RUTGERS
Cancer Institute
of New Jersey

Rutgers, The State University of New Jersey
195 Little Albany Street
New Brunswick, NJ 08903-2681

cinj.org
p. 732-235-2465

Title: "TLC FIT": A Novel Mobile Health Fitness Program for Adolescent and Young Adult (AYA) Childhood Cancer Survivors

Principal Investigator: Katie Devine, PhD, MPH
Assistant Professor
Rutgers Cancer Institute of New Jersey
195 Little Albany Street, Room 5571
New Brunswick, NJ 08903
Telephone: (732) 235-7549; Fax: (732) 235-6225
Email: katie.devine@rutgers.edu

Subinvestigators:

Sharon Manne, PhD Rutgers Co-investigator (Mentor)	
Margaret Masterson, MD Rutgers Co-investigator	Jerod Stapleton, PhD Rutgers Co-Investigator
Shawn Arent, PhD, CSCS Rutgers Co-Investigator	Pamela Ohman-Strickland, PhD Rutgers Co-Investigator (Biostatistician)

Rutgers Cancer Institute of New Jersey
Operations Center
Office of Human Research Services
195 Little Albany Street
New Brunswick, NJ 08903
Telephone: (732) 235-8675
FAX: (732) 235-7690

Rutgers Cancer Institute of New Jersey
Biostatistical Center
Biometrics Division
195 Little Albany Street
New Brunswick, NJ 08903
Telephone: (732) 235-6791
FAX: (732) 235-7350

Supported by:
This project is funded by NCI (K07 CA174728). Dr. Devine's start-up funds will pay for additional costs not covered by the grant.

Drug(s) Under Investigation: N/A

TABLE OF CONTENTS

1. PURPOSE/SPECIFIC OBJECTIVES 4

2. BACKGROUND AND SIGNIFICANCE 5

3. PARTICIPATING INSTITUTIONS 7

4. EXPERIMENTAL DESIGN AND METHODS 8

4.1 Procedures 8
4.2 Duration of Study 10

5. PATIENT SELECTION CRITERIA 11

5.1 Inclusion Criteria 11
5.2 Exclusion Criteria 11
5.3 Inclusion of Women and Minorities 12
5.4 Participation of Children 12
5.5 Sources or Methods of Recruitment 12
5.6 Study Enrollment Procedures 12

6. STUDY PARAMETERS/MEASURES 13

7. DATA COLLECTION AND RECORDS TO BE KEPT 15

7.1 Research Charts 15
7.2 Reports 16

8. DATA AND SAFETY MONITORING 16

9. STATISTICAL CONSIDERATIONS 16

9.1 Primary and Secondary Hypotheses and Endpoints 16
9.2 Sample Size Justification 17
9.3 Methods for Masking, Randomization and Stratification 17
9.4 Statistical Analysis 17
9.5 Compliance and Missing Data 18

10. HUMAN SUBJECTS 18

10.1 Subject Population 19
10.2 Potential Risks 19
10.3 Consent Procedures 20
10.4 Potential Benefits 20
10.5 Risk-Benefit Ratio 20
10.6 Gender and Minorities 21

11. ECONOMIC/FINANCIAL CONSIDERATIONS 21

12. PUBLICATION OF RESEARCH FINDINGS 21

REFERENCES 22

LIST OF ABBREVIATIONS

TLC FIT	Teens Living with Cancer – Fitness Improvement Training
AYA	Adolescent and Young Adult
CINJ	Cancer Institute of New Jersey
LITE	Long-term, Information, Treatment effects, and Evaluation program
IRB	Institutional Review Board
NCI	National Cancer Institute
NIH	National Institutes of Health
PI	Principal Investigator
PA	Physical Activity
HRQOL	Health-Related Quality of Life
CCSS	Childhood Cancer Survivor Study
SCT	Social Cognitive Study

The K07 is a 5-year training grant and part of the training plan is for Dr. Devine to learn how to design and implement the studies outlined in the proposal (i.e., development of a mobile application "app" and evaluation of a behavioral intervention incorporating the newly developed app). In this application, we have described the general procedures of the project but the exact project details will be finalized during the grant period. We will modify the protocol on an ongoing basis as needed to reflect the development of project materials (i.e., mobile app) or any changes in procedures. We will obtain IRB approval for all study procedures and materials prior to their utilization in the project.

1. Purpose/Specific Objectives

The goal of this project is to develop and evaluate the feasibility of "TLC FIT" (Teens Living with Cancer Fitness Improvement Training), a technology-enhanced fitness program for adolescent and young adult (AYA) survivors of childhood cancers. Advances in treatment have fortunately led to a growth in the number of childhood cancer survivors in the US. Unfortunately, these survivors are at-risk for negative late effects from treatment, including cardiovascular disease and early death. Physical inactivity can exacerbate these risks. Adolescent survivors of childhood cancers in particular have reported significant declines in physical activity that persist following treatment. In preliminary work, we designed an eight-session group-based fitness program for AYA survivors using social cognitive theory. This program incorporated the FitBit, a novel commercially available electronic accelerometer, which allowed for self-monitoring of activity. The FitBit also provided an internet-based website for social networking among participants. The program was feasible and acceptable to participants, and they suggested lengthening the program to 12 weeks. Further, participants reported low levels of engagement with the FitBit website and a strong interest in on-the-go access to program materials outside of weekly group sessions. Therefore, the next step is to significantly enhance the technology by creating a cancer-specific smartphone application (app) that motivates participants to engage in and *sustain* behavior change. *Phase* 1 of this project involves the development of the mobile app. Following app development and validation, in *Phase 2* we will conduct a randomized pilot trial (n = 88) of TLC FIT to evaluate feasibility and effectiveness.

1.1 Primary Objectives

Aim 1: Develop and evaluate the usability of cancer-specific and motivational tools in the mobile app (Phase 1).
AYA survivors will help design the functionality requirements for the initial prototype. An experienced app development company will program the app with identified tools such as goal setting, self-monitoring, exercise instructions, and social networking. Usability testing will be conducted in an iterative manner with AYA survivors, refining the app based on user feedback (total n = 20).

Aim 2: Evaluate the feasibility of the technology-enhanced (electronic accelerometer + app + 8 weekly group sessions) fitness program in a pilot randomized clinical trial (Phase 2).

Hypothesis 1: AYAs will agree to participate in the program, demonstrate engagement in the program via > 80% attendance at group-based sessions, and use one or more components of the app at least weekly.

1.2 Secondary Objectives

Aim 3: Determine the effectiveness of the technology-enhanced fitness program on participants' cardiorespiratory fitness and muscular fitness.
Hypothesis 2: Participants in the intervention group will demonstrate greater improvement in cardiorespiratory fitness (objective submax treadmill test) and muscular fitness (objective 10-repetition tests) from baseline than wait-list control participants at the post-intervention assessment.

Aim 4: Examine the effects of the program on secondary outcomes of health-related quality of life (HRQOL) and fatigue.
Hypothesis 3: Participants in the intervention group will demonstrate greater improvement in HRQOL (PedsQL Generic Core Scale) and fatigue (PedsQL Multidimensional Fatigue Scale) from baseline than the wait-list control group at the post-intervention assessment.

2. Background and Significance

Physical inactivity is a significant problem for childhood cancer survivors. Advances in therapy have resulted in survival rates of almost 80% for children diagnosed with cancer,[1] and there are now over 350,000 childhood cancer survivors in the US.[2] These survivors are at risk for negative late effects from treatment, and almost two-thirds will develop at least one chronic health condition.[3,4] Premature cardiovascular morbidity and mortality, physical inactivity, and obesity are serious concerns.[5-10] A sedentary lifestyle is a risk factor for health problems and may exacerbate late effects of treatment, increasing the risk of cardiovascular disease, osteoporosis, and early mortality.[6] Physical activity (PA) is well known to reduce risk for cardiovascular disease and early mortality.[11,12] In healthy children and adolescents, increased PA is associated with benefits such as improved cardiorespiratory fitness, muscular fitness, bone health, and body composition.[13] PA is also positively associated with quality of life.[14-16] Because survivors of childhood cancers are inherently at risk for serious late health effects, programs to promote PA are especially important for this population. A recent systematic review of PA in childhood cancer survivors indicated the need for evidence-based behavioral interventions to promote physical activity.[17] Despite a need and interest in PA promotion programs for this group,[18] there are very few controlled studies of PA interventions for adolescent and young adult (AYA) survivors.[10,16,19] The proposed work will evaluate the effectiveness of a highly-engaging technology-enhanced PA intervention program designed specifically for AYA survivors.

Adolescents and young adults (AYAs) are especially important to target. AYA survivors are recognized as a unique group that warrants further attention to treatment and survivorship issues as they transition from pediatric to adult health care settings.[20] There are many barriers to successful transition, and AYA survivors may be lost to follow-up or receive inadequate care if the transition is not successful,[21] reducing opportunities for counseling regarding the benefits of PA and other health promotion behaviors. A report from the Childhood Cancer Survivor Study (CCSS) indicated that adult survivors of childhood cancers are less likely to meet CDC

guidelines for PA and more likely to report an inactive lifestyle than siblings.[22] Because health behaviors adopted by AYAs are likely to be "carried over" into adulthood,[19,23] intervention during this time period is likely to improve PA trajectories into adulthood and reduce disparities between adult survivors and siblings. Further, intervening earlier may produce better outcomes, as AYAs are unlikely to have chronic de-conditioning like older adults and more likely to have plasticity of body tissues.[24]

Factors associated with physical activity in AYA survivors of childhood cancers. As pictured in Figure 1, treatments for childhood cancers, including radiation and various chemotherapies (e.g., anthracyclines, vincristine), can lead to adverse acute and long-term health effects, including deficits in fitness and health-related quality of life (HRQOL).[6,25] These adverse changes reduce AYAs' beliefs in their abilities to engage in physical activity (self-efficacy for PA) and may prompt reduced support for PA from parents and peers, leading to reductions in physical activity. Sedentary habits can exacerbate functional deficits and fatigue, becoming a self-perpetuating cycle.[24] Social Cognitive Theory (SCT)[26,27] proposes that behavior is reciprocally influenced by multiple personal/cognitive and environmental/social factors. Emphasis is placed on self-efficacy, or belief in one's capability to conduct the intended behavior (physical activity) and overcome perceived barriers to a behavior, and outcome expectancies, or beliefs that the behavior will have the desired effect (e.g., improve fitness). Social modeling, or learning through observation of others' experiences, and social support for the activity are also key components. For AYA survivors, self-efficacy and support for PA are critical components to target. Specifically, self-efficacy is positively associated with physical activity in young adult cancer survivors and healthy AYAs.[28-30] Greater family and peer support for PA have been associated with increased PA.[31-36] Peer support is particularly important for adolescents.[35,36] Certain demographic factors, including male gender and younger age, are also consistently correlated with PA.[22,30,32] The proposed intervention is guided by Social Cognitive Theory and will evaluate the role of self-efficacy and support for PA in AYA survivors of childhood cancers. What is learned will contribute to the broader understanding of health promotion for AYA survivors.

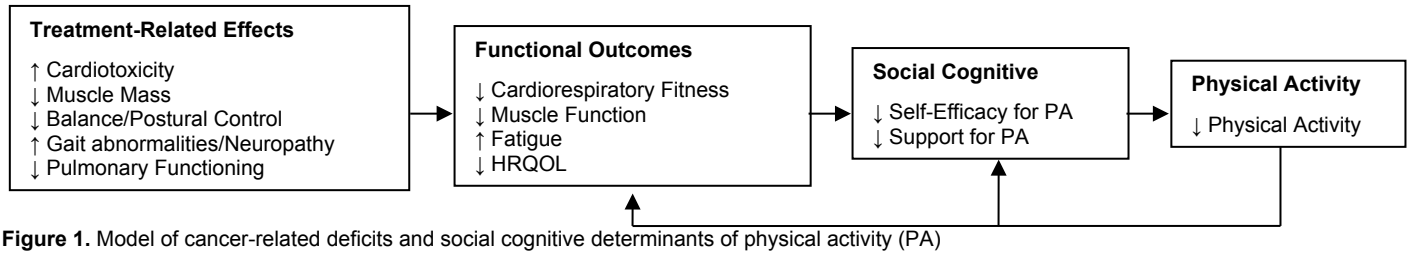

Figure 1. Model of cancer-related deficits and social cognitive determinants of physical activity (PA)

2.1 Supporting Data and Rationale. Guided by Social Cognitive Theory, we developed an 8-week group intervention with four primary components: (1) educational modules, (2) physical exercise, (3) goal-setting and self-monitoring, and (4) social support. Each session was detailed in a manual. This program incorporated the "FitBit," a small electronic accelerometer that uploads data wirelessly to a personalized account for monitoring PA. Because participants could modify their behavior based on viewing activity levels using FitBit, this technology was used as part of the intervention but not as an outcome measurement. Participants met weekly and provided social support in-person as well as through a private forum on the FitBit website.

Nine participants completed baseline and post-intervention measures (100% retention). On average, participants attended 6 out of 7 weekly exercise sessions (the 8th week was an

assessment only). There were no serious adverse events during the study. Our preliminary work demonstrated feasibility in enrolling participants, retaining participants, and completing the various assessment measures. There was evidence of improvement in time spent in physical activity, muscle strength, health-related quality of life, and fatigue that warrants further study. Participants reported high satisfaction with the program and FitBit. Despite increases in PA by actigraphy, we did not see large improvements in cardiovascular fitness (Mile Run/Walk). As a result, we will modify session structure to devote more attention to aerobic training. Further, participant feedback indicated interest in more fitness sessions (12 instead of 8), increased intensity of cardiovascular exercises, and additional structure to individualized exercise plans outside of session. These suggested refinements to the program are included in this proposed study.

Interest in mobile app development. Although participants reported that the FitBit website and group forum were easy to use, they reported logging in only "rarely" or "sometimes" because going to a computer to log in was a barrier. Participants are more likely to engage if access is immediate and available wherever they are. Hence, a primary goal of developing a mobile app is to increase engagement with study materials outside of the weekly sessions. In response to a survey, six out of 9 (67%) participants expressed "quite a bit" or "extreme" interest in trying an app to promote PA. Of the three who did not express high levels of interest, two indicated that they were uninterested because they do not currently own a smartphone, but expressed high interest if they were to be given a smartphone or iPod touch as part of the intervention. Of those who expressed an interest, participants indicated a high level of interest in functions like messaging/texting with a coach, tracking calories consumed and burned, goal setting, goal tracking, and messaging/texting with other survivors. Additional suggested features included a list of exercises for individual workouts, making steps and activities viewable by all group members for motivation and support, and awarding a weekly prize or badge for being the most active.

3. Participating Institutions

Project planning, recruitment, data collection, data management, and data analyses will take place at the Rutgers Cancer Institute of New Jersey. Because this is a K07 award, Dr. Devine has selected a team of mentors to provide training in their respective areas of expertise and facilitate the successful completion of the proposed project. ITX Corporation will program the app based on the requirements defined by the research team. They have completed necessary paperwork to partner with Rutgers Cancer Institute of New Jersey researchers on this project. Hackensack University Medical Center will participate as a site with IRB approval from the HackensackMeridian IRB.

4. Experimental Design and Methods

Overall Study Design: The primary goal of the proposed study is to develop and evaluate the feasibility and effectiveness of TLC FIT, a technology-enhanced intervention to promote physical activity in AYA childhood cancer survivors. Phase 1 includes development and usability testing of the smartphone application (Aim 1). Employing user-centered design methods,[37,38] we will work with AYA survivors ("end users") to design and refine prototype versions of the app. Technology consultants (contract to be determined) will create the app using theoretically-based features identified as desirable in our previous work. We will recruit a total of 20 AYA survivors to assist in the development and usability testing of the mobile app. This will be an iterative process such that AYAs will give ideas about desired features, assist in critiques of prototypes, and later test a working version of the product. Next, in Phase 2 we will conduct a pilot RCT (n = 88) of the 12-week TLC FIT (8 group meetings + electronic accelerometer + app) versus wait-list control (WLC) group (Aims 2-4). We will evaluate the feasibility of the fitness program, including recruitment, retention, and adherence to the intervention (Aim 2), and test the hypothesis that technology-enhanced intervention will increase AYAs' muscle strength and cardiorespiratory fitness (Aim 3). We will also explore the effects of the program on secondary outcomes of HRQOL, and fatigue (Aim 4). A randomized wait-list control design is particularly appropriate for this feasibility study, as all recruited individuals receive the intervention, allowing intervention adherence and program satisfaction data to be obtained from all study participants. Such a design can also increase the appeal of random assignment to study participants. The Phase 2 study design is presented in Figure 2.

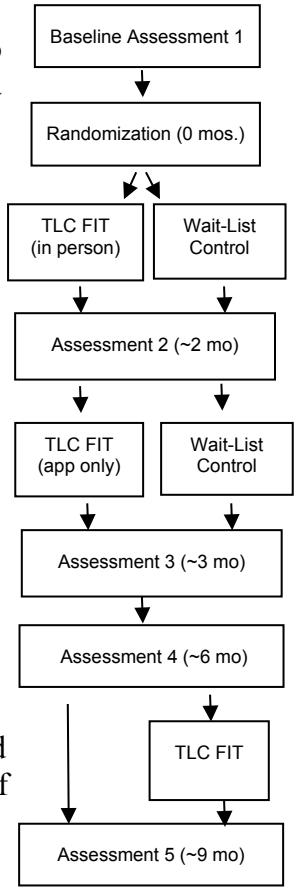

Figure 2. Phase 2 Study Schema

4.1 Procedures

Phase 1. Development of smartphone application
We gathered information about functionality requirements for the smartphone app in our preliminary work with AYA cancer survivors. We will recruit a total of 20 AYA survivors for this phase of the study. We will use individual or small group interviews conducted by the PI or a trained research assistant to gain additional input about desired features for the app. We will also get feedback on mock designs for the app. We will record these interviews and they will be transcribed for analysis by a member of the research team. The exact number of interviews conducted will depend on the data gathered; we will analyze the data as we go and we will stop interviewing when we reach saturation (i.e., no new themes emerge from the data).

Next, we will work with the technology consultants to develop a prototype based on AYA preferences. The exact content of the app will be determined in the development phase but it will reflect the content of the original TLC FIT program (based on Social Cognitive Theory)

and include tailored cancer-specific fitness information (e.g., potential effects of radiation/chemotherapy and issues to consider when exercising based on up-to-date COG guidelines). Users will create a private login. Data from an electronic accelerometer will be directly imported into the app and used to unlock achievement awards. Individuals will set personal goals, monitored in real-time. Instruction videos of the trainer demonstrating exercises will allow for instruction 24/7. A qualified trainer with experience working with adolescents and young adults will be used for this study. Engagement with the app will unlock achievements and there will be optional social support messaging between individuals in the study. The PI and/or trainer will initiate challenges and prompt participants to continue working on goals between sessions. All user data will be continuously stored in an encrypted and cached environment on the device itself. When an internet connection is available, the device will securely transmit the data to our servers for downloading by researchers.

The app will be created using an iterative development process. Product development is broken into logical pieces, prioritized, and completed in iterations. Usability testing is conducted after each piece. Usability testing at this stage involves observation of participants completing defined tasks, time to complete tasks, errors in use, and subjective assessment of satisfaction, ease of learning the app, and memorability of the app.[38] This can be done in person or remotely via computer and phone. Usability tests are completed using a rapid iterative procedure, in which design changes are made after receipt of one set of participants' feedback (usually four participants) and then tested with the next set of participants. The app is refined to eliminate issues that impede usability. The final usability tests would include a field trial of using the app for up to one week and providing feedback regarding use in daily life. Having a smartphone is not required to participate; we will loan iPod touches to anyone who does not have a personal smartphone for the duration of the study. We have planned for 12-18 months for total development time. We expect it will take 3-6 months to design and refine the health and cancer-specific content for the app, 3-4 months to design the app, and 3 months to conduct usability testing with the app. Our goal is to minimize frustration with technology. Individual participation may include a one-time interview or usability test (approximately 1-2 hours) or a field trial of using the app for up to a week.

Phase 2: Pilot RCT

Recruitment will occur in waves, such that 10-20 participants will be randomized within cohorts, and each arm will have 5-10 patients at a time. After obtaining informed consent/assent, participants will complete baseline assessments (Time 1) conducted either in group formats or individually as done in our preliminary study. The assessments will be conducted by trained research personnel. Participants will then be randomized to either TLC FIT (8 group sessions + electronic accelerometer + App) or wait-list control (WLC). Randomization will be stratified by cohort (since enrolled in waves) and age (13-17 vs. 18-25). All participants will be asked to complete assessments at Time 2 (~2 months, after the in-person sessions are completed for the TLC FIT group), Time 3 (~3 months; after the full in-person plus app intervention for TLC FIT group), Time 4 (,~6 months), and Time 5 (~9 months; after the waitlist control participants receive the intervention). Waitlist control participants will also be asked to complete the objective fitness tests during the last session of the in-person groups; they will be given feedback on their results but no additional monetary compensation for these tests. Assessments and the group fitness program will be conducted in at the Center for Health and Human Performance (directed by Co-Investigator Dr. Shawn

Arent) at the Institute for Food, Nutrition, and Health on Rutgers Cook Campus in New Brunswick. This is a facility equipped with appropriate equipment and space for group exercise. The trainer will be a qualified professional trainer or member of the Center for Health and Human Performance with appropriate experience and expertise who will be closely supervised by Dr. Arent and the PI.

TLC FIT (Technology-Enhanced Intervention): TLF FIT is composed of the group fitness program, use of an electronic accelerometer, private Facebook group and the mobile app. The group fitness program is manualized and will be led by a qualified trainer. The PI will teach the trainer the manualized program and treatment integrity will be evaluated during the program. The group program has four primary components: (1) cancer-specific and general educational modules, (2) physical exercise, (3) goal-setting and self-monitoring, and (4) social support. The original program consisted of eight weekly group sessions; however, participants expressed interest in adding exercise sessions, which would likely increase the impact on participants' fitness. Therefore, the program is now 8 weekly group sessions lasting 90 minutes each plus 4 weeks of using the app without in-person groups. In-person sessions will consist of approximately 20 minutes of education regarding fitness and administrative tasks, 10 minutes of goal-setting/monitoring, and 60 minutes of instructor-led exercise and cool-down (~30 minutes of aerobic exercise and 30 minutes of muscle strengthening and balance exercises). Exercises are age-appropriate and the intensity of participation is individualized – that is, any exercise can be modified to be more or less strenuous for each participant based on participants' ratings of perceived exertion as well as any physical limitations due to cancer treatment (such as hip problems). The trainer will have experience in assisting teens and young adults in modifying exercises to a level appropriate to their current fitness and physical abilities. Participants will wear a commercially available electronic accelerometer daily throughout the intervention to self-monitor progress. Data from the accelerometer will be electronically extracted into the app for easy monitoring and sharing of goals/progress. Social support for physical activity will be fostered through group interactions at each session and group messaging within the app and Facebook private groups. During the follow-up period, participants continue to use the app, set physical activity goals, and monitor progress. We will remotely download data regarding app use weekly throughout the intervention and follow-up.

4.2 Duration of Study

The K07 training grant is a 5-year grant. The app development and refinement (Phase 1) will occur in years 1-2 and the pilot RCT (Phase 2) will occur in years 3-5.

Phase 1: App Development. We have planned for a period of 12-18 months for development, usability testing, and refinement. Information will be gathered from childhood cancer survivors about desired features of the app via interview. During development, feedback about the quality of the program and design elements will be sought. Once a usable app is developed, individuals will be asked to field test the app for a brief period (e.g., a few days or a week, depending on needs identified during development) to evaluate usability in a real-world setting prior to beginning Phase 2.

Phase 2: Pilot RCT. Recruitment will occur in waves, such that cohorts of 10-20 participants will be randomized simultaneously, and each arm will have 5-10 patients at a

time. Following individual consent/assent and completion of a baseline assessment, individuals will be randomized either to the Technology-Enhanced Intervention (TLC FIT) arm or the Waitlist Control (WLC) arm (see Figure 2). Individual data collection will last approximately 9 months, with assessments conducted at approximately 2, 3, 6, and 9 months following randomization. Individuals randomized to the waitlist will receive the intervention after the 6-month assessment. Recruitment and data collection for Phase 2 are expected to span two to three years.

Overview of Study Duration

Study Year	**1→**				**2→**				**3→**				**4→**				**5→**			
Quarter	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
Phase 1: App Development																				
Training in App Development																				
IRB & study prep																				
App development/Refinement																				
Phase 2: Pilot RCT																				
IRB & study prep																				
Recruitment																				
Data Collection																				
Data Analysis																				
Manuscript Prep																				
Write/Submit Grant																				

5. Patient Selection Criteria

5.1 Inclusion Criteria

Phase 1: A patient is eligible for enrollment if all of the following criteria are met:

5.1.1 Any diagnosis of cancer prior to age 21
5.1.2 Current age 13-25
5.1.3 Off treatment
5.1.4 For patients < 18 years, parents must give informed consent and patient must give assent. Patients ≥ 18 must give informed consent.

Phase 2: A patient is eligible for enrollment if all of the following criteria are met:

5.1.5 Any diagnosis of cancer prior to age 21
5.1.6 Current age 13-25
5.1.7 Off treatment for at least 6 months
5.1.8 For patients < 18 years, parents must give informed consent and patient must give assent. Patients ≥ 18 must give informed consent.

5.2 Exclusion Criteria

Phase 1: A patient is not eligible for enrollment if any of the following criteria are met:

5.2.1 Non-English speaking
5.2.2 Significant developmental delay per patient, parent, or physician report
5.2.3 Pregnant (per patient report)

Phase 2: A patient is not eligible for enrollment if any of the following criteria are met:

5.2.4 Any medical contraindication to exercise according to a physician or physician's designee

5.2.5 Non-English speaking

5.2.6 Current physical activity level exceeding CDC guidelines for activity (60 min of moderate-vigorous exercise/day for 5+ days/wk including 3+ days of vigorous intensity activities and muscle-strengthening exercises on 3+ days/wk and bone-strengthening exercises on 3+ days/wk for children <18 and 150 min of moderate-vigorous exercise or 75 min of vigorous exercise/wk and 2+ days of muscle-strengthening activities for adults ≥ 18). The CDC guidelines are used to determine exercise prescription in our intervention; individuals already exceeding the guidelines would be unlikely to benefit from participating.

5.2.7 Significant developmental delay per patient, parent, or physician report

5.2.8 Pregnant (per patient report)
For Phase 2, if participant becomes pregnant during the course of the study, she will be removed from further participation

5.3 Inclusion of Women and Minorities

Males and females and members of all ethnic groups are eligible for this study. We expect the distribution of sex and race/ethnicity to reflect that of the Rutgers CINJ.

5.4 Participation of Children

This study includes children, as the primary goal is to evaluate an intervention specifically designed for adolescents and young adults ages 13-25. To protect children who are considered a vulnerable population, we will obtain both individual assent and parent consent for participation in the study for all children under the age of 18. We will also clearly explain and document that participation in the study in no way influences medical care. The PI and mentor, Dr. Manne, have significant experience and expertise in working with children of this age range and their families. Co-Investigator Arent has experience conducting exercise interventions with children.

5.5 Sources or Methods of Recruitment

Patients will be recruited through the Rutgers CINJ LITE (Long-term, Information, Treatment effects, and Evaluation) program, which provides long-term evaluation, support, and health education for childhood cancer survivors, through their routine office visit or mail. Patients will also be recruited through physician or staff referral in the Division of Pediatric Hematology/Oncology. Patients will also be recruited through flyers posted or available in relevant places (e.g., community support centers for teens and young adults with cancer). Flyers will be posted in the LITE clinic space and advertisements will be posted in the Rutgers CINJ LITE newsletter to recruit; these materials will be submitted and approved by the IRB prior to use. We will make information about the study available via webpage, www.cinj.org/fitsurvivor. We will also post advertisements with a link to the study webpage or IRB-approved flyer on social media sites, including Facebook and Twitter. The study team will also periodically (approximately 4-6 times per year) hold informational meetings for potentially eligible participants to learn about the program and ask questions. Study

information will be sent to the faculty and staff via Rutgers email lists or online news media, such as the Faculty & Staff Bulletin and Rutgers Today or Research News.

5.6 Study Enrollment Procedures

For Phase 1, potential participants may be recruited during their Rutgers CINJ LITE office visit. The PI or trained study staff will approach potentially eligible patients and families to provide a brief description of the study, answer any questions, and obtain informed consent/parental permission and assent (for children 13-17). Participants will be given as much time as needed to read the consent/assent materials and ask any questions. Dr. Masterson, the Director of the Rutgers CINJ LITE program and a Co-Investigator on this study, and Susan Stephens, LCSW, the primary social worker for the LITE program, will assist in recruiting by identifying potentially eligible patients from patient records. For those who are not due for a routine LITE visit, the study team will mail an invitation with an insert noting available interview dates and follow-up with a phone call to answer any questions and arrange for an in-person meeting to obtain consent/parental permission/assent and conduct the interview about desired features for the app. Phone calls can be made up to three times per week, with a maximum of one message per week, for up to three weeks. A recruitment flyer will be handed out or hung in clinic or sent via mail with the study invitation. For participants who contact the PI or research staff regarding participation via email or phone, research staff will respond in the same mode of contact. Participants will be paid $20 for each interview or usability session completed.

For Phase 2, we will use the existing LITE program mailing list to mail invitational letters to all LITE parents and/or patients ages 13-25 informing them of the study. The LITE program maintains a clinical contact list to send periodic newsletters and mailings to patients. This letter will be written from Dr. Masterson, the patient's physician and Medical Director of the LITE program who has routine contact with these patients, and the PI of the study, to invite potential participants to contact the research team to ask questions or enroll in the study as well as inform potential participants of in-person informational meetings to be held by the PI and study team at Rutgers CINJ. We will follow-up by phone to answer any questions and determine interest in participating. Phone calls can be made up to three times per week, with a maximum of one message per week, for up to three weeks. We will arrange for in-person meetings to obtain informed consent/assent; if it is not possible to schedule, we will mail consent/assent forms, discuss via phone, and have participants return completed forms via mail. Initial invitations will include a post card that the recipient may return to indicate that they are not interested in the study and we will remove them from the mailing list. Because we will recruit in cohorts, we will hold informational meetings about four to six times per year. These meetings are to provide information about the study, answer any questions, and obtain consent/parental permission/assent to individuals ready to enroll. All materials will be submitted to the IRB for approval prior to use. Informed consent/parental permission and assent (for children 13-17) will be obtained prior to any study procedure. Participants will be given as much time as needed to read the consent/assent materials and ask any questions. If any participant turns 18 during the study period, the participant will be re-consented using the appropriate approved consent form as soon as possible. Participants will be paid $20 for completion of each assessment, for a total of $100. Any participant who completes all

assessments will be entered into a raffle to win a fitness gift basket, including items such as water bottles, healthy snacks, and fitness equipment (valued at $150).

6. Study Parameters/Measures

Phase 1: App Development. We will interview participants individually or in small focus groups regarding desired content and functional features of the app. The PI or a trained research assistant will conduct interviews in person or via phone using a guide. Interviews will be recorded and transcribed by a member of the team for content analysis. Usability testing will involve assessment of satisfaction, ease of learning the app, and memorability of the app. Usability testing may be done in person or via telephone while the participant is interacting with the application online. At the time of accrual, a medical chart review will be conducted by trained study personnel to assess type of cancer, treatment history (surgery, chemotherapy, radiation therapy), time since treatment completion, and general demographic information (i.e., gender, age, race, and ethnicity).

Phase 2: Pilot RCT. All measures selected for this study have demonstrated adequate validity and reliability (see Table 1). With the exception of the demographic survey, all measures will be administered at baseline (Time 1), Time 3 (~3 months), Time 4 (~6 months), and Time 5 (~ 9 months). Only the muscular fitness tests, cardiorespiratory fitness test, body composition measures, accelerometry, and self-reported physical activity and sedentary behavior will be administered at Time 2 (~2 months). The *primary outcomes* are muscular fitness and cardiorespiratory fitness as measured by the 10-repetition max tests and submaximal treadmill testing (Aim 3). *Secondary outcomes* include health-related quality of life (HRQOL) and fatigue (Aim 4). We will also examine other constructs from Social Cognitive Theory, including exercise motivations, barriers to PA, body esteem, and psychological functioning. Finally, we will examine measures of physical activity (objectively measured via accelerometers or "actigraphs"), sleep, and anthropometric body measurements. Accelerometers have been extensively validated as measures of physical activity in children and adolescents.[39] Data regarding usage of the intervention app and electronic accelerometer will also be collected. Physical fitness measures are expected to take 40-45 minutes to complete plus the 7-days of actigraph wear during usual activities. Surveys are anticipated to take up to 45 minutes to complete. At the time of accrual, a medical chart review will be conducted by trained study personnel to assess cancer type, treatment history (surgery, chemotherapy, radiation therapy), time since treatment completion, and general demographic information (i.e., gender, age, race, and ethnicity).

Table 1. Measures

Construct	Measure	Description	Type	Time to Complete
Muscle Strength	10-Repetition Max Test (Upper & Lower Body)	*Primary Outcome;* Yields maximum resistance that can be lifted throughout the full range of motion using good form for 10 times for upper and lower body	O	15-20 min
Cardiorespiratory Fitness	Submaximal Treadmill Test[40,41]	Standardized graded treadmill test; yields estimated VO_2 max	O	20 min
Health-Related Quality of Life	PedsQL Generic Core[42,43]	Physical, Emotional, Social, and Cognitive domains	P	5 min
Fatigue	PedsQL Multidimensional Fatigue Scale.[44]	Fatigue	P	5 min

Physical Activity	Accelerometry (actigraph): 7-day activity	Objective measure of activity counts and time spent in sedentary, light, moderate, and vigorous activity	O	7-day wear
	FitBit Tracker physical activity data	Used as part of intervention, steps counts and time in various levels of activity will be collected weekly	O	---
	Modified International Physical Activity Questionnaire (IPAQ-SF)[45]	Self-reported physical activity within past 7 days	P	< 5 min
Sedentary Activity	Sedentary Habits Questionnaire	Sedentary habits within past 7 days	P	< 5 min
Body Composition	Height & Weight	Height & weight measurements	O	< 5 min
	Waist Circumference	Waist circumference	O	< 5 min
	BodPod[46] [Optional for participants who agree]	The Bod Pod is a gold standard in body composition measurement. It is an air displacement plethysmograph which uses whole-body densitomtry to determing body composition (fat and fat-free mass) in adults and children. This will be optional for participants who sign an additional consent for this test.	O	< 5 min
Barriers to PA	Barriers to Exercise Scale[47]	Barriers to PA	P	< 5 min
Exercise Motivation	Motivation for Exercise Item	Motivation for exercise	P	2 min
Psychological Symptoms	PROMIS Anxiety and PROMIS Depression measures[48] – Pediatric and Adult forms depending on age	Symptoms of depression and anxiety	P	5 min
Body Esteem	Child & Youth Self-Perception Inventory[49]	Body self-esteem and overall self-esteem	P	10 min
Sleep Quality	Pittsburgh Sleep Quality Index[50]	Sleep quality	P	5 min
Demographics	Information Survey	Age, gender, race/ethnicity, socioeconomic status	P	< 5 min
Intervention Feedback	Feedback Questionnaire	Given after intervention to assess satisfaction and ideas for improving intervention	P	5 min

Note. Type of Measure: O = Objective; P = Patient-reported. The BodPod body composition test will be optional for participants who agree to it; evaluating changes in body composition is exploratory and will provide pilot data for future studies.

Table 2. Assessment Schedule

Measure	**Time of Assessment**				
	Baseline (0 Mo.)	**Time 2 (~2 Mo)**	**Time 3 (~3-Mo)**	**Time 4 (~6-Mo)**	**Time 5 (~9-Mo)**
10-Repetition Max (Upper & Lower)	√	√	√	√	√
Submaximal Treadmill Test	√	√	√	√	√
Height, Weight, Waist Circumference	√	√	√	√	√
BodPod body composition [optional]	√		√		√
Actigraphy	√	√	√	√	√
Demographic/Medical Information	√				
Modified IPAQ-SF	√	√	√	√	√
Sedentary Habits	√	√	√	√	√
Barriers to Exercise Scale	√		√	√	√
Motivation for Exercise Item	√		√	√	√
PedsQL: Generic Core	√		√	√	√
PedsQL: Multidimensional Fatigue Scale	√		√	√	√
PROMIS Anxiety & PROMIS Depression	√		√	√	√
Child & Youth Self-Perception Inventory	√		√	√	√
Pittsburgh Sleep Quality Index	√		√	√	√

Feedback Questionnaire	√[a]	√[b]

Note. [a] For intervention group only; [b] For waitlist control group only. If individuals miss or need to reschedule assessments, they should be completed within 4 weeks of the scheduled time point.

7. Data Collection and Records to be Kept

7.1 Research Charts

Hard copies of data for each patient enrolled will be kept in a locked filing cabinet in the PI's locked office. Electronic files of interviews from Phase 1 will be downloaded from the recording device to a folder on the PI's secure departmental drive as soon as possible after the interview. It will then be erased from the recorder and only authorized study personnel will have access to the electronic files. Interviews will be transcribed as soon as possible and any identifying information will be removed in the written transcript. The electronic file will be destroyed at the end of study procedures (i.e., after transcription is complete and verified to be accurate by the PI). In Phase 2, patients will be registered for the trial using OnCore. All data (i.e., surveys, medical review sheet, fitness data) for each participant will be identified with an identification number rather than patient information and the key linking patient name and identification number will be kept locked in a separate file. Signed informed consent/permission and assent forms will also be kept in a locked cabinet separately from research files. Only authorized research personnel will have access to these files. We will also maintain an electronic database of potentially eligible patients we have contacted and track if any person returns a postcard asking to be removed from our contact list. This database will be stored on the PI's departmental drive and password protected. The key that links patient names and identification numbers will be destroyed after all procedures are complete and data is checked, by the close of the study.

7.2 Reports

Publications and annual reports for submission to the IRB will be written by the Cancer Institute of New Jersey PI using the data captured in the electronic database and the OnCore system.

8. Data and Safety Monitoring

The PI will convene a Data and Safety Monitoring Board (DSMB) composed of a behavioral scientist and a clinician to be named. The PI will conduct quarterly reviews of data and patient safety and send these reports to the DSMB for review. All unexpected and/or serious adverse events occurring during the active portion of the intervention or up to 30 days after the last fitness program session, will be reported to the Rutgers CINJ Office of Human Research Services and the IRB in accordance with IRB policy.

9. Statistical Considerations

9.1 Primary and Secondary Hypotheses and Endpoints

Aim 1: Develop and evaluate the usability of cancer-specific and motivational tools in the mobile app (Phase 1).

AYA survivors will help design the functionality requirements for the initial prototype. An experienced app development company will program the app with identified tools such as goal setting, self-monitoring, exercise instructions, and social networking. Usability testing will be conducted in an iterative manner with AYA survivors, refining the app based on user feedback (total $n = 20$).

Aim 2: Evaluate the feasibility of the technology-enhanced (electronic accelerometer + app + 8 weekly group sessions) fitness program in a pilot RCT (Phase 2).
Hypothesis 1: AYAs will agree to participate in the program, demonstrate engagement in the program via > 80% attendance at group-based sessions, and use one or more components of the app at least weekly.

Aim 3: Determine the effectiveness of the technology-enhanced fitness program on participants' cardiorespiratory fitness and muscular strength.
Hypothesis 2: Participants in the intervention group will demonstrate greater improvement in cardiorespiratory fitness (objective submaximal treadmill testing) and muscular strength (objective 10-repetition max testing) from baseline than wait-list control participants at the post-intervention assessment (Time 3).

Aim 4: Examine the effects of the program on secondary outcomes of health-related quality of life (HRQOL), and fatigue.
Hypothesis 3: Participants in the intervention group will demonstrate greater improvement in HRQOL (PedsQL Generic Core Scale) and fatigue (PedsQL Multidimensional Fatigue Scale) from baseline than the wait-list control group at the post-intervention assessment (Time 3).

9.2 Sample Size Justification

The focus of this work is to determine feasibility and estimate the effect size. Since this is a feasibility study, we intend to enroll 88 patients and expect 10% attrition, resulting in 80 patients with evaluable data. With a sample size of 40 per group and alpha set at .05, we calculate that we will have 80% power to detect a medium effect size (Cohen's $d = .32$) for differences between groups in muscular strength scores using ANCOVA. While we recognize that this study is underpowered for small effects, the primary aim is feasibility.

9.3 Methods for Masking, Randomization and Stratification

A randomization scheme will be determined prior to the start of recruitment in accordance with the Standard Operating Procedures of the Biometrics Division of the Rutgers Cancer Institute of New Jersey. Randomization will be stratified by cohort (due to recruitment in waves) and age (13-17 and 18-25). Randomization will occur after baseline measures are completed. Trained personnel who conduct the assessments will be masked to the assignment (intervention vs. WLC) of the participants.

9.4 Statistical Analysis

Preliminary data analysis will include descriptive statistics, assessment of reliability of surveys (Cronbach's alpha), and evaluation of distributions of each variable. If distributions are skewed or fail to meet assumptions for parametric analyses, transformations or non-parametric procedures will be used as appropriate. Strategies for handling missing data will

be chosen based on the type, nature, and extent of the problem, and could range from replacing a single item on a scale with the mean of the subscale, dropping a subscale/measure, or multiple imputation for the primary endpoint.

Aim 1: Participants will initially provide input for development based on individual interviews, which will be transcribed and analyzed to identify desirable components for inclusion in the app. For usability testing, participants are given a defined set of tasks to complete and observed to determine the ease with which participants can navigate tools and success in utilizing various aspects of the app (e.g., error rates, time to complete tasks). Participants will also provide qualitative and quantitative feedback regarding satisfaction with features, ease of use, and likeability of the app. Usability tests will be completed using a rapid iterative procedure, in which design changes are completed after receipt of a set of participants' feedback and then tested with the next set of participants. The app will be refined to eliminate issues that impede usability. A total n of 20 participants is anticipated to achieve saturation on issues identified during testing.

Aim 2: Feasibility will be evaluated using enrollment rates, assessment completion rates, attendance at weekly sessions, adherence to exercise prescription outside of sessions, and usage of the electronic accelerometer and app. The primary hypothesis is that AYAs will agree to participate in the intervention and demonstrate engagement via > 80% attendance at group-based sessions and use one or more components of the app at least weekly. Descriptive analyses (means, frequencies) will be used.

Aim 3: This aim is to determine the effectiveness of the program on the primary outcomes, objectively-measured cardiorespiratory fitness and muscular fitness. The primary hypothesis is that participants in the intervention group will demonstrate greater improvement in cardiorespiratory fitness (measured via the Submaximal Treadmill test) and muscular fitness (measured via the objective 10-repetition max tests) from baseline than wait-list control participants at the 3-month assessment (after the intervention group completes TLC FIT). To test this hypothesis, the two groups' outcome scores at the post assessment will be compared using ANCOVA, controlling for baseline scores. To account for enrollment in cohorts, cohort will be included as a covariate and removed if not significant. The primary analysis will be performed on an "intent-to-treat" basis; i.e., once a subject is randomized, data on that subject will be analyzed according to assignment, regardless of the degree to which the subject participates.

Aim 4: This aim will evaluate the effects of the program on the secondary outcomes of HRQOL and fatigue. We will test the hypothesis that participants in the intervention group will demonstrate greater improvement in HRQOL and fatigue from baseline than the wait-list control group at the 3-month assessment using ANCOVA.

9.5 Compliance and Missing Data

Based on preliminary work and other similar published interventions, 10% dropout is expected and the sample size was calculated to account for this rate. Phone, email, and/or text message reminders regarding assessments will be used to minimize dropout rate. Compliance with the intervention program will be evaluated by examining attendance at sessions and utilization of the app. All subjects will be asked to complete assessment regardless of their attendance at weekly sessions.

10. Human Subjects

10.1 Subject Population

Phase 1 participants will be 20 AYA survivors of childhood cancer and Phase 2 participants will be 88 AYA survivors of childhood cancer. Inclusion criteria for Phase 1: (1) any diagnosis of cancer prior to age 21; (2) current age 13 to 25; (3) off-treatment. Exclusion criteria for Phase 1 are: (1) non-English speaking; (2) significant developmental delay per patient, parent, or physician report; and (3) pregnant per patient report. Inclusion criteria for Phase 2: (1) any diagnosis of cancer prior to age 21; (2) current age 13 to 25; (3) off-treatment for at least 6 months. Exclusion criteria for Phase 2 are: (1) medical contraindication to exercise according to physician or physician's designee (form to be completed by patient's primary physician, oncologist, or physician's designee); (2) non-English speaking; (3) current activity level exceeding CDC guidelines for activity (60 min of moderate-vigorous exercise/day for 5+ days/wk including 3+ days of vigorous-intensity activities and 3+ days of muscle-strengthing activities and 3+ days of bone-strengthening activities for children <18 and 150 min of moderate-vigorous exercise or 75 min of vigorous exercise/wk and 2+ days of muscle-strengthening activities for adults ≥ 18); (4) significant developmental delay per patient, parent, or physician report; and (5) pregnant per patient report. The CDC guidelines are used to determine exercise prescription in our intervention; individuals already exceeding the guidelines would be unlikely to benefit from participating. The Rutgers CINJ LITE program maintains a contact list of approximately 300 CCS, who receive regular newsletters and other mailings. Nearly half of the patients in the LITE program were seen at CINJ for follow-up care in 2010 and 2011. The approximate age distribution of LITE participants is: 0-8 years old = 6%; 9-12 years = 17%; 13-17 years = 29%, and aged 18 or older = 50%. This suggests that approximately 79% of LITE patients or 237 patients will be eligible for screening. With a conservative enrollment rate of 30% (we had 39% in our preliminary work using one source of survivors; other similar studies have reported enrollment rates from 27-85%[51-54]), we could enroll about 71 patients per year, reaching our accrual goal of 88 in 18 months.

10.2 Potential Risks

Potential risks are considered minimal. In Phase 1, the risks are the same as encountered in daily life. The interviews will focus on app design and development and individuals' perceptions of its usefulness in daily life. In Phase 2, increased physical activity may result in muscle soreness or injury; however, each participant will be required to have their physician, oncologist, or physician's designee complete a form prior to enrollment clearing the participant for engagement in a physical activity program. Physical fitness testing will be done by trained personnel. Dr. Arent, a mentor and Co-Investigator on this project, is a certified strength and conditioning specialist and will provide expert guidance to Dr. Devine for hiring and training qualified personnel. It should be noted that the fitness tests utilize standard exercise testing protocols. To protect the participants against risks of injury, the trainer will have adequate experience and training in working with AYAs, with a preference for certification in working with cancer survivors. All exercises will be age-appropriate and the intensity can be modified according to individual comfort. Further, the trainer will have each participants' emergency contact information with them during all sessions in the event that an injury occurs. Adolescents and young adults may feel uncomfortable answering

questions regarding physical or emotional functioning, and will be free not to answer any question. Participants are permitted to refuse to participate in any aspect of the research, and may withdraw from the study at any time for any reason. To minimize risk of breach of confidentiality when using the app, data will be stored in an encrypted and cached environment on the device itself and securely transmitted to our servers for downloading by researchers. All data storage and transmission will be encrypted and logged for audit-ability to meet the applicable HIPAA standards. Questionnaire data will be coded with an ID number and stored in locked filing cabinets that are only accessible to appropriate research personnel. The key linking ID number and personal identification will be kept separately from research files. The mHealth app and private Facebook group will be kept private only to individuals in the study. Messaging between participants will be monitored by the PI and trainer, who will remove any negative or questionable comments as soon as discovered (i.e., if a participant sends a message teasing another participant or using a curse word, it will be removed as soon as discovered). Confidentiality will be further maintained by reporting only group data in study publications and presentations.

10.3 Consent Procedures

Patients and parents will be informed of the study by the study team via letter, flyers, in person at clinic, or telephone. The PI or a trained member of the study team will explain the study to the potential subject and answer all questions. We will obtain informed assent from patients ages 13-17 and consent from their parents; we will obtain informed consent from patients ages 18-25. Participants will be given a signed copy of consent/assent documents, along with the phone numbers of the investigators to call if they have questions.

10.4 Potential Benefits

There are no direct benefits for participating in Phase 1, design of the mobile app. Although not guaranteed, the potential benefits of participating in Phase 2, the randomized trial of the technology-enhanced intervention, include improved cardiorespiratory fitness, muscular fitness, health-related quality of life, and fatigue. All participants, including those in the waitlist control, will have the opportunity to participate in the exercise program for free. This study has the potential to yield important information regarding health promotion behaviors for AYA survivors of pediatric cancers, an important but understudied population.

10.5 Risk-Benefit Ratio

The minimal risk involved in this study is reasonable in relation to the anticipated benefits of the research. Alternatives to participating are not participating; choosing not to participate does not affect patients' medical care. Results of the proposed research will inform the feasibility and preliminary effectiveness of a technology-enhanced fitness intervention to improve physical fitness in AYA survivors of pediatric cancers. Information on the incorporation of a mHealth application is particularly novel and will guide our understanding of the application of mHealth technology to this area of research. Data from this study will be used to generate a sample size estimate and refine research procedures for a future R01 application that will evaluate the efficacy of a technology-enhanced fitness intervention for AYA cancer survivors. The benefit of improved health outcomes outweighs the minimal risks associated with participation. This approach may also inform interventions to improve motivation for other healthy behaviors in this population.

10.6 Gender and Minorities

There are no exclusion criteria based on gender or minority status. We expect to enroll participants of both genders and minority status.

11. Economic/Financial Considerations

This study will be financed through a pending grant from the National Cancer Institute. Dr. Devine will use some of her start-up funds to pay for costs not covered through the K07 grant.

12. Publication of Research Findings

The policies and procedures of the Rutgers University legal department (see: Investigator's Handbook) will govern publication of the trial. It is expected that the results of this trial will be submitted for publication in a timely manner following the conclusion. The Cancer Institute of New Jersey PI, and all co-authors prior to submission or use, must review any abstract or manuscript.

References

1. Altekruse S, Kosary C, Krapcho M, et al. SEER Cancer Statistics Review, 1975-2007, National Cancer Institute. Bethesda, MD.
2. Howlader N, Noone A, Krapcho M, et al. SEER cancer statistics review, 1975-2008. *Bethesda, MD: National Cancer Institute.* 2011.
3. Blaauwbroek R, Groenier K, Kamps W, Meyboom-de Jong B, Postma A. Late effects in adult survivors of childhood cancer: the need for life-long follow-up. *Annals of oncology.* 2007;18:1898-1902.
4. Oeffinger K, Mertens A, Sklar C, et al. Chronic health conditions in adult survivors of childhood cancer. *New England Journal of Medicine.* 2006;355(15):1572-1582.
5. Lipshultz SE, Colan SD. Cardiovascular trials in long-term survivors of childhood cancer. *Journal of Clinical Oncology.* 2004;22(5):769-773.
6. Florin TA, Fryer GE, Miyoshi T, et al. Physical inactivity in adult survivors of childhood acute lymphoblastic leukemia: a report from the childhood cancer survivor study. *Cancer Epidemiol Biomarkers Prev.* Jul 2007;16(7):1356-1363.
7. Oeffinger KC, Buchanan GR, Eshelman DA, et al. Cardiovascular risk factors in young adult survivors of childhood acute lymphoblastic leukemia. *J Pediatr Hematol Oncol.* Oct 2001;23(7):424-430.
8. Reilly J, Brougham M, Montgomery C, Richardson F, Kelly A, Gibson B. Effect of glucocorticoid therapy on energy intake in children treated for acute lymphoblastic leukemia. *Journal of Clinical Endocrinology & Metabolism.* 2001;86(8):3742-3745.
9. Oeffinger K, Mertens A, Sklar C, et al. Obesity in adult survivors of childhood acute lymphoblastic leukemia: a report from the Childhood Cancer Survivor Study. *Journal of Clinical Oncology.* 2003;21(7):1359-1365.
10. Winter C, Muller C, Hoffmann C, Boos J, Rosenbaum D. Physical activity and childhood cancer. *Pediatr Blood Cancer.* Apr 2010;54(4):501-510.
11. Leon AS, Connett J, Jacobs DR, Rauramaa R. Leisure-time physical activity levels and risk of coronary heart disease and death. *JAMA: the journal of the American Medical Association.* 1987;258(17):2388.
12. Sattelmair J, Pertman J, Ding EL, Kohl HW, Haskell W, Lee I-M. Dose Response Between Physical Activity and Risk of Coronary Heart Disease / Clinical Perspective. *Circulation.* August 16, 2011 2011;124(7):789-795.
13. Health UDo, Services H. 2008 physical activity guidelines for Americans. *Be active, healthy, and happy.* 2008. http://www.health.gov/paguidelines. Accessed February 26, 2012.
14. Paxton RJ, Jones LW, Rosoff PM, Bonner M, Ater JL, Demark-Wahnefried W. Associations between leisure-time physical activity and health-related quality of life among adolescent and adult survivors of childhood cancers. *Psychooncology.* Sep 2010;19(9):997-1003.
15. Courneya KS, Friedenreich CM. Physical exercise and quality of life following cancer diagnosis: a literature review. *Annals of Behavioral Medicine.* 1999;21(2):171-179.
16. Keats MR, Culos-Reed SN. A community-based physical activity program for adolescents with cancer (project trek): Program feasibility and preliminary findings. *Journal of Pediatric Hematology/Oncology.* 2008;30(4):272-280.

17. Stolley MR, Restrepo J, Sharp LK. Diet and physical activity in childhood cancer survivors: a review of the literature. *Ann Behav Med.* Jun 2010;39(3):232-249.
18. Rabin C, Simpson N, Morrow K, Pinto B. Behavioral and psychosocial program needs of young adult cancer survivors. *Qual Health Res.* Jun 2011;21(6):796-806.
19. San Juan AF, Wolin K, Lucía A. Physical activity and pediatric cancer survivorship. Recent Results Cancer Res. *Physical Activity and Cancer.* 2011:319-347.
20. Zebrack B, Mathews-Bradshaw B, Siegel S. Quality cancer care for adolescents and young adults: a position statement. *J Clin Oncol.* Nov 10 2010;28(32):4862-4867.
21. Henderson TO, Friedman DL, Meadows AT. Childhood cancer survivors: transition to adult-focused risk-based care. *Pediatrics.* 2010;126(1):129-136.
22. Ness KK, Leisenring WM, Huang S, et al. Predictors of inactive lifestyle among adult survivors of childhood cancer: a report from the Childhood Cancer Survivor Study. *Cancer.* May 1 2009;115(9):1984-1994.
23. Hallal PC, Victora CG, Azevedo MR, Wells JCK. Adolescent physical activity and health: a systematic review. *Sports Medicine.* 2006;36(12):1019-1030.
24. Lucía A, Earnest C, Pérez M. Cancer-related fatigue: can exercise physiology assist oncologists? *The Lancet Oncology.* 2003;4(10):616.
25. Van Brussel M, Takken T, Lucia A, Van der Net J, Helders P. Is physical fitness decreased in survivors of childhood leukemia? A systematic review. *Leukemia.* 2004;19(1):13-17.
26. Bandura A. Self-efficacy: toward a unifying theory of behavioral change. *Psychological review.* 1977;84(2):191.
27. Bandura A. *Self-efficacy: The exercise of control.*: W. H. Freemann and Company; 1997.
28. Rovniak LS, Anderson ES, Winett RA, Stephens RS. Social cognitive determinants of physical activity in young adults: A prospective structural equation analysis. *Annals of Behavioral Medicine.* 2002;24(2):149-156.
29. Motl RW, Dishman RK, Saunders RP, et al. Examining social-cognitive determinants of intention and physical activity among Black and White adolescent girls using structural equation modeling. *Health Psychology.* 2002;21(5):459.
30. Finnegan L, Wilkie DJ, Wilbur J, Campbell RT, Zong S, Katula S. Correlates of physical activity in young adult survivors of childhood cancers. *Oncol Nurs Forum.* Sep 2007;34(5):E60-69.
31. Dishman RK, Dunn AL, Sallis JF, Vandenberg RJ, Pratt CA. Social-cognitive correlates of physical activity in a multi-ethnic cohort of middle-school girls: two-year prospective study. *Journal of Pediatric Psychology.* 2010;35(2):188-198.
32. Sallis JF, Prochaska JJ, Taylor WC. A review of correlates of physical activity of children and adolescents. *Medicine & Science in Sports & Exercise.* 2000;32(5):963-975.
33. Anderssen N, Wold B. Parental and peer influences on leisure-time physical activity in young adolescents. *Research quarterly for exercise and sport.* 1992;63(4):341.
34. Trost SG, Sallis JF, Pate RR, Freedson PS, Taylor WC, Dowda M. Evaluating a model of parental influence on youth physical activity. *American journal of preventive medicine.* 2003;25(4):277-282.
35. Gilliam MB, Madan-Swain A, Whelan K, Tucker DC, Demark-Wahnefried W, Schwebel DC. Social, demographic, and medical influences on physical activity in child and adolescent cancer survivors. *Journal of Pediatric Psychology.* 2012;37:198-208.

36. Heitzler CD, Lytle LA, Erickson DJ, Barr-Anderson D, Sirard JR, Story M. Evaluating a model of youth physical activity. *American journal of health behavior.* 2010;34(5):593-606.
37. Wolpin S, Stewart M. A Deliberate and Rigorous Approach to Development of Patient-Centered Technologies. *Semin Oncol Nurs.* 2011;27:183-191.
38. Zhang D, Adipat B. Challenges, methodologies, and issues in the usability testing of mobile applications. *International Journal of Human-Computer Interaction.* 2005;18(3):293-308.
39. Sirard JR, Pate RR. Physical activity assessment in children and adolescents. *Sports Medicine.* 2001;31(6):439-454.
40. Bruce RA, Kusumi F, Hosmer D. Maximal oxygen intake and nomographic assessment of functional aerobic impairment in cardiovascular disease. *American heart journal.* 1973;85(4):546-562.
41. Gumming GR, Everatt D, Hastman L. Bruce treadmill test in children: normal values in a clinic population. *The American journal of cardiology.* 1978;41(1):69-75.
42. Varni JW, Limbers CA. The PedsQL™ 4.0 Generic Core Scales Young Adult Version. *Journal of health psychology.* 2009;14(4):611.
43. Varni JW, Seid M, Kurtin PS. PedsQL (TM) 4.0: Reliability and validity of the Pediatric Quality of Life Inventory (TM) version 4.0 Generic Core Scales in healthy and patient populations. *Medical care.* 2001;39(8):800.
44. Varni JW, Burwinkle TM, Katz ER, Meeske K, Dickinson P. The PedsQL™ in pediatric cancer. *Cancer.* 2002;94(7):2090-2106.
45. Booth ML, Ainsworth BE, Pratt M, et al. International physical activity questionnaire: 12-country reliability and validity. *Med sci sports Exerc.* 2003;195(9131/03):3508-1381.
46. Fields DA, Goran MI, McCrory MA. Body-composition assessment via air-displacement plethysmography in adults and children: a review. *The American Journal of Clinical Nutrition.* March 1, 2002 2002;75(3):453-467.
47. Arroyave WD, Clipp EC, Miller PE, et al. Childhood cancer survivors' perceived barriers to improving exercise and dietary behaviors. *Oncol Nurs Forum.* 2008;35:121-130.
48. Pilkonis PA, Choi SW, Reise SP, Stover AM, Riley WT, Cella D. Item banks for measuring emotional distress from the Patient-Reported Outcomes Measurement Information System (PROMIS®): depression, anxiety, and anger. *Assessment.* 2011;18(3):263-283.
49. Eklund RC, Whitehead JR, Welk GJ. Validity of the children and youth physical self-perception profile: A confirmatory factor analysis. *Research Quarterly for Exercise and Sport.* 1997;68(3):249-256.
50. Buysse DJ, Reynolds CF, Monk TH, Berman SR, Kupfer DJ. The Pittsburgh Sleep Quality Index: a new instrument for psychiatric practice and research. *Psychiatry research.* 1989;28(2):193-213.
51. Marchese VG, Chiarello LA, Lange BJ. Effects of physical therapy intervention for children with acute lymphoblastic leukemia. *Pediatric Blood & Cancer.* 2004;42(2):127-133.
52. Jarvela LS, Niinikoski H, Lahteenmaki PM, et al. Physical activity and fitness in adolescent and young adult long-term survivors of childhood acute lymphoblastic leukaemia. *J Cancer Surviv.* Dec 2010;4(4):339-345.

53. Takken T, van der Torre P, Zwerink M, et al. Development, feasibility and efficacy of a community based exercise training program in pediatric cancer survivors. *Psycho Oncology.* 2009;18(4):440-448.
54. Tan SY, Poh BK, Chong HX, et al. Physical activity of pediatric patients with acute leukemia undergoing induction or consolidation chemotherapy. *Leukemia research.* 2012.