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Design and Methods of a Randomized Telehealth-Based Intervention to Improve Fitness in Survivors of Childhood Cancer with Exercise Intolerance

Arun Maharaj[a], **John L. Jefferies**[b], **Daniel A. Mulrooney**[c], **Gregory T. Armstrong**[d], **Tara M. Brinkman**[e], **Sean T. O'Neil**[f], **Sarah Terrell**[g], **Robyn E. Partin**[h], **Deo Kumar Srivastava**[i], **Melissa M. Hudson**[j], **Zhaoming Wang**[k], **Kirsten K. Ness**[l]

[a]Department of Epidemiology and Cancer Control, St. Jude Children's Research Hospital, 262 Danny Thomas Place, MS-735, Memphis, TN 38105 USA

[b]Department of Medicine, University of Tennessee Health Science Center, 920 Madison Avenue, Memphis, TN 38163 USA

[c]Department of Oncology, St. Jude Children's Research Hospital, 262 Danny Thomas Place, MS-260, Memphis, TN 38105 USA

[d]Department of Epidemiology and Cancer Control, St. Jude Children's Research Hospital, 262 Danny Thomas Place, MS-735, Memphis, TN 38105 USA

[e]Department of Psychology and Biobehavioral Sciences, St. Jude Children's Research Hospital, 262 Danny Thomas Place, MS-740, Memphis, TN 38105 USA

[f]Department of Epidemiology and Cancer Control, St. Jude Children's Research Hospital, 262 Danny Thomas Place, MS-735, Memphis, TN 38105 USA

[g]Department of Epidemiology and Cancer Control, St. Jude Children's Research Hospital, 262 Danny Thomas Place, MS-735, Memphis, TN 38105 USA

[h]Department of Epidemiology and Cancer Control, St. Jude Children's Research Hospital, 262 Danny Thomas Place, MS-735, Memphis, TN 38105 USA

[i]Department of Biostatistics, St. Jude Children's Research Hospital, 262 Danny Thomas Place, MS-768, Memphis, TN 38105 USA

Corresponding Author: Kirsten K. Ness, PT, PhD, FAPTA, St. Jude Children's Research Hospital, 262 Danny Thomas Place, MS-735, Memphis, TN 38105, kiri.ness@stjude.org.

CRediT authorship contribution statement

Arun Maharaj: Writing – original draft, Writing – review & editing. **John L. Jefferies:** Writing – review & editing, Conceptualization, Investigation, Supervision. **Daniel A. Mulrooney:** Writing – review & editing, Conceptualization, Supervision. **Gregory T. Armstrong:** Writing – review & editing, Conceptualization. **Tara M. Brinkman:** Writing – review & editing, Conceptualization. **Sean T. O'Neil:** Writing – review & editing, Investigation. **Sarah Terrell:** Writing – Conceptualization. **Robyn E. Partin:** Writing – review & editing, Investigation. **Deo Kumar Srivastava:** Writing – review & editing, Conceptualization, Formal analysis, Methodology. **Melissa M. Hudson:** Writing – review & editing, Conceptualization, Supervision. **Zhaoming Wang:** Writing – review & editing, Conceptualization. **Kirsten K. Ness:** Writing – review & editing, Conceptualization, Supervision, Funding acquisition, Investigation.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

[j]Departments of Oncology and Epidemiology and Cancer Control, St. Jude Children's Research Hospital, 262 Danny Thomas Place, MS-735, Memphis, TN 38105 USA

[k]Departments of Epidemiology and Cancer Control and Computational Biology, St. Jude Children's Research Hospital, 262 Danny Thomas Place, MS-735, Memphis, TN 38105 USA

[l]Department of Epidemiology and Cancer Control, St. Jude Children's Research Hospital, 262 Danny Thomas Place, MS-735, Memphis, TN 38105 USA

Abstract

Background—Exercise intolerance among childhood cancer survivors substantially increases risk for early mortality, reduced cognitive function, poor quality of life, emotional distress, and sub-optimal participation in social roles. Fortunately, exercise intolerance is modifiable, even among individuals with impaired cardiopulmonary and neuromuscular health. This study aims to evaluate the impact of tailored exercise intervention remotely supervised by fitness professionals in survivors with exercise intolerance. Telehealth-based delivery of the intervention aims to enhance uptake by removing the burden of travel and allowing participants to gain confidence with exercise and physical activity at home.

Methods—This is an ongoing single-blind, two-arm, prospective, clinical trial that will randomize 160 participants 1:1 to intervention (n=80) and attention control (n=80) groups. The intervention group receives an individually tailored exercise prescription based on results from baseline assessments performed remotely via a Health Insurance Portability and Accountability Act-compliant virtual platform and personal preferences for aerobic exercise. Each prescription includes aerobic and strengthening components designed to progress gradually to 150–300-minutes of moderate aerobic activity and twice weekly strengthening exercises over 20-weeks. The first two weeks are supervised for 6 sessions, tapering to twice/week for weeks 3–4, once/week for weeks 5–8, every other week for weeks 9–16 and once midway between weeks 17–20. The schedule is modifiable depending on participant need, adherence, and response to exercise. Each session is approximately one hour.

Conclusion—This study tests the efficacy of an individually prescribed, virtually supervised exercise intervention on exercise intolerant childhood cancer survivors.

Clinicaltrials.gov registration: NCT04714840

Keywords

childhood cancer survivors; exercise intolerance; physical activity; fitness; remote; telehealth-based; web-based

1. Introduction

Survival following a childhood cancer diagnosis exceeds 85% in developed countries, with over 500,000 survivors living in the United States today [1]. Unfortunately, cure is not without consequences. Late effects are well-documented in this vulnerable population, who are five times more likely than siblings to report severe, disabling, life threatening or fatal chronic conditions [2], suggesting risk for accelerated aging. Chronic conditions,

including impairments of cardiac, pulmonary, autonomic, musculoskeletal, and neurosensory function [3], and specific biomarkers of aging, including shortened leukocyte telomere length [4], reduced mitochondrial deoxyribonucleic acid (DNA) copy number [5] and DNA methylation-based epigenetic age acceleration (EAA) [6] are present in childhood cancer survivors, and are associated with previous cancer treatment exposures.

In the general and in diseased populations, chronic conditions [7–9] and biomarkers of aging [10–13] respond favorably to interventions designed to optimize health behaviors, including those that deliver prescribed exercise with the goal of improving exercise tolerance. Thus, although childhood cancer survivors cannot change treatment exposures, they may be able to optimize health outcomes by engaging in regular exercise. Unfortunately, nearly 33% of childhood cancer survivors report that they do not participate in any regular physical activity, and an additional 27% fail to meet weekly recommendations of 150-minutes of moderate physical activity [14]. Engaging in activity is difficult for anyone, especially in persons whose initial responses to exercise are blunted and uncomfortable from cancer or treatment related organ system dysfunction [15]. Discomfort during exercise is likely discouraging [16], and meaningful behavioral change is difficult without specific guidance [17]. Evidence to support interventions that promote exercise among childhood cancer survivors is scarce [18]; current standard of care is simply to encourage activity [19]. Interventions tailored to accommodate survivor-specific impairments are needed.

Recent meta-analyses and systematic reviews indicate that individualized home-based exercise interventions can improve exercise capacity in persons with heart failure [20], in older adults [21], in survivors of adult-onset cancers [22, 23], and that providing direct remote feedback (video or telephone) has similar positive effects on exercise capacity to supervised center-based exercise [21]. Thus, individualized interventions designed to increase exercise capacity, supervised remotely, and delivered in a home setting have potential for success in childhood cancer survivors. This study is powered on its primary aim, which is to test the impact of an individually tailored, supervised, home-delivered aerobic and strengthening intervention on exercise capacity in survivors of childhood cancer. We will further examine the effects of the intervention on cardiac, pulmonary, musculoskeletal, and neurosensory function as well as emotional health, participation in family and community activities, quality of life and cognitive function. Additionally, we will evaluate the impact of exercise on aging biomarkers. Those in the intervention (INT) group will be compared to an attention control (AC) group. Supervision is tapered over 20-weeks. If effective, this study will move the standard of care (encouraging physical activity) for exercise intolerance from its current state, ineffective for many survivors, to a clinically actionable, practical, sustainable, relatively low cost and generalizable intervention.

2. Methods

2.1. Study design and participants

This is a single-blind two-arm, prospective, randomized clinical trial currently enrolling participants from the St. Jude Lifetime Cohort (SJLIFE), a retrospective cohort study designed to assess childhood cancer survivors surviving ≥5-years from cancer diagnosis. Potentially eligible participants have exercise capacity <85% of predicted VO_{2peak}. Figure

1 outlines the study design and overview. Consented participants are randomized after baseline testing to either the INT or AC group. Outcomes are evaluated at baseline, after the intervention (20-weeks; primary outcome assessment) and 6-months after completion of the intervention (durability outcome). This study is approved and monitored by the St. Jude Children's Research Hospital Institutional Review and Data Safety Monitoring Boards, respectively.

2.2. Participant eligibility and recruitment

This study will enroll 160 SJLIFE participants for approximately 11-months. Participants will undergo remote assessment to confirm eligibility, assess baseline outcomes and receive medical clearance from study physicians. Assessment team members are blinded to group assignments.

Inclusion and exclusion criteria are outlined in Table 1. Pregnant females, those enrolled in a formal exercise intervention, or who self-report engaging in >150-minutes/week of moderate physical activity, those endorsing significant psychological distress or those requiring immediate medical intervention are ineligible. The Alcohol Use Disorders Identification Test (AUDIT) and Drug Abuse Screen Test (DAST-10) are used to screen for those who have active alcohol or drug use disorders before baseline testing. If a participant indicates alcohol or drug abuse, participants are taken off study and not randomized. Participants then receives referral for local treatment services. This study was opened for recruitment on February 8, 2021, and 133 participants were enrolled as of August 18, 2023.

2.3. Consent and randomization

Initial eligibility criteria are confirmed before obtaining consent. If approached in person, the participant is provided with a hard copy of the consent to review. Otherwise, the consent is emailed to the participant for review before the consent discussion, where the study staff reviews the document and answers questions. All participants are informed that, if randomized to the AC group, they will be offered the intervention once the study is complete. No additional data collection is planned for AC participants who choose to receive the intervention. Upon agreement to participate, participants and the study team member sign the document. A copy of the signed consent form is provided to the participant.

Participants complete a baseline medical screening/impairment assessment, performance testing and study questionnaires remotely via a commercially available, Health Insurance Portability and Accountability Act (HIPAA) compliant online platform (Moterum Technologies Inc, Salt Lake City, UT). Participants are stratified by age (18–29 and 30–39-years), sex, race, and baseline estimate (from 2-minute step in place test; 2MSPT) of percent predicted VO_{2peak} (<70%, >70%) and randomized 1:1 between the study arms.

2.4. Study materials

Participants are provided with written instructions, videos of strengthening exercises, a Bluetooth enabled heart rate (HR) monitor worn on the arm (OH1+ or Verity, Polar Electro, Kempele, Republic of Finland) and an iPad (Generation 9 or 10, OS 15.3.1 or 16.5, Apple Inc., Cupertino, CA) pre-loaded with a shortcut to Moterum. This platform

provides a secure log-in where participants access their personalized account to connect with their exercise specialist via video session or access their individualized exercise plans. Participants in the intervention group receive exercise equipment (bands, weights). Once participants receive the testing equipment, they are instructed to familiarize themselves with each item and set up their web-based fitness platform account. An assessment only exercise specialist schedules an orientation video session to familiarize the participant with the online platform and all testing equipment. The baseline assessment is scheduled at the end of the virtual orientation session. After baseline testing, the participant is contacted by an intervention exercise specialist to review the results of their baseline assessment and receive group assignment. The first supervised exercise session is then scheduled and includes reviewing the components and proposed progression of their exercise program. Aerobic and strengthening exercises are demonstrated, the participant practices, receives feedback and is encouraged to ask questions.

2.5. Intervention

Exercise specialists (American College of Sports Medicine Certified Clinical Exercise Physiologist (ACSM-CEP)) establish visit times with each participant for initial video communication supervised visits. During the first two weeks, supervision and guidance is provided for six sessions (3/week, divided between aerobic and strengthening sessions) via the web-based fitness platform, allowing for visualization of exercise performance and two-way communication. Supervision is tapered to twice/week in weeks 3–4, once/week in weeks 5–8, every other week in weeks 9–16 and once midway between weeks 17–20. Participants' goal is to exercise 3x/week for the entire intervention duration so as supervised sessions taper, they exercise independently (following individualized exercise programs written by the exercise specialist) with increasing frequency [12, 24]. For resistance training, the goal is a load that elicits fatigue after 3 sets of 10–12 repetitions on 8–10 exercises 2 days/week. Participants who have difficulty with their exercises or adherence to their program are provided with additional sessions as needed as part of the tailored approach in the study design. Each visit lasts approximately one-hour. The progression of the intervention is estimated a priori but is monitored by the specialist during visits and delayed or accelerated as appropriate. The intervention exercise specialists have cell phones and email accounts, so they can be contacted during working hours (including evenings) to answer questions.

At each visit, ability to adhere to the program is reviewed. Participants having difficulty with adherence (<80% of the prescribed intervention over a rolling two-week interval) complete a specific problem-solving session with the exercise specialist, and with assistance from the study psychologist. The exercise specialist helps identify potential barriers to adherence and discusses possible solutions. Upon identification of potential barriers, the participant selects one solution that they are willing to implement over the next month and it is operationalized. Participants who need more frequent supervision because of difficulties performing an exercise or because of a lapse in adherence may select additional supervision as a potential solution. Participants are not removed from the intervention trial due to poor adherence. Intervention sessions are monitored via the web-based platform. iPads are provided by the

study, so remote technology support is available as needed. Replacement iPads and HR monitor devices are provided to participants within 24-hours of failure notification.

Participants randomized to AC are provided with results of their baseline assessment and a handout outlining the Physical Activity Guidelines for Americans. The exercise specialist answers general questions about their performance and encourages them to engage in physical activity. A specific prescription is not provided. Participants are asked to answer general questions about recent exercise habits and to complete the PROMIS ability to participate 8a Short Forms.

2.6. Study Outcomes

The primary outcome of this study is exercise capacity, remotely assessed by the 2MSPT. Testing also includes measures of organ system dysfunction, emotional health, ability to participate in family, social and work activities, and quality of life. Before any fitness testing begins, study staff asks physical activity related health history questions, as well as questions from the Physical Activity Readiness Questionnaire (PAR-Q) [25–27], to ensure exercise is appropriate and safe. If further follow up is needed, a study physician will contact the participant to obtain additional information to determine the safety of further testing and participation in exercise. Data collection is completed at baseline, 20-weeks, and six-months after the intervention is complete in both INT and AC groups. Participants complete PROMIS forms each week during the first eight-weeks and every four-weeks during weeks 9–20. Study outcomes include exercise capacity (2MSPT), resting HR, HR variability (HRV), oxygen saturation and blood pressure (BP), body weight, lung function (spirometry), neurosensory integrity, measurements of physical function (muscle strength) and PA, and questionnaires related to alcohol and drug abuse, PA readiness, health history, anxiety, and activity impairment (Table 2).

2.7. Vital signs, sensory testing, and spirometry

Body weight is obtained twice on an electronic scale without shoes. Oxygen saturation (SpO_2) and resting HR are measured using a pulse oximeter (FL400, FaceLake, Buffalo Grove, IL) placed on the index finger. The participant is seated and rests for 5-minutes before documentation. Once HR and SpO_2 have stabilized, the participant reports the values. Blood pressure is measured using a wireless BP monitor (7350, Omron Healthcare, Kyoto, Japan). The exercise specialist instructs the participant to place the BP monitor on the left upper arm and to start the device after 5-minutes of seated rest. A second reading is taken on the left arm after a one-minute rest. If both readings are >10 mmHg different for either systolic or diastolic pressures, a third measurement is taken. Peripheral sensation and motor function are evaluated using the sensory and motor symptom questions from the modified total neuropathy scale [28]. A total score out of 8 is documented. Scores of >2 are considered impaired. Spirometry is assessed with a portable flowmeter (PF100, Microlife, Widnau, Switzerland). Peak expiratory flow (PEF) and forced expiratory volume in one-second (FEV_1) are measured. Participants are instructed to take a deep breath and fully exhale into the mouthpiece as forcefully and quickly as possible. Peak expiratory flow and FEV_1 are measured digitally on the screen. Participants have three attempts, and the highest values are documented.

2.8. Physical performance and biospecimen collection

Exercise capacity is measured using the 2MSPT [29]. The participant stands directly next to a blank wall keeping a stable chair nearby for safety. They place two pieces of tape; one at the patella and another at the iliac crest. The exercise specialist verbally assists the participant with palpating the anatomical sites. Using the supplied measuring tape, the participant measures the distance between the two tape marks, then places the 3rd piece of tape at the halfway point of the patella and iliac crest tape marks. The participant then removes the patella and iliac crest marks leaving only the halfway point tape. The exercise specialist instructs the participant to start and counts the number of times the right knee completes a step in two-minutes, ensuring the knee meets or passes the tape mark each time. Feedback is provided if the participant needs to lift the knees higher to meet the tape mark. Pulse oximetry is used to capture HR, documented prior to and immediately after the test, and one- and two-minutes into recovery. The participant is asked to rate how hard they felt they were working during the test using the RPE scale.

Handgrip strength is measured using a digital dynamometer (Jamar, Patterson, Warrenville, IL). The participant holds the dynamometer with fingertips in the grooves, with the elbow bent to 90 degrees, and squeezes as hard as possible for 2–3-seconds. Peak force is recorded in kilograms. Participants perform the sit-to-stand test to measure leg strength using a standard-sized chair next to a table or wall for safety. With arms crossed at the shoulders, participants attempt to stand and sit as quickly as possible for 30-seconds. The number of times the participant stands and sits again are recorded. Physical activity, HR and HRV are measured using an accelerometer (xGT3X-BT, ActiGraph, LLC, Pensacola, FL) and a Polar HR monitor. Participants wear the accelerometer on an elastic belt around the waist and the HR monitor around the chest, snug against the skin, to collect physical activity data, HR and HRV over 3-days at each assessment timepoint.

Optionally, after signing the appropriate consent forms, participants in both groups provide saliva samples at baseline, after the intervention and 6-months after completion of the intervention. Deoxyribonucleic acid is then extracted from saliva samples, and a DNA methylation EPIC array is used for methylation profiling [30]. Quantitative polymerase chain reaction (qPCR) is then used to simultaneously quantify telomere length and mitochondrial DNA copy number [31, 32].

Participants complete global physical and mental health (PROMIS) short form measures (2-items each) weekly during weeks 1–8 and every fourth week during weeks 9–20. Social and work participation is evaluated with the PROMIS ability to participate in social roles and activities Short Form [33], the work productivity and activity impairment questionnaire (WPAI) [34, 35] and the work and social adjustment scale (WSAS) [36, 37]. Emotional health is assessed using the Patient Health Questionnaire 8 (PHQ-8) for depression [38, 39]. The Generalized Anxiety Disorder 7 (GAD-7) questionnaire is used to assess mild, moderate and severe anxiety [40, 41], and the Medical Outcomes Survey Short Form (SF-36) to assess quality of life [42, 43]. Cognitive function is evaluated via the Childhood Cancer Survivor Study Neurocognitive Questionnaire (CCSS-NCQ) – Revised. The CCSS-NCQ is a 32 item self-report questionnaire evaluating four domains of neurocognitive function: (1) memory; (2) task efficiency; (3) organization; and (4) emotional regulation [44]. Lastly,

two constructs related to participant experience with the intervention are assessed at the end of and six months after the intervention is complete. The Service User Technology Acceptability Questionnaire (SUTAQ) [45] includes 22 statements to which participants use a 6-point Likert-type scale to rate agreement. The System Usability Scale (SUS) is a 10-item questionnaire, which measures agreement (i.e., strongly agree to strongly disagree) on a five-point scale [46].

2.9. Data management

Registration, enrollment, randomization, and data collection/entry are done at St. Jude Children's Research Hospital. Data from the assessment and the survey are recorded by study personnel by participant identification number on optical recognition forms and downloaded daily onto a computer server with restricted access to the research team. The medical records are abstracted, and the data are recorded using an established database. All files are password protected. Identifying information is stored separately and the files are linked by identification number. Paper forms are stored in a locked file cabinet.

2.10. Sample size calculation

With a sample size of 129, we have 80% power using a two-sided two sample t-test and an alpha value of 0.05 to detect a difference of 3.75 ml/kg/min (0.5 standard deviation (SD)) between groups on the VO_{2peak} assessed with the 2MSPT. We estimate 20% missing data at week 20. We plan to enroll a total of 163 participants on the study to ensure adequate power. This sample size accounts for interim analysis when 65 survivors have been randomized and followed for 20-weeks. We will only stop for futility if the p-value is larger than 0.724 in the interim analysis. During the interim analysis, we will also obtain estimates of the variability and correlation in peak VO_2/2MSPT measurements and missingness proportions. We will use this information to revise the sample size upwards if required. The sample size will not be reduced.

2.11. Data analysis

For each of the continuous outcomes in Aims 1 and 3, differences between two groups will be compared using two-sample t-tests, where the two peak VO_2/2MSPT (or other outcomes) measurements at end of intervention and baseline post randomization are denoted by Y_{W20}^{INT} and Y_B^{INT} for the INT group and Y_{W20}^{AC} and Y_B^{AC} for the AC group, and $D_i^{INT} = Y_{i,\,20W}^{INT} - Y_{i,\,B}^{INT}$, and $D_i^{AC} = Y_{i,\,20W}^{AC} - Y_{i,\,B}^{AC}$ for $i = 1, 2, \ldots 64$ denote differences b the 2 groups. It is important to note that even when original distributions are not normal (distributions of Y_i's), the distribution of the differences (D_i's) are often close to normal. However, we will test assumptions of normality for the differences, and if normality assumptions are not met, we will appropriately transform the data before applying t-tests for analysis.

For each of the outcomes in aim 2, because they can be represented both as continuous measures and dichotomies (impaired/normal), we will evaluate both mean changes in the differences between groups as described above and compare the proportions of those whose values indicate impairment at end of intervention between groups, adjusting for the baseline prevalence of the specific impairment. These analyses will utilize Generalized Estimating Equation (GEE) [47], specifying a binomial distribution in PROC GENMOD in SAS v9.4

with compound symmetry as the working covariance structure to account for correlation among repeated observations.

Analyses to also be conducted to determine the sustainability of changes in our outcome measures (6 months post-intervention) in a similar manner, as discussed above, by taking the differences between the measurement obtained at 6 months after end of intervention and baseline measurement and comparing the proportions of those whose values indicate impairment 6 months after end of intervention between groups. In addition, since we will have observations at three time points for all outcome measures, and at many time points for the PROMIS Global Health Instruments, we will also use GEE approaches to assess patterns of change over time using PROC GENMOD in SAS v9.4, with compound symmetry as the working covariance structure to account for correlation among repeated observations.

For analysis of the biomarkers, let DM_{1j} and DY_{1j}, j=1, 2,…n denote differences from after the intervention to baseline in the marker level and outcome measure for n individuals on the trial. Similarly, DM_{2j} and DY_{1j}, j=1, 2,…n denote differences from 6 months after the intervention to after the intervention in the marker level and outcome measure for n individuals on the trial. Generalized linear regression will be used to compare the changes in the biomarker levels between the intervention and the control group with baseline values of the biomarker as a covariate in the model. Generalized linear regression will be used to assess the relationship between changes in biomarker levels and changes in outcome measures and the models will be appropriately adjusted for other covariates of interest.

2.12 Missing and incomplete data

We do not expect >20% missing data but have increased the sample size to ensure adequate power. However, if there are missing data, irrespective of the missingness percentage, a multiple imputation approach will be established, assuming that data are missing at random, as described in Fitzmaurice, et al. [47], to test the null hypothesis and assess sensitivity of the results.

3. Discussion

Evidence suggests that regular exercise is difficult and/or uncomfortable for childhood cancer survivors because of underlying organ system impairments [14, 15], reducing motivation to perform physical activity, maintain quality of life and substantially increases mortality risk. This study employs a telehealth-based strategy to test the efficacy of individually prescribed exercise training on exercise tolerance in childhood cancer survivors. Results from this study will highlight the importance of improving cardiorespiratory fitness to reduce late effects as well as increase motivation, confidence, and independence to encourage lifelong physical activity.

This study is innovative for various reasons. It engages an individualized, progressive exercise prescription that accommodates survivor-specific organ-based impairments within the context of American Heart Association and/or American College of Sports Medicine Exercise guidelines for persons with chronic disease. This study also provides supervision and/or guidance from an exercise specialist to reassure survivors lacking confidence that

they can be successful, and that starting an exercise program is naturally progressive. Importantly, this study tapers supervision over time, allowing survivors to become progressively independent with the exercises. Further, both intervention and assessments are designed to be completely home-based and all materials (equipment, written and video instruction, supervision/monitoring devices) are provided, removing barriers of fitness center travel, access, recurring cost, and self-consciousness. This study is also flexible, addressing adherence concerns, and engages the survivor in identifying barriers and selecting solutions that work for them. This study is also assessing the sustainability of outcomes six months post- intervention, testing long-term adherence to the exercise program.

This intervention is not without limitations. Using telehealth-based assessment and intervention strategies requires internet access. To counteract this, internet hot spots are sent to participants with unreliable internet access. Scheduling limitations can also hinder participant progress. It may become difficult to schedule live sessions for those working nightshifts or multiple jobs. However, our exercise specialists have successfully worked through scheduling conflicts in the past. Lastly, like all intervention studies, adherence to the regimen can be a challenge when conducting virtual sessions. Since supervision is tapered over time, participants become more inclined to miss or skip sessions. Participants will not be dropped for poor adherence. Instead, we have participants identify barriers that are causing poor adherence and help find solutions.

4. Conclusion

This study is an ongoing, telehealth-based intervention designed to improve overall fitness and mental health to perform exercise among exercise intolerant survivors of childhood cancer. Exercise intolerance substantially increases their risk for early mortality, reduced cognitive function, poor quality of life, emotional distress, and sub-optimal participation in social roles [48–56]. Fortunately, exercise intolerance is modifiable, even among individuals with impaired cardiac [57, 58], pulmonary [59], and neuromuscular health [60]. Nevertheless, survivors do not, on average, engage in exercise [14]. Findings from this study will shed light on the efficacy of using a telehealth-based system to improve exercise tolerance and motivate childhood cancer survivors to engage in physical activity and improve long-term health.

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Data availability

Protocol documents are available upon request to the corresponding author. Study data will be made publicly available when the study is complete at https://www.stjude.cloud/ [61] and www.zenodo.com [62].

Abbreviations

2MSPT	2-minute step in place test
AC	attention control group
AUDIT	alcohol use disorders identification test
BP	blood pressure
CCSS-NCQ	Childhood Cancer Survivor Study Neurocognitive Questionnaire
DAST	drug abuse screening test
DNA	Deoxyribonucleic acid
EAA	epigenetic age acceleration
FEV_1	forced expiratory volume in 1 second
GAD-7	Generalized Anxiety Disorder – 7
HR	heart rate
HRV	heart rate variability
INT	intervention group
PAR-Q	physical activity readiness questionnaire
PEF	peak expiratory flow
PHQ-8	patient health questionnaire-8
PROMIS	Patient Reported Outcomes Measurement Information System global physical and mental health short forms
SF v2.0	PROMIS ability to participate
SF-36	medical outcomes survey short form
SJLIFE	St. Jude Lifetime Cohort
SPO_2	oxygen saturation
SUS	system usability scale
SUTAQ	Service User Technology Questionnaire

VO_{2peak}	relative peak oxygen uptake
WASA	work and social adjustment scale
WPAI	work productivity and activity impairment questionnaire

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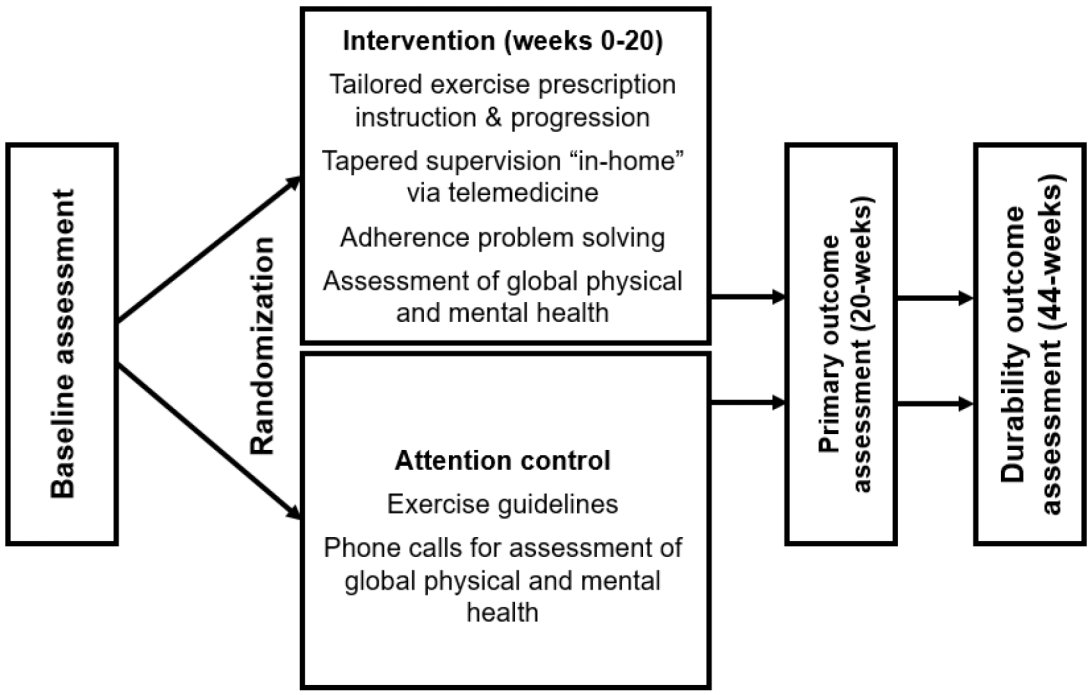

Figure 1.
Study Design and overview

Table 1.

Study inclusion and exclusion criteria

Inclusion Criteria	Exclusion Criteria
18 to 39-years of age at enrollment	Enrolled in a formal exercise intervention
SJLIFE participant (have history of cancer diagnosed and treated at St. Jude Children's Research Hospital, alive ≥5 years after cancer diagnosis)	Self-report of >150-mins/week of moderate physical activity
VO_{2peak} <85% predicted calculated from 2MSPT (during remote baseline testing)	Currently pregnant
Understanding of directions for use of web-based fitness platform on the study provided iPad and HR monitor	Significant psychological distress (e.g., suicidal ideation)
Clearance for participation in exercise by a study physician	Conditions requiring immediate medical intervention (e.g., angina, decompensated heart failure)
	Alcohol or drug abuse in the past year (AUDIT >=13/women and >=15/men or DAST - 10 >=3)

Abbreviations: 2MSPT = 2-minute step in place test; AUDIT = Alcohol Use Disorders Identification Test; DAST = Drug Abuse Screening Test; HR, heart rate; mins, minutes; SJLIFE, St. Jude Lifetime Cohort; VO_{2peak}, relative peak oxygen uptake

Table 2.

Outcome collection timeline

Measure	Time point		
	BL	20-wk	6-mo
Informed Consent	X		
Screening Questionnaires:	X		
Alcohol Use Disorders Identification Test (AUDIT)			
Drug Abuse Screen Test (DAST-10)			
Pregnancy test (urine), if applicable	X		
2-minute step in place test	X	X	X
Resting HR, oxygen saturation and blood pressure	X	X	X
Weight	X	X	X
Spirometry	X	X	X
Muscle Strength	X	X	X
Neurosensory integrity	X	X	X
Physical activity and HR/HR variability	X	X	X
Questionnaire:	X	X	X
Physical activity Readiness Questionnaire (PAR-Q)			
Questionnaires:	X	X	X
Physical Activity Related Health History			
Patient Health Questionnaire (PHQ-8)			
Generalized Anxiety Disorder (GAD-7)			
PROMIS Ability to Participate 8a (SF v2.0)			
Work Productivity and Activity Impairment Questionnaire (WPAI)			
Work and Social Adjustment Scale (WSAS)			
Medical Outcomes Survey Short Form (SF-36)			
Childhood Cancer Survivor Study Neurocognitive			
Questionnaire – Revised (CCSS-NCQ)			
Questionnaire (Acceptability Measures):		X	X
Service User Technology Acceptability Questionnaire (SUTAQ)			
System Usability Scale (SUS)			
OPTIONAL: Biomarkers (saliva), if applicable	X	X	X

Abbreviations: BL, baseline; HR, heart rate; mo, month; wk, week