Preventive Medicine Reports 35 (2023) 102288

Contents lists available at ScienceDirect

Preventive Medicine Reports

journal homepage: www.elsevier.com/locate/pmedr

The impact of high intensity interval training in a diverse group of cancer survivors: CAPABLE, a pilot study

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ARTICLE INFO

Keywords:
Physical activity
Exercise
Metabolic markers
Cancer survivorship
Quality of life
Body mass index

ABSTRACT

Purpose: Given the well-documented benefits of regular exercise to cancer survivors, current American Cancer Society guidelines recommend that patients engage in a minimum of 150 min per week of moderate-to-vigorous physical activity with a minimum of two days of strength training. However, few survivors meet this goal, particularly among minorities.

Methods: The CAPABLE study is a single-arm, pilot exercise intervention that introduced 48 cancer survivors to a high intensity interval and strength training program three days a week for 12 weeks. We evaluated the impact of this unique training method on bodyweight, % body fat, serum markers correlated with an adverse cardiometabolic profile and health-related quality of life (HRQoL). Measures were summarized at baseline and program exit. Paired t-tests were used to assess change in each of these measures over time.

Results: We observed losses in weight, body mass index, and % body fat, and glycosylated hemoglobin (HbA1c) levels over 12-weeks. There were also clinically meaningful improvements in reported overall HRQoL (FACTG total change +9.5 (95% CI, 4.6, 14.4)) and in each one of the individual domains (physical, social, emotional, and functional well-being).

Conclusions: We observed meaningful improvements in body composition, HbA1c and quality of life over 12 weeks among cancer survivors participating in a high-intensity interval training program. Future work will include a control arm for comparison and address barriers to participation and adherence which will be important in using this intervention and others like it to improve outcomes and reduce cancer health disparities.

1. Introduction

It has been estimated that there are >17 million cancer survivors in the United States, a number that has been growing over the past several decades with the introduction of wide-spread screening for the early-detection of the most commonly diagnosed cancers as well as advances in cancer treatments (Miller et al., 2022). This number is expected to increase by >5 million over the next decade which will place an ever increasing demand on limited health care resources (Miller et al., 2019). The growing number of cancer survivors strengthens the need to develop, refine and promote strategies to improve both short and long term outcomes in this growing population. The benefits of low to moderate intensity exercise for cancer survivors have been well-documented, so much so that in 2012, the American Cancer Society (ACS) convened a panel of experts in nutrition, physical activity and cancer to examine the evidence and develop best clinical practice guidelines to assist health care providers and cancer survivors along the cancer continuum (Rock et al., 2012). The panel recommended that cancer survivors avoid inactivity and return to normal daily activities as soon as possible following diagnosis. The panel specifically recommended that survivors should aim to engage in moderate to vigorous physical activity for at least 150 min per week, and that strength training at a minimum of two days per week should be a part of the activity regimen (Rock et al., 2012). A published analysis of National Health Interview Survey linked mortality data suggested that cancer survivors who reported adhering to the complete ACS physical activity guidelines

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https://doi.org/10.1016/j.pmedr.2023.102288
Received 25 January 2023; Received in revised form 15 May 2023; Accepted 16 June 2023
Available online 22 June 2023

had a significantly lower risk of all-cause, cancer-specific and cardiovascular disease-specific mortality (Tarasenko et al., 2018). ACS published an update to the recommendation in 2022 suggesting the ultimate goal for cancer survivors is to adhere to their guidelines for cancer prevention which includes 150–300 min of moderate intensity exercise or 75–150 min of vigorous exercise weekly with a minimum of 2 days of strength training (Rock, 2022).

There is a wealth of evidence to indicate that regular exercise improves cancer specific outcomes including quality of life, reducing cancer treatment related fatigue, reversing the adverse metabolic effects of hormone therapy and prolonging cancer-specific survival (Boisen et al., 2016; Friedenreich et al., 2016; Kenfield et al., 2011; Newton et al., 2018; Phillips et al., 2015; Trinh et al., 2022; Ussing et al., 2022; Han et al., 2021; Montaño-Rojas et al., 2020; Friedenreich et al., 2020; Wu et al., 2016; Garcia and Thomson, 2014). Very little is known about the impact of high-intensity interval training (or HIIT training) on the health and quality of life specifically in cancer survivors. The majority of interventional trials have focused on HIIT have been conducted in women diagnosed with breast cancer. These studies suggest that these programs are well-tolerated by survivors, with few adverse events and significant improvements in cardiovascular fitness and quality of life (Adams et al., 2018; Adams et al., 2017; Lee et al., 2018a,b; Mijwel, 2019; Schlüter et al., 2019; Schmitt et al., 2016; Toohey et al., 2016; Tsuji et al., 2019; Wallen et al., 2020; Slomski, 2021; Lavín-Pérez et al., 2021; Lavín-Pérez et al., 2021; Schutz, 2021). Unfortunately, we and others have shown that just a fraction of cancer survivors meet ACS guidelines with even lower participation in racial and ethnic minorities and in rural populations.. The current pilot exercise intervention was conducted in a racially diverse group of cancer survivors living in the city of Detroit and the surrounding Metropolitan area examining the impact of such a program on fitness body composition and health-related quality of life.

2. Methods

The **C**ross-training **A**nd **P**hysical **A**ctivity for a **B**etter **L**ife **E**xperience (**CAPABLE**) study is a twelve-week, single-arm pilot exercise intervention. The research was approved by the Institutional Review Board (IRB) of Wayne State University (WSU), McLaren Health Care IRB and is registered as a National Clinical Trial (ID: NCT03750981) The protocol introduces cancer survivors to a training method which mixes high-intensity interval and strength building exercises with an overarching goal to improve upon fitness metrics, quality of life and longer-term outcomes, both cancer-specific and overall, in this population. Study eligibility criteria included 1) age 18 and older at the time of program recruitment; 2) diagnosed with an invasive cancer; 3) cleared from their physician to participate in the program; 4) not currently participating in any regular fitness program indicated on the screening questionnaire, and 5) available transportation. In addition, we excluded patients with widely metastatic cancer to bone or brain.

Participation in this trial was voluntary and potentially eligible participants were identified using a variety of methods including 1) referral from treating physician, 2) advertisement material in oncology clinics, 3) participation in other WSU cancer survivorship trials and providing consent for re-contact for future trial opportunities and 4) local health events. Each potentially eligible participant and their treating physician were sent a study packet including 1) an introductory letter stating the goals of the program; and 2) a schedule including a description of the types of activity that participants would be engaged in. Written documentation of medical clearance by their treating physician was required prior to participant consent. Once medical clearance was obtained, each participant received a short survey to complete indicating their personal goals for the program (i.e. weight loss/gain, increase strength, mobility, agility). Participants were then contacted by study staff to participate in a short telephone-administered health screener to verify study eligibility and gather information on comorbid conditions, treatment and medications in the event that the treating physician of record may not have their complete medical history. Study informed consent was obtained prior to baseline testing on the first day of the program, as well as a liability waiver for participation required by each performance site. The program was offered at no cost to all eligible participants. Program participants chose ahead of baseline testing one of two performance sites located in Detroit and the surrounding Metropolitan area to complete all 12 weeks of the program at that site.

At baseline, enrolled participants completed the following: 1) a review of their unique goals with one of the coaches; 2) a baseline survey to collect information on health behaviors, emotional response to exercise, and health related quality of life (HRQoL) measured using the Functional Assessment of Cancer Therapy (FACT-General) instrument (Cella et al., 1993; Webster et al., 2003); 3) measurement of height and weight using protocols standardized by the National Institute of Health; and 4) percent body fat measured using a handheld OMRON HBF-306C body fat monitor. The scale to assess the emotional response to exercise was developed specifically for this study (F.K.H.). Based on previous research (Schutzer and Graves, 2004), the scale was composed of a series of Likert scale questions related to the feelings evoked during and after exercise (strong, happy, healthy, proud, confident, optimistic, sore, tired, defeated, weak). “On a scale of 1 to 5, with 1 being strongly disagree and 5 strongly agree, please rate how you feel, or expect to feel, after exercising”. Scales on the last 4 negative emotions were reversed to produce a summary score with higher scores indicating a better relationship between exercise and mood. Baseline body mass index was then calculated from measured weight and height (in kg/m^2). Lastly, participants could opt-in for a blood draw performed by staff phlebotomists for measurement of blood glucose, HbA1c, and a lipid panel (triglycerides, LDL, VLDL, HDL and total cholesterol).

Introduction to all movements, teaching and baseline assessments for all fitness tests took place during the first three one-hour sessions. At this time, appropriate scaling options (or modifications) for each movement for individual participants were determined. One of the unique characteristics of this particular method was that all of the activities involved in the program, including the baseline tests, were infinitely and individually scalable thus allowing for participation regardless of their baseline fitness level. To ensure the standardization of baseline testing across performance sites, the start dates of the program at each performance site were staggered by one week so that study staff and program director (D.G.F.) could supervise all baseline enrollment, training and testing activities. The baseline testing for all participants was performed under the supervision of the coach and one additional judge, using a variety of standard tests commonly used in CrossFit® programming. For example, improvement for all strength-based tests (e.g. deadlifts and squats) is measured by the amount of weight moved whereas improvement in all time-based conditioning tests (e.g. time to finish 500 m on rowing machine) would be measured as time to completion. All tests and subsequent program activities were focused on improving each participant’s functional movement, flexibility, strength, and aerobic capacity.

For each of the following weeks, the intervention consisted of three one-hour sessions led by a Level-1 or higher certified CrossFit® coach. Each session was planned with the intention to build capacity in one or more of four aforementioned areas. At each session, the program director and coaches first reviewed the movement standards for each session, provided close supervision to all participants, established reasonable goals for the group, and provided individual modifications as needed based upon the ability of each participant. Program adherence was defined as participation in at least 75% of the sessions. One additional make-up session was offered to participants each month. The last three sessions of the intervention were reserved for final testing at which time the standardized tests used in the baseline assessment, with identical modifications if necessary, were repeated to measure changes in the functional performance of each participant. On the last day of the program, body composition measurements were collected and an end of

study survey was administered which collected identical health behaviors, emotional response to exercise, and HRQoL data as in the baseline survey. Post-intervention focus groups conducted by study staff assessed overall satisfaction with the program and participants' emotional response to exercise, and helped identify barriers and facilitators to participation in the intervention. Surveys were also administered to participants who either withdrew (n = 5) or were considered non-adherent (n = 6) to address additional barriers to participation.

3. Statistical methods

All analyses were performed using SAS software (Cary, NC) version 9.4).The distribution of age at enrollment, gender, self-reported race, and cancer site was summarized using counts and percentages. The mean and 95% confidence intervals (CIs) for measures of interest (body composition, emotional response to exercise, all serum measures, and trainer assessments) were calculated at baseline and study exit. In addition, the mean change between the two time points was calculated and evaluated using paired t-tests. Body composition was summarized for all patients, and for those who would be considered over-weight (BMI $\geq$25 kg/m^2) at study entry. The mean and 95% CIs were also calculated for FACT-G total and the 4 individual domains (physical, social, emotional, and functional well-being), All analyses were further stratified by participant race and gender to explore potential effect modification; however, the sample size was prohibitively small therefore formal tests of interaction by these characteristics were not performed.

4. Results

Forty-eight participants were initially enrolled into CAPABLE, with 37 (77%) of participants considered adherent based upon program requirements ($\geq$75% of sessions including completion of all post-intervention tests). Table 1 summarizes the baseline characteristics of the 37 adherent participants. The mean age at time of enrollment was 58.5 years (range 38–79 years). Sixty-eight percent of participants were female and 73% were African American. Most participants were diagnosed with breast cancer (54%) followed by prostate (27%) and endometrial cancer (11%). Reasons for non-adherence or withdrawals included 1) work conflicts (N = 5), 2) complications of cancer treatment (N = 2), 3) illness (N = 1), 4) increased caregiver responsibilities (N = 1), 5) program difficulty (N = 1), or 6) injury unrelated to program (N = 1). The demographics (age, gender, race, and cancer site) of non-adherent participants did not significantly differ from adherent participant (data not shown).

Table 2 provides summary measures of the changes in measures of body composition. Most participants were considered obese at baseline exam, with the mean BMI at 32.8 kg/m^2. There was a mean reduction in BMI of 1.1 kg/m^2 over the study period. This reflects the mean weight loss among participants of 7 lbs. and a 2.8% decrease in body fat over the same period. In the subset of participants with BMI > 25.0 kg/m^2, the reduction in BMI and body weight were slightly more demonstrable, 1.5 kg/m^2 and 9 lbs., but reduction in % body fat was similar to all participants combined. Table 3 summarizes the change over time among the 21 adherent participants who provided a blood sample for serum measures of glucose, HbA1c and lipids. We observed improvements, albeit modest for most measures, among participants over 12 weeks. Importantly HbA1c, considered more stable measure of blood glucose, decreased by 0.4%.

Table 4 summarizes the change over time in reported HRQoL measured using the FACT-G survey and emotional response to exercise. We observed improvements in reported quality of life irrespective of domain over the study period. The summary score improved from 85.7 to 95.2 (+9.5, 95% CI, +4.6, +14.4). The largest observed change in any individual domain was in social well-being (+3.1, 95% CI, +0.9, +5.3). We also observed a 3.5-point improvement in the mean scores for the emotional response to exercise measure (95% CI, 0.9, 6.1). Supplementary Table 1 provides a both a description of and a summary of changes in trainer assessments (as secondary outcomes) between baseline and end of study. We observed uniformly positive changes in measures of strength and endurance. No appreciable differences were seen in the analyses stratified by race and gender (Supplementary Table 2a & 2b).

Table 1
Participant demographics for the Cross-training And Physical Activity for a Better Life Experience (CAPABLE) study.

	N	%
Total	37	
Age at Enrollment		
<50	6	16
50–59	13	35
60–69	12	32
70–79	6	16
Mean (std)	58.5 (10.5)	
Median (range)	38–79	
Gender		
Male	12	32
Female	25	68
Race		
White	10	27
African American	27	73
Cancer Site		
Breast	20	54
Prostate	10	27
Endometrial	4	11
Hodgkin's lymphoma	1	3
Kidney	1	3
Kidney & bladder	1	3
Medical History		
Arthritis	15	41
COPD or emphysema	1	3
Depression	4	11
Diabetes	7	19
Heart attack	5	14
High cholesterol	10	27
High blood pressure	22	59
Thyroid disease	4	11
Count of conditions		
None	7	19
1	8	22
2	11	30
3 or more	11	30

* Adherent to intervention protocol (>75% of sessions).

5. Discussion

Our findings from this single-arm, high-intensity interval training pilot intervention suggest multiple benefits in a diverse group of cancer survivors including weight and fat loss, improvement in HbA1c levels, and better quality of life. The training program implemented in this study is the first of its kind with an emphasis on community building and social support among athletes and the practice of functional movements required for daily living activities as well as the nature of the outcomes under investigation.

The majority of cancer survivors in CAPABLE were diagnosed with female breast or prostate cancer (>80%), as with most of the U.S., the most common cancers diagnosed within the Metropolitan Detroit area. (Miller et al., 2019; Siegel et al., 2022) Generally, the 5-year relative survival for these cancers is high, reaching 90% for breast cancer and

Table 2
Changes in weight, BMI (in kg/m^2) and % body fat over 12-week exercise intervention.

	N	Baseline	Exit	Change	p-value
Among all participants					
BMI	31				<0.001
Mean (std)		32.8 (29.1, 36.5)	31.7 (28.1, 35.2)	−1.1 (-1.7, −0.1)	
Range		19.4, 63.1	20.1, 61.7	−4.7, 0.7	
Weight	31				<0.001
Mean (std)		210 (184, 236)	203 (178, 228)	−7 (-10, −4)	
Range		113, 403	117, 394	−26, 4	
% body fat	30				<0.001
Mean (std)		38.3 (35.3, 41.4)	35.5 (32.0, 39.0)	−2.8 (-4.2, −1.5)	
Range		25.5, 63.1	10.7, 59.7	−14.8, 3.6	
Among participants with a BMI ≥ 25 kg/m^2 at study entry					
BMI	22				<0.001
Mean (std)		36.8 (32.7, 40.9)	35.3 (31.3, 39.3)	−1.5 (-2.1, −0.8)	
Range		25.3, 63.1	24.4, 61.7	−4.7, 0.5	
Weight	22				<0.001
Mean (std)		239 (211, 268)	230 (203, 257)	−9 (-13, −6)	
Range		159, 403	154, 394	−26, 3.2	
% body fat	22				0.001
Mean (std)		40.9 (37.5, 44.2)	38.5 (35.0, 42.0)	−2.4 (-3.7, −1.1)	
Range		29.8, 63.1	26.4, 59.7	−11.8, 3.6	

exceeding 99% for prostate cancer.(Siegel et al., 2022) Therefore, given a relatively good prognosis from cancer, the issue of co-morbidity or competing risks for mortality in breast and prostate cancer survivors is critical when developing post-treatment survivorship care plans.(Cho et al., 2013; Patnaik et al., 2011; Basen-Engquist et al., 2017) The majority (81%) of CAPABLE participants reported one or more comorbid conditions at baseline interview prior to the intervention. Hypertension, obesity, and hyperlipidemia are common comorbidities in cancer survivors, as they are in the population at large, with the prevalence higher and the severity of symptoms often greater among African Americans compared with other race and ethnic groups.(Killelea et al., 2019; Smith et al., 2005; Beebe-Dimmer et al., 2007) Regular exercise and weight loss among individuals who are overweight or obese and adoption of a diet with a high intake of fresh fruits and vegetables, and low intake of sugar and processed foods is important in the prevention and control for all comorbidities including cancer and has shown to result in improved cancer specific and other non-cancer outcomes including mortality. (Tarasenko et al., 2018; Rock, 2022; Kenfield et al., 2011; Friedenreich et al., 2020; Ferrer et al., 2011).

There was marked improvement in participant reported quality of life was over12-weeks. The magnitude of the observed change (+9.5) in the FACTG scores was beyond the range (+3 to +7) considered to be a minimally important difference (MID) (Yost and Eton, 2005). By comparison, we previously reported in the Detroit Research on Cancer Survivors (ROCS) cohort, the largest cohort conducted exclusively among African American cancer survivors, that meeting ACS guidelines for physical activity among survivors who were previously inactive was associated with +2.0 change in FACTG over one year (Beebe-Dimmer et al., 2020). However, given the absence of a randomized control arm, results should be interpreted with caution. Future work will include controls who have similar contact with a health professional.

Our findings are largely in agreement with other studies, also pilot in nature, of high-intensity interval training or HIIT methods on outcomes among cancer survivors with evidence of a greater benefit to other exercise programs.(Mijwel, 2019; Toohey et al., 2016; Slomski, 2021; Kenfield et al., 2021; Newton et al., 2018; Ficarra et al., 2022; Hooshmand Moghadam et al., 2021) Results from the ERASE trial, a phase 2 randomized clinical trial (RCT) examined HIIT training among 52 men diagnosed with prostate cancer on active surveillance. At the end of 12 weeks (36 sessions), it was reported that men assigned to the HIIT intervention, compared with usual care group, had improved peak V02 (a measure of oxygen consumption during exercise), but also had declines in prostate specific antigen (PSA) and PSA velocity over the same period (Kang et al., 2021). After a 12-week RCT conducted among breast

Table 4
Changes in reported Health Related Quality of Life (HRQoL) and emotional response to exercise in CAPABLE participants.

	Baseline	Exit	Change	p-value
FACT-G Summary Score*				<0.001
Mean (std)	85.7 (15.2)	95.2 (11.4)	9.5 (14.0)	
Range	38, 113	63, 110	−10, 40	
Physical Well Being				0.005
Mean (std)	22.7 (4.4)	25.1 (3.8)	2.4 (4.7)	
Range	9, 28	9, 28	−10, 19	
Social Well Being				0.007
Mean (std)	22.4 (7.0)	25.4 (4.2)	3.1 (6.3)	
Range	0, 34	9, 33	−8, 24	
Emotional Well Being				0.005
Mean (std)	19.9 (3.2)	21.4 (2.8)	1.5 (2.7)	
Range	12, 24	15, 24	−3, 6	
Functional Well Being				0.027
Mean (std)	20.7 (6.8)	23.2 (5.1)	2.5 (6.4)	
Range	1, 30	10, 32	−9, 27	
Emotional Response to Exercise				0.010
Mean (std)	40.7 (5.3)	44.2 (4.2)	3.5 (7.6)	
Range	26, 50	34, 50	−16, 24	

*A higher score represents better reported quality of life.

Table 3
Change in serum metabolic markers over 12 weeks in CAPABLE participants.

		Baseline		Exit		Change		
Serum Marker	N	Mean	95% CI	Mean	95% CI	Mean	95% CI	p-value
Glucose (mg/dL)	21	90.7	82.4, 98.9	89.5	81.4, 97.6	−1.2	−4.7, 2.3	0.487
HbA1c (%)	20	5.7	5.3, 6.0	5.3	5.1, 5.6	−0.4	−0.5, −0.2	<0.001
Total Cholesterol (mg/dL)	21	190.7	174.9, 206.4	189.8	174.0, 205.6	−0.9	−8.8, 7.1	0.824
Triglycerides (mg/dL)	21	99.0	80.4, 117.7	85.4	66.7, 104.1	−13.7	−30.4, 3.1	0.105
HDL (mg/dL)	21	62.4	54.6, 70.2	63.0	56.1, 69.8	0.6	−2.6, 3.7	0.711
LDL (mg/dL)	17	108.5	93.6, 123.3	118.1	102.2, 134.0	1.3	−6.6, 9.2	0.734
VLDL (mg/dL)	16	19.8	15.9, 23.7	18.7	14.5, 23.0	−2.3	−6.7, 2.2	0.298

*4 participants had recorded Triglyceride levels < 50 mg/dL and therefore LDL and VLDL results were unavailable.

cancer survivors comparing a HIIT training program to one characterized by moderate intensity continuous training (MICT) and a control group, HITT participants were found to have greater declines in overall body mass and fat mass, serum concentrations of pro-inflammatory cytokines TNFα and leptin and improvements in lower body strength compared with MICT (Hooshmand Moghadam et al., 2021). Another study in breast cancer survivors following treatment with chemotherapy found that patients participating in HIIT experienced less cancer-related fatigue, reported improvements in HRQoL, gains in measured muscle strength (hand-grip test) and decreased body mass (Mijwel, 2019). In a small RCT of 18 patients diagnosed with Chronic Lymphocytic Leukemia (CLL), after 12 weeks of 150 min per week of HIIT and strength training; compared with a controls arm, patients participating in the intervention demonstrated superior improvements in muscle strength. In addition, the immunologic function, measured by Natural Killer (NK) and B-cell activity, was significantly improved (MacDonald, 2021). Finally, in a study of 24 female cancer survivors participating in a 12 week intervention comparing HIIT to a low-to-moderate intensity training program, significant improvements were observed in 13 of the 23 measured endpoints, the breadth of which covered measures of body composition (e.g. body mass, % body fat), cardiovascular fitness (e.g. resting heart rate, blood pressure), HRQoL, and chronic inflammation (CRP, WBC, insulin) (Toohey et al., 2016). All of these trials were demonstrated to be feasible, well-tolerated by participants, and the vast majority of participants considered adherent to protocols with few drop-outs.

Among the strengths of the current investigation include the diversity of our patient population, not just by race, but by gender, age and cancer type. An exploratory analysis of the outcomes of interest by race and gender suggest no differences in the observed improvements by participant race, however the baseline measures of body composition and HbA1c were higher among black participants compared with white (Supplementary Table 2). As these measures are markers of cardiometabolic health, this would suggest that black cancer survivors in particular stand to benefit greatly from this program and similar ones. The current pilot was adequately powered to detect outcomes under investigation given the magnitude of the observed changes over time. However, a larger sample size in future iterations of this intervention will be required to examine the impact of this program by additional participant characteristics. In this single-arm trial, all of the outcomes of interest were measured as change over time, appropriate given its pilot nature. However, future studies will include one or more control groups of survivors randomized to undergo usual care or participation in other (non-HIIT) forms of exercise. The training protocol, including baseline and end of study testing, was conducted by trained professionals with decades of experience in the exercise techniques used, increasing the likelihood of repeatable, reliable, and objective measures of performance. Finally, though not a measured endpoint, end of study focus group participation has provided some preliminary feedback to help future studies planned to understand barriers to participation and adherence to improve the program.

6. Conclusions

The benefits of regular physical activity on outcomes among cancer survivors is important and exercise, to the extent possible, is encouraged throughout the cancer survivorship continuum from time of diagnosis through palliative stages. The American Cancer Society has recommended that cancer survivors regularly participate in moderate to vigorous physical activity coupled with strength training as soon as possible following diagnosis. Unfortunately, post-treatment survivorship care plans do not adequately address exercise following treatment and the discussion between treating physicians and their patients surrounding physical activity is not optimal. African American cancer survivors have been a particularly difficult group to reach with these messages, but is a group that stands to benefit greatly from changes in health behaviors like physical activity. Our findings suggest that this unique single arm HIIT and strength training format is well-tolerated with uniformly positive outcomes over a 12-week period. Future work will include a randomized control arm in larger groups of survivors, and include an examination of longer-term outcomes.

Funding

Barbara Ann Karmanos Cancer Institute.

CRediT authorship contribution statement

Jennifer L. Beebe-Dimmer: Conceptualization, Investigation, Methodology, Writing – original draft. **David G. Finlay:** Conceptualization, Investigation, Methodology, Writing – original draft, Writing – review & editing. **Julie J. Ruterbusch:** Data curation, Formal analysis. **Tara Baird:** Investigation, Methodology, Writing – review & editing. **Michael S. Simon:** Writing – review & editing. **Judith Abrams:** Data curation, Formal analysis, Writing – review & editing. **Felicity W.K. Harper:** Writing – review & editing. **Izabela Podgorski:** Writing – review & editing. **Elisabeth I. Heath:** Conceptualization, Writing – review & editing.

Declaration of Competing Interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Jennifer Beebe-Dimmer reports financial support was provided by National Cancer Institute.

Data availability

The data that has been used is confidential.

Acknowledgements

This work was supported by the Epidemiology Research Core and the National Cancer Institute Center Grant (P30CA022453) awarded to the Karmanos Cancer Institute at Wayne State University. We would also like to thank the coaches at Detroit Athletix and Northville Athletix for their contribution to the CAPABLE program.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.pmedr.2023.102288.

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