daily chores such as standing up and sitting down a chair.

This capability was verified during the initial contact by phone and in-person during the initial assessments.

(h) Not regularly practicing physical exercise (more than once a week) for the past 3 months.

(i) In case the patient has undergone some surgical procedure, they must have medical clearance for exercise training before participating in the study.

Exclusion criteria for both breast and prostate cancer patients

(a) Patients presenting metastatic disease or active loco-regional prior to their enrollment.

(b) Inability to understand the terms and study conditions, language, hearing and cognition difficulties, or any major psychiatric issues or hindrances.

(c) Simultaneous participation or a family member in the same household, already engaged in the study.

(d) Moving plans or a trip that causes an absence greater than 2 weeks throughout the study length.

(e) Medical history of cardiovascular disease (with the exception of hypertension under the use of medication) or severe cardiopulmonary disease, such as history of heart attack, revascularization procedures, deep venous thrombosis, cerebrovascular accident, or pulmonary embolism in the past 12 months.

(f) Chronic pulmonary disease requiring use of oxygen or corticosteroid therapy.

(g) Kidney disease with use or about to initiate dialysis, or yet, on the waitlist for a kidney transplant.

(h) Severe nausea, anorexia, or any other condition that does not allow the performance of exercise;

(i) Presentation of a medical report stating any contraindications or medical conditions that are incompatible with exercise training.

Patient consent

During the screening phone call, the researcher will kindly inquire whether the patient would be willing to provide consent for sharing their data in an anonymous format as part of open science initiatives, fostering a culture of openness and collaboration in scientific research. Should the patient opt not to participate in this aspect, their data will be securely retained solely for the use of our research team and will not be disseminated on open science platforms. In addition, this study utilized two consent form procedures: a remote form, sent by email for the patient to read and decide his/her consent to participate in the study, and a printed form, which the patient signs during the face-to-face meeting, as requested by the local IRB. The final patient consent is set by the reading, clarifications, and agreement of the informed consent form (available at https://osf.io/3zcfn/files/osfstorage#). Additionally, the printed consent form has two consenting parts: one related to consent to participate in the study and another related to data sharing in an anonymized approach, in a public repository. In addition, if the patient, by any reason, cannot go to the hospital facilities to take part in the evaluations, the research team can visit the patient at his/her home or other agreed location to perform the procedures .

Recruitment methods

We commenced recruitment in April 2022 and concluded in August 2023, utilizing various recruitment methods. These included a query (a list of patients requested from the hospital), the hospital's Facebook page and website, as well as its mailing list. Additionally, we utilized the UFRGS website, printed and virtual flyers, Instagram, WhatsApp, and face-to-face contact in the outpatient clinic. Posters were also displayed at a health center and we relied on word of mouth for further outreach.

Additionally, we pursued other avenues for recruitment that yielded no patients or substantial responses. These included attempts to connect with two medical doctors who are also professors, initiating phone calls, and sending detailed trial information via mail to specialized oncology clinics, as well as contacting medical doctors specializing in cancer care through social media platforms.

Screening and storing processes

Study data were collected and managed using REDCap electronic data capture tools hosted at Hospital de Clínicas de Porto Alegre [27,28] REDCap (Research Electronic Data Capture) is a secure, web-based software platform designed to support data capture for research studies, providing 1) an intuitive interface for validated data capture; 2) audit trails for tracking data manipulation and export procedures; 3) automated export procedures for seamless data downloads to common statistical packages; and 4) procedures for data integration and interoperability with external sources.

Participants' sociodemographic, health characteristics and physical activity levels assessment

Participants were contacted by phone to provide information regarding their age and race/ethnicity, which was categorized as black, brown, white, indigenous, oriental, and other. In either a virtual or face-to-face interaction, participants were queried about their educational attainment, specifically whether they had completed elementary school, high school, or higher education. Additionally, information about their health status, such as smoking, alcohol consumption and physical activity levels, throughout the International Physical Activity Questionnaire (IPAQ), on its long version, were collected.

Evaluations

Initial evaluations

Fatigue and quality of life questionnaires

The questionnaires were answered after the completion of the informed consent form. To note, sanitary recommendations set by the WHO [31] were followed, in case of in-person contact. The measurements of fatigue and quality of life scores were achieved through answering of specific scales for each sex: women answered to the Functional Assessment Cancer Therapy Breast (FACT-B) questionnaire, on its Portuguese version, whereas men will answered to the Functional Assessment Cancer Therapy Prostate (FACT-P) questionnaire, on its Portuguese version. Such questionnaires are derived from the questionnaire

Functional Assessment of Cancer Therapy—General (FACT-G): FACT-B and FACT-P comprise the instrument FACT-G and the domain “Additional Worries,” composed by 10 and 12 questions regarding specifically to symptoms and issues from breast and prostate cancer, respectively. In total, we have 37 and 39 questions divided into 5 domains (physical well-being, social/family, emotionally, functionally, and additional worries). Each answer may vary from 0 (worst state of health) to 4 (best state of health). In addition, the Functional Assessment of Chronic Illness Therapy: Fatigue Scale (FACIT-F), was applied to both men and women in this trial. This instrument is composed of 13 questions that assesses self-reported fatigue and its impact upon daily activities and function.

Anthropometric profile

To characterize the anthropometric profile, body mass (kg), height (cm), and abdominal circumference (cm) were measured following the National Society for Advances in Kinanthropometry (ISAK). Besides this, there were measures of lymphedema control for patients female patients, with measurements at four circumference points: metacarpophalangeal joint, fist, 10 cm away from the lateral epicondyle and 12 cm in proximity to the lateral epicondyle regarding the superior limbs from each female patient, in a pre-/post-format. Differences larger than 2 cm at any point would represent a statistical difference and, therefore, a lymphedema [32].

Handgrip test

The handgrip strength was assessed by manual dynamometry in both hands. The test consists of 3 attempts in each hand, with a minute apart from each attempt. The individual stood up, with elbows flexed in a 90° angle and performed the maximum possible strength for 4 s. The highest value was chosen as the result of the test [33].

Six-minute walk test (6 MW)

The 6-min walk test 6 MW assesses an individual functional capacity to continuous walking for 6 min at a steady pace, aiming to cover the highest distance in meters. This procedure was held in a flat environment, 27 m wide, with visual markers placed every 3 m. The subjective effort was measured by the Borg scale at

the beginning and at the end of the test. Standard stimuli were given to each individual at every minute of the test [34].

Training simulation

The research team provided training simulations of the exercises when the participants visited the laboratory (or would receive at-home visits). In addition, participants received virtual, and/or printed material as a visual aid for their workouts, as well as an elastic band to perform the exercises in our program. The research team recorded the technical aspects (e.g., movement specificities) regarding the exercise performance so that these could be approached, if needed, in the follow-up telephone calls.

Intervention, contacts, and adverse events

The trial intervention was designed taking into account three major aims: (1) to offer a pragmatic intervention that could be adaptable for the public health system and scaled up depending upon the available setting for exercise training, (2) to implement an exercise program jointly to an educational component, and (3) to implement the intervention as remotely as possible so that the intervention could reduce accessibility and mobility barriers to exercise. Both breast and prostate cancer patients received, prior to the beginning of the trial, the same instructions to exercise at their homes, parks, or other places they feel comfortable, three times a week, at hours and days of their choice. The 12-week training routine followed this order: a warm-up (~2 minutes), followed by walking, strength exercises (wall push ups, sit-to-stand from a bench or chair, wide row with elastic band, hip bridge on the floor or bed and sit-ups on the floor or bed) and stretching (~ 5 minutes). Patients initially walked for 15 minutes, gradually increasing the time to 30 minutes. Similarly, strength exercises started with one set and progressively increased to three sets. Telephone calls, text messaging, and e-mail were conducted to follow up the patients' progression and their health status, to record possible issues and to motivate them to continue exercising (all material is available at https://osf.io/3zcfn/). During the weekly contact with the participant, adverse events that could have occurred were accounted for. Events or issues throughout the study length (e.g., sickness, fall, neuromuscular injury) were computed as adverse events, being classified according to their severity (mild, moderate, severe), predictability

(expected or unexpected), and potential relation with study procedures (definitely related, possibly related, or unrelated).

Final evaluations

Aside from the participant's informed consent, the fatigue and quality of life questionnaires, anthropometric and functional capacity evaluations were carried out again, in a remote format, for the questionnaires, whenever it was possible or taken together with the anthropometric and functional capacity evaluations at the laboratory (or participants' home, if needed). After completing the final evaluations, we invited all participants to engage in an in-person focused group discussion. This informal, pressure-free setting aimed to discuss physical activity and exercise in the context of cancer, including cancer patients' views and feelings towards exercise and their participation in our study.

Statistical considerations

We followed intention-to-treat principles (ITT), therefore accounting for all participants in analyses, regardless of their level of adherence. One participant was considered to be entered in analysis (analysis set) after completing baseline assessments. If a participant withdraws before the completion of baseline assessments, he/she would be presented in the flowchart, but would be considered a loss before the intervention's allocation. Continuous data adhere to a descriptive format, delineating the total count, occurrence percentages, mean, median, minimum and maximum values, as well as standard deviation, contingent upon the specific outcome. Categorical data are presented in absolute and relative frequencies. The Shapiro–Wilk test was carried out to assess whether the main continuous outcomes follow a normal distribution. We used general estimating equations (GEE) to compare means over time (pre-post-assessments). For categorical variables, we used the Wilcoxon test, comparing data regarding the pre-and post-intervention moments. Regarding missing data, we have employed different strategies for different variables. For the quality of life and fatigue scores, the last observation carried forward (LOCF) imputation method was used. For the training sessions, a missed value was considered as a non-attendance, since the trial accounts for multiple forms of contact that can verify if the participant performed or not the session.The recruitment yields for women were determined by dividing the total

number of women contacted by the number who consented to participate in our trial. This method was equally applied to men. Additionally, we stratified these figures based on the form of recruitment, identifying the most effective method in both reaching and obtaining consent from participants for our trial.

All the results were analyzed in Google Sheets and in RStudio software, in its desktop version 4.3.2, with our data and codes publicly available at https://osf.io/3zcfn/files/osfstorage#. Regarding the focus group results, the primary analysis was performed on the Google Colaboratory platform, in the GPU environment, "Whisper" was installed within the platform using the command "!!pip install git+https://github.com/openai/whisper.git!sudo apt update && sudo apt install ffmpeg". The audio file was transferred into the Colaboratory environment, and the transcription command "!whisper "FILE NAME" --model medium" was applied. All these processes were performed in order to facilitate the transcription, however, after this initial analysis, a peer review process was applied, to ensure a proper transcription and the results were analyzed, also in a peer review format, in order to identify barriers and facilitators when it comes to exercise practice (Content Analyses).

Results

Figure 1 below depicts the flowchart detailing the process of screening and entrance for patients participating in our trial. The results of our statistical analyses revealed that all of our databases exhibited a normal distribution, except for handgrip performance in both the overall sample and specifically among female patients, during the pre-trial period.

For male patients, given their small number (only three), we opted to provide an additional file containing all the results, accessible through the following link: https://osf.io/3zcfn/files/osfstorage. For the male sample, in general, there was a single adverse event observed in a male patient, unrelated to our trial. Nevertheless, all three male patients successfully met our adherence outcome criteria.

Flowchart

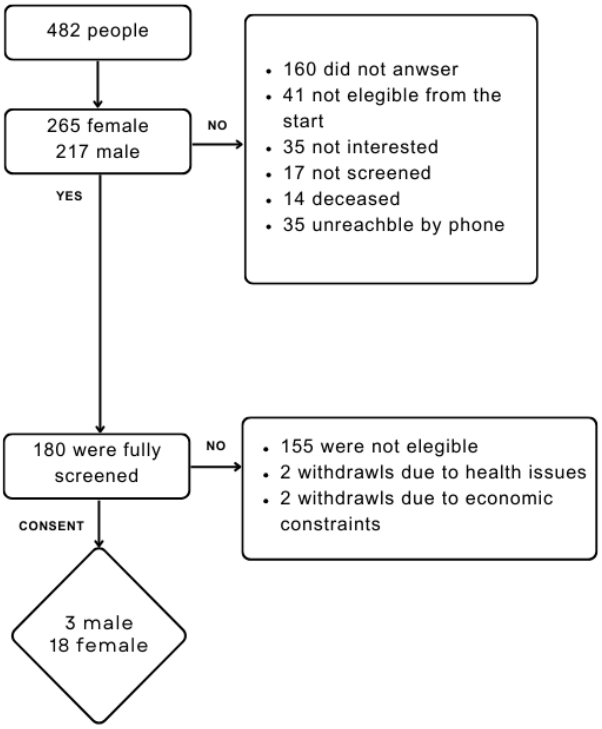

Figure 1: flowchart of patients contacted in the trial.

A total of 482 individuals were contacted for potential participation. From these, 265 (54.9%) were female and 217 (45.1%) were male subjects. We could fully screen 180 individuals and, from these, 21 consented to participate in our trial (Figure 1). There were 95 women and 85 men fully screened for this trial. For the women, there were 71 patients who were white, followed by 10 black, 8 brown, 1 indigenous and 5 patients who considered themselves as mixed races. For the men, the majority were still white, with 59 patients, followed by 13 brown, 8 black, 1 indigenous and 4 patients who considered themselves as mixed races.

Table 1 depicts age, residential area, and body mass index (BMI) by sex and race/ethnicity among women and men in our sample.

Table 1

Patients' characteristics						
	Ethnicity	**Age**	**Metastasis**	**Hormonal blockade**	**Living area**	**BMI**
		Mean ± sd	**Positive %**	**Positive %**	**Metropolitan region**	**Mean ± sd**
Women	71 white (74.7%)	53 ± 11	11.5%	62.1%	61 (85.9%)	29.4 ± 5.5
	10 black (10.5%)	56 ± 8	0%	8.4%	10 (100%)	30.5 ± 4.5
	8 brown (8.4%)	55 ± 8	0%	6.3%	5 (62.5%)	28.0 ± 3.8
	1 indigenous (1.1%)	66.0	0%	1.0%	1 (100%)	31.6
	5 other ethnicities (5.3%)	71 ± 9	0%	3.1%	5 (100%)	25.0 ± 2.2
Men	59 white (69.4%)	66 ± 7	15.2%	16.4%	53 (89.8%)	27.4 ± 3.8
	8 black (9.4%)	69 ± 7	1.1%	4.7%	7 (87.5%)	29.9 ± 5.6
	13 brown (15.3%)	68 ± 5	2.3%	5.8%	12 (92.3%)	26.8 ± 4,1
	1 indigenous (1.2%)	57	0%	1.1%	1 (100%)	27.3
	4 other ethnicities (4.7%)	68 ± 7	1.1%	0%	2 (50%)	23.0 ± 3.5

Age: values in years; sd: standard deviation; BMI: body mass index values in kg/m^2.

Recruitment methods results

The most common recruitment method was through institutional queries (electronic health records), constituting 67.77% of our recruitment efforts. Following, outpatient clinic contact with our research team accounted for 12.19%, while doctor referrals to contact us at the outpatient represented 5.77%. Other methods included Whatsapp (4.4%), Instagram (3.3%), Word of mouth (2.8%), Flyers (2.2%), Contact in other outpatient clinic (1.10%; not at the Hospital de Clínicas), Hospital's web page

(0.55%), UFRGS' web page (0,55%), E-mail (mailing list for Hospital's employees; 0.55%), and Health center posters (0.55%) (Figure 2).

Figure 2

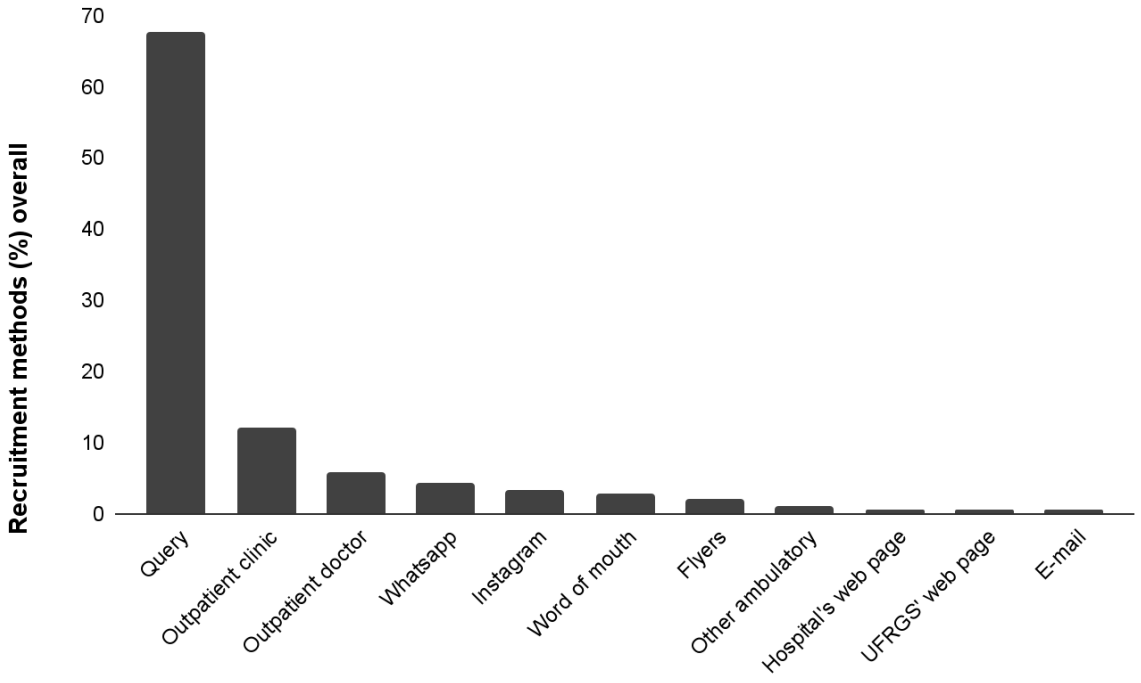

Figure 2: Number of people achieved through the different methods of recruitment, for both breast and prostate cancer.

Recruitment yield rates

In Figure 3, the chart illustrates the quantity of individuals contacted, indicating the number who provided consent and actively participated in our trial, categorized by cancer type. The overall recruitment rates were 19.0% and 3.5% for patients with breast and prostate cancer, respectively. The electronic health records obtained by the institutional query method provided the highest yield rate (11.6%) for recruiting breast cancer patients.

Figure 3

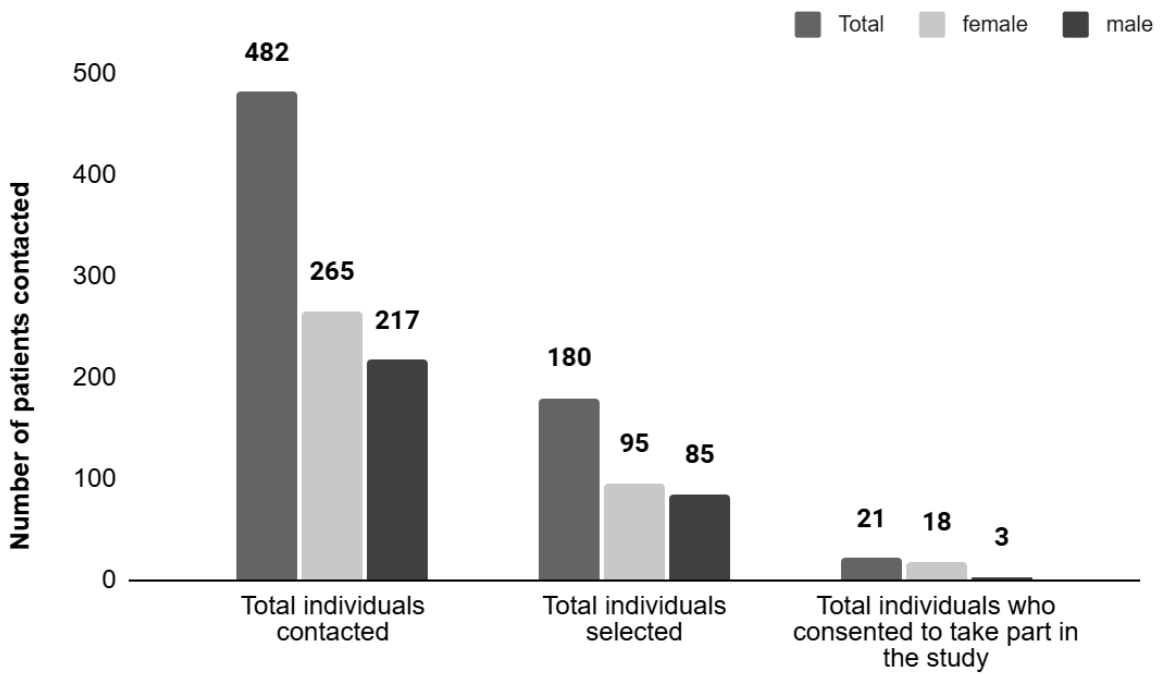

Figure 3: Number of individuals contacted and how many consented in participating in the trial.

Absolute recruitment per cancer type

In Figure 4, the chart illustrates the quantity of individuals contacted, categorized by gender, and specifies the method of contact applied. It is evident that, among the 95 female and the 85 male patients, the most prevalent method was the query, followed by the contact with the patients at the outpatient clinic.

Figure 4

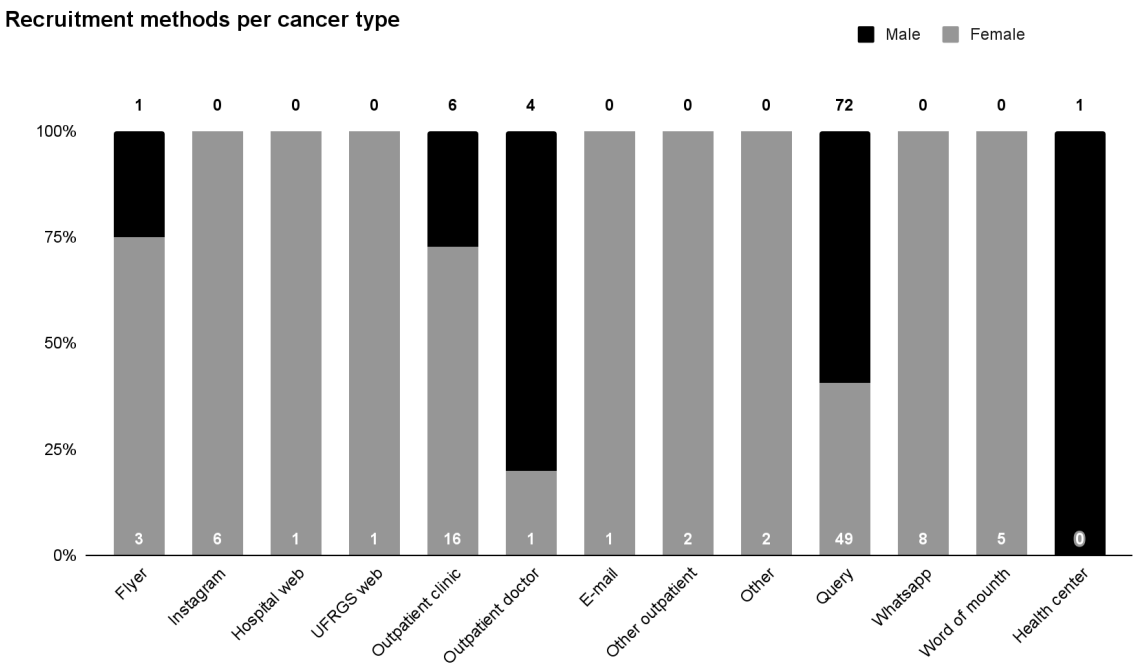

Figure 4: Number of individuals contacted by sex and which method of recruitment was employed.

Eligibility status

As stated in the flowchart (figure 1), out of the 180 subjects screened, a large portion of our sample was not eligible, since only 21 patients have engaged in our trial. As we can see in Table 1, there was a significant portion of patients who were at a metastasis stage and/or were not being under hormone blockade treatment, with this being a most common factor among the male sample. Other aspects that influenced the eligibility status among men were: one was not a cancer patient, four had health situations that prevented them from engaging in the trial, three exercised on a regular basis, more than one time per week and two didn't answer our returning calls. As for the women, four were not cancer patients, one had a health condition that prevented her from engaging in our trial, four had a physical impairment that prevented them from exercising in safety, on their own, twenty four exercised on a regular basis, more than one time per week, four dropped out before before signing

the consent form (2 due to health issues and 2 due to economic constraints) and fifteen didn't answer our returning calls.

Technology literacy

The majority (76,66%; 138 patients) of our screened patients reported having the abilities to use a smartphone or computer to engage in social applications, send and open a photograph and read an email. Only 40 patients (8 female and 32 male) reported not having the necessary skills for that, and 2 male and 2 female patients did not answer. For the 21 patients engaged in our trial, we have collected data regarding scholarly status, and a few health indicators, such as physical activity levels and alcohol consumption.

Scholarly status

The educational background of the patients in the study reveals a diverse range of academic achievements. Notably, all male patients and eleven female patients successfully completed their high school education, showcasing a substantial portion of the sample with this academic milestone. Additionally, one male and six female participants attained a completed college degree, with all of them belonging to the white ethnic group. However, one male and one female patient had not completed their college education. In terms of elementary education, all male and sixteen female patients had completed their elementary school. However, two female patients did not finish their elementary school.

Primary outcomes results

Adverse events

Throughout the entire trial, there were observed five adverse events **not related** to the trial: four events in the female sample and one in the male sample. However, in the interest of transparency and to help other researchers to learn from our experiences and to develop better trials, we have reported them all to the IRB Committee and the details can be found here: https://osf.io/bxndg**.**

Adherence

To be considered adherent to our trial, we previously have established that the patient should have engaged in at least two weekly sessions, in a complete or

incomplete format, for the first eight weeks to the trial and, for the trial to be successful in terms of adherence, this behavior should accompany 40% or more of our sample. With 85.71% of our sample, including 15 female patients and all 3 male patients, meeting these criteria, we have successfully reached our adherence outcome cutting point.

For the women, 53,24% of the twelve week training program was performed in a complete form, that is, without reducing any set or diminishing the walking time or not performing one part of the training program. For the men, this number was 75,92%. Only three women did not exercise three times a week, showing a more irregular frequency and missed training sessions. There was one female patient who exercised every day for the first 10 weeks of training and one who had her house fluted with water and lost her elastic band. She took two weeks to return to the training routine, the 7th and 8th she did not exercise and, even though, she was adherent to our trial. After the rain stopped, another elastic band was sent to her.

Another aspect addressed with the patients pertained to the implementation of training sheets. Specifically, patients were instructed to document their training sessions, either on paper or digitally, by annotating their perceptions of effort before and after walking, as well as following resistance exercises. Additionally, patients were requested to record the training days, details about exercise completion, and any additional difficulties or comments. Regrettably, this measure encountered poor acceptance among patients, leading us to omit its presentation.

Secondary outcomes

Patients' physical characteristics and functional capacity outcomes

The table below displays pre- and post-trial values for age, body mass index, abdominal circumference, hand grip performance, and the 6-minute walk performance test. The Wilcoxon test showed no significant differences for the BORG scale scores across evaluated moments: before and after the 6-minute walk test in both pre- and post-trial periods. Pre-trial BORG scores ranged from 6 to 13, with 6 being the most common, indicating no effort. Post-trial pre-test scores ranged from 6 to 15, with 6 being the most common. Post-trial post-test scores ranged from 7 to 17, with 7 being the most common, representing very light effort.

During the trial, technical issues with handgrip equipment necessitated transitioning from manual to digital equipment. Six patients used the original, and six used the digital version, with nine undergoing pre-trial testing with one type and post-trial testing with the other. Despite this deviation, minimal impact on data collection or interpretation is anticipated. Additionally, the pre-trial assessment of women's right hand did not exhibit a normal distribution.

Table 2

Age, physical characteristics and functional capacity outcomes for the female patients

	Age (years)	51.8 ± 9.98
Outcome	**Moment**	
	Pre	**Post**
BMI (kg/m2)	30.0 ± 3.66	29.5 ± 4.0
Abdominal circumference (cm)	103.0 ±9.9	99.3 ± 9.6
Left hand grip force (kg.f)	23.4 ± 6.6	24.6 ± 5.7
Right hand grip force (kg.f)	24.6 ± 6.8	26.1 ± 6.5
6 min walk distance (m)	388.0 ± 79.9	456.0 ± 98.9

The results are presented in mean ± sd: standard deviation. BMI: body mass index values in kg/m^2; min: minute.

Table 2. Characteristics of women participants.

There was a maintenance in the BMI indexes, an apparent reduction in abdominal circumference and an apparent small increase in the hand grip performance in left (from 20.13 ± 26.5kg.f to 20.95 ± 28.2kg.f CI95%), right hand (from 21.6 ± 27.4kg.f to 23.0 ± 29.3kg.f CI95%) and a more pronounced increase in the six minute walk test (from 236-492m to 305-632m CI95%).

Lymphedema status

No instances of lymphedema were observed among participants during our trial period. The measurements, conducted to identify potential swelling (exceeding two centimeters) in all female patients were analyzed individually. Detailed data is accessible through the provided link: https://osf.io/s348q.

Fatigue and quality of life scores

For the fatigue and quality of life questionnaires, we used three different questionnaires, whose scores are listed below: Functional Assessment of Chronic Illness Therapy: Fatigue Scale (FACIT-F), Functional Assessment of Cancer Therapy: Breast (FACT-B) and the Functional Assessment of Cancer Therapy: Prostate (FACT-P). The scores' positive correlation implies that as the score increases, both fatigue and quality of life improve.

The FACIT -F scores for women prior to the trial were 32.0 ± 9.5, increasing to 41.0 ± 7.5 post-trial (median ± standard deviation).

The table below illustrates the FACT-B scores during the pre and post-trial periods.

Table 3

Functional Assessment of Cancer Therapy: Breast (FACT-B) Scores		
	Moment	
	Pre	**Post**
Physical well being	21.0 ± 5.3	23.0 ± 4.9
Social well being	20.0 ± 5.7	22.0 ± 6.3
Emotional well being	19.0 ± 3.7	18.0 ± 4.6
Functional well being	15.5 ± 6.3	17.0 ± 6.3
Additional worries	23.5 ± 7.3	23.0 ± 6.7

The results are presented in median ± sd: standard deviation.

Table 3. Characteristics of women participants.

Open feedback from participants

The hearing took place in a face-to-face setting at the hospital's facilities, with groups comprising two to three female patients. Despite efforts to recruit additional participants, these attempts were unsuccessful due to time constraints and cancellations. Through the dynamics of the focus group discussions, we identified reported barriers and facilitators to exercise at different stages of cancer among our breast cancer patients:

- Prior to diagnosis
- During the surgery and recovery period
- Throughout chemotherapy and/or radiotherapy

- During the hormone blockade period (current phase)
- Throughout the trial period

Barriers and facilitators to exercise before the diagnosis

The patients acknowledged that they had not prioritized exercise during this stage of their lives, primarily due to the demands of work and household responsibilities. While they engaged in physical activity through tasks like house chores, active commuting to work or other activities, such as walking, they did not follow a structured exercise regimen.

Barriers and facilitators to exercise during the surgery period

The patients lacked motivation to engage in physical activity and faced movement constraints resulting from the surgery. Nonetheless, they acknowledged the significance of exercise for their overall health. One patient shared a concerning situation where her doctor informed her that she would be unable to perform certain tasks indefinitely, rather than for a specified recovery period, as described in her statement below:

> *"...Another thing that most like is to to hoe. He said no. I love it. I love to do these things, but he said that we couldn't do it all. So, if it 's not for me to do it, I won't do it. And then my daughter said… But you are only 67 years old, how can you not do it?"*

Barriers and facilitators to exercise during the chemotherapy and/or radiotherapy period

The patients reported experiencing nausea, weakness, body pain, and a lack of motivation to exercise. One patient expressed a particularly alarming concern:

> *"...Ah, if I do something. It will hurt me again and then create it again… So, I was afraid that it (the cancer) would come back and develop it again. I didn't hung up clothes, didn't hung up anymore, just on the drying rack. I didn't sweep the house. My daughter who swept for me".*

In contrast, another patient, whose son is a personal trainer, encouraged her to move through this period and beyond.

"... I got too debilitated, because of it all, right, all treatment. But after that, this son of mine, whom is graduated, graduated on your field (Physical Education/Fitness), also was there, instructed me to do exercises in bed, and I got up. I am very much to get up; I remember my mother saying, the bed is the worst thing, the worst disease that you can have, so do not make bed, my daughter; if you can get up, get up, in the of God. So, I looked at that, I'll get up…"

Barriers and facilitators to exercise during the hormone blockade period (actual period)

The patients reported that their inconsistency in exercising stemmed from a lack of organization and making excuses. However, during their participation in our trial, they felt motivated to exercise consistently. They also mentioned feeling a sense of contribution to society, which further fueled their motivation to continue exercising.

Barriers and facilitators to exercise during the trial

All patients expressed that they found the trial too short; they desired a longer duration, ideally lasting at least six months, but preferably extending to a year. They collectively valued the trial assessments, materials provided, and the selection of exercises. Regarding our interactions with the patients, they all expressed satisfaction and made no suggestions for changes, except for one individual who requested increased weekly contact. Furthermore, all patients expressed a preference for more face-to-face interaction, either in group settings or individually. Finally, all patients expressed deep gratitude for our warm reception, the opportunity to engage with the research team, and the chance to interact with their peers.

Non enrollment numbers after consent

As described in our protocol (BENEFIT CA protocol), this trial accounted for two consent formats: online and physical. The online version was an initial consent, which allowed us to go on with the questionnaires that could be performed in a remote manner. However, the IRB Committee insisted for us to perform an additional consent form, the physical one, at the moment the patient met our research team, in order to continue the process. So, this was the final consent. Depending on the

patient's skills, the remote consent form was not possible to be performed, and this was not an issue. However, it was mandatory that the consent form was physically signed at the moment the research team met the patient. There were no exclusions for this trial after the patient signed the consent form, on its physical format.

Discussion

This study demonstrates the findings from the BENEFIT CA trial, a feasibility home based exercise with a 12 week duration study. The trial primarily involved white female breast cancer patients, with query being the most common recruitment method. We initially expected to recruit more patients through the query method, given that these individuals were already utilizing the Hospital's facilities. However, what we did not anticipate was the significant difficulty in recruiting participants through our other recruitment methods. It was also expected that we would find and recruit more female breast cancer patients, as the existing literature provides more data on breast cancer than prostate cancer in the context of exercise. This discrepancy could be attributed to cultural and gender differences, as women are often observed to seek medical services more frequently than men [35,36], and societal pressures related to aesthetics tend to affect women more than men [37,38].

For instance, if we had included individuals who were already physically fit, despite potentially skewing adherence results, we could have monitored their activity levels throughout the trial and gained insights into their engagement with physical activity across a wider spectrum. This could have led to the inclusion of more participants and encouraged greater increases in physical activity, which is critical for both health and quality of life. In the case of prostate cancer, we recognize that the side effects of treatment—or the lack thereof in patients undergoing only surgical procedures—would differ from those under active treatment. Nevertheless, these patients are still considered cancer survivors and could benefit from exercise just as much as their counterparts with other types of cancer.

Additional factors also influenced our recruitment outcomes, such as the absence of hormone blockade treatment and the presence of metastasis, which was more common among the male participants in our sample (21%) but also present in approximately 13% of the female participants. These findings lead us to reflect: who are we actually recruiting for our trials? Perhaps with broader eligibility criteria, we

might have reached a larger number of prostate and breast cancer patients, potentially revealing different patterns of adherence and other outcomes.

For instance, if we had included individuals who were already physically fit, despite potentially skewing adherence results, we could have monitored their activity levels throughout the trial and gained insights into their engagement with physical activity across a wider spectrum. This could have led to the inclusion of more participants and encouraged greater increases in physical activity, which is critical for both health and quality of life. In the case of prostate cancer, we recognize that the side effects of treatment—or the lack thereof in patients undergoing only surgical procedures—would differ from those under active treatment. Nevertheless, these patients are still considered cancer survivors and could benefit from exercise just as much as their counterparts.

Our study highlights a racial/ethnic disparity in our sample, with a higher representation of white individuals, despite living in a diverse country. A 2020 study [39] using data from Surveillance, Epidemiology and End Results (SEER) data on 547,703 women found that African American women with breast cancer had higher all-cause and breast cancer-specific mortality compared to Caucasian women. Additionally, a 2011 observational study in Southern Brazil indicated that black women had a higher risk of not undergoing early detection for breast cancer and were twice as likely as white women to have never had a pap-smear examination. While some researchers attribute these disparities to socioeconomic status rather than race, the study found that inequalities persisted even after controlling for economic and demographic factors, particularly affecting older black women. A cohort study conducted in Rio de Janeiro (2010–2016) revealed that participation in the Brazilian Government's Family Health Strategy (ESF) was associated with a lower mortality risk among low-income populations, particularly within disadvantaged ethnic and racial groups [40]. These findings highlight the importance of strengthening approaches within the health care system to address inequalities, not only in preventive and post-cancer care but also in expanding access to physical exercise for economically disadvantaged groups.

In this trial, we determined the critical points related to our primary outcomes, namely adherence and adverse events, since there were none related to our trial

and no drop-outs after consent. Our adherence rates showed our program was consistent in encouraging and engaging our patients to exercise, even without the face to face component. Other studies have highlighted the importance of maintaining the motivation and communication constant across the trial [2,41,42], and we believe this was an important factor that favored the adherence results.

Regarding the patients' physical characteristics, the patients showed a maintenance in BMI and an apparent decline in abdominal circumference values. These findings are similar with findings from other trials in the literature, such as Stefani et al. 2018, that compared a home based aerobic and resistance exercise program for cancer survivors to a control situation for one year, finding significant waist circumference and body weight reductions after six and twelve months of trial [43]. Although our trial was not designed to promote weight loss, this issue holds significance in the overall health status, since cardiac diseases and events exhibit a strong correlation with excessive body weight and increased abdominal circumference [44]. Some authors suggest that a 3% weight loss or less is associated with benefits on glucose levels [45,46]. Another systematic review and meta analysis [47] from 2020 states that an increase by 10 cm in the waist circumference for men and women, results in an 8 and 12% increase risk of all cause mortality, respectively. Our trial emphasizes the importance of these measures, which serve as vital indicators. From a public health perspective, evaluating BMI and abdominal circumference proves to be a cost-effective and easily implementable strategy. This assessment not only provides valuable insights for us as researchers but also promotes heightened awareness among patients regarding their overall health status.

As for handgrip strength and six-minute walk performance, we could observe a small positive increase for both hands, with the left one being a more pronounced increase, and a more consistent improvement for the distance in the six-minute walk test. Although the six-minute walk test may not be the gold standard for assessing aerobic capacity, it holds substantial clinical relevance and demonstrates a positive association with improvements in both aerobic and functional capacity [48,49]. Our results are consistent with prior research with female breast cancer survivors that used a multidisciplinary approach including an exercise component over a three-month period [50,51]. This outcome is particularly crucial for cancer patients,

considering its implications for their overall well-being. Moreover, enhanced aerobic capacity serves as a well-established protective factor against cardiovascular and cardiorespiratory conditions [52,53]. This holds true not only for the general population but particularly for cancer patients who may face treatment-related side effects [2,3,54,55]. Recognizing the significance of improving aerobic capacity becomes imperative in mitigating these potential health challenges for individuals undergoing cancer treatments. For the female participants, it is crucial to acknowledge the diverse nature of their post-surgical recoveries, leading to varying levels of strength and abilities. Even years after their procedures, significant disparities may persist between the affected and unaffected arms. A study working with patients undergoing adjuvant aromatase inhibitors or tamoxifen therapy noted that both groups of patients had a pronounced decline in the hand grip strength, with a more pronounced decline for the aromatase inhibitors group [56]. In addition, a cross sectional study found an association between lower handgrip values and lower quality of life scores among cancer survivors [57], which is consistent with other literature findings. Hand grip strength, a crucial metric for assessing muscle function, is particularly relevant for the aging population [58–60] beyond evaluation, actively maintaining or improving these values is vital for overall health.

Our findings regarding lymphedema align with existing literature [61,62], demonstrating the absence of additional swelling in the upper limbs upon completion of our trial, with a potential decrease in the swelling [62]. This outcome holds particular significance as it provides patients with tangible evidence that no detrimental effects were incurred during the intervention. The visible and understandable nature of this result is crucial in reassuring patients and fostering a sense of well-being, assuring them that the trial did not cause any harm. Notably, one of our patients received advice from her doctor to refrain from lifting anything exceeding five kilograms and to avoid certain activities, such as weeding, indefinitely. While certain restrictions are warranted immediately after surgery and during subsequent weeks, blanket prohibitions should be approached with caution. Regrettably, despite compelling evidence to the contrary, unfounded claims persist, contributing to unnecessary fears among patients. During the focus group discussion, this same patient expressed a lingering fear from the time of her diagnosis that certain activities who require physical effort might trigger a recurrence

of cancer. Addressing such myths is paramount, and it underscores the importance of collaborative efforts between the healthcare team and the patient. By working together, patients can gain a clearer understanding of their individual situations, empowering them to navigate their recovery more effectively and dispelling unnecessary fears.

Our findings appear to indicate improvement in the FACIT-F scores and a maintenance in the FACT-B scores over the course of our trial. While we haven't conducted further analyses on this data, we believe it aligns with observations made by other researchers [63–66]. An interesting meta analysis with colorectal cancer patients revealed that, when reaching at least 80% of adherence, supervised and home-based exercise can modify quality of life rates and functional capacity [67]. A systematic review regarding female breast cancer survivors (those who have completed primary care for at least 10 years) participating in home-based multidimensional programmes revealed the programmes appear to have a short-term beneficial effect of improving breast cancer-specific quality of life and global quality of life. In addition, the authors state that the programmes were associated with a reduction in anxiety, fatigue and insomnia immediately after the intervention [68].

In our comprehensive analysis, insights from open feedback sessions with patients proved exceptionally valuable. It was evident that, before their cancer diagnosis, exercise wasn't a focal point for them, whether employed or homemakers, and the idea of incorporating it for health benefits was not prominent. Despite evolving perspectives post-diagnosis and trial completion, patients faced ongoing challenges integrating exercise, despite recognizing its significance. Notably, fatigue during surgery, chemotherapy or radiotherapy emerged as a prevalent barrier, shared among our cancer patients. In subsequent months, especially during hormone blockade stage, organizational issues and, intriguingly, a sense of laziness were identified as barriers to regular exercise, even for those not currently employed. A Swiss trial on female breast cancer patients highlighted more psychological barriers for unsupervised home-based exercise compared to supervised center-based exercise, emphasizing the importance of structured programs. The authors stressed the need for a special focus on the transition from supervised to self-organized exercise for long-term participation [31]. These findings align with our

own, revealing that our patients, actively participating in our trial, expressed newfound motivation for engagement in our exercise program. Intriguingly, they unanimously expressed a desire for the trial duration to extend beyond the initial 12 weeks, suggesting durations of at least six months to a year. This underscores a noteworthy aspect: when individuals feel motivated and perceive accountability, they demonstrate a willingness to engage in regular exercise.

Limitations:

Our biggest limitation was related to recruitment. We failed to reach an expressive number of prostate cancer patients. However, despite a number below the desired, we were able to reach a substantial amount of breast cancer patients. allowing us to think that, for now, it is possible to move forward with this trial in this population.

Final considerations

We express our sincere gratitude to the patients whose generous contributions made this collaborative scientific endeavor possible. Despite recruitment rates falling short of the initial goal, we successfully met the feasibility progression criterion for a phase three randomized controlled trial in breast cancer patients. However, for prostate cancer patients, the predefined eligibility criteria did not yield the target recruitment rate. Moving forward, we believe that future trials should broaden their inclusion criteria to allow a greater portion of cancer patients to benefit from exercise interventions. While this may require adjusting outcomes and analyses to better isolate the effects of the trial, such modifications would enable us to capture the diversity of responses across different cancer patient populations.

This feasibility trial was designed with a focus on adherence and adverse events, laying the groundwork for larger, more definitive studies. It upheld principles of real-world applicability, inclusivity, low cost, and transparency, all while embracing open science practices. In particular, patient feedback played a critical role in shaping the trial, and we are committed to carrying this emphasis on patient input into future initiatives. Notably, we experienced no dropouts, a significant achievement for a remote trial of this nature.

Patients consistently expressed a desire for a longer intervention period, which suggests that extending the trial duration to six months or even a year, where resources permit, could provide valuable insights into the long-term effects of exercise interventions on adherence, well-being, and functional capacity. Such an extension would enrich our understanding of the efficacy of these interventions.

In conclusion, our findings underscore the importance of developing more diverse recruitment strategies to include underrepresented demographic groups. Expanding the pool of trial participants will offer a more comprehensive understanding of the distinct challenges faced by various cancer patient populations when engaging in exercise regimens. Additionally, a stronger emphasis should be placed on promoting exercise through the primary healthcare system, recognizing its well-established role in cancer prevention, treatment, and management, as well as in reducing recurrence and improving overall quality of life.

Abbreviations

BENEFIT CA The home-based exercise for breast and prostate cancer patients during treatment: a feasibility trial" (BENEFIT CA trial)

CAPES Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (Coordination for the Improvement of Higher Education Personnel)

COVID-19 Coronavirus Disease 2019

ESF Family Health Strategy

FAPERGS Fundação de Amparo à Pesquisa do Estado do Rio Grande do Sul (Research Support Foundation of the State of Rio Grande do Sul)

FIPE Fundo de Incentivo à Pesquisa

GEE General Estimating Equations

HCPA Hospital de Clínicas de Porto Alegre-City Hospital at Porto Alegre

HDI Human Development Index

IATS National Institute of Science and Technology for Health Technology Assessment (IATS/HCPA)

INCA National Institute of Cancer

IPAQ International Physical Activity Questionnaire

IRB Institutional Review Board

OSF Open Science Framework

PA Physical activity

REDCap Research Electronic Data Capture

RCT Randomized controlled trial

SEER Surveillance, Epidemiology and End Results

SWAT Study within a trial

UFRGS Universidade Federal Do Rio Grande Do Sul, Porto Alegre, RS, Brazil (Federal University of Rio Grande do Sul, Porto Alegre, Brazil).

WHO World Health Organization

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Authors' contributions

LXNS, FDM, ACI, YFS, JPSC and DU contributed to the original draft preparation, reviewing, editing, and critical review. During the intervention, LXNS was involved in patient's recruitment. LXNS were involved in remote informed consent procedures and remote evaluations. LXNS, FDM and ACI were involved in face-to-face evaluations. ACI was involved in data's organization and conference. LXNS was involved in patient's communication. LXNS, ACI, JPSC and YFS were involved in data analysis. LXNS and DU are involved in data dissemination. DU oversaw all the study procedures. All authors have read and approved the manuscript. Funding This study was financed in part by Coordenação de Aperfeiçoamento de Pessoal de Nível

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