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Community-based Exercise for Health Promotion and Secondary Cancer Prevention: Protocol for a Hybrid Effectiveness-Implementation Study

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ABSTRACT

Introduction

Cancer care has expanded from a disease-focused, survival-oriented model to an approach that now considers how survivors can live well in the aftermath of intensive therapy, where they may deal with significant changes to their bodies, mental health, or emotional well-being. Research evidence supports the benefit of exercise during and following cancer treatments for cancer-related symptoms, physical functioning and fitness, and health-related quality of life. To move this efficacy evidence into practice, we designed and launched a five-year study to evaluate the relative benefit from implementing a clinic-to-community-based cancer and exercise model of care.

Methods

A hybrid effectiveness and implementation trial design is being used to evaluate the effectiveness of delivery of community-based exercise and to collect data on implementation of the program. Key features of the exercise program include (1) training of community exercise specialists to deliver the program, (2) screening, referral and support for community-based exercise programming, and (3) stakeholder engagement in the design, development and delivery of the program. Participants are adult cancer survivors (N = 2500) from all tumour groups and stages, and at any time point along their cancer treatment trajectory, up to three years post treatment completion. Survivors take part in exercise twice weekly for a 12-week period. The RE-AIM framework will be utilized to capture individual and organizational-level impact of the exercise program at 12 and 24 weeks, and one-year follow-up.

Ethics and Dissemination

The study was approved by the Health Research Ethics Board of Alberta. The study will help to answer critical questions on the value of cancer-specific community-based exercise programming, and allow us to determine both the short and long-term effectiveness of exercise. Collectively, the findings will help to inform the acceptability, adoption, feasibility, reach, and sustainability of community-based exercise, and simultaneously evaluate integration of exercise into clinical care.

Trial Registration

ClinicalTrials.gov: NCT02984163 (prospectively registered)

Strengths and Limitations of this Study

- The study involves patients and other stakeholders in the design and ongoing delivery of exercise programming.
- External validity of the program is supported by the community-based implementation focus, with novel aspects of supervision by cancer-trained exercise specialists and support provided by study personnel.
- We will determine both the short and long-term effectiveness of community-based exercise, and identify important intervention-implementation interactions.
- The main limitation of the ACE hybrid effectiveness-implementation study is related to the single-group design that does not allow for comparison of findings to usual care.

Key words: cancer survivorship, exercise, physical activity, quality of life, supportive care, implementation, knowledge translation

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Introduction

The growing population of individuals living with or beyond a diagnosis of cancer highlights the long-term impact of cancer and its therapies on the body, the mind and on overall health of survivors. This necessitates an expansion of focus from merely survival to how to live in the aftermath of intensive therapy with an altered body and attendant psychological changes. There is an immediate and emergent need to disseminate strategies that can improve the health of cancer survivors.

Exercise is a low cost and safe intervention for cancer survivors with beneficial effects on physical functioning and all aspects of health-related fitness, including aerobic and muscular fitness, and body composition.[1-3] Exercise also benefits psychosocial well-being, including mental and emotional health, and overall quality of life.[3] Moreover, targeted programs that include tailored exercise prescriptions are more successful in helping individuals with chronic disease to incorporate physical activity and exercise into their daily routines.[4] Given the low physical activity prevalence, and the negative impact cancer and its associated treatments have on the survivors' physical fitness and physical activity levels[5], efforts are needed to address this evidence-to-practice gap.[6,7]

In addition to implementing exercise, there is also a need to evaluate its effectiveness on overall health, considering both physical and psychosocial outcomes. Most research evidence to date comes from lab-based studies.[3] While positive, these results may not translate into the same benefits seen from community-based programs.[8] At a pragmatic and policy level, we also need to understand the costs, and potential for cost savings, of such programs.[9] To achieve widespread adoption, projects must benefit participants, and must be cost-effective and reduce health care utilization. There are limited data on these key aspects of community-based exercise programs.

In order to move the efficacy evidence into practice, we designed and launched a five-year hybrid

effectiveness and implementation study to evaluate the relative benefit from an Alberta wide clinic-to-community-based cancer and exercise model of care – the Alberta Cancer Exercise (ACE) program, and to evaluate the implementation of such an initiative. The overarching goal of the ACE program is to provide, support, and evaluate high quality, timely and personalized exercise for the survivor after a cancer diagnosis.

Objectives

The specific objectives of this study are to:

1) Determine the utility of facilitated referral of survivors to appropriate exercise programming within their respective communities, as a strategy for increasing adoption of exercise.
2) Determine the immediate and long-term effectiveness of community-based programming on the survivors' health-related quality of life (QoL), physical fitness, other patient-reported outcomes and healthcare utilization.
3) Identify strategic opportunities for enhancing implementation of the ACE clinic-to-community strategy, including knowledge translation, program sustainability, and strategies for integrating exercise into clinical care pathways.

Methods

A hybrid effectiveness and implementation trial design is being used to evaluate the effectiveness of delivery of community-based exercise and to collect data on implementation of the program.[10] The study opened in January 2017 and will run for a 5-year period (to 2021). We chose this trial design because: 1) there is strong evidence from efficacy trials supporting the benefit of exercise for survivors both during and following cancer treatment, 2) there is a limited body of evidence supporting implementation of programming in the community and evidence supporting objective outcomes and long-term adoption are currently lacking; and 3) with appropriate pre-exercise evaluation and screening, there is minimal risk in implementing a community-based exercise

intervention. The hybrid design provides important data on the effectiveness of community exercise programming while fast-tracking translation of research findings into clinical practice and survivorship care pathways.

Participants

Participants are adult cancer survivors from all tumour groups and stages, and at any time point along their cancer treatment trajectory into the survivorship post-cancer treatment period, up to three years post treatment completion. This inclusionary focus will allow us to build a clinic-to-community model that is sustainable and meets the needs of most cancer survivors. Ethical approval was received from the Health Research Ethics Board of Alberta: Cancer Committee and all participants are required to provide written informed consent.

Setting

The exercise programming intervention takes place at local YMCAs and municipal fitness centres across the province, as well as Wellspring (a non-profit cancer support organization in Alberta) and University-based cancer-specific fitness or rehabilitation centres.

Eligibility: Inclusion criteria

Participants are screened for eligibility over the phone by the respective site coordinator (Alberta north or Alberta south) and must: 1) have a diagnosis of cancer; 2) be over the age of 18 years; 3) be able to participate in mild levels of activity at minimum; 4) be pretreatment, *or* receiving active cancer treatment (e.g., surgery, systemic therapy and/or radiation therapy), *or* have received cancer treatment within the past 3 years *or* have existing long-term or late presenting effects of their cancer treatment; and 5) be able to provide informed written consent in English.

Screening

Consenting participants complete a cancer-specific intake form and Physical Activity Readiness Questionnaires (PAR-Q+) to determine appropriateness for community-based exercise programming. Data are collected on *exercise preferences* as well as the participant's *Physical Activity Stages of Change* to inform the participant's status in terms of preferences, attitudes and

behaviors towards increasing physical activity. A Certified Exercise Physiologist (CEP), who has graduate level training or certification in exercise physiology, and experience in the cancer field, performs the screening for safety. The CEP oversees baseline physical fitness testing, and evaluates testing results. The CEP then triages the participant to local programming based on his/ her current health, baseline physical fitness, cancer-related symptoms and exercise preferences**.** If safety issues emerge during screening, the CEP consults with the participant's oncologist or family physician on the need for further evaluation and/ or referral to rehabilitation services or medically supervised exercise programming.

Implementation Components and Framework (Figure 1)

1. Cancer-specific Education and Support for Community-based Exercise Specialists

All community-based exercise programming is administered by exercise specialists who have undergone the *Cancer and Exercise: Training for Fitness Professionals* online course offered through the University of Calgary. The ACE CEP provides additional in-person training to ensure community-based exercise professionals have the skills and knowledge required to work with the cancer population, as well as ongoing support to ensure success of the program implementation. This training aids in the dissemination of the ACE program's critical knowledge to key community fitness partners.

2. Screening, Referral and Support for Community-based Exercise Programming

The ACE program bridges the gap between Healthcare Professionals (HCPs) and community exercise programming by facilitating referral of survivors to appropriate cancer-specific exercise programming. The CEPs provide education and onsite support to HCPs within the major centres (Calgary and Edmonton), and via online and telephone-based support to HCPs working with survivors in rural locations.

3. Patient and other Stakeholder Engagement in the Design, Development and Delivery of ACE

Our ACE clinic-to-community based exercise program works with survivors and families, community exercise specialists, HCPs and end-users to improve the survivor exercise experience.

The goal is to ensure that all stakeholders contribute to the design, development and delivery of the ACE exercise strategy from clinic-to-community. Cancer survivors were involved in the design and delivery of ACE from inception, and a series of focus groups and semi-structured interviews are planned to elicit feedback from participants, HCPs and exercise specialists over the course of ACE implementation.

Exercise Intervention

Intervention options are geared to the various settings where ACE is being implemented. Participants take part in a combination of aerobic, resistance, balance, and flexibility exercises delivered in a circuit-type class setting or group personal training format, twice weekly for a 12-week period. The exercise sessions are conducted in small groups of 8-15 participants under the direct supervision of the community-based ACE trained exercise specialist. Two options for community-based exercise programming exist: group fitness classes or supervised fitness centre access. Participating community sites offer one or more of these options depending on available resources and demand. Active support and ongoing mentoring by the CEP is provided to community-based exercise specialists in the participating community program for the duration of ACE programming. To encourage longer-term exercise adherence, a second 12-week optional maintenance program is offered, where possible, at low to no cost to survivors.

Participants assessed as having high needs due to active cancer, metastatic disease or with severe symptoms (where their disease or symptoms pose a risk in terms of safety of community-based exercise participation) are referred to ACE medically supervised programming or local cancer rehabilitation services.

Outcomes to Support Effectiveness of Programming

Health-related aspects of both physical fitness and QoL in cancer survivors are assessed. Exercise testing takes place at the University sites or at the fitness facilities offering the programming, and is performed both before (baseline) and after the exercise program (at week 12) across all sites, with

further follow-up testing at 24-weeks and one-year at the tertiary sites. Exercise testing includes:

- Physical activity level: Godin Leisure Time Physical Activity Questionnaire;
- Body composition: height, weight (calculation of body mass index);
- Aerobic endurance: six minute walk test;
- Musculoskeletal fitness: grip strength, timed sit-to-stand, shoulder flexion (flexibility) and one-legged stance (balance);
- Cancer-related symptoms: Edmonton Symptom Assessment Scale and Screening for Distress;

Health-related QoL is assessed using the Functional Assessment of Cancer Therapy-General scale, and RAND Short Form Instrument (SF-36), and EQ5D-5L at baseline, 12-weeks, 24-weeks, and one-year for all participants. Participants will have the option for further follow-up at year 2 and 3 following the program. The study database was created in the REDCap system provided by the Women and Children's Health Research Institute (WCHRI) and hosted in the University of Alberta's Faculty of Medicine & Dentistry's data centre. Data collection and storage will comply with the measures outlined in WCHRI's REDCap privacy document.

Additional tests performed where available**:** (i) 1or 8 repetition maximum bench press and 1 or 8 repetition maximum leg press to determine muscular strength; (ii) Sit-and-reach test to assess flexibility; (iii) plank muscular endurance test; (iv) push-up test.

Safety is monitored during exercise testing and training by the CEP and the ACE trained exercise specialists in community locations. The CEPs and ACE exercise specialist record rates of adverse events (minor to serious adverse events including cardiovascular events, falls or musculoskeletal injuries). Participants are asked to report any issues, injuries, or falls, related and unrelated to exercise participation to the ACE exercise specialist at the respective site. Attendance at the exercise sessions is tracked as a marker of acceptability. Reasons for missed sessions are recorded. Exercise adherence includes attendance at supervised exercise sessions and average exercise minutes per

week over the study period. A priori targets for physical fitness, symptoms and quality of life outcomes will be used to inform effectiveness and safety of the intervention (Table 1).

Outcomes to Support Implementation

The RE-AIM framework will be utilized to evaluate and enhance the external validity of the ACE program. The RE-AIM framework presents a means to evaluate the impact of a community-based intervention as a function of 5 factors: reach, effectiveness, adoption, implementation and maintenance. This framework has been used to evaluate health and lifestyle behaviours to determine the public health impact of the intervention.[11,12] Embedded within RE-AIM is a cost description analysis pertaining to the survivor (individual costs) and the institutions (Community fitness facilities, Universities, and CancerControl Alberta). A proposed RE-AIM evaluation plan to assess the impact of the ACE program has been developed based on existing research (Table 2).[11]

Health Care Utilization Evaluation

The proposed methods for health care utilization include evaluation of usage among participants compared to that of matched controls, before and after the exercise program. Using personal health numbers (PHN) for consenting participants who provide permission, the PHN will be linked to the Cancer Registry to obtain: tumor type, year of diagnosis, age and stage at diagnosis, and provincial zone of residence. These five variables will be used to match each participant (1:1, as closely as possible) to a control identified from the Cancer Registry. For each matched pair, "time 0" will be the date the participant joined the exercise program. Relative to this date, the Cancer Registry records will be linked to administrative data sources to capture all physician visits, emergency room visits and hospitalizations, one year prior to and one year following "time 0". For physician visits, we will link to Alberta Health physician claims data. The following variables will be collected: date of visit, health service type code and category, primary/secondary/tertiary diagnoses, and health service(s) performed. Health care utilization will be examined overall (summed for each database) and by subgroups of interest (e.g., diagnostic groupings, services provided, resource intensity weights), before and after "time 0", separately for cases and controls. Differences in health care

utilization across the two time periods will be described for both groups. The analysis will be performed for all participants, and stratified by tumor type.

Analyses and Dissemination

Sample size

The overall sample size goal is to accrue up to 2500 survivors via the ACE five-year roll out across the province of Alberta (18-20 sites). The primary objective outcome to assess study effectiveness is the number of participants meeting public health guidelines for physical activity at one-year follow-up. The current estimate for the number of cancer survivors meeting public health guidelines of 150 minutes or more of moderate intensity exercise per week is 25.8%.[13] According to the Conference Board of Canada, by simply getting 10% of Canadians with suboptimal levels of physical activity to exercise more would reduce incidence rates for major chronic conditions including cancer, and result in significant savings in healthcare costs.[14] Thus, assuming a 10% increase in the proportion of participants meeting the guidelines for physical activity (minimally important difference of 10%) at one-year ($p < 0.05$; 80% power), a sample size of 161 survivors would be required. As the aim of the study is to evaluate both effectiveness and implementation, evaluating site-specific effects and implementation issues is of utmost importance, and we anticipate variability across sites in study outcomes. To obtain or exceed a minimally important difference for physical fitness outcomes a minimum of 40 participants is required. Therefore, our aim is to recruit a minimum of 50 participants to each participating site over the study period in order to evaluate site-specific effectiveness.

Within the sample, we will aim to recruit a minimum of 60% of survivors from the three target cancer types with evidence supporting secondary prevention: breast (30%), prostate (20%), and colorectal (10%). These samples will allow for subgroup analyses across sites and cancer groups. The cohort of survivors participating in the study will allow for long-term evaluation of rates of

cancer recurrence, secondary cancers, and other chronic diseases (e.g., cardiovascular diseases, diabetes) beyond the funding period.

Statistical Analysis Plan

Descriptive analyses will be performed to evaluate participant demographic, medical and exercise related variables, as well as RE-AIM components including an economic evaluation of the program. A single proportion inference test and confidence interval will be performed to determine the proportion of eligible survivors who provide informed consent and complete the program, as well as adherence rates to the program. Generalized linear mixed models will be utilized to examine the changes over time in the program participants on the patient-reported outcomes, including fitness, activity levels, and indices of QoL (i.e., baseline, 12-weeks, 24-weeks and One-year). The cohort of survivors participating in the study will allow for long-term evaluation of rates of cancer recurrence and secondary cancers beyond the study period.

In recent years, the focus of research in the oncology exercise field has expanded from determining efficacy through randomized controlled trial designs to include "real world" effectiveness studies focusing on implementation of exercise into cancer care.[15-18] A wide variety of approaches to promote exercise among cancer survivors are available, including programs that are medically supervised, community-based, or self-directed/ home-based.[8] Advantages of community-based programs include high accessibility, safety and supervision of exercise, and social interaction.[19] Importantly, systematic review evidence supports greater and more consistent benefits when exercise is delivered in a group or supervised setting when compared to a home-based or unsupervised setting.[20] Moreover, surveys of cancer survivors show a high interest in exercise, with reported preference for exercise programs that are offered in a supportive environment where treating and managing cancer are understood, and at a location that focuses on health promotion rather than illness.[21-24] Community-based studies performed to date, while demonstrating short-term effectiveness, are lacking data supporting long-term effectiveness. Moreover, studies commonly

report low adherence and high dropout rates.[8,11] Given the infancy of implementation efforts in regards to community-based programming, further research with greater attention to implementation science aspects appears warranted.

We propose that our hybrid effectiveness-implementation study will help to answer critical questions on the value of cancer-specific community-based exercise programming. The ACE study will allow us to determine both the short and long-term effectiveness of exercise, and enhance our ability to identify important intervention-implementation interactions. Collectively, the findings will help to inform the acceptability, adoption, feasibility, reach, and sustainability of community-based exercise, and simultaneously evaluate integration of exercise into clinical care.[25]

Consistent with the design of an effectiveness study, the ACE program is a cancer-specific exercise intervention with broad eligibility criteria that reflect "real-world" conditions. As many survivors report feeling neither physically nor psychologically prepared to engage in community-based exercise programs designed for the general public[24], a feature of ACE is the built-in flexibility of the exercise prescription such that participants self-select the exercise intensity based on presenting symptoms, "down days", or personal preference. While participants are expected to meet a minimal goal of two hours per week of at least light intensity exercise, the participant is encouraged to exceed this goal if able and desired.

To address issues seen with less than optimal adherence and completion rates in previous implementation studies, key strategies built into ACE include monitoring of exercise adherence and behavior change support for exercise.[18] The primary behavioral supports within the ACE program are the supervised and supportive aspects of the programming, along with exercise behaviour change education, goal setting and self-monitoring of activities. An ACE trained exercise specialist at the community site leads exercise classes and sessions. An ACE CEP and physical therapist are

available to provide additional support to the survivor to address issues related to cancer treatment effects. This supportive format allows for modification and tailoring of the exercise, as needed, to the survivor's cancer type, capabilities and preferences.[26] In theory, if the program meets the needs of survivors, adherence and completion rates should be high, reflecting program acceptability.

Recently published guidelines from Australia endorse the integration of exercise into cancer care as a means to lessen some of the negative effects of cancer and its treatment.[7] Importantly, the guidelines identify the need for cancer HCPs to discuss the role of exercise in cancer recovery, and recommend referral of survivors to a CEP and/or physical therapist with experience in cancer care.[7] Implementation studies, to date, have largely focused on the delivery and effectiveness of an exercise intervention rather than studying the processes and outcomes associated with implementation within the healthcare system. Despite guidelines supporting exercise [2,27,28], challenges exist with implementing exercise counseling and referral due to the existing complexity and competing priorities in the cancer clinical setting.[29] Our ACE integrated knowledge translation strategy involves stakeholders in the design and ongoing delivery of ACE (i.e. survivors, end-users, administrators and policy-makers) and aims to address HCPs barriers and facilitators to exercise counseling and referral within the local cancer clinical setting.

There are important limitations to note in the design of the ACE hybrid effectiveness-implementation study related to the single-group design that does not allow for comparison of findings to usual care. As such, threats to internal validity exist including maturation, history, testing and regression to the mean. To address these concerns, specific fitness outcome targets were determined, a priori, based on previous randomized controlled trial findings. Moreover, to reduce bias associated with testing, ACE assessors, who are blinded to previous results, conduct the evaluations and the participants complete the patient-reported outcomes electronically at home. External validity of the program is supported by the community-based implementation focus, with

novel aspects of supervision by cancer-trained exercise specialists and support provided by ACE CEPs and physical therapists. Importantly, evaluation of the program is guided by the RE-AIM framework and includes a robust suite of endpoints.

Conclusions

ACE is a healthy lifestyle initiative, encouraging and supporting cancer survivors to take a role in their own wellbeing by increasing capacity for, and accessibility to cancer-specific exercise in the community, and by facilitating referral to programming. Through this research, we will better understand the effectiveness of the program at the level of the individual and institution, and evaluate processes to support future implementation and sustainability. Supporting improved rates of exercise adoption and sustained adherence to an active lifestyle among survivors of cancer will improve physical fitness and QoL, and may lower rates of cancer recurrence, secondary cancers, and other chronic diseases for cancer survivors in Alberta.

Declarations:

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Availability of data and material

Data sharing is not applicable to this article as no datasets were generated or analyzed (i.e., study protocol paper). Material developed to support this study is available from the corresponding author on reasonable request.

Author contributions

All authors developed the study concept and protocol. MLM, SNCR, CS, and TW assisted in further development of the exercise and implementation protocol. All authors will oversee the implementation of the protocol and contribute to the acquisition, analysis and interpretation of data. MLM and SNCR drafted the manuscript, all authors contributed to revisions and all authors approved the final manuscript.

Competing interests

We acknowledge the support and funding received from the Alberta Innovates Cancer Prevention Research Opportunity and the Alberta Cancer Foundation.

The authors declare that they have no competing interests.

Consent for publication

Not applicable.

Ethics approval and consent to participate

The study was approved by the Health Research Ethics Board of Alberta: Cancer Committee (ID: HREBA.CC-16-0905) and all participants are required to provide written informed consent.

REFERENCES

1. Speck RM, Courneya KS, Masse LC, et al. An update of controlled physical activity trials in cancer survivors: a systematic review and meta-analysis. *J Cancer Surviv* 2010;4(2):87-100. doi: 10.1007/s11764-009-0110-5 [published Online First: 2010/01/07]
2. Rock CL, Doyle C, Demark-Wahnefried W, et al. Nutrition and physical activity guidelines for cancer survivors. *CA Cancer J Clin* 2012;62(4):243-74. doi: 10.3322/caac.21142 [published Online First: 2012/04/28]
3. Cormie P, Zopf EM, Zhang X, et al. The Impact of Exercise on Cancer Mortality, Recurrence, and Treatment-Related Adverse Effects. *Epidemiol Rev* 2017;39(1):71-92. doi: 10.1093/epirev/mxx007
4. Macera CA. Promoting Healthy Eating and Physical Activity for a Healthier Nation. Healthier People 2010. Centers for Disease Control and Prevention National Center for Chronic Disease, 2013.
5. Courneya KS, Katzmarzyk PT, Bacon E. Physical activity and obesity in Canadian cancer survivors: population-based estimates from the 2005 Canadian Community Health Survey. *Cancer* 2008;112(11):2475-82. doi: 10.1002/cncr.23455 [published Online First: 2008/04/23]
6. Santa Mina D, Sabiston CM, Au D, et al. Connecting people with cancer to physical activity and exercise programs: a pathway to create accessibility and engagement. *Curr Oncol* 2018;25(2):149-62. doi: 10.3747/co.25.3977
7. Cormie P, Atkinson M, Bucci L, et al. Clinical Oncology Society of Australia position statement on exercise in cancer care. *Med J Aust* 2018.
8. Hardcastle SJ, Cohen PA. Effective Physical Activity Promotion to Survivors of Cancer Is Likely to Be Home Based and to Require Oncologist Participation. *J Clin Oncol* 2017;35(32):3635-37. doi: 10.1200/JCO.2017.74.6032
9. Abu-Omar K, Rutten A, Burlacu I, et al. The cost-effectiveness of physical activity interventions: A systematic review of reviews. *Prev Med Rep* 2017;8:72-78. doi: 10.1016/j.pmedr.2017.08.006
10. Curran GM, Bauer M, Mittman B, et al. Effectiveness-implementation hybrid designs: combining elements of clinical effectiveness and implementation research to enhance public health impact. *Medical care* 2012;50(3):217-26. doi: 10.1097/MLR.0b013e3182408812
11. White SM, McAuley E, Estabrooks PA, et al. Translating physical activity interventions for breast cancer survivors into practice: an evaluation of randomized controlled trials. *Ann Behav Med* 2009;37(1):10-9. doi: 10.1007/s12160-009-9084-9 [published Online First: 2009/03/04]
12. Glasgow RE, Emmons KM. How can we increase translation of research into practice? Types of evidence needed. *Annu Rev Public Health* 2007;28:413-33. doi: 10.1146/annurev.publhealth.28.021406.144145 [published Online First: 2006/12/08]
13. Neil SE, Gotay CC, Campbell KL. Physical activity levels of cancer survivors in Canada: findings from the Canadian Community Health Survey. *J Cancer Surviv* 2014;8(1):143-9. doi: 10.1007/s11764-013-0322-6
14. Bounajm F, Dinh T, Theiault L. Moving Ahead. The Economic Impact of Reducing Physical Inactivity and Sedentary Behaviour. Ottawa: The Conference Board of Canada, 2014:1-37.
15. Translating Exercise Oncology Research into Practice: Effectiveness of a Community-Based Exercise Program for Cancer Patients and Survivors. MASCC/ISOO Annual Meeting Supportive Care in Cancer; 2015; Copenhagen Supportive Care in Cancer.
16. Heston AH, Schwartz AL, Justice-Gardiner H, et al. Addressing physical activity needs of survivors by developing a community-based exercise program: LIVESTRONG(R) at the YMCA. *Clinical journal of oncology nursing* 2015;19(2):213-7. doi: 10.1188/15.CJON.213-217
17. Haas BK, Kimmel G, Hermanns M, et al. Community-based FitSTEPS for life exercise program

for persons with cancer: 5-year evaluation. *Journal of oncology practice / American Society of Clinical Oncology* 2012;8(6):320-4, 2 p following 24. doi: 10.1200/JOP.2012.000555

18. Cheifetz O, Park Dorsay J, Hladysh G, et al. CanWell: meeting the psychosocial and exercise needs of cancer survivors by translating evidence into practice. *Psycho-oncology* 2014;23(2):204-15. doi: 10.1002/pon.3389
19. Santa Mina D, Au D, Brunet J, et al. Effects of the community-based Wellspring Cancer Exercise Program on functional and psychosocial outcomes in cancer survivors. *Curr Oncol* 2017;24(5):284-94. doi: 10.3747/co.23.3585
20. Segal R, Zwaal C, Green E, et al. Exercise for people with cancer: a systematic review. *Curr Oncol* 2017;24(4):e290-e315. doi: 10.3747/co.24.3619
21. Rogers LQ, Malone J, Rao K, et al. Exercise preferences among patients with head and neck cancer: prevalence and associations with quality of life, symptom severity, depression, and rural residence. *Head Neck* 2009;31(8):994-1005. doi: 10.1002/hed.21053 [published Online First: 2009/04/03]
22. Rogers LQ, Markwell SJ, Verhulst S, et al. Rural breast cancer survivors: exercise preferences and their determinants. *Psycho-oncology* 2009;18(4):412-21. doi: 10.1002/pon.1497 [published Online First: 2009/02/26]
23. Rogers LQ, Courneya KS, Verhulst S, et al. Factors associated with exercise counseling and program preferences among breast cancer survivors. *J Phys Act Health* 2008;5(5):688-705. [published Online First: 2008/09/30]
24. Blaney JM, Lowe-Strong A, Rankin-Watt J, et al. Cancer survivors' exercise barriers, facilitators and preferences in the context of fatigue, quality of life and physical activity participation: a questionnaire-survey. *Psycho-oncology* 2013;22(1):186-94. doi: 10.1002/pon.2072 [published Online First: 2013/01/09]
25. Bernet AC, Wilens DE, Bauer M. Effectiveness-implementation hybrid designs: implications for quality improvement science. *Implementation Science* 2013;8 (Supplement 1)(S2):1-2.
26. Buffart LM, Ros WJ, Chinapaw MJ, et al. Mediators of physical exercise for improvement in cancer survivors' quality of life. *Psycho-oncology* 2014;23(3):330-8. doi: 10.1002/pon.3428
27. Schmitz KH, Courneya KS, Matthews C, et al. American College of Sports Medicine roundtable on exercise guidelines for cancer survivors. *Med Sci Sports Exerc* 2010;42(7):1409-26. doi: 10.1249/MSS.0b013e3181e0c112
28. Tomasone J, Zwaal C, Kim GM, et al. Moving guidelines into action: A report from cancer care Ontario's event let's get moving: Exercise and rehabilitation for cancer patients. *Curr Oncol Journal Translated Name Current Oncology* 2017;24(1):e65-e74. doi: http://dx.doi.org/10.3747/co.24.3422
29. Smith-Turchyn J, Richardson J, Tozer R, et al. Physical Activity and Breast Cancer: A Qualitative Study on the Barriers to and Facilitators of Exercise Promotion from the Perspective of Health Care Professionals. *Physiother Can* 2016;68(4):383-90. doi: 10.3138/ptc.2015-84

Table 1. Effectiveness Outcomes

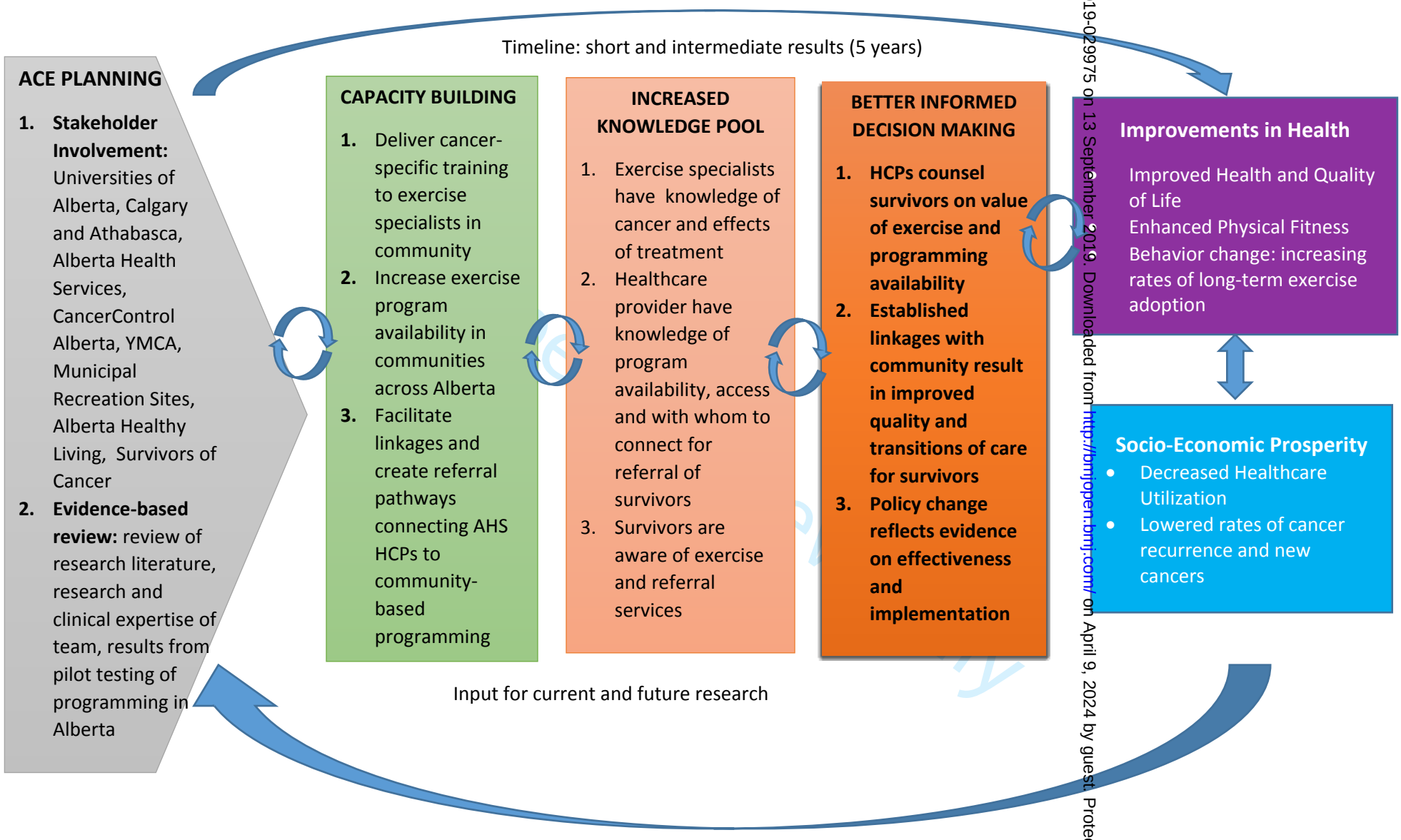
Outcome Category	**Outcome measure/ measurement**	**Target for improvement in outcome score**
Physical activity behavior	Godin Leisure-time questionnaire and exercise adherence diary	+10% or more of survivors are engaging in PA at one-year
Body Composition	Waist circumference	+10% survivors with reduction to below disease risk cut-point
Aerobic Endurance	6-Minute walk test	+35 metres
Grip strength	Hand-grip dynamometry	+10% meeting or exceeding age-specific average score
Timed sit-to-stand	30 second sit-to-stand	+10% meeting age-specific functional level
Upper limb flexibility	Shoulder Flexion Range Goniometry	+10% meeting or exceeding age-specific average score
Lower limb flexibility	Sit and reach test	+10% meeting or exceeding age-specific average score
One-legged balance	Number attaining 45 second maximum time	+10% meeting age-specific level
Cancer-related Quality of Life (QoL)	Functional Assessment of Cancer Therapy (FACT) – General Scale	+ 3 points
Fatigue	FACT-Fatigue	+ 6 points
General health-related QoL	RAND Short Form-36	12% change from baseline
Generic Health Status	EQ5D -5L	+0.06 from baseline
Adherence	Attendance at sessions	> 70% attendance at exercise sessions

Table 2. RE-AIM Framework

Components/ Categories	1	2	3	4
Reach (Individual Level)	Methods used to recruit survivors	Efficiency of referral and screening processes	Participation rate: absolute numbers and proportions	Characteristics of participating survivors; stage of change; # tumour groups reached
Effectiveness (Individual & Institutional Level)	Outcomes – patient rated outcomes, and fitness measures	Attrition from the program and reasons: random/ non-random	Safety: adverse events rate related to exercise participation	Cost of overall programming to the individual, to community organization & CancerControl
Adoption (Institutional Level)	HCPs referral to programming: number & programs accessed	Programming options: number, type and location	# cancer trained exercise specialists in community	Characteristics of adoption/ nonadoption across centres
Implementa-tion (Community)	Type and intensity level of activity	Extent exercise protocol delivered as intended	Consistency in program availability	Implementation of cancer-specific exercise into general community centre programming
Maintenance (Individual, Institutional & Community)	Individual physical activity levels at a minimum 1 year follow-up	Individual physical fitness at a minimum 1 year follow-up	Exercise referral implemented into institutional practice and policy	Sustainability of exercise in community-based centre (# ongoing fee-for-service memberships)

Figure Legends:

Figure 1. ACE Research to Impact Framework (Adapted from AIHS Research to Impact Framework)



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Community-based Exercise for Health Promotion and Secondary Cancer Prevention in Canada: Protocol for a Hybrid Effectiveness-Implementation Study

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ABSTRACT

Introduction

Cancer care has expanded from a disease-focused, survival-oriented model to an approach that now considers how survivors can live well in the aftermath of intensive therapy, where they may deal with significant changes to their bodies, mental health, or emotional well-being. Research evidence supports the benefit of exercise during and following cancer treatments for cancer-related symptoms, physical functioning and fitness, and health-related quality of life. To move this efficacy evidence into practice, we designed and launched a five-year study to evaluate the relative benefit from implementing a clinic-to-community-based cancer and exercise model of care.

Methods

A hybrid effectiveness and implementation trial design is being used to evaluate the effectiveness of delivery of community-based exercise and to collect data on implementation of the program. The study opened in January 2017, with estimated completion by January 2022. The program will be delivered in seven cities across the province of Alberta Canada, with sites including three academic institutions, six YMCA locations, Wellspring Edmonton and Calgary, and six municipal fitness centres. Participants are adult cancer survivors (N = 2500) from all tumour groups and stages, and at any time point along their cancer treatment trajectory, up to three years post treatment completion. Survivors take part in a minimum of 60 minutes of mild-to-moderate intensity full body exercise twice weekly for a 12-week period. The primary effectiveness outcome is the proportion of participants meeting or exceeding 150-minutes of moderate-intensity exercise per week at one-year follow-up. The Reach, Effectiveness, Adoption, Implementation and Maintenance (RE-AIM) framework will be utilized to capture individual and organizational-level impact of the exercise program at 12 and 24 weeks, and one-year follow-up. The cohort of survivors participating in the study will allow for long-term (5-year) evaluation of rates of cancer recurrence and secondary cancers beyond the funding period.

Ethics and Dissemination

The study was approved by the Health Research Ethics Board of Alberta. The study is funded by Alberta Innovates and the Alberta Cancer Foundation. The study will help to answer critical questions on the effectiveness of cancer-specific community-based exercise programming in both the short and long-term. Collectively, the findings will help to inform the acceptability, adoption, feasibility, reach, and sustainability of community-based exercise.

Trial Registration

ClinicalTrials.gov: NCT02984163 (prospectively registered)

Strengths and Limitations of this Study

- The study involves patients and other stakeholders in the design and ongoing delivery of exercise programming.
- External validity of the program is supported by the community-based implementation focus, with novel aspects of supervision by cancer-trained exercise specialists and support provided by study personnel.
- We will determine both the short and long-term effectiveness of community-based exercise, and identify important intervention-implementation interactions.
- The main limitation of the ACE hybrid effectiveness-implementation study is related to the single-group design that does not allow for comparison of findings to usual care.

Key words: cancer survivorship, exercise, physical activity, quality of life, supportive care, implementation, knowledge translation

Introduction

In 2019, there will be an estimated 20,473 new cancer cases diagnosed in Alberta Canada. By 2030, this number is expected to exceed 27,000.[1] The growing population of individuals living with or beyond a diagnosis of cancer highlights the long-term impact of cancer and its therapies on the body, the mind and on overall health of survivors. This necessitates an expansion of focus from merely survival to how to live in the aftermath of intensive therapy with an altered body and attendant psychological changes. There is an immediate and emergent need to disseminate strategies that can improve the health of cancer survivors.

Exercise is a low cost and safe intervention for cancer survivors with beneficial effects on physical functioning and all aspects of health-related fitness, including aerobic and muscular fitness, and body composition.[2-4] Exercise reduces the severity of treatment-related side effects such as pain, fatigue and lymphedema[5-8], and also benefits psychosocial well-being, including mental and emotional health, and overall quality of life.[4] Evidence from randomized controlled trials has shown that supervised exercise results in better chemotherapy completion rates, thus potentially optimizing treatment outcomes.[5,6] Importantly, for three of the four most common cancers, representing 50% of all cancer survivors, exercise may prove valuable for ***secondary cancer prevention***.[7-11] Despite the known benefits of exercise, including the prevention of secondary cancers, less than one third of cancer survivors self-report that they are meeting the public health guidelines recommendations for physical activity.[3] This proportion is lower than the self-reported estimates of the general population (52%) in Canada.[12]

In recent years, strong evidence supporting the efficacy of exercise for cancer survivors has resulted in the development of cancer-specific exercise guidelines.[3,13,14] As a result, implementation of programming in the community-based setting and preliminary data evaluating effectiveness of programming have begun to emerge.[4,15-20] While positive results have been seen with lab-based

studies[4], these results may not translate into the same benefits when implemented in a community-based setting.[21] To date, published cancer-specific exercise implementation studies report significant short term benefit from exercise for physical activity[22], six minute walk test (6MWT) distance[17,22], fatigue[23], quality of life[22,23] and medical costs.[23] However, high program attrition[19,24-26] suggests the need for further exploration on the extent and nature (random or nonrandom) of program dropouts and withdrawals. Moreover, the overall uptake of community-based exercise by cancer survivors relative to the larger population of survivors appears low. Finally, there is a lack of data from implementation studies supporting the long-term effectiveness of programming for physical fitness and quality of life outcomes, overall health including healthcare utilization, and long-term survivorship, including survival rates.[27]

In order to move the efficacy evidence into practice, we designed and launched a five-year hybrid effectiveness and implementation study to evaluate the relative benefit from an Alberta wide clinic-to-community-based cancer and exercise model of care – the Alberta Cancer Exercise (ACE) program, and to evaluate the implementation of such an initiative. The overarching goal of the ACE program is to provide and support high quality, timely and personalized exercise for the survivor after a cancer diagnosis. In addition to implementing exercise programming, our hybrid effectiveness-implementation study was designed to better evaluate exercise effectiveness on overall health, considering both physical and psychosocial outcomes. At a pragmatic and policy level, we will aim to capture the costs, and potential for cost savings, of such a program.[28] To achieve widespread adoption, we acknowledge that our program must benefit participants, and must be cost-effective and reduce health care utilization. At present, there are limited data on these key aspects of community-based exercise programs.

Objectives

The specific objectives of this study are to:

1) Determine the utility of facilitated referral of survivors, where participants are screened for

inclusion in exercise programming within their respective communities, as a strategy for increasing adoption of exercise, with the primary aim to increase physical activity levels of participating cancer survivors.

2) Determine the immediate and long-term effectiveness of community-based programming on the survivors' health-related quality of life (QoL), physical fitness, patient-reported symptoms including fatigue and distress, as well as healthcare utilization.
3) Identify strategic opportunities for enhancing implementation of the ACE clinic-to-community strategy by formalizing screening methods, referral processes, and incorporating clinical evaluation of physical function.

Methods

A hybrid effectiveness and implementation trial design is being used to evaluate the effectiveness of delivery of community-based exercise and to collect data on implementation of the program.[29] The study opened in January 2017 and will run for a 5-year period to January 2022. We chose this trial design because: 1) there is strong evidence from efficacy trials supporting the benefit of exercise for survivors both during and following cancer treatment, 2) there is a limited body of evidence supporting implementation of programming in the community and evidence supporting objective outcomes and long-term adoption are currently lacking; and 3) with appropriate pre-exercise evaluation and screening, there is minimal risk in implementing a community-based exercise intervention. The hybrid design provides important data on the effectiveness of community exercise programming while fast-tracking translation of research findings into clinical practice and survivorship care pathways (Figure 1: Study Schema).

Participants

Participants are adult cancer survivors from all tumour groups and stages, and at any time point along their cancer treatment trajectory into the survivorship post-cancer treatment period, up to three years post treatment completion. Participants can self-refer to the program or be referred by their healthcare professional. This inclusionary focus will allow us to build a clinic-to-community model

that is sustainable and meets the needs of most cancer survivors. Ethical approval was received from the Health Research Ethics Board of Alberta: Cancer Committee and all participants are required to provide written informed consent.

We will aim to recruit a minimum of 60% of survivors from the three target cancer types with evidence supporting secondary prevention: breast, prostate, and colorectal. These samples will allow for subgroup analyses across sites and cancer groups. This cohort of survivors participating in the study will allow for long-term evaluation of rates of cancer recurrence, secondary cancers, and other chronic diseases (e.g., cardiovascular diseases, diabetes) beyond the funding period.

Setting

The exercise programming intervention takes place at six YMCAs and six municipal fitness centres, three Wellspring locations (a non-profit cancer support organization) in Calgary (two sites) and Edmonton (one site), as well as three Academic fitness facilities (two of which are cancer-specific facilities). See Figure 2: ACE Programming Sites Map.

Eligibility: Inclusion criteria

Participants are screened for eligibility over the phone by the respective site coordinator (Alberta north or Alberta south) and must: 1) have a diagnosis of cancer of any type; 2) be over the age of 18 years; 3) be able to participate in mild levels of activity at minimum; 4) be pretreatment, *or* receiving active cancer treatment (e.g., surgery, systemic therapy and/or radiation therapy), *or* have received cancer treatment within the past 3 years *or* have existing long-term or late presenting effects of their cancer treatment (e.g. radiation fibrosis syndrome, lymphedema, communication deficits related to cancer treatment, or incontinence); and 5) be able to provide informed written consent in English.

Screening

Two Certified Exercise Physiologist (CEP), with graduate level training or certification in exercise physiology[30], and > five years of experience in the cancer field, perform the screening for exercise safety (one CEP north, one CEP south). The CEPs report to the respective study Principal

Investigators at the Tertiary centres in the north and south of Alberta. For screening purposes, consenting participants complete a cancer-specific intake form and Physical Activity Readiness Questionnaires (PAR-Q+) online to determine appropriateness for community-based exercise programming. If any clarification on responses or status are needed, the CEP contacts the participant via telephone or meets with them in-person. Data are collected on *exercise preferences* as well as the participant's *Physical Activity Stages of Change* to inform the participant's status in terms of preferences, attitudes and behaviors towards increasing physical activity. The CEP oversees baseline objective assessments, and evaluates testing results. The CEP then triages the participant to local programming based on his/ her current health, findings of baseline objective assessment, cancer-related symptoms, and exercise and location preferences**.** If safety issues emerge during screening (e.g. uncontrolled seizures, history of falls, presence of metastatic disease, recent surgery or hospitalization), the CEP consults with the participant's oncologist or family physician on the need for further evaluation and/ or referral to rehabilitation services or medically supervised exercise programming.

Implementation Components and Framework

1. Cancer-specific Education and Support for Community-based Exercise Specialists

All community-based exercise programming is administered by exercise specialists (i.e. certified personal trainer, kinesiologist or group exercise instructor) who have undergone the *ACE Cancer and Exercise: Training for Fitness Professionals* online course offered through the University of Calgary. The training involves 16 hours of cancer-specific content related to cancer biology, cancer incidence, treatment and treatment-related effects, exercise evidence and prescription for cancer survivors, and health behavior change. The ACE CEP provides additional in-person training to ensure community-based exercise professionals have the skills and knowledge required to work with the cancer population, as well as ongoing support to ensure success of the program implementation. This training aids in the dissemination of the ACE program's critical knowledge to key community fitness partners.

2. Screening, Referral and Support for Community-based Exercise Programming

The ACE program bridges the gap between Healthcare Professionals (HCPs) and community exercise programming by facilitating the referral of survivors to appropriate cancer-specific exercise programming. The CEPs provide education and onsite support to HCPs within the tertiary centres (Calgary and Edmonton), and via online and telephone-based support to HCPs working with survivors in smaller communities.

Patient and Public Involvement

Our ACE clinic-to-community based exercise program works with survivors and families, community exercise specialists, HCPs and end-users to improve the survivor exercise experience. All stakeholders, including cancer survivors, contributed to the design and delivery of ACE from inception, including providing input towards the funding application and during pilot testing. Survivors informed the format of the study (e.g. no control group, implementation focus), recruitment (e.g. self-referral option), eligibility (e.g. including all cancer types and stage of disease) and intervention design in terms of preferences for exercise location (e.g. community locations, ease of parking), format (e.g. supervised program, group class, mild-to-moderate intensity exercise, instructors with knowledge in cancer), days per week (i.e. two), and time commitment (i.e. 60-90 minutes per session). A series of future focus groups and semi-structured interviews are planned to elicit feedback from participants, HCPs and exercise specialists over the course of ACE implementation.

Dissemination and utilization of our research findings will involve partnering with cancer groups such as Canadian Cancer Survivorship Network, Prostate Cancer Canada, the Canadian Cancer Society, the Canadian Partnership Against Cancer, the Canadian Physiotherapy Association Oncology Division, and the Psychosocial and Palliative Oncology Network. Collaboration with these agencies will ensure that information from the study will be widely disseminated to local as well as the broader cancer survivor community across Canada.

Exercise Intervention

Intervention options are geared to the various settings where ACE is being implemented. Participants take part in a combination of aerobic, resistance, balance, and flexibility exercises delivered in a standardized circuit-type class setting or group personal training format, twice weekly for a minimum of 60 minutes per session (approximately 3-4 metabolic equivalent units per session) for a 12-week period. The exercise sessions are conducted in small groups of 8-15 participants under the direct supervision of the community-based ACE trained exercise specialist. Two options for community-based exercise programming exist: group fitness classes or supervised fitness centre access. The program includes options for low-to-moderate intensity exercise, and is progressed in intensity over the 12-week program duration (from 3 to 5 metabolic equivalent units per session) as a means to progress participants towards recommended physical activity levels. Participating community sites offer one or more of these options depending on available resources and demand. Attendance at the exercise sessions is tracked as a marker of acceptability. Reasons for missed sessions are recorded. Exercise adherence includes attendance at supervised exercise sessions and average exercise minutes per week over the study period. Intensity is monitored using the 10-point Borg Rating of Perceived Exertion scale.[31,32] Active support and ongoing mentoring by the CEP is provided to community-based exercise specialists in the participating community program for the duration of ACE programming. Fidelity checks are performed by the respective CEP at scheduled times during the 12-week exercise session. Participants record exercise sessions in minutes and intensity in their training log, and other physical activity in their exercise diary. To encourage longer-term exercise adherence, participants are offered a second 12-week optional maintenance program, where possible, at low to no cost to survivors.

Participants assessed as having high needs (e.g. mobility issues, high risk of falling, risk of bone fracture, cognitive issues) due to active cancer, metastatic disease or with severe symptoms (where their disease or symptoms pose a risk in terms of safety of community-based exercise participation)

are referred to ACE medically supervised programming or local cancer rehabilitation services.

Outcomes to Support Effectiveness of Programming

The CEPs perform the objective assessments at the University sites or at the respective fitness facilities offering the programming both before (baseline) and after the exercise program (at week 12), with further follow-up objective testing at 24-weeks and one-year at the tertiary sites. The respective CEPs travel to the smaller cities in the North and South to conduct the baseline and 12-week assessments.

Objective and subjective physical outcome measures with demonstrated validity and reliability include:

- Physical activity level: Godin Leisure Time Physical Activity Questionnaire[33-35];
- Height, weight (calculation of body mass index);
- Waist and hip circumference[36];
- Six-minute walk test[37];
- Other objective measures: grip strength[38-40], timed sit-to-stand[41], shoulder flexion[42] (flexibility), and one-legged stance (balance)[43];
- Cancer-related symptoms: Edmonton Symptom Assessment Scale and Screening for Distress[44];

Health-related QoL is assessed using the Functional Assessment of Cancer Therapy-General[45] and Fatigue scales[46], and RAND Short Form Instrument (SF-36)[47], and EQ5D-5L[48] at baseline, 12-weeks, 24-weeks, and one-year for all participants. Participants will have the option for further follow-up yearly for the duration of the study. The study database was created in the REDCap system provided by the Women and Children's Health Research Institute (WCHRI) and hosted in the University of Alberta's Faculty of Medicine & Dentistry's data centre. Data collection and storage will comply with the measures outlined in WCHRI's REDCap privacy document.

Additional tests performed where equipment, time and resources are available: (i) 1or 8 repetition

maximum bench press and 1 or 8 repetition maximum leg press to determine muscular strength; (ii) Sit-and-reach test to assess flexibility; (iii) plank muscular endurance test; (iv) push-up test.

Safety is monitored during exercise testing and training by the CEP and the ACE trained exercise specialists in community locations. Participants are asked to report any issues, injuries, or falls, related and unrelated to exercise participation to the ACE exercise specialist at the respective site. Where necessary, the medical advisor and rehabilitation team at the cancer centre are consulted. The CEPs and ACE exercise specialist record rates of adverse events (minor to serious adverse events including cardiovascular events, falls or musculoskeletal injuries) on the REDCap database with serious adverse events also reported to the Research Ethics Board. A priori targets for objective outcomes, symptoms and quality of life outcomes will be used to inform effectiveness and safety of the intervention (Table 1).

Outcomes to Support Implementation

The reach, effectiveness, adoption, implementation and maintenance (RE-AIM) framework will be utilized to evaluate and enhance the external validity of the ACE program, and presents a means to evaluate the impact of a community-based intervention as a function of these five factors. This framework has been used to evaluate health and lifestyle behaviours to determine the public health impact of the intervention.[27,49] Embedded within RE-AIM is a cost description analysis pertaining to the survivor (individual costs) and the institutions (Community fitness facilities, Universities, and CancerControl Alberta). A proposed RE-AIM evaluation plan to assess the impact of the ACE program has been developed based on existing research (Table 2).[27]

Health Care Utilization Evaluation

The proposed methods for health care utilization include evaluation of usage among participants compared to that of matched controls, before and after the exercise program. Using personal health numbers (PHN) for consenting participants who provide permission, the PHN will be linked to the

Cancer Registry to obtain: tumor type, sex, year of diagnosis, age and stage at diagnosis, and provincial zone of residence. These six variables will be used to match each participant (1:1, as closely as possible) to a control identified from the Cancer Registry. For each matched pair, "time 0" will be the date the participant joined the exercise program. Relative to this date, the Cancer Registry records will be linked to administrative data sources to capture all physician visits, emergency room visits and hospitalizations, one year prior to and one year following "time 0". For physician visits, we will link to Alberta Health physician claims data. The following variables will be collected: date of visit, health service type code and category, primary/secondary/tertiary diagnoses, and health service(s) performed. Health care utilization will be examined overall (costs summed for each service component and each database) and by subgroups of interest (e.g., diagnostic groupings, services provided, resource intensity weights), before and after "time 0", separately for cases and controls. Differences in health care utilization across the two time periods will be described for both groups. The analysis will be performed for all participants, and stratified by tumor type.

Analyses and Dissemination

Sample size

The overall sample size goal is to accrue up to 2500 survivors via the ACE five-year roll out across the province of Alberta (7 cities: 18 sites) to inform implementation. The primary objective outcome to assess study effectiveness is the number of participants meeting public health guidelines for physical activity at one-year follow-up. The current estimate for the number of cancer survivors meeting public health guidelines of 150 minutes or more of moderate intensity exercise per week is 25.8%.[50] According to the Conference Board of Canada, by simply getting 10% of Canadians with suboptimal levels of physical activity to exercise more would reduce incidence rates for major chronic conditions including cancer, and result in significant savings in healthcare costs.[51] Thus, assuming a 10% increase in the proportion of participants meeting the guidelines for physical activity (minimally important difference of 10%) at one-year ($p < 0.01$; 90% power), a sample size of approximately 305 survivors would be required. As the aim of the study is to evaluate both

effectiveness and implementation, evaluating site-specific effects and implementation issues is of utmost importance, and thus our sample will allow adequate power for subgroup analyses given the number of sites and outcomes, and the anticipated variability among participants, cancer types, and disease stages.

Statistical Analysis Plan

Descriptive analyses will be performed to evaluate participant demographic, medical and exercise related variables, as well as RE-AIM components including an economic evaluation of the program. We will perform checks of data integrity including evaluating statistical power, test assumptions, and missing data. A single proportion inference test and confidence interval will be performed to determine the proportion of eligible survivors who provide informed consent and complete the program, as well as adherence rates to the program. Generalized linear mixed models will be utilized to examine the changes over time in the program participants on the patient-reported outcomes, including objective outcomes, activity levels, and indices of QoL (i.e., baseline, 12-weeks, 24-weeks and One-year). The cohort of survivors participating in the study will allow for long-term evaluation of rates of cancer recurrence and secondary cancers beyond the study period.

DISCUSSION

In recent years, the focus of research in the oncology exercise field has expanded from determining efficacy through randomized controlled trial designs to include "real world" effectiveness studies focusing on implementation of exercise into cancer care.[17,19,20,23] A wide variety of approaches to promote exercise among cancer survivors are available, including programs that are medically supervised, community-based, or self-directed/ home-based.[21] Advantages of community-based programs include high accessibility, safety and supervision of exercise, and social interaction.[18] Importantly, systematic review evidence supports greater and more consistent benefits when exercise is delivered in a group or supervised setting when compared to a home-based or unsupervised setting.[52] Moreover, surveys of cancer survivors show a high interest in exercise, with reported preference for exercise programs that are offered in a supportive environment where

treating and managing cancer are understood, and at a location that focuses on health promotion rather than illness.[53-55] Community-based studies performed to date, while demonstrating short-term effectiveness, are lacking data supporting long-term effectiveness. Moreover, studies commonly report low adherence and high dropout rates.[21,27] Given the infancy of implementation efforts in regards to community-based programming, further research with greater attention to implementation science aspects appears warranted.

We propose that our hybrid effectiveness-implementation study will help to answer critical questions on the value of cancer-specific community-based exercise programming. The ACE study will allow us to determine both the short and long-term effectiveness of exercise, and enhance our ability to identify important intervention-implementation interactions. Collectively, the findings will help to inform the acceptability, adoption, feasibility, reach, and sustainability of community-based exercise, and simultaneously evaluate integration of exercise into clinical care.[56]

Consistent with the design of an effectiveness study, the ACE program is a cancer-specific exercise intervention with broad eligibility criteria that reflect "real-world" conditions. As many survivors report feeling neither physically nor psychologically prepared to engage in community-based exercise programs designed for the general public[55], a feature of ACE is the built-in flexibility of the exercise prescription such that participants self-select the exercise intensity based on presenting symptoms, "down days", or personal preference. While participants are expected to meet a minimal goal of two hours per week of at least light intensity exercise, the participant is encouraged to exceed this goal if able and desired.

Our ACE integrated knowledge translation strategy involves stakeholders in the design and ongoing delivery of ACE (i.e. survivors, end-users, administrators and policy-makers) and aims to address HCPs barriers and facilitators to exercise counseling and referral within the local cancer clinical

setting. To address issues seen with less than optimal adherence and completion rates in previous implementation studies, key strategies built into ACE include monitoring of exercise adherence and behavior change support for exercise.[17] The primary behavioral supports within the ACE program are the supervised and supportive aspects of the programming, along with exercise behaviour change education, goal setting and self-monitoring of activities. An ACE trained exercise specialist at the community site leads exercise classes and sessions. An ACE CEP and physical therapist are available to provide additional support to the survivor to address issues related to cancer treatment effects. This supportive format allows for modification and tailoring of the exercise, as needed, to the survivor's cancer type, capabilities and preferences.[57] In theory, if the program meets the needs of survivors, then adherence and completion rates should be high, reflecting program acceptability.

Recently published guidelines from Australia endorse the integration of exercise into cancer care as a means to lessen some of the negative effects of cancer and its treatment.[13] Importantly, the guidelines identify the need for cancer HCPs to discuss the role of exercise in cancer recovery, and recommend referral of survivors to a CEP and/or physical therapist with experience in cancer care.[13] Implementation studies, to date, have largely focused on the delivery of an exercise intervention rather than studying the processes and outcomes associated with implementation within the healthcare system. Despite guidelines supporting exercise [3,14,58], challenges exist with implementing exercise counseling and referral into practice due to the existing complexity and competing priorities in the cancer clinical setting.[59] Embedding CEP positions within our inter-professional supportive care team has the potential to address these challenges, and is seen as a sustainable care model that will add measurable value to our efforts to integrate exercise into clinical care.[60,61]

There are important limitations to note in the design of the ACE hybrid effectiveness-implementation study related to the single-group design that does not allow for comparison of findings to usual care. As such, threats to internal validity exist including maturation, history, testing

and regression to the mean. To address these concerns, specific objective outcome targets were determined, a priori, based on previous randomized controlled trial findings. Moreover, to reduce bias associated with testing, ACE assessors, who are specially trained and blinded to previous results, conduct the evaluations and the participants complete the patient-reported outcomes electronically at home. External validity of the program is supported by the community-based implementation focus, with novel aspects of supervision by cancer-trained exercise specialists and support provided by ACE CEPs and physical therapists. Importantly, evaluation of the program is guided by the RE-AIM framework and includes a robust suite of endpoints.

Conclusions

ACE is a healthy lifestyle initiative, encouraging and supporting cancer survivors to take a role in their own wellbeing by increasing capacity for, and accessibility to cancer-specific exercise in the community, and by facilitating referral to programming. Through this research, we will better understand the effectiveness of the program at the level of the individual and institution, and evaluate processes to support future implementation and sustainability. Supporting improved rates of exercise adoption and sustained adherence to an active lifestyle among survivors of cancer will improve physical fitness and QoL, and may lower rates of cancer recurrence, secondary cancers, and other chronic diseases for cancer survivors in Alberta.

Declarations:

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Availability of data and material

Data sharing is not applicable to this article as no datasets were generated or analyzed (i.e., study protocol paper). Material developed to support this study is available from the corresponding author on reasonable request.

Author contributions

MLM, CS, TW, MSB, AAJ, HYL, JCE, ADM, JKV, KSC, JRM, MBP, and SNCR developed the study concept and protocol. MLM, SNCR, CS, and TW assisted in further development of the exercise and implementation protocol. All authors will oversee the implementation of the protocol and contribute to the acquisition, analysis and interpretation of data. MLM and SNCR drafted the manuscript, MLM, CS and SNCR contributed to revisions and MLM, CS, TW, MSB, AAJ, HYL, JCE, ADM, JKV, KSC, JRM, MBP, and SNCR approved the final manuscript.

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Competing interests

The authors declare that they have no competing interests.

Consent for publication

Not applicable.

Ethics approval and consent to participate

The study was approved by the Health Research Ethics Board of Alberta: Cancer Committee (ID: HREBA.CC-16-0905) and all participants are required to provide written informed consent.

REFERENCES

1. Surveillance and Reporting. The 2019 Report on Cancer Statistics in Alberta. Edmonton: Cancer Control Alberta, 2019.

2. Speck RM, Courneya KS, Masse LC, et al. An update of controlled physical activity trials in cancer survivors: a systematic review and meta-analysis. *J Cancer Surviv* 2010;4(2):87-100. doi: 10.1007/s11764-009-0110-5

3. Rock CL, Doyle C, Demark-Wahnefried W, et al. Nutrition and physical activity guidelines for cancer survivors. *CA Cancer J Clin* 2012;62(4):243-74. doi: 10.3322/caac.21142

4. Cormie P, Zopf EM, Zhang X, et al. The Impact of Exercise on Cancer Mortality, Recurrence, and Treatment-Related Adverse Effects. *Epidemiol Rev* 2017;39(1):71-92. doi: 10.1093/epirev/mxx007

5. van Waart H, Stuiver MM, van Harten WH, et al. Effect of Low-Intensity Physical Activity and Moderate- to High-Intensity Physical Exercise During Adjuvant Chemotherapy on Physical Fitness, Fatigue, and Chemotherapy Completion Rates: Results of the PACES Randomized Clinical Trial. *J Clin Oncol* 2015;33(17):1918-27.

6. Courneya KS SR, Mackey JR, et al:. Effects of aerobic and resistance exercise in breast cancer patients receiving adjuvant chemotherapy: A multicenter randomized controlled trial. *J Clin Oncol* 2007;25(28):4396-404. doi: http://dx.doi.org/10.1200/JCO.2006.08.2024 Embase Accession Number 2007524017 PMID 17785708 [http://www.ncbi.nlm.nih.gov/pubmed/?term=17785708]

7. Ibrahim EM, Al-Homaidh A. Physical activity and survival after breast cancer diagnosis: meta-analysis of published studies. *Med Oncol* 2011;28(3):753-65. doi: 10.1007/s12032-010-9536-x

8. Kenfield SA, Stampfer MJ, Giovannucci E, et al. Physical activity and survival after prostate cancer diagnosis in the health professionals follow-up study. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology* 2011;29(6):726-32. doi: 10.1200/JCO.2010.31.5226 [published Online First: 2011/01/06]

9. Ballard-Barbash R, Friedenreich CM, Courneya KS, et al. Physical activity, biomarkers, and

disease outcomes in cancer survivors: a systematic review. *J Natl Cancer Inst* 2012;104(11):815-40. doi: 10.1093/jnci/djs207

10. Meyerhardt JA, Giovannucci EL, Holmes MD, et al. Physical activity and survival after colorectal cancer diagnosis. *J Clin Oncol* 2006;24(22):3527-34. doi: 10.1200/JCO.2006.06.0855

11. Meyerhardt JA, Heseltine D, Niedzwiecki D, et al. Impact of physical activity on cancer recurrence and survival in patients with stage III colon cancer: findings from CALGB 89803. *J Clin Oncol* 2006;24(22):3535-41. doi: 10.1200/JCO.2006.06.0863

12. Colley RC, Garriguet D, Janssen I, et al. Physical activity of Canadian adults: accelerometer results from the 2007 to 2009 Canadian Health Measures Survey. *Health reports* 2011;22(1):7-14.

13. Cormie P, Atkinson M, Bucci L, et al. Clinical Oncology Society of Australia position statement on exercise in cancer care. *Med J Aust* 2018

14. Schmitz KH, Courneya KS, Matthews C, et al. American College of Sports Medicine roundtable on exercise guidelines for cancer survivors. *Med Sci Sports Exerc* 2010;42(7):1409-26. doi: 10.1249/MSS.0b013e3181e0c112

15. Leach HJ, Danyluk JM, Culos-Reed SN. Design and implementation of a community-based exercise program for breast cancer patients. *Curr Oncol* 2014;21(5):267-71. doi: 10.3747/co.21.2079

16. Leach HJ, Danyluk JM, Nishimura KC, et al. Evaluation of a Community-Based Exercise Program for Breast Cancer Patients Undergoing Treatment. *Cancer Nurs* 2015;38(6):417-25. doi: 10.1097/NCC.0000000000000217

17. Cheifetz O, Park Dorsay J, Hladysh G, et al. CanWell: meeting the psychosocial and exercise needs of cancer survivors by translating evidence into practice. *Psycho-oncology* 2014;23(2):204-15. doi: 10.1002/pon.3389

18. Santa Mina D, Au D, Brunet J, et al. Effects of the community-based Wellspring Cancer Exercise Program on functional and psychosocial outcomes in cancer survivors. *Curr Oncol* 2017;24(5):284-94. doi: 10.3747/co.23.3585

19. Haas BK, Kimmel G, Hermanns M, et al. Community-based FitSTEPS for life exercise program

for persons with cancer: 5-year evaluation. *Journal of oncology practice / American Society of Clinical Oncology* 2012;8(6):320-4, 2 p following 24. doi: 10.1200/JOP.2012.000555

20. Heston AH, Schwartz AL, Justice-Gardiner H, et al. Addressing physical activity needs of survivors by developing a community-based exercise program: LIVESTRONG(R) at the YMCA. *Clinical journal of oncology nursing* 2015;19(2):213-7. doi: 10.1188/15.CJON.213-217

21. Hardcastle SJ, Cohen PA. Effective Physical Activity Promotion to Survivors of Cancer Is Likely to Be Home Based and to Require Oncologist Participation. *J Clin Oncol* 2017;35(32):3635-37. doi: 10.1200/JCO.2017.74.6032

22. Irwin ML, Cartmel B, Harrigan M, et al. Effect of the LIVESTRONG at the YMCA exercise program on physical activity, fitness, quality of life, and fatigue in cancer survivors. *Cancer* 2017;123(7):1249-58. doi: 10.1002/cncr.30456

23. Translating Exercise Oncology Research into Practice: Effectiveness of a Community-Based Exercise Program for Cancer Patients and Survivors. MASCC/ISOO Annual Meeting Supportive Care in Cancer; 2015; Copenhagen Supportive Care in Cancer.

24. Santa Mina D, Au D, Auger LE, et al. Development, implementation, and effects of a cancer center's exercise-oncology program. *Cancer* 2019 doi: 10.1002/cncr.32297

25. Cheifetz O, Dorsay JP, MacDermid JC. Exercise facilitators and barriers following participation in a community-based exercise and education program for cancer survivors. *Journal of exercise rehabilitation* 2015;11(1):20-9. doi: 10.12965/jer.150183

26. Leach HJ, Danyluk JM, Nishimura KC, et al. Benefits of 24 versus 12 weeks of exercise and wellness programming for women undergoing treatment for breast cancer. *Support Care Cancer* 2016;24(11):4597-606. doi: 10.1007/s00520-016-3302-3

27. White SM, McAuley E, Estabrooks PA, et al. Translating physical activity interventions for breast cancer survivors into practice: an evaluation of randomized controlled trials. *Ann Behav Med* 2009;37(1):10-9. doi: 10.1007/s12160-009-9084-9

28. Abu-Omar K, Rutten A, Burlacu I, et al. The cost-effectiveness of physical activity

interventions: A systematic review of reviews. *Prev Med Rep* 2017;8:72-78. doi: 10.1016/j.pmedr.2017.08.006

29. Curran GM, Bauer M, Mittman B, et al. Effectiveness-implementation hybrid designs: combining elements of clinical effectiveness and implementation research to enhance public health impact. *Medical care* 2012;50(3):217-26. doi: 10.1097/MLR.0b013e3182408812

30. Canadian Society for Exercise Physiology. CSEP Certified Exercise Physiologist Ottawa, Ontario: Canadian Society for Exercise Physiology 2019 [Available from: https://www.csep.ca/view.asp?ccid=534.

31. Marks LE, Borg G, Ljunggren G. Individual differences in perceived exertion assessed by two new methods. *Percept Psychophys* 1983;34(3):280-8.

32. Borg G. Ratings of perceived exertion and heart rates during short-term cycle exercise and their use in a new cycling strength test. *Int J Sports Med* 1982;3(3):153-8. doi: 10.1055/s-2008-1026080

33. Amireault S, Godin G. The Godin-Shephard leisure-time physical activity questionnaire: validity evidence supporting its use for classifying healthy adults into active and insufficiently active categories. *Percept Mot Skills* 2015;120(2):604-22. doi: 10.2466/03.27.PMS.120v19x7

34. Amireault S, Godin G, Lacombe J, et al. The use of the Godin-Shephard Leisure-Time Physical Activity Questionnaire in oncology research: a systematic review. *BMC Med Res Methodol* 2015;15:60. doi: 10.1186/s12874-015-0045-7

35. Amireault S, Godin G, Lacombe J, et al. Validation of the Godin-Shephard Leisure-Time Physical Activity Questionnaire classification coding system using accelerometer assessment among breast cancer survivors. *J Cancer Surviv* 2015;9(3):532-40. doi: 10.1007/s11764-015-0430-6

36. Barrios P, Martin-Biggers J, Quick V, et al. Reliability and criterion validity of self-measured waist, hip, and neck circumferences. *BMC Med Res Methodol* 2016;16:49. doi: 10.1186/s12874-016-0150-2

37. Schmidt K, Vogt L, Thiel C, et al. Validity of the six-minute walk test in cancer patients. *Int J Sports Med* 2013;34(7):631-6. doi: 10.1055/s-0032-1323746

38. Bellace JV, Healy D, Besser MP, et al. Validity of the Dexter Evaluation System's Jamar dynamometer attachment for assessment of hand grip strength in a normal population. *J Hand Ther* 2000;13(1):46-51.

39. Hamilton GF, McDonald C, Chenier TC. Measurement of grip strength: validity and reliability of the sphygmomanometer and jamar grip dynamometer. *J Orthop Sports Phys Ther* 1992;16(5):215-9. doi: 10.2519/jospt.1992.16.5.215

40. Reuter SE, Massy-Westropp N, Evans AM. Reliability and validity of indices of hand-grip strength and endurance. *Aust Occup Ther J* 2011;58(2):82-7. doi: 10.1111/j.1440-1630.2010.00888.x

41. McAllister LS, Palombaro KM. Modified 30-Second Sit-to-Stand Test: Reliability and Validity in Older Adults Unable to Complete Traditional Sit-to-Stand Testing. *J Geriatr Phys Ther* 2019 doi: 10.1519/JPT.0000000000000227

42. Kolber MJ, Hanney WJ. The Reliability and Concurrent Validity of Shoulder Mobility Measurements Using a Digital Inclinometer and Goniometer: A Technical Report. *Int J Sports Phys Ther* 2012;7(3):306-13.

43. Franchignoni F, Tesio L, Martino MT, et al. Reliability of four simple, quantitative tests of balance and mobility in healthy elderly females. *Aging (Milano)* 1998;10(1):26-31.

44. Richardson LA, Jones GW. A review of the reliability and validity of the Edmonton Symptom Assessment System. *Curr Oncol* 2009;16(1):55. doi: 10.3747/co.v16i1.261

45. Cella DF, Tulsky DS, Gray G, et al. The Functional Assessment of Cancer Therapy scale: development and validation of the general measure. *J Clin Oncol* 1993;11(3):570-9. doi: 10.1200/JCO.1993.11.3.570

46. Yellen SB, Cella DF, Webster K, et al. Measuring fatigue and other anemia-related symptoms with the Functional Assessment of Cancer Therapy (FACT) measurement system. *J Pain Symptom Manage* 1997;13(2):63-74.

47. Jenkinson C, Wright L, Coulter A. Criterion validity and reliability of the SF-36 in a population

sample. *Qual Life Res* 1994;3(1):7-12.

48. Pickard AS, Wilke CT, Lin HW, et al. Health utilities using the EQ-5D in studies of cancer. *Pharmacoeconomics* 2007;25(5):365-84.

49. Glasgow RE, Emmons KM. How can we increase translation of research into practice? Types of evidence needed. *Annu Rev Public Health* 2007;28:413-33. doi: 10.1146/annurev.publhealth.28.021406.144145 [published Online First: 2006/12/08]

50. Neil SE, Gotay CC, Campbell KL. Physical activity levels of cancer survivors in Canada: findings from the Canadian Community Health Survey. *J Cancer Surviv* 2014;8(1):143-9. doi: 10.1007/s11764-013-0322-6

51. Bounajm F, Dinh T, Theiault L. Moving Ahead. The Economic Impact of Reducing Physical Inactivity and Sedentary Behaviour. Ottawa: The Conference Board of Canada, 2014:1-37.

52. Segal R, Zwaal C, Green E, et al. Exercise for people with cancer: a systematic review. *Curr Oncol* 2017;24(4):e290-e315. doi: 10.3747/co.24.3619

53. Rogers LQ, Malone J, Rao K, et al. Exercise preferences among patients with head and neck cancer: prevalence and associations with quality of life, symptom severity, depression, and rural residence. *Head Neck* 2009;31(8):994-1005. doi: 10.1002/hed.21053 [published Online First: 2009/04/03]

54. Rogers LQ, Courneya KS, Verhulst S, et al. Factors associated with exercise counseling and program preferences among breast cancer survivors. *J Phys Act Health* 2008;5(5):688-705.

55. Blaney JM, Lowe-Strong A, Rankin-Watt J, et al. Cancer survivors' exercise barriers, facilitators and preferences in the context of fatigue, quality of life and physical activity participation: a questionnaire-survey. *Psycho-oncology* 2013;22(1):186-94. doi: 10.1002/pon.2072

56. Bernet AC, Wilens DE, Bauer M. Effectiveness-implementation hybrid designs: implications for quality improvement science. *Implementation Science* 2013;8 (Supplement 1)(S2):1-2.

57. Buffart LM, Ros WJ, Chinapaw MJ, et al. Mediators of physical exercise for improvement in cancer survivors' quality of life. *Psycho-oncology* 2014;23(3):330-8. doi: 10.1002/pon.3428

58. Tomasone J, Zwaal C, Kim GM, et al. Moving guidelines into action: A report from cancer care Ontario's event let's get moving: Exercise and rehabilitation for cancer patients. *Curr Oncol Journal Translated Name Current Oncology* 2017;24(1):e65-e74. doi: http://dx.doi.org/10.3747/co.24.3422

59. Smith-Turchyn J, Richardson J, Tozer R, et al. Physical Activity and Breast Cancer: A Qualitative Study on the Barriers to and Facilitators of Exercise Promotion from the Perspective of Health Care Professionals. *Physiother Can* 2016;68(4):383-90. doi: 10.3138/ptc.2015-84

60. Fortier MS, Hogg W, O'Sullivan TL, et al. Impact of integrating a physical activity counsellor into the primary health care team: physical activity and health outcomes of the Physical Activity Counselling randomized controlled trial. *Applied Physiology, Nutrition, & Metabolism = Physiologie Appliquee, Nutrition et Metabolisme* 2011;36(4):503-14.

61. Santa Mina D, Sabiston CM, Au D, et al. Connecting people with cancer to physical activity and exercise programs: a pathway to create accessibility and engagement. *Curr Oncol* 2018;25(2):149-62. doi: 10.3747/co.25.3977

62. Government of Canada. Canadian Guidelines for Body Weight Classification in Adults 2011 [Available from: https://www.canada.ca/en/health-canada/services/food-nutrition/healthy-eating/healthy-weights/canadian-guidelines-body-weight-classification-adults/questions-answers-public.html#a4.

63. Bohannon RW, Crouch R. Minimal clinically important difference for change in 6-minute walk test distance of adults with pathology: a systematic review. *J Eval Clin Pract* 2017;23(2):377-81.

64. Record Owner NLM. What is the minimum clinically important difference in grip strength?

65. Statistics Canada. Musculoskeletal fitness in Canada 2007 to 2009: Government of Canada; 2015 [Available from: https://www150.statcan.gc.ca/n1/pub/82-625-x/2010001/article/11089-eng.htm accessed July 5, 2019.

66. Muir SW, Corea CL, Beaupre L. Evaluating change in clinical status: reliability and measures of agreement for the assessment of glenohumeral range of motion. *N Am J Sports Phys Ther* 2010;5(3):98-110.

67. Lemmink KA, Kemper H, Greef MH. The Validity of the Sit-and-Reach Test and the Modified Sit-and-Reach Test in Middle-Aged to Older Men and Women. *Res Q Exerc Sport* 2003;74(3):331-36.

68. Goldberg A, Casby A, Wasielewski M. Minimum detectable change for single-leg-stance-time in older adults. *Gait Posture* 2011;33(4):737-9. doi: 10.1016/j.gaitpost.2011.02.020

69. Wood-Dauphinee S. The Canadian SF-36 health survey: normative data add to its value. *Cmaj* 2000;163(3):283-4.

70. Pickard AS, De Leon MC, Kohlmann T, et al. Psychometric comparison of the standard EQ-5D to a 5 level version in cancer patients. *Medical care* 2007;45(3):259-63. doi: 10.1097/01.mlr.0000254515.63841.81

71. Pickard AS, Neary MP, Cella D. Estimation of minimally important differences in EQ-5D utility and VAS scores in cancer. *Health Qual Life Outcomes* 2007;5:70. doi: 10.1186/1477-7525-5-70

72. Rivera-Torres S, Fahey TD, Rivera MA. Adherence to Exercise Programs in Older Adults: Informative Report. *Gerontol Geriatr Med* 2019;5:2333721418823604. doi: 10.1177/2333721418823604

73. Coretti S, Ruggeri M, McNamee P. The minimum clinically important difference for EQ-5D index: a critical review. *Expert Rev Pharmacoecon Outcomes Res* 2014;14(2):221-33. doi: 10.1586/14737167.2014.894462

Table 1. Effectiveness Outcomes

Outcome measure/ measurement	**Minimal Clinically Important Difference*/ Established Cut point**	**Study target for improvement in outcome score**
Godin Leisure-time questionnaire	10% change in physical activity behaviour at one year	+10% or more of survivors are engaging in > 150 minutes of moderate intensity PA at one-year
Waist circumference	Cut points for health[62]: Men: 102 cm Women: 88 cm	+10% survivors with reduction to below disease risk cut-point based on age and gender
6-Minute Walk Test Distance	24 to 30.5 metres[63]	+30 metres
Hand-grip dynamometry	6.5 kg[64,65]	+10% meeting or exceeding age-specific average score
30 second sit-to-stand	Not established in cancer	+10% in the number of participants meeting age-specific functional level
Shoulder Flexion Range Goniometry	>10 degrees[66]	+10% meeting or exceeding age-specific average score
Sit and reach test	Population values[65,67] Men 0 to +5 cm Women 0 to +10cm	+10% meeting or exceeding age-specific average score
Single leg balance:	24 seconds[68]	+10% meeting 45 seconds maximum time
One repetition maximum test	MCID: 1-3%	+10% increase
Functional Assessment of Cancer Therapy (FACT) – General Scale	Population value[45]: score 88 MCID: 3 points	+ 3 points
FACT-Fatigue subscale	Population value[46]: score of 40 MCID: 3-6 points	+ 6 points
RAND Short Form-36	Population value[69]: 67-87/ 100 across domains; MCID 6-7 points	12% change from baseline
EQ5D -5L	EQ5D index: 0.06 [48,70,71]	+0.06 from baseline
Attendance at sessions	Population values in older adults: 58% to 77%[72]	> 70% attendance at exercise sessions

*The minimum clinically important difference (MCID) is the minimum difference that the patient is able to recognize and appreciate[73]

Table 2. RE-AIM Framework

Components/ Categories	Reporting outcomes
Reach (Individual Level)	• Methods used to recruit survivors • Efficiency of referral and screening processes • Participation rate: absolute numbers and proportions • Characteristics of participating survivors; stage of change; # tumour groups reached
Effectiveness (Individual & Institutional Level)	• Patient-reported and objective outcomes • Attrition from the program and reasons: random/ non-random • Safety: adverse events rate related to exercise participation • Cost of overall programming to the individual and to community organization
Adoption (Institutional Level)	• HCPs referral to programming: number & programs accessed • Programming options: number, type and location • Number of cancer trained exercise specialists in community • Characteristics of adoption/ nonadoption across centres
Implementa-tion (Community)	• Type and intensity level of activity • Extent exercise protocol delivered as intended • Consistency in program availability • Implementation of cancer-specific exercise into general community centre programming
Maintenance (Individual, Institutional & Community)	• Individual physical activity levels at a minimum 1 year follow-up • Individual physical fitness at a minimum 1 year follow-up • Exercise referral implemented into institutional practice and policy • Sustainability of exercise in community-based centre (# ongoing fee-for-service memberships)

Figure Legends:

Figure 1. Study Schema

Figure 2. ACE Programming Sites

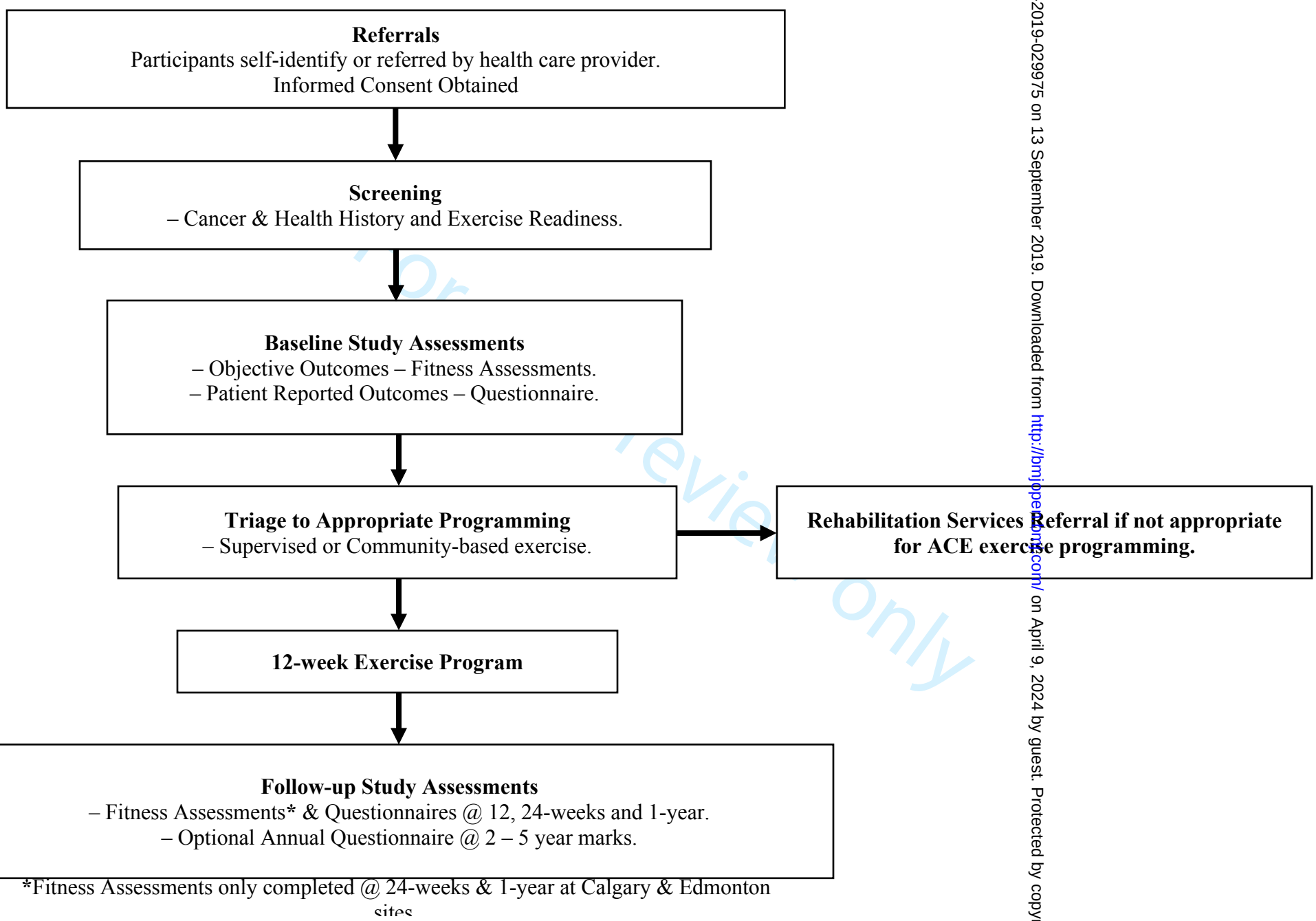

Figure 1. Study Schema

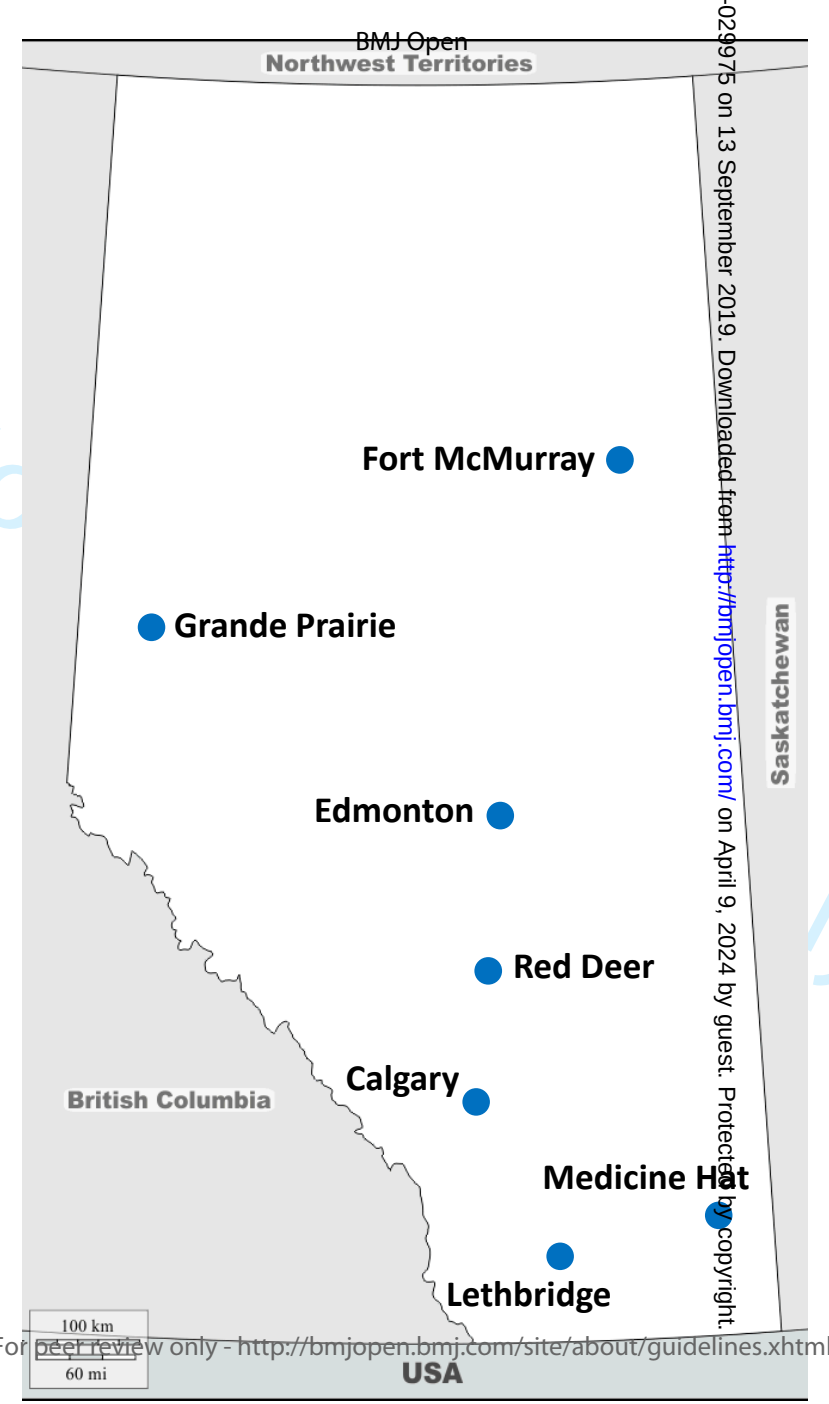

Figure 2: ACE Programming Sites

SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents*

Section/item	Item No	Description	Response/ location in manuscript
Administrative information			
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	The Alberta Cancer Exercise "ACE" Hybrid Effectiveness Implementation Study: A Protocol"
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry	Clinical Trials.gov: NCT02984163
	2b	All items from the World Health Organization Trial Registration Data Set	N/A
Protocol version	3	Date and version identifier	Protocol Version: March 2017
Funding	4	Sources and types of financial, material, and other support	Alberta Innovates: Cancer Prevention Research Opportunity: $1,250,000 Alberta Cancer Foundation: $400,000
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors	See title page 2: last paragraph All authors developed the study concept and protocol. MLM, SNCR, CS, and TW assisted in further development of the exercise and implementation protocol. All authors will oversee the implementation of the protocol and contribute to the

			acquisition, analysis and interpretation of data. MLM and SNCR drafted the manuscript, all authors contributed to revisions and all authors approved the final manuscript.
	5b	Name and contact information for the trial sponsor	**Mike Christen**, BComm Officer, Initiatives & Innovations (Health) **TEL:** 780.809.2557 mike.christen@albertainnovates.ca 1500 10104 103 Avenue NW Edmonton, Alberta, Canada T5J 0H8 Theresa Radwell Vice President, Program Investment Alberta Cancer Foundation 710, 10123- 99th Street Edmonton, AB. T5J 3H1 Email: Theresa.Radwell@albertacancer.ca
	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	Study sponsors were not involved in any aspect of the study from design to publication, and will not have any authority over activities related to the project.
	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	Coordinating centre: University of Alberta Oversight: Clinical Trials Unit, Cross Cancer Institute
Introduction			
Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for	Page 4-5: Paragraphs 1-4

		each intervention	
	6b	Explanation for choice of comparators	N/A: implementation study
Objectives	7	Specific objectives or hypotheses	Page 5 last sentence and Page 6
Trial design	8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory)	Page 5: Paragraph 2 - Hybrid effectiveness implementation study (single group)
Methods: Participants, interventions, and outcomes			
Study setting	9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	Page 7: Paragraph 3
Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	Page 7: Paragraph 4
Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	Page 8, Paragraph 3 and Page 9: Paragraph 1 &2: Implementation aspects Page 9 Paragraph 3: Exercise intervention
	11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease)	Page 10, Paragraph 2: referral to medically supervised exercise or cancer rehabilitation services
	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests)	Page 10, Paragraph 1:
	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	No restrictions in terms of usual activities.
Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis	Page 10, Paragraph 2: outcomes to support effectiveness Page 12, Paragraph 1: outcome to support implementation

		metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	Page 12, Paragraph 2: outcomes related to healthcare utilization
Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	Page 6 : 2nd paragraph: Screening Page 8: screening; baseline assessment, 12 week intervention, post (12-week) intervention assessment, 24-week and one-year follow-ups. Figure 1: Study Schema
Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	Page12, paragraph 1: sample of 1500. As this is an implementation study, the sample size was based on building capacity in the community. For the purposes of effectiveness a sample of approximately 305 participants are needed for our primary outcome. Page 13 (Sample size). An Alpha of 0.01 was used due to the large proposed sample size (risk of Type I error). We also set the power to .9 to avoid a Type II error. The larger sample will allow for subgroup analyses.
Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size	Passive recruitment strategies: brochures, posters. Active recruitment by healthcare professionals in oncology clinics.
Methods: Assignment of interventions (for controlled trials)			
Allocation:			
Sequence generation	16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	N/A

Allocation concealment mechanism	16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	N/A Implementation study
Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	N/A Implementation study
Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	N/A Participants are aware they are exercising.
	17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	N/A
Methods: Data collection, management, and analysis			
Data collection methods	18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	REDCap database, Page 11: 2nd paragraph: Self-reported outcomes are assessed at baseline, 12-weeks, 24 weeks, and one-year for all participants. Participants will have the option for further follow-up at year 2 and 3 following the program.
	18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	N/A: implementation study, thus, retention and completion rates are being monitored as outcomes.
Data management	19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	Two step data entry process: data is entered by one ACE staff person and verified by a second independent person. To improve data quality, REDCap validation rules have been set. For example, minimum and maximum values that can be accepted, and units as well as rules to ensure that valid dates are entered. All items of self-reported questionnaires are

			required and must be answered prior to moving on to next question.
Statistical methods	20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	Page 13: Paragraph 2
	20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	N/A
	20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	N/A
Methods: Monitoring			
Data monitoring	21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	N/A - Implementation study
	21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	N/A – Implementation study
Harms	22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	Page 11, last paragraph: Safety is monitored during exercise testing and training by the CEP and the ACE trained exercise specialists in community locations. The CEPs and ACE exercise specialists record rates of adverse events (minor to serious adverse events including cardiovascular events, falls or musculoskeletal injuries). Participants are asked to report any issues, injuries, or falls, related and unrelated to exercise participation to the ACE exercise specialist at the respective

			site.
Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	N/A: implementation study. Oversight is provided by the External advisory committee, Clinical Trials Unit at the Cross Cancer Institute and the Health Research Ethics Board of Alberta: Cancer Committee.
Ethics and dissemination			
Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval	Research Ethics approval is in place: HREBA.CC-16-0905
Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators)	Amendments will be submitted to the ethics board for any protocol changes including sub-studies related to the implementation process.
Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	Consent is obtained by the site principal investigators and research coordinators.
	26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	N/A
Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	Participants recruited to the study are provided with a unique study ID. All data is housed on the secure REDCap database (supported by the Faculty of Medicine and Dentistry at the University of Alberta). Data will be de-identified prior to any analyses.
Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site	N/A The authors declare no conflicts of interest.
Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	N/A: implementation study focus. Access to final data set undetermined.

Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	N/A: in the event of injury or harm, healthcare services will be provided as per standard of care
Dissemination policy	31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	An integrated knowledge translation plan is in place and available on our website: https://www.albertacancerexercise.com/knowledge-translation. End of study: The end of grant KT will focus on dissemination of the long-term effectiveness of programming on outcomes of survivors, including markers supporting secondary cancer prevention and healthcare utilization. Initial knowledge translation (KT) efforts will utilize academic peer-reviewed publications and conference presentations to disseminate new knowledge to the researcher/academic audiences working in the field of exercise and cancer survivorship. Survivors: Dissemination and utilization of our research findings will involve partnering with cancer groups such as the Canadian Breast Cancer Foundation, Prostate Cancer Canada, the Canadian Cancer Society, the Canadian Partnership Against Cancer, the Canadian Physiotherapy Association Oncology Division, and the Psychosocial and Palliative Oncology Network. Collaboration with these agencies will ensure that information from the study will be widely disseminated to local as well as the broader cancer survivor community across Canada.
	31b	Authorship eligibility guidelines and any intended use of professional writers	No professional writers will be used. Authorship must be warranted based on contribution to the study.
	3	Plans, if any, for granting public access to the full protocol,	No plans at this time.

	1c	participant-level dataset, and statistical code	
Appendices			
Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates	Consent forms developed for each region. Attached as an appendices.
Biological specimens	33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	N/A – no biological specimens are being collected.

*It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated. The SPIRIT checklist is copyrighted by the SPIRIT Group under the Creative Commons "Attribution-NonCommercial-NoDerivs 3.0 Unported" license.

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Community-based Exercise for Health Promotion and Secondary Cancer Prevention in Canada: Protocol for a Hybrid Effectiveness-Implementation Study

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ABSTRACT

Introduction

Cancer care has expanded from a disease-focused, survival-oriented model to an approach that now considers how survivors can live well in the aftermath of intensive therapy, where they may deal with significant changes to their bodies, mental health, or emotional well-being. Research evidence supports the benefit of exercise during and following cancer treatments for cancer-related symptoms, physical functioning and fitness, and health-related quality of life. To move this efficacy evidence into practice, we designed and launched a five-year study to evaluate the relative benefit from implementing a clinic-to-community-based cancer and exercise model of care.

Methods and Analysis

A hybrid effectiveness and implementation trial design is being used to evaluate the effectiveness of delivery of community-based exercise and to collect data on implementation of the program. The study opened in January 2017, with estimated completion by January 2022. The program will be delivered in seven cities across the province of Alberta Canada, with sites including three academic institutions, six YMCA locations, Wellspring Edmonton and Calgary, and six municipal fitness centres. Participants are adult cancer survivors (N = 2500) from all tumour groups and stages, and at any time point along their cancer treatment trajectory, up to three years post treatment completion. Survivors take part in a minimum of 60 minutes of mild-to-moderate intensity full body exercise twice weekly for a 12-week period. The primary effectiveness outcome is the proportion of participants meeting or exceeding 150-minutes of moderate-intensity exercise per week at one-year follow-up. The Reach, Effectiveness, Adoption, Implementation and Maintenance (RE-AIM) framework will be utilized to capture individual and organizational-level impact of the exercise program at 12 and 24 weeks, and one-year follow-up. The cohort of survivors participating in the study will allow for long-term (5-year) evaluation of rates of cancer recurrence and secondary cancers beyond the funding period.

Ethics and Dissemination

The study was approved by the Health Research Ethics Board of Alberta. The study is funded by Alberta Innovates and the Alberta Cancer Foundation. The study will help to answer critical questions on the effectiveness of cancer-specific community-based exercise programming in both the short and long-term. Collectively, the findings will help to inform the acceptability, adoption, feasibility, reach, and sustainability of community-based exercise.

Trial Registration

ClinicalTrials.gov: NCT02984163 (prospectively registered)

Strengths and Limitations of this Study

- The study involves patients and other stakeholders in the design and ongoing delivery of exercise programming.
- External validity of the program is supported by the community-based implementation focus, with novel aspects of supervision by cancer-trained exercise specialists and support provided by study personnel.
- We will determine both the short and long-term effectiveness of community-based exercise, and identify important intervention-implementation interactions.
- The main limitation of the ACE hybrid effectiveness-implementation study is related to the single-group design that does not allow for comparison of findings to usual care.

Key words: cancer survivorship, exercise, physical activity, quality of life, supportive care, implementation, knowledge translation

Introduction

In 2019, there will be an estimated 20,473 new cancer cases diagnosed in Alberta Canada. By 2030, this number is expected to exceed 27,000.[1] The growing population of individuals living with or beyond a diagnosis of cancer highlights the long-term impact of cancer and its therapies on the body, the mind and on overall health of survivors. This necessitates an expansion of focus from merely survival to how to live in the aftermath of intensive therapy with an altered body and attendant psychological changes. There is an immediate and emergent need to disseminate strategies that can improve the health of cancer survivors.

Exercise is a low cost and safe intervention for cancer survivors with beneficial effects on physical functioning and all aspects of health-related fitness, including aerobic and muscular fitness, and body composition.[2-4] Exercise reduces the severity of treatment-related side effects such as pain, fatigue and lymphedema[5-8], and also benefits psychosocial well-being, including mental and emotional health, and overall quality of life.[4] Evidence from randomized controlled trials has shown that supervised exercise results in better chemotherapy completion rates, thus potentially optimizing treatment outcomes.[5,6] Importantly, for three of the four most common cancers, representing 50% of all cancer survivors, exercise may prove valuable for ***secondary cancer prevention***.[7-11] Despite the known benefits of exercise, including the prevention of secondary cancers, less than one third of cancer survivors self-report that they are meeting the public health guidelines recommendations for physical activity.[3] This proportion is lower than the self-reported estimates of the general population (52%) in Canada.[12]

In recent years, strong evidence supporting the efficacy of exercise for cancer survivors has resulted in the development of cancer-specific exercise guidelines.[3,13,14] As a result, implementation of programming in the community-based setting and preliminary data evaluating effectiveness of programming have begun to emerge.[4,15-20] While positive results have been seen with lab-based

studies[4], these results may not translate into the same benefits when implemented in a community-based setting.[21] To date, published cancer-specific exercise implementation studies report significant short term benefit from exercise for physical activity[22], six minute walk test (6MWT) distance[17,22], fatigue[23], quality of life[22,23] and medical costs.[23] However, high program attrition[19,24-26] suggests the need for further exploration on the extent and nature (random or nonrandom) of program dropouts and withdrawals. Moreover, the overall uptake of community-based exercise by cancer survivors relative to the larger population of survivors appears low. Finally, there is a lack of data from implementation studies supporting the long-term effectiveness of programming for physical fitness and quality of life outcomes, overall health including healthcare utilization, and long-term survivorship, including survival rates.[27]

In order to move the efficacy evidence into practice, we designed and launched a five-year hybrid effectiveness and implementation study to evaluate the relative benefit from an Alberta wide clinic-to-community-based cancer and exercise model of care – the Alberta Cancer Exercise (ACE) program, and to evaluate the implementation of such an initiative. The overarching goal of the ACE program is to provide and support high quality, timely and personalized exercise for the survivor after a cancer diagnosis. In addition to implementing exercise programming, our hybrid effectiveness-implementation study was designed to better evaluate exercise effectiveness on overall health, considering both physical and psychosocial outcomes. At a pragmatic and policy level, we will aim to capture the costs, and potential for cost savings, of such a program.[28] To achieve widespread adoption, we acknowledge that our program must benefit participants, and must be cost-effective and reduce health care utilization. At present, there are limited data on these key aspects of community-based exercise programs.

Objectives

The specific objectives of this study are to:

1) Determine the utility of facilitated referral of survivors, where participants are screened for

inclusion in exercise programming within their respective communities, as a strategy for increasing adoption of exercise, with the primary aim to increase physical activity levels of participating cancer survivors.

2) Determine the immediate and long-term effectiveness of community-based programming on the survivors' health-related quality of life (QoL), physical fitness, patient-reported symptoms including fatigue and distress, as well as healthcare utilization.
3) Identify strategic opportunities for enhancing implementation of the ACE clinic-to-community strategy by formalizing screening methods, referral processes, and incorporating clinical evaluation of physical function.

Methods and analysis

A hybrid effectiveness and implementation trial design is being used to evaluate the effectiveness of delivery of community-based exercise and to collect data on implementation of the program.[29] The study opened in January 2017 and will run for a 5-year period to January 2022. We chose this trial design because: 1) there is strong evidence from efficacy trials supporting the benefit of exercise for survivors both during and following cancer treatment, 2) there is a limited body of evidence supporting implementation of programming in the community and evidence supporting objective outcomes and long-term adoption are currently lacking; and 3) with appropriate pre-exercise evaluation and screening, there is minimal risk in implementing a community-based exercise intervention. The hybrid design provides important data on the effectiveness of community exercise programming while fast-tracking translation of research findings into clinical practice and survivorship care pathways (Figure 1: Study Schema).

Participants

Participants are adult cancer survivors from all tumour groups and stages, and at any time point along their cancer treatment trajectory into the survivorship post-cancer treatment period, up to three years post treatment completion. Participants can self-refer to the program or be referred by their healthcare professional. This inclusionary focus will allow us to build a clinic-to-community model

that is sustainable and meets the needs of most cancer survivors.

We will aim to recruit a minimum of 60% of survivors from the three target cancer types with evidence supporting secondary prevention: breast, prostate, and colorectal. These samples will allow for subgroup analyses across sites and cancer groups. This cohort of survivors participating in the study will allow for long-term evaluation of rates of cancer recurrence, secondary cancers, and other chronic diseases (e.g., cardiovascular diseases, diabetes) beyond the funding period.

Setting

The exercise programming intervention takes place at six YMCAs and six municipal fitness centres, three Wellspring locations (a non-profit cancer support organization) in Calgary (two sites) and Edmonton (one site), as well as three Academic fitness facilities (two of which are cancer-specific facilities). See Figure 2: ACE Programming Sites Map.

Eligibility: Inclusion criteria

Participants are screened for eligibility over the phone by the respective site coordinator (Alberta north or Alberta south) and must: 1) have a diagnosis of cancer of any type; 2) be over the age of 18 years; 3) be able to participate in mild levels of activity at minimum; 4) be pretreatment, *or* receiving active cancer treatment (e.g., surgery, systemic therapy and/or radiation therapy), *or* have received cancer treatment within the past 3 years *or* have existing long-term or late presenting effects of their cancer treatment (e.g. radiation fibrosis syndrome, lymphedema, communication deficits related to cancer treatment, or incontinence); and 5) be able to provide informed written consent in English.

Screening

Two Certified Exercise Physiologist (CEP), with graduate level training or certification in exercise physiology[30], and > five years of experience in the cancer field, perform the screening for exercise safety (one CEP north, one CEP south). The CEPs report to the respective study Principal Investigators at the Tertiary centres in the north and south of Alberta. For screening purposes, consenting participants complete a cancer-specific intake form and Physical Activity Readiness

Questionnaires (PAR-Q+) online to determine appropriateness for community-based exercise programming. If any clarification on responses or status are needed, the CEP contacts the participant via telephone or meets with them in-person. Data are collected on *exercise preferences* as well as the participant's *Physical Activity Stages of Change* to inform the participant's status in terms of preferences, attitudes and behaviors towards increasing physical activity. The CEP oversees baseline objective assessments, and evaluates testing results. The CEP then triages the participant to local programming based on his/ her current health, findings of baseline objective assessment, cancer-related symptoms, and exercise and location preferences**.** If safety issues emerge during screening (e.g. uncontrolled seizures, history of falls, presence of metastatic disease, recent surgery or hospitalization), the CEP consults with the participant's oncologist or family physician on the need for further evaluation and/ or referral to rehabilitation services or medically supervised exercise programming.

Implementation Components and Framework

1. Cancer-specific Education and Support for Community-based Exercise Specialists

All community-based exercise programming is administered by exercise specialists (i.e. certified personal trainer, kinesiologist or group exercise instructor) who have undergone the *ACE Cancer and Exercise: Training for Fitness Professionals* online course offered through the University of Calgary. The training involves 16 hours of cancer-specific content related to cancer biology, cancer incidence, treatment and treatment-related effects, exercise evidence and prescription for cancer survivors, and health behavior change. The ACE CEP provides additional in-person training to ensure community-based exercise professionals have the skills and knowledge required to work with the cancer population, as well as ongoing support to ensure success of the program implementation. This training aids in the dissemination of the ACE program's critical knowledge to key community fitness partners.

2. Screening, Referral and Support for Community-based Exercise Programming

The ACE program bridges the gap between Healthcare Professionals (HCPs) and community

exercise programming by facilitating the referral of survivors to appropriate cancer-specific exercise programming. The CEPs provide education and onsite support to HCPs within the tertiary centres (Calgary and Edmonton), and via online and telephone-based support to HCPs working with survivors in smaller communities.

Patient and Public Involvement

Our ACE clinic-to-community based exercise program works with survivors and families, community exercise specialists, HCPs and end-users to improve the survivor exercise experience. All stakeholders, including cancer survivors, contributed to the design and delivery of ACE from inception, including providing input towards the funding application and during pilot testing. Survivors informed the format of the study (e.g. no control group, implementation focus), recruitment (e.g. self-referral option), eligibility (e.g. including all cancer types and stage of disease) and intervention design in terms of preferences for exercise location (e.g. community locations, ease of parking), format (e.g. supervised program, group class, mild-to-moderate intensity exercise, instructors with knowledge in cancer), days per week (i.e. two), and time commitment (i.e. 60-90 minutes per session). A series of future focus groups and semi-structured interviews are planned to elicit feedback from participants, HCPs and exercise specialists over the course of ACE implementation.

Exercise Intervention

Intervention options are geared to the various settings where ACE is being implemented. Participants take part in a combination of aerobic, resistance, balance, and flexibility exercises delivered in a standardized circuit-type class setting or group personal training format, twice weekly for a minimum of 60 minutes per session (approximately 3-4 metabolic equivalent units per session) for a 12-week period. The exercise sessions are conducted in small groups of 8-15 participants under the direct supervision of the community-based ACE trained exercise specialist. Two options for community-based exercise programming exist: group fitness classes or supervised fitness centre access. The program includes options for low-to-moderate intensity exercise set at 3 to 4 metabolic

equivalent (MET) units per session (360-480 MET-minutes per week) and is progressed in intensity to 4 to 5 METs over the 12-week program duration (480-600 MET-minutes per week) as a means to progress participants towards recommended physical activity levels (500-1000 MET-minutes per week).[31] In terms of intensity, this would be similar to prescribing walking at a comfortable pace (4 km per hour) initially and then slowly progressing to a brisk walking pace (6 km per hour) over a 12-week period. Participating community sites offer one or more of these options depending on available resources and demand. Attendance at the exercise sessions is tracked as a marker of acceptability. Reasons for missed sessions are recorded. Exercise adherence includes attendance at supervised exercise sessions and average exercise minutes per week over the study period. Intensity is monitored using the 10-point Borg Rating of Perceived Exertion scale.[32,33] Active support and ongoing mentoring by the CEP is provided to community-based exercise specialists in the participating community program for the duration of ACE programming. Fidelity checks are performed by the respective CEP at scheduled times during the 12-week exercise session. Participants record exercise sessions in minutes and intensity in their training log, and other physical activity in their exercise diary. To encourage longer-term exercise adherence, participants are offered a second 12-week optional maintenance program, where possible, at low to no cost to survivors.

Participants assessed as having high needs (e.g. mobility issues, high risk of falling, risk of bone fracture, cognitive issues) due to active cancer, metastatic disease or with severe symptoms (where their disease or symptoms pose a risk in terms of safety of community-based exercise participation) are referred to ACE medically supervised programming or local cancer rehabilitation services.

Outcomes to Support Effectiveness of Programming

The CEPs perform the objective assessments at the University sites or at the respective fitness facilities offering the programming both before (baseline) and after the exercise program (at week 12), with further follow-up objective testing at 24-weeks and one-year at the tertiary sites. The

respective CEPs travel to the smaller cities in the North and South to conduct the baseline and 12-week assessments.

Objective and subjective physical outcome measures with demonstrated validity and reliability include:

- Physical activity level: Godin Leisure Time Physical Activity Questionnaire[34-36];
- Height, weight (calculation of body mass index);
- Waist and hip circumference[37];
- Six-minute walk test[38];
- Other objective measures: grip strength[39-41], timed sit-to-stand[42], shoulder flexion[43] (flexibility), and one-legged stance (balance)[44];
- Cancer-related symptoms: Edmonton Symptom Assessment Scale and Screening for Distress[45];

Health-related QoL is assessed using the Functional Assessment of Cancer Therapy-General[46] and Fatigue scales[47], and RAND Short Form Instrument (SF-36)[48], and EQ5D-5L[49] at baseline, 12-weeks, 24-weeks, and one-year for all participants. Participants will have the option for further follow-up yearly for the duration of the study. The study database was created in the REDCap system provided by the Women and Children's Health Research Institute (WCHRI) and hosted in the University of Alberta's Faculty of Medicine & Dentistry's data centre. Data collection and storage will comply with the measures outlined in WCHRI's REDCap privacy document.

Additional tests performed where equipment, time and resources are available**:** (i) 1or 8 repetition maximum bench press and 1 or 8 repetition maximum leg press to determine muscular strength; (ii) Sit-and-reach test to assess flexibility; (iii) plank muscular endurance test; (iv) push-up test. A priori targets for objective outcomes, symptoms and quality of life outcomes will be used to inform effectiveness and safety of the intervention (Table 1).

Outcomes to Support Implementation

The reach, effectiveness, adoption, implementation and maintenance (RE-AIM) framework will be

utilized to evaluate and enhance the external validity of the ACE program, and presents a means to evaluate the impact of a community-based intervention as a function of these five factors. This framework has been used to evaluate health and lifestyle behaviours to determine the public health impact of the intervention.[27,50] Embedded within RE-AIM is a cost description analysis pertaining to the survivor (individual costs) and the institutions (Community fitness facilities, Universities, and CancerControl Alberta). A proposed RE-AIM evaluation plan to assess the impact of the ACE program has been developed based on existing research (Table 2).[27]

Health Care Utilization Evaluation

The proposed methods for health care utilization include evaluation of usage among participants compared to that of matched controls, before and after the exercise program. Using personal health numbers (PHN) for consenting participants who provide permission, the PHN will be linked to the Cancer Registry to obtain: tumor type, sex, year of diagnosis, age and stage at diagnosis, and provincial zone of residence. These six variables will be used to match each participant (1:1, as closely as possible) to a control identified from the Cancer Registry. For each matched pair, "time 0" will be the date the participant joined the exercise program. Relative to this date, the Cancer Registry records will be linked to administrative data sources to capture all physician visits, emergency room visits and hospitalizations, one year prior to and one year following "time 0". For physician visits, we will link to Alberta Health physician claims data. The following variables will be collected: date of visit, health service type code and category, primary/secondary/tertiary diagnoses, and health service(s) performed. Health care utilization will be examined overall (costs summed for each service component and each database) and by subgroups of interest (e.g., diagnostic groupings, services provided, resource intensity weights), before and after "time 0", separately for cases and controls. Differences in health care utilization across the two time periods will be described for both groups. The analysis will be performed for all participants, and stratified by tumor type.

Sample size

The overall sample size goal is to accrue up to 2500 survivors via the ACE five-year roll out across

the province of Alberta (7 cities: 18 sites) to inform implementation. The primary objective outcome to assess study effectiveness is the number of participants meeting public health guidelines for physical activity at one-year follow-up. The current estimate for the number of cancer survivors meeting public health guidelines of 150 minutes or more of moderate intensity exercise per week is 25.8%.[51] According to the Conference Board of Canada, by simply getting 10% of Canadians with suboptimal levels of physical activity to exercise more would reduce incidence rates for major chronic conditions including cancer, and result in significant savings in healthcare costs.[52] Thus, assuming a 10% increase in the proportion of participants meeting the guidelines for physical activity (minimally important difference of 10%) at one-year ($p < 0.01$; 90% power), a sample size of approximately 305 survivors would be required. As the aim of the study is to evaluate both effectiveness and implementation, evaluating site-specific effects and implementation issues is of utmost importance, and thus our sample will allow adequate power for subgroup analyses given the number of sites and outcomes, and the anticipated variability among participants, cancer types, and disease stages.

Statistical Analysis Plan

Descriptive analyses will be performed to evaluate participant demographic, medical and exercise related variables, as well as RE-AIM components including an economic evaluation of the program. We will perform checks of data integrity including evaluating statistical power, test assumptions, and missing data. A single proportion inference test and confidence interval will be performed to determine the proportion of eligible survivors who provide informed consent and complete the program, as well as adherence rates to the program. Generalized linear mixed models will be utilized to examine the changes over time in the program participants on the patient-reported outcomes, including objective outcomes, activity levels, and indices of QoL (i.e., baseline, 12-weeks, 24-weeks and One-year). The cohort of survivors participating in the study will allow for long-term evaluation of rates of cancer recurrence and secondary cancers beyond the study period.

Ethics and dissemination

Ethical approval was received from the Health Research Ethics Board of Alberta: Cancer Committee and all participants are required to provide written informed consent.

Safety

Safety is monitored during exercise testing and training by the CEP and the ACE trained exercise specialists in community locations. Participants are asked to report any issues, injuries, or falls, related and unrelated to exercise participation to the ACE exercise specialist at the respective site. Where necessary, the medical advisor and rehabilitation team at the cancer centre are consulted. The CEPs and ACE exercise specialist record rates of adverse events (minor to serious adverse events including cardiovascular events, falls or musculoskeletal injuries) on the REDCap database with serious adverse events also reported to the Research Ethics Board.

Dissemination

We propose that our hybrid effectiveness-implementation study will help to answer critical questions on the value of cancer-specific community-based exercise programming. The ACE study will allow us to determine both the short and long-term effectiveness of exercise, and enhance our ability to identify important intervention-implementation interactions. Collectively, the findings will help to inform the acceptability, adoption, feasibility, reach, and sustainability of community-based exercise, and simultaneously evaluate integration of exercise into clinical care.[53]

The end of grant KT will focus on dissemination of the long-term effectiveness of programming on outcomes of survivors, including markers supporting secondary cancer prevention and healthcare utilization. Initial KT efforts will utilize academic peer-reviewed publications and conference presentations to disseminate new knowledge to academic audiences working in the field of exercise and cancer survivorship. Further dissemination and utilization of our research findings will involve partnering with cancer groups such as Canadian Cancer Survivorship Network, Prostate Cancer Canada, the Canadian Cancer Society, the Canadian Partnership Against Cancer, the Canadian

Physiotherapy Association Oncology Division, and the Psychosocial and Palliative Oncology Network. Collaboration with these agencies will ensure that information from the study will be widely disseminated to local as well as the broader cancer survivor community across Canada.

Discussion

In recent years, the focus of research in the oncology exercise field has expanded from determining efficacy through randomized controlled trial designs to include "real world" effectiveness studies focusing on implementation of exercise into cancer care.[17,19,20,23] A wide variety of approaches to promote exercise among cancer survivors are available, including programs that are medically supervised, community-based, or self-directed/ home-based.[21] Advantages of community-based programs include high accessibility, safety and supervision of exercise, and social interaction.[18] Importantly, systematic review evidence supports greater and more consistent benefits when exercise is delivered in a group or supervised setting when compared to a home-based or unsupervised setting.[54] Moreover, surveys of cancer survivors show a high interest in exercise, with reported preference for exercise programs that are offered in a supportive environment where treating and managing cancer are understood, and at a location that focuses on health promotion rather than illness.[55-58] Community-based studies performed to date, while demonstrating short-term effectiveness, are lacking data supporting long-term effectiveness. Moreover, studies commonly report low adherence and high dropout rates.[21,27] Given the infancy of implementation efforts in regards to community-based programming, further research with greater attention to implementation science aspects appears warranted.

Our ACE integrated knowledge translation (KT) strategy involves stakeholders in the design and ongoing delivery of ACE (i.e. survivors, end-users, administrators and policy-makers) and aims to address HCPs barriers and facilitators to exercise counseling and referral within the local cancer clinical setting. To address issues seen with less than optimal adherence and completion rates in previous implementation studies, key strategies built into ACE include monitoring of exercise

adherence and behavior change support for exercise.[17] The primary behavioral supports within the ACE program are the supervised and supportive aspects of the programming, along with exercise behaviour change education, goal setting and self-monitoring of activities. An ACE trained exercise specialist at the community site leads exercise classes and sessions. An ACE CEP and physical therapist are available to provide additional support to the survivor to address issues related to cancer treatment effects. This supportive format allows for modification and tailoring of the exercise, as needed, to the survivor's cancer type, capabilities and preferences.[59] In theory, if the program meets the needs of survivors, then adherence and completion rates should be high, reflecting program acceptability.

Consistent with the design of an effectiveness study, the ACE program is a cancer-specific exercise intervention with broad eligibility criteria that reflect "real-world" conditions. As many survivors report feeling neither physically nor psychologically prepared to engage in community-based exercise programs designed for the general public[58], a feature of ACE is the built-in flexibility of the exercise prescription such that participants self-select the exercise intensity based on presenting symptoms, "down days", or personal preference. While participants are expected to meet a minimal goal of two hours per week of at least light intensity exercise, the participant is encouraged to exceed this goal if able and desired.

Recently published guidelines from Australia endorse the integration of exercise into cancer care as a means to lessen some of the negative effects of cancer and its treatment.[13] Importantly, the guidelines identify the need for cancer HCPs to discuss the role of exercise in cancer recovery, and recommend referral of survivors to a CEP and/or physical therapist with experience in cancer care.[13] Implementation studies, to date, have largely focused on the delivery of an exercise intervention rather than studying the processes and outcomes associated with implementation within the healthcare system. Despite guidelines supporting exercise [3,14,60], challenges exist with implementing

exercise counseling and referral into practice due to the existing complexity and competing priorities in the cancer clinical setting.[61] Embedding CEP positions within our inter-professional supportive care team has the potential to address these challenges, and is seen as a sustainable care model that will add measurable value to our efforts to integrate exercise into clinical care.[62,63]

Limitations

There are important limitations to note in the design of the ACE hybrid effectiveness-implementation study related to the single-group design that does not allow for comparison of findings to usual care. As such, threats to internal validity exist including maturation, history, testing and regression to the mean. To address these concerns, specific objective outcome targets were determined, a priori, based on previous randomized controlled trial findings. Moreover, to reduce bias associated with testing, ACE assessors, who are specially trained and blinded to previous results, conduct the evaluations and the participants complete the patient-reported outcomes electronically at home. External validity of the program is supported by the community-based implementation focus, with novel aspects of supervision by cancer-trained exercise specialists and support provided by ACE CEPs and physical therapists. Importantly, evaluation of the program is guided by the RE-AIM framework and includes a robust suite of endpoints.

Through this research, we will better understand the effectiveness of the program at the level of the individual and institution, and evaluate processes to support future implementation and sustainability. Supporting improved rates of exercise adoption and sustained adherence to an active lifestyle among survivors of cancer will improve physical fitness and QoL, and may lower rates of cancer recurrence, secondary cancers, and other chronic diseases for cancer survivors in Alberta.

Declarations:

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Availability of data and material

Data sharing is not applicable to this article as no datasets were generated or analyzed (i.e., study protocol paper). Material developed to support this study is available from the corresponding author on reasonable request.

Author contributions

MLM, CS, TW, MSB, AAJ, HYL, JCE, ADM, JKV, KSC, JRM, MBP, and SNCR developed the study concept and protocol. MLM, SNCR, CS, and TW assisted in further development of the exercise and implementation protocol. All authors will oversee the implementation of the protocol and contribute to the acquisition, analysis and interpretation of data. MLM and SNCR drafted the manuscript, MLM, CS and SNCR contributed to revisions and MLM, CS, TW, MSB, AAJ, HYL, JCE, ADM, JKV, KSC, JRM, MBP, and SNCR approved the final manuscript.

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Competing interests

The authors declare that they have no competing interests.

Consent for publication

Not applicable.

Ethics approval and consent to participate

The study was approved by the Health Research Ethics Board of Alberta: Cancer Committee (ID: HREBA.CC-16-0905) and all participants are required to provide written informed consent.

REFERENCES

1. Surveillance and Reporting. The 2019 Report on Cancer Statistics in Alberta. Edmonton: Cancer Control Alberta, 2019.

2. Speck RM, Courneya KS, Masse LC, et al. An update of controlled physical activity trials in cancer survivors: a systematic review and meta-analysis. *J Cancer Surviv* 2010;4(2):87-100. doi: 10.1007/s11764-009-0110-5 [published Online First: 2010/01/07]

3. Rock CL, Doyle C, Demark-Wahnefried W, et al. Nutrition and physical activity guidelines for cancer survivors. *CA Cancer J Clin* 2012;62(4):243-74. doi: 10.3322/caac.21142 [published Online First: 2012/04/28]

4. Cormie P, Zopf EM, Zhang X, et al. The Impact of Exercise on Cancer Mortality, Recurrence, and Treatment-Related Adverse Effects. *Epidemiol Rev* 2017;39(1):71-92. doi: 10.1093/epirev/mxx007

5. van Waart H, Stuiver MM, van Harten WH, et al. Effect of Low-Intensity Physical Activity and Moderate- to High-Intensity Physical Exercise During Adjuvant Chemotherapy on Physical Fitness, Fatigue, and Chemotherapy Completion Rates: Results of the PACES Randomized Clinical Trial. *J Clin Oncol* 2015;33(17):1918-27.

6. Courneya KS SR, Mackey JR, et al:. Effects of aerobic and resistance exercise in breast cancer patients receiving adjuvant chemotherapy: A multicenter randomized controlled trial. *J Clin Oncol* 2007;25(28):4396-404. doi: http://dx.doi.org/10.1200/JCO.2006.08.2024 Embase Accession Number 2007524017 PMID 17785708 [http://www.ncbi.nlm.nih.gov/pubmed/?term=17785708]

7. Ibrahim EM, Al-Homaidh A. Physical activity and survival after breast cancer diagnosis: meta-analysis of published studies. *Med Oncol* 2011;28(3):753-65. doi: 10.1007/s12032-010-9536-x [published Online First: 2010/04/23]

8. Kenfield SA, Stampfer MJ, Giovannucci E, et al. Physical activity and survival after prostate cancer diagnosis in the health professionals follow-up study. *Journal of clinical oncology :*

official journal of the American Society of Clinical Oncology 2011;29(6):726-32. doi: 10.1200/JCO.2010.31.5226 [published Online First: 2011/01/06]

9. Ballard-Barbash R, Friedenreich CM, Courneya KS, et al. Physical activity, biomarkers, and disease outcomes in cancer survivors: a systematic review. *J Natl Cancer Inst* 2012;104(11):815-40. doi: 10.1093/jnci/djs207 [published Online First: 2012/05/10]
10. Meyerhardt JA, Giovannucci EL, Holmes MD, et al. Physical activity and survival after colorectal cancer diagnosis. *J Clin Oncol* 2006;24(22):3527-34. doi: 10.1200/JCO.2006.06.0855
11. Meyerhardt JA, Heseltine D, Niedzwiecki D, et al. Impact of physical activity on cancer recurrence and survival in patients with stage III colon cancer: findings from CALGB 89803. *J Clin Oncol* 2006;24(22):3535-41. doi: 10.1200/JCO.2006.06.0863
12. Colley RC, Garriguet D, Janssen I, et al. Physical activity of Canadian adults: accelerometer results from the 2007 to 2009 Canadian Health Measures Survey. *Health reports* 2011;22(1):7-14.
13. Cormie P, Atkinson M, Bucci L, et al. Clinical Oncology Society of Australia position statement on exercise in cancer care. *Med J Aust* 2018
14. Schmitz KH, Courneya KS, Matthews C, et al. American College of Sports Medicine roundtable on exercise guidelines for cancer survivors. *Med Sci Sports Exerc* 2010;42(7):1409-26. doi: 10.1249/MSS.0b013e3181e0c112
15. Leach HJ, Danyluk JM, Culos-Reed SN. Design and implementation of a community-based exercise program for breast cancer patients. *Curr Oncol* 2014;21(5):267-71. doi: 10.3747/co.21.2079
16. Leach HJ, Danyluk JM, Nishimura KC, et al. Evaluation of a Community-Based Exercise Program for Breast Cancer Patients Undergoing Treatment. *Cancer Nurs* 2015;38(6):417-25. doi: 10.1097/NCC.0000000000000217
17. Cheifetz O, Park Dorsay J, Hladysh G, et al. CanWell: meeting the psychosocial and exercise

needs of cancer survivors by translating evidence into practice. *Psycho-oncology* 2014;23(2):204-15. doi: 10.1002/pon.3389

18. Santa Mina D, Au D, Brunet J, et al. Effects of the community-based Wellspring Cancer Exercise Program on functional and psychosocial outcomes in cancer survivors. *Curr Oncol* 2017;24(5):284-94. doi: 10.3747/co.23.3585
19. Haas BK, Kimmel G, Hermanns M, et al. Community-based FitSTEPS for life exercise program for persons with cancer: 5-year evaluation. *Journal of oncology practice / American Society of Clinical Oncology* 2012;8(6):320-4, 2 p following 24. doi: 10.1200/JOP.2012.000555
20. Heston AH, Schwartz AL, Justice-Gardiner H, et al. Addressing physical activity needs of survivors by developing a community-based exercise program: LIVESTRONG(R) at the YMCA. *Clinical journal of oncology nursing* 2015;19(2):213-7. doi: 10.1188/15.CJON.213-217
21. Hardcastle SJ, Cohen PA. Effective Physical Activity Promotion to Survivors of Cancer Is Likely to Be Home Based and to Require Oncologist Participation. *J Clin Oncol* 2017;35(32):3635-37. doi: 10.1200/JCO.2017.74.6032
22. Irwin ML, Cartmel B, Harrigan M, et al. Effect of the LIVESTRONG at the YMCA exercise program on physical activity, fitness, quality of life, and fatigue in cancer survivors. *Cancer* 2017;123(7):1249-58. doi: 10.1002/cncr.30456
23. Translating Exercise Oncology Research into Practice: Effectiveness of a Community-Based Exercise Program for Cancer Patients and Survivors. MASCC/ISOO Annual Meeting Supportive Care in Cancer; 2015; Copenhagen Supportive Care in Cancer.
24. Santa Mina D, Au D, Auger LE, et al. Development, implementation, and effects of a cancer center's exercise-oncology program. *Cancer* 2019 doi: 10.1002/cncr.32297
25. Cheifetz O, Dorsay JP, MacDermid JC. Exercise facilitators and barriers following participation in a community-based exercise and education program for cancer survivors. *Journal of exercise rehabilitation* 2015;11(1):20-9. doi: 10.12965/jer.150183

26. Leach HJ, Danyluk JM, Nishimura KC, et al. Benefits of 24 versus 12 weeks of exercise and wellness programming for women undergoing treatment for breast cancer. *Support Care Cancer* 2016;24(11):4597-606. doi: 10.1007/s00520-016-3302-3

27. White SM, McAuley E, Estabrooks PA, et al. Translating physical activity interventions for breast cancer survivors into practice: an evaluation of randomized controlled trials. *Ann Behav Med* 2009;37(1):10-9. doi: 10.1007/s12160-009-9084-9 [published Online First: 2009/03/04]

28. Abu-Omar K, Rutten A, Burlacu I, et al. The cost-effectiveness of physical activity interventions: A systematic review of reviews. *Prev Med Rep* 2017;8:72-78. doi: 10.1016/j.pmedr.2017.08.006

29. Curran GM, Bauer M, Mittman B, et al. Effectiveness-implementation hybrid designs: combining elements of clinical effectiveness and implementation research to enhance public health impact. *Medical care* 2012;50(3):217-26. doi: 10.1097/MLR.0b013e3182408812

30. Canadian Society for Exercise Physiology. CSEP Certified Exercise Physiologist Ottawa, Ontario: Canadian Society for Exercise Physiology 2019 [Available from: https://www.csep.ca/view.asp?ccid=534.

31. Ainsworth BE, Haskell WL, Herrmann SD, et al. 2011 Compendium of Physical Activities: a second update of codes and MET values. *Med Sci Sports Exerc* 2011;43(8):1575-81. doi: 10.1249/MSS.0b013e31821ece12

32. Marks LE, Borg G, Ljunggren G. Individual differences in perceived exertion assessed by two new methods. *Percept Psychophys* 1983;34(3):280-8.

33. Borg G. Ratings of perceived exertion and heart rates during short-term cycle exercise and their use in a new cycling strength test. *Int J Sports Med* 1982;3(3):153-8. doi: 10.1055/s-2008-1026080

34. Amireault S, Godin G. The Godin-Shephard leisure-time physical activity questionnaire: validity evidence supporting its use for classifying healthy adults into active and insufficiently active

categories. *Percept Mot Skills* 2015;120(2):604-22. doi: 10.2466/03.27.PMS.120v19x7

35. Amireault S, Godin G, Lacombe J, et al. The use of the Godin-Shephard Leisure-Time Physical Activity Questionnaire in oncology research: a systematic review. *BMC Med Res Methodol* 2015;15:60. doi: 10.1186/s12874-015-0045-7

36. Amireault S, Godin G, Lacombe J, et al. Validation of the Godin-Shephard Leisure-Time Physical Activity Questionnaire classification coding system using accelerometer assessment among breast cancer survivors. *J Cancer Surviv* 2015;9(3):532-40. doi: 10.1007/s11764-015-0430-6

37. Barrios P, Martin-Biggers J, Quick V, et al. Reliability and criterion validity of self-measured waist, hip, and neck circumferences. *BMC Med Res Methodol* 2016;16:49. doi: 10.1186/s12874-016-0150-2

38. Schmidt K, Vogt L, Thiel C, et al. Validity of the six-minute walk test in cancer patients. *Int J Sports Med* 2013;34(7):631-6. doi: 10.1055/s-0032-1323746

39. Bellace JV, Healy D, Besser MP, et al. Validity of the Dexter Evaluation System's Jamar dynamometer attachment for assessment of hand grip strength in a normal population. *J Hand Ther* 2000;13(1):46-51.

40. Hamilton GF, McDonald C, Chenier TC. Measurement of grip strength: validity and reliability of the sphygmomanometer and jamar grip dynamometer. *J Orthop Sports Phys Ther* 1992;16(5):215-9. doi: 10.2519/jospt.1992.16.5.215

41. Reuter SE, Massy-Westropp N, Evans AM. Reliability and validity of indices of hand-grip strength and endurance. *Aust Occup Ther J* 2011;58(2):82-7. doi: 10.1111/j.1440-1630.2010.00888.x

42. McAllister LS, Palombaro KM. Modified 30-Second Sit-to-Stand Test: Reliability and Validity in Older Adults Unable to Complete Traditional Sit-to-Stand Testing. *J Geriatr Phys Ther* 2019 doi: 10.1519/JPT.0000000000000227

43. Kolber MJ, Hanney WJ. The Reliability and Concurrent Validity of Shoulder Mobility

Measurements Using a Digital Inclinometer and Goniometer: A Technical Report. *Int J Sports Phys Ther* 2012;7(3):306-13.

44. Franchignoni F, Tesio L, Martino MT, et al. Reliability of four simple, quantitative tests of balance and mobility in healthy elderly females. *Aging (Milano)* 1998;10(1):26-31.

45. Richardson LA, Jones GW. A review of the reliability and validity of the Edmonton Symptom Assessment System. *Curr Oncol* 2009;16(1):55. doi: 10.3747/co.v16i1.261

46. Cella DF, Tulsky DS, Gray G, et al. The Functional Assessment of Cancer Therapy scale: development and validation of the general measure. *J Clin Oncol* 1993;11(3):570-9. doi: 10.1200/JCO.1993.11.3.570

47. Yellen SB, Cella DF, Webster K, et al. Measuring fatigue and other anemia-related symptoms with the Functional Assessment of Cancer Therapy (FACT) measurement system. *J Pain Symptom Manage* 1997;13(2):63-74.

48. Jenkinson C, Wright L, Coulter A. Criterion validity and reliability of the SF-36 in a population sample. *Qual Life Res* 1994;3(1):7-12.

49. Pickard AS, Wilke CT, Lin HW, et al. Health utilities using the EQ-5D in studies of cancer. *Pharmacoeconomics* 2007;25(5):365-84.

50. Glasgow RE, Emmons KM. How can we increase translation of research into practice? Types of evidence needed. *Annu Rev Public Health* 2007;28:413-33. doi: 10.1146/annurev.publhealth.28.021406.144145 [published Online First: 2006/12/08]

51. Neil SE, Gotay CC, Campbell KL. Physical activity levels of cancer survivors in Canada: findings from the Canadian Community Health Survey. *J Cancer Surviv* 2014;8(1):143-9. doi: 10.1007/s11764-013-0322-6

52. Bounajm F, Dinh T, Theiault L. Moving Ahead. The Economic Impact of Reducing Physical Inactivity and Sedentary Behaviour. Ottawa: The Conference Board of Canada, 2014:1-37.

53. Bernet AC, Wilens DE, Bauer M. Effectiveness-implementation hybrid designs: implications for quality improvement science. *Implementation Science* 2013;8 (Supplement 1)(S2):1-2.

54. Segal R, Zwaal C, Green E, et al. Exercise for people with cancer: a systematic review. *Curr Oncol* 2017;24(4):e290-e315. doi: 10.3747/co.24.3619

55. Rogers LQ, Malone J, Rao K, et al. Exercise preferences among patients with head and neck cancer: prevalence and associations with quality of life, symptom severity, depression, and rural residence. *Head Neck* 2009;31(8):994-1005. doi: 10.1002/hed.21053 [published Online First: 2009/04/03]

56. Rogers LQ, Markwell SJ, Verhulst S, et al. Rural breast cancer survivors: exercise preferences and their determinants. *Psycho-oncology* 2009;18(4):412-21. doi: 10.1002/pon.1497 [published Online First: 2009/02/26]

57. Rogers LQ, Courneya KS, Verhulst S, et al. Factors associated with exercise counseling and program preferences among breast cancer survivors. *J Phys Act Health* 2008;5(5):688-705. [published Online First: 2008/09/30]

58. Blaney JM, Lowe-Strong A, Rankin-Watt J, et al. Cancer survivors' exercise barriers, facilitators and preferences in the context of fatigue, quality of life and physical activity participation: a questionnaire-survey. *Psycho-oncology* 2013;22(1):186-94. doi: 10.1002/pon.2072 [published Online First: 2013/01/09]

59. Buffart LM, Ros WJ, Chinapaw MJ, et al. Mediators of physical exercise for improvement in cancer survivors' quality of life. *Psycho-oncology* 2014;23(3):330-8. doi: 10.1002/pon.3428

60. Tomasone J, Zwaal C, Kim GM, et al. Moving guidelines into action: A report from cancer care Ontario's event let's get moving: Exercise and rehabilitation for cancer patients. *Curr Oncol Journal Translated Name Current Oncology* 2017;24(1):e65-e74. doi: http://dx.doi.org/10.3747/co.24.3422

61. Smith-Turchyn J, Richardson J, Tozer R, et al. Physical Activity and Breast Cancer: A Qualitative Study on the Barriers to and Facilitators of Exercise Promotion from the Perspective of Health Care Professionals. *Physiother Can* 2016;68(4):383-90. doi: 10.3138/ptc.2015-84

62. Fortier MS, Hogg W, O'Sullivan TL, et al. Impact of integrating a physical activity counsellor into the primary health care team: physical activity and health outcomes of the Physical Activity Counselling randomized controlled trial. *Applied Physiology, Nutrition, & Metabolism = Physiologie Appliquee, Nutrition et Metabolisme* 2011;36(4):503-14.

63. Santa Mina D, Sabiston CM, Au D, et al. Connecting people with cancer to physical activity and exercise programs: a pathway to create accessibility and engagement. *Curr Oncol* 2018;25(2):149-62. doi: 10.3747/co.25.3977

64. Government of Canada. Canadian Guidelines for Body Weight Classification in Adults 2011 [Available from: https://www.canada.ca/en/health-canada/services/food-nutrition/healthy-eating/healthy-weights/canadian-guidelines-body-weight-classification-adults/questions-answers-public.html#a4.

65. Bohannon RW, Crouch R. Minimal clinically important difference for change in 6-minute walk test distance of adults with pathology: a systematic review. *J Eval Clin Pract* 2017;23(2):377-81.

66. Record Owner NLM. What is the minimum clinically important difference in grip strength?

67. Statistics Canada. Musculoskeletal fitness in Canada 2007 to 2009: Government of Canada; 2015 [Available from: https://www150.statcan.gc.ca/n1/pub/82-625-x/2010001/article/11089-eng.htm accessed July 5, 2019.

68. Muir SW, Corea CL, Beaupre L. Evaluating change in clinical status: reliability and measures of agreement for the assessment of glenohumeral range of motion. *N Am J Sports Phys Ther* 2010;5(3):98-110.

69. Lemmink KA, Kemper H, Greef MH. The Validity of the Sit-and-Reach Test and the Modified Sit-and-Reach Test in Middle-Aged to Older Men and Women. *Res Q Exerc Sport* 2003;74(3):331-36.

70. Goldberg A, Casby A, Wasielewski M. Minimum detectable change for single-leg-stance-time in older adults. *Gait Posture* 2011;33(4):737-9. doi: 10.1016/j.gaitpost.2011.02.020

71. Wood-Dauphinee S. The Canadian SF-36 health survey: normative data add to its value. *Cmaj* 2000;163(3):283-4.

72. Pickard AS, De Leon MC, Kohlmann T, et al. Psychometric comparison of the standard EQ-5D to a 5 level version in cancer patients. *Medical care* 2007;45(3):259-63. doi: 10.1097/01.mlr.0000254515.63841.81

73. Pickard AS, Neary MP, Cella D. Estimation of minimally important differences in EQ-5D utility and VAS scores in cancer. *Health Qual Life Outcomes* 2007;5:70. doi: 10.1186/1477-7525-5-70

74. Rivera-Torres S, Fahey TD, Rivera MA. Adherence to Exercise Programs in Older Adults: Informative Report. *Gerontol Geriatr Med* 2019;5:2333721418823604. doi: 10.1177/2333721418823604

75. Coretti S, Ruggeri M, McNamee P. The minimum clinically important difference for EQ-5D index: a critical review. *Expert Rev Pharmacoecon Outcomes Res* 2014;14(2):221-33. doi: 10.1586/14737167.2014.894462

Table 1. Effectiveness Outcomes

Outcome measure/ measurement	**Minimal Clinically Important Difference*/ Established Cut point**	**Study target for improvement in outcome score**
Godin Leisure-time questionnaire	10% change in physical activity behaviour at one year	+10% or more of survivors are engaging in > 150 minutes of moderate intensity PA at one-year
Waist circumference	Cut points for health[64]: Men: 102 cm Women: 88 cm	+10% survivors with reduction to below disease risk cut-point based on age and gender
6-Minute Walk Test Distance	24 to 30.5 metres[65]	+30 metres
Hand-grip dynamometry	6.5 kg[66,67]	+10% meeting or exceeding age-specific average score
30 second sit-to-stand	Not established in cancer	+10% in the number of participants meeting age-specific functional level
Shoulder Flexion Range Goniometry	>10 degrees[68]	+10% meeting or exceeding age-specific average score
Sit and reach test	Population values[67,69] Men 0 to +5 cm Women 0 to +10cm	+10% meeting or exceeding age-specific average score
Single leg balance:	24 seconds[70]	+10% meeting 45 seconds maximum time
One repetition maximum test	MCID: 1-3%	+10% increase
Functional Assessment of Cancer Therapy (FACT) – General Scale	Population value[46]: score 88 MCID: 3 points	+ 3 points
FACT-Fatigue subscale	Population value[47]: score of 40 MCID: 3-6 points	+ 6 points
RAND Short Form-36	Population value[71]: 67-87/ 100 across domains; MCID 6-7 points	12% change from baseline
EQ5D -5L	EQ5D index: 0.06 [49,72,73]	+0.06 from baseline
Attendance at sessions	Population values in older adults: 58% to 77%[74]	> 70% attendance at exercise sessions

*The minimum clinically important difference (MCID) is the minimum difference that the patient is able to recognize and appreciate[75]

Table 2. RE-AIM Framework

Components/ Categories	Reporting outcomes
Reach (Individual Level)	• Methods used to recruit survivors • Efficiency of referral and screening processes • Participation rate: absolute numbers and proportions • Characteristics of participating survivors; stage of change; # tumour groups reached
Effectiveness (Individual & Institutional Level)	• Patient-reported and objective outcomes • Attrition from the program and reasons: random/ non-random • Safety: adverse events rate related to exercise participation • Cost of overall programming to the individual and to community organization
Adoption (Institutional Level)	• HCPs referral to programming: number & programs accessed • Programming options: number, type and location • Number of cancer trained exercise specialists in community • Characteristics of adoption/ nonadoption across centres
Implementa-tion (Community)	• Type and intensity level of activity • Extent exercise protocol delivered as intended • Consistency in program availability • Implementation of cancer-specific exercise into general community centre programming
Maintenance (Individual, Institutional & Community)	• Individual physical activity levels at a minimum 1 year follow-up • Individual physical fitness at a minimum 1 year follow-up • Exercise referral implemented into institutional practice and policy • Sustainability of exercise in community-based centre (# ongoing fee-for-service memberships)

Figure Legends:

Figure 1. Study Schema

Figure 2. ACE Programming Sites

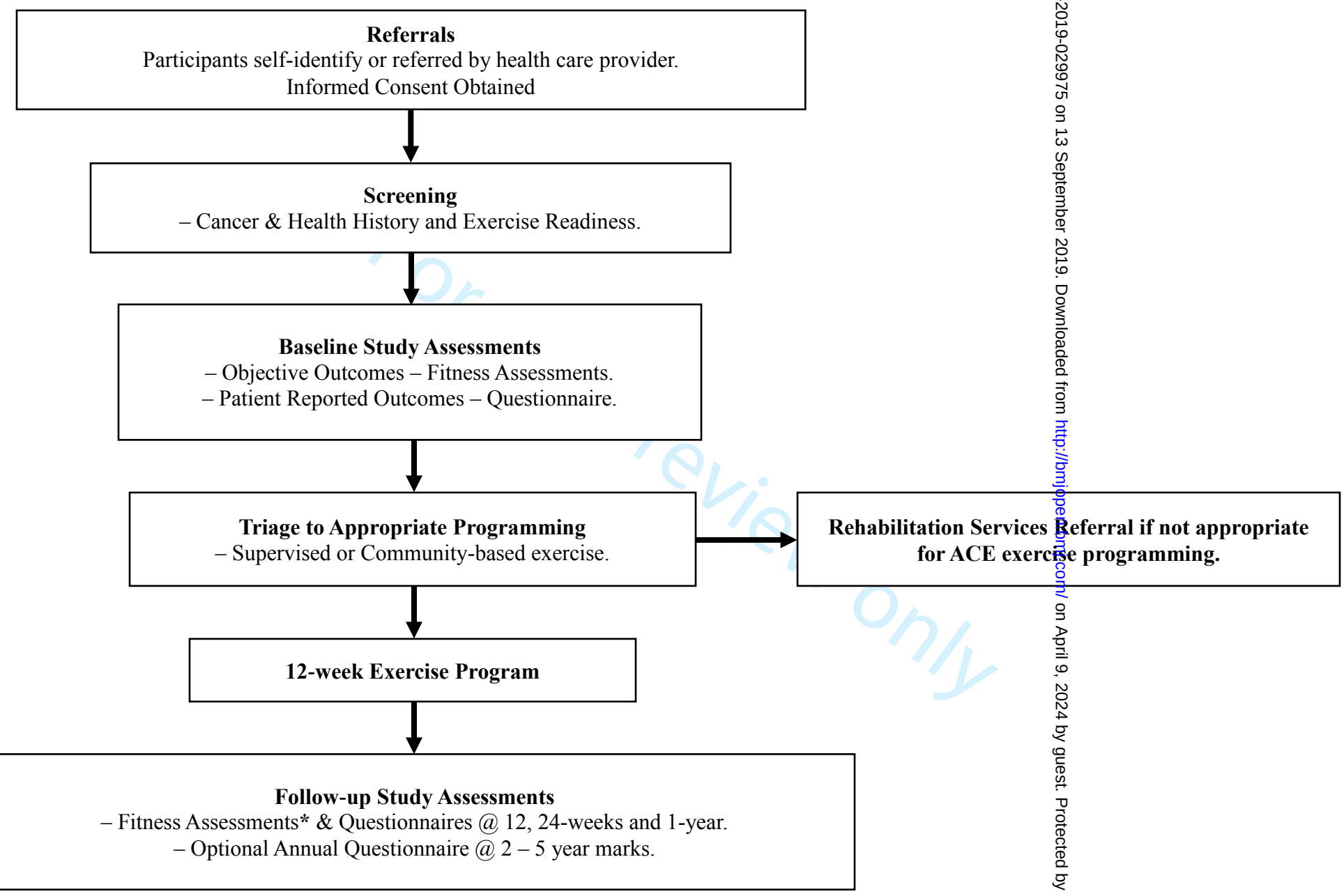

Figure 1. Study Schema

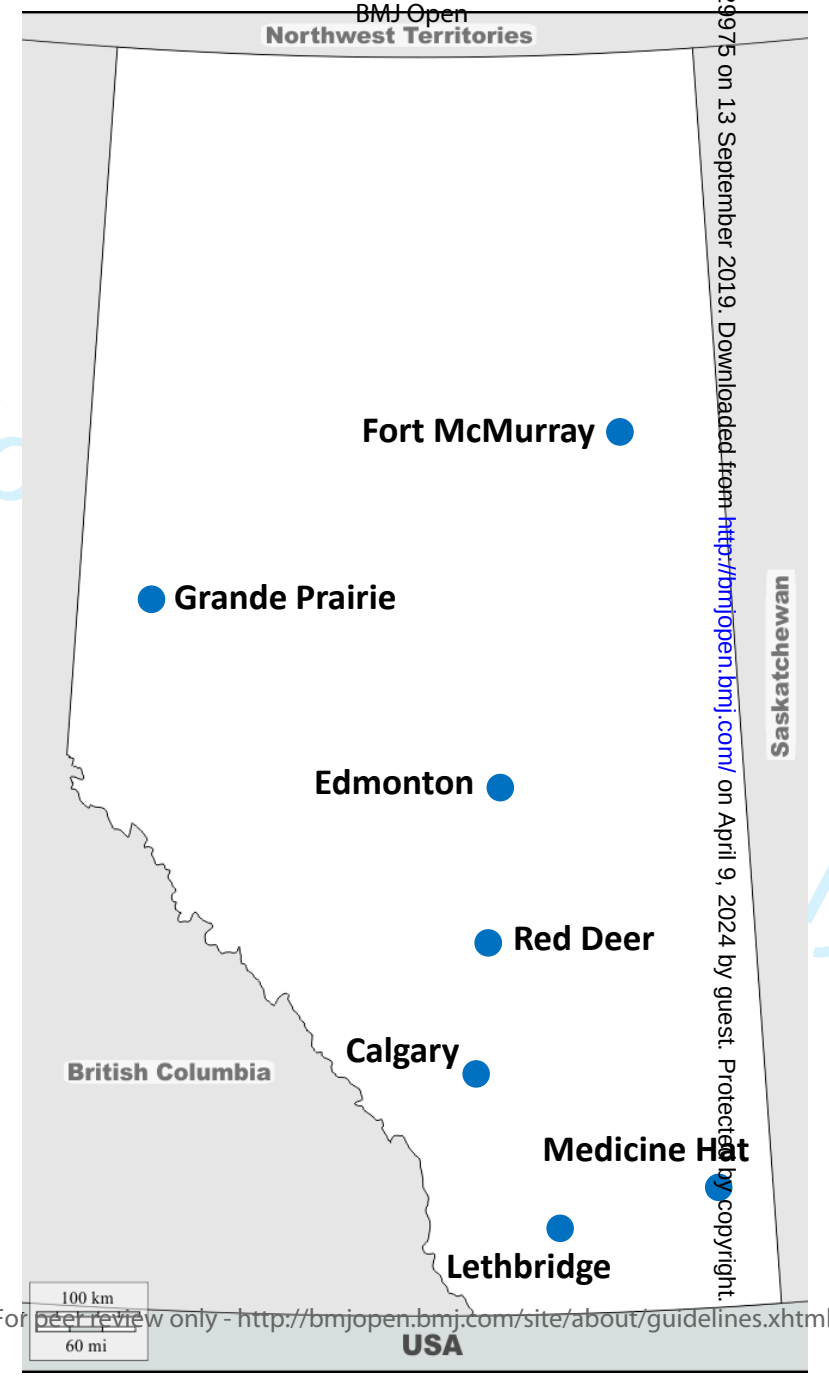

Figure 2: ACE Programming Sites

SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents*

Section/item	Item No	Description	Response/ location in manuscript
Administrative information			
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	The Alberta Cancer Exercise "ACE" Hybrid Effectiveness Implementation Study: A Protocol"
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry	Clinical Trials.gov: NCT02984163
	2b	All items from the World Health Organization Trial Registration Data Set	N/A
Protocol version	3	Date and version identifier	Protocol Version: March 2017
Funding	4	Sources and types of financial, material, and other support	Alberta Innovates: Cancer Prevention Research Opportunity: $1,250,000 Alberta Cancer Foundation: $400,000
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors	See title page 2: last paragraph All authors developed the study concept and protocol. MLM, SNCR, CS, and TW assisted in further development of the exercise and implementation protocol. All authors will oversee the implementation of the protocol and contribute to the

			acquisition, analysis and interpretation of data. MLM and SNCR drafted the manuscript, all authors contributed to revisions and all authors approved the final manuscript.
	5b	Name and contact information for the trial sponsor	**Mike Christen**, BComm Officer, Initiatives & Innovations (Health) **TEL:** 780.809.2557 mike.christen@albertainnovates.ca 1500 10104 103 Avenue NW Edmonton, Alberta, Canada T5J 0H8 Theresa Radwell Vice President, Program Investment Alberta Cancer Foundation 710, 10123- 99th Street Edmonton, AB. T5J 3H1 Email: Theresa.Radwell@albertacancer.ca
	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	Study sponsors were not involved in any aspect of the study from design to publication, and will not have any authority over activities related to the project.
	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	Coordinating centre: University of Alberta Oversight: Clinical Trials Unit, Cross Cancer Institute
Introduction			
Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for	Page 4-5: Paragraphs 1-4

		each intervention	
	6b	Explanation for choice of comparators	N/A: implementation study
Objectives	7	Specific objectives or hypotheses	Page 5 last sentence and Page 6
Trial design	8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory)	Page 5: Paragraph 2 - Hybrid effectiveness implementation study (single group)
Methods: Participants, interventions, and outcomes			
Study setting	9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	Page 7: Paragraph 3
Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	Page 7: Paragraph 4
Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	Page 8, Paragraph 3 and Page 9: Paragraph 1 &2: Implementation aspects Page 9 Paragraph 3: Exercise intervention
	11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease)	Page 10, Paragraph 2: referral to medically supervised exercise or cancer rehabilitation services
	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests)	Page 10, Paragraph 1:
	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	No restrictions in terms of usual activities.
Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis	Page 10, Paragraph 2: outcomes to support effectiveness Page 12, Paragraph 1: outcome to support implementation

		metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	Page 12, Paragraph 2: outcomes related to healthcare utilization
Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	Page 6 : 2nd paragraph: Screening Page 8: screening; baseline assessment, 12 week intervention, post (12-week) intervention assessment, 24-week and one-year follow-ups. Figure 1: Study Schema
Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	Page12, paragraph 1: sample of 1500. As this is an implementation study, the sample size was based on building capacity in the community. For the purposes of effectiveness a sample of approximately 305 participants are needed for our primary outcome. Page 13 (Sample size). An Alpha of 0.01 was used due to the large proposed sample size (risk of Type I error). We also set the power to .9 to avoid a Type II error. The larger sample will allow for subgroup analyses.
Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size	Passive recruitment strategies: brochures, posters. Active recruitment by healthcare professionals in oncology clinics.
Methods: Assignment of interventions (for controlled trials)			
Allocation:			
Sequence generation	16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	N/A

Allocation concealment mechanism	16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	N/A Implementation study
Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	N/A Implementation study
Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	N/A Participants are aware they are exercising.
	17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	N/A
Methods: Data collection, management, and analysis			
Data collection methods	18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	REDCap database, Page 11: 2nd paragraph: Self-reported outcomes are assessed at baseline, 12-weeks, 24 weeks, and one-year for all participants. Participants will have the option for further follow-up at year 2 and 3 following the program.
	18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	N/A: implementation study, thus, retention and completion rates are being monitored as outcomes.
Data management	19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	Two step data entry process: data is entered by one ACE staff person and verified by a second independent person. To improve data quality, REDCap validation rules have been set. For example, minimum and maximum values that can be accepted, and units as well as rules to ensure that valid dates are entered. All items of self-reported questionnaires are

			required and must be answered prior to moving on to next question.
Statistical methods	20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	Page 13: Paragraph 2
	20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	N/A
	20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	N/A
Methods: Monitoring			
Data monitoring	21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	N/A - Implementation study
	21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	N/A – Implementation study
Harms	22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	Page 11, last paragraph: Safety is monitored during exercise testing and training by the CEP and the ACE trained exercise specialists in community locations. The CEPs and ACE exercise specialists record rates of adverse events (minor to serious adverse events including cardiovascular events, falls or musculoskeletal injuries). Participants are asked to report any issues, injuries, or falls, related and unrelated to exercise participation to the ACE exercise specialist at the respective

			site.
Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	N/A: implementation study. Oversight is provided by the External advisory committee, Clinical Trials Unit at the Cross Cancer Institute and the Health Research Ethics Board of Alberta: Cancer Committee.
Ethics and dissemination			
Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval	Research Ethics approval is in place: HREBA.CC-16-0905
Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators)	Amendments will be submitted to the ethics board for any protocol changes including sub-studies related to the implementation process.
Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	Consent is obtained by the site principal investigators and research coordinators.
	26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	N/A
Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	Participants recruited to the study are provided with a unique study ID. All data is housed on the secure REDCap database (supported by the Faculty of Medicine and Dentistry at the University of Alberta). Data will be de-identified prior to any analyses.
Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site	N/A The authors declare no conflicts of interest.
Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	N/A: implementation study focus. Access to final data set undetermined.

Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	N/A: in the event of injury or harm, healthcare services will be provided as per standard of care.
Dissemination policy	31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	An integrated knowledge translation plan is in place and available on our website: https://www.albertacancerexercise.com/knowledge-translation. End of study: The end of grant KT will focus on dissemination of the long-term effectiveness of programming on outcomes of survivors, including markers supporting secondary cancer prevention and healthcare utilization. Initial knowledge translation (KT) efforts will utilize academic peer-reviewed publications and conference presentations to disseminate new knowledge to the researcher/academic audiences working in the field of exercise and cancer survivorship. Survivors: Dissemination and utilization of our research findings will involve partnering with cancer groups such as the Canadian Breast Cancer Foundation, Prostate Cancer Canada, the Canadian Cancer Society, the Canadian Partnership Against Cancer, the Canadian Physiotherapy Association Oncology Division, and the Psychosocial and Palliative Oncology Network. Collaboration with these agencies will ensure that information from the study will be widely disseminated to local as well as the broader cancer survivor community across Canada.
	31b	Authorship eligibility guidelines and any intended use of professional writers	No professional writers will be used. Authorship must be warranted based on contribution to the study.
	3	Plans, if any, for granting public access to the full protocol,	No plans at this time.

	1c	participant-level dataset, and statistical code	
Appendices			
Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates	Consent forms developed for each region. Attached as an appendices.
Biological specimens	33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	N/A – no biological specimens are being collected.

*It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated. The SPIRIT checklist is copyrighted by the SPIRIT Group under the Creative Commons "Attribution-NonCommercial-NoDerivs 3.0 Unported" license.