Study Protocol Cover Page for ClinicalTrials.gov Record

Official Study Title:

Improving Symptom Management for Survivors of Young Adult Cancer

Brief Title:

Symptom Management for YA Cancer Survivors

NCT #: NCT04035447

Duke University Health System (DUHS) Protocol #: Pro00103249

Document Version Date: 30-APR-2025

Document Name: Study Protocol (including Statistical Analysis Plan)

DUHS IRB Application (Version 1.38)

General Information

***Please enter the full title of your protocol:**

Improving Symptom Management for Survivors of Young Adult Cancer

***Please enter the Short Title you would like to use to reference the study:**

Symptom Management for YA cancer survivors
* This field allows you to enter an abbreviated version of the Study Title to quickly identify this study.

Add Study Organization(s):

List Study Organizations associated with this protocol:

Primary Dept?	Department Name
◯	**DUHS** - Behavioral Medicine

Assign key study personnel (KSP) access to the protocol

*** Please add a Principal Investigator for the study:**

(Note: Before this study application can be submitted, the PI MUST have completed CITI training)

Dorfman, Caroline

3.1 If applicable, please select the Key Study personnel: (Note: Before this study application can be submitted, all Key Personnel MUST have completed CITI training)
*** Denotes roles that are not recognized in OnCore. Please select an appropriate role that is recognized in all clinical research applications (iRIS, OnCore, eREG, etc.)**

A) Additional Investigators, Primary Study Coordinator (CRC), and the Primary Regulatory Coordinator (PRC):

B) All Other Key Personnel

Arrato, Nicole
Collaborator
Berchuck, Samuel
Collaborator
Diachina, Allison
Collaborator
Divakaran, Smrithi

Clinical Research Specialist/Study Assistant
Erkanli, Alaattin
Statistician
Falkovic, Margaret Barry
Other
Fish, Laura
Other
Keefe, Francis
Collaborator (Duplicate)*
Lachman, Sage
Collaborator
Makarushka, Christina
Other
Neish, Drew
Statistician
Oeffinger, Kevin
Collaborator
Parnell, Heather
Other
Rogers, Maggie
Data Manager
Shelby, Rebecca
Collaborator (Duplicate)*
Somers, Tamara
Collaborator
Stalls, Juliann
Collaborator (Duplicate)*
Thomas, Samantha
Statistician
Weinfurt, Kevin Phil
Collaborator (Duplicate)*
Willis, Michael
Regulatory Coordinator
Willis, Michael
Study Coordinator (CRC/CRNC/RPL)
Youssef, Daniel
Clinical Research Specialist/Study Assistant

***Please add a Study Contact:**

Dorfman, Caroline

The Study Contact(s) will receive all important system notifications along with the Principal Investigator. (e.g., The study contact(s) are typically the Principal Investigator, Study Coordinator, and Regulatory Coordinator.)

Oncore

Please select the Library for your Protocol:

This field is used in OnCore and determines the Reference Lists, Forms, Protocol Annotations, Notifications, and Signoffs available for the protocol. Protocols that require reporting to the NCI (National Cancer Institute), must select the Oncology library.

- (•) Oncology
- ( ) Non-Oncology

Protocol Application Type

Select the type of protocol you are creating:

Please see additional criteria and information in the policy titled, "Reliance on the IRB of Another Institution, Organization, or an Independent IRB", on the **IRB web site**.

- (●) Regular Study Application - Most common. The IRB will determine if the study is eligible for expedited review or requires full board review upon submission.
- ( ) Application for Exemption from IRB Review - Includes Exempt, Not Human Subject Research, & Not Research.
- ( ) External IRB Application - Any study using an external IRB as the IRB-of-Record.
- ( ) Trainee Research While Away from Duke - Research conducted by medical students overseen by the Office of Curriculum & other student/trainee research away from Duke.
- ( ) Individual Patient Expanded Access, Including Emergency Use - Use of an investigational product under expanded access, including emergency use of an investigational drug or biologic or emergency use of an unapproved device.

Conflict of Interest

Are any key personnel an inventor of any of the drugs, devices or technologies used in this research?

( ) Yes (●) No

Do any key personnel have a conflict of interest management plan issued by DOSI-COI related to this research?

( ) Yes (●) No

Oversight Organization Selection

CRU (Clinical Research Unit) or Oversight Organization Selection:

Please select the CRU.

Psychiatry

The Clinical Research Unit that takes responsibility for this study.

- Please select **Medicine** as the CRU **only** if the PI is in one of these Divisions or Institutes: Endocrinology, Gastroenterology, General Internal Medicine, Geriatrics, Hematology, Infectious Diseases, Nephrology, Pulmonary, Rheumatology & Immunology, Center for Applied Genomics and Precision Medicine, Center for the Study of Aging and Human Development, Duke Molecular Physiology Institute.
- More information on CRUs can be found on the Duke Office of Clinical Research (DOCR) website, **http://docr.som.duke.edu**
- Questions concerning CRU selection should be directed to docr.help@dm.duke.edu.
- For questions about the Campus Oversight Organization, please visit **Campus Oversight Organization**.

List all Key Personnel on the study who are outside Duke:

- In the panel below, "PHI" is Protected Health Information.
- Note: If outside key personnel will have access to Duke PHI, you will need the following:

- Attach the documentation of Human Subjects Certification for each individual, if they have completed the certification somewhere other than Duke.
- A data transfer agreement AND external site IRB approval (or IRB authorization agreement). See HRPP policy **Use of Research Data by Former Duke Students or Former Duke Faculty and Employees**

Entry 1

Name	
Study Role	
Email Address	
Institution / Organization	
Will he/she have access to Duke P.H.I.?	○ Yes ○ No
Is he/she an unpaid volunteer at Duke on the study?	○ Yes ○ No

Describe Role of External Personnel:

N/A

Indicate the Protocol source below:

The protocol source is the author of the protocol. If the protocol is a joint authorship between multiple sources, select the primary author.

An IRB fee may be assessed for all research that is supported by for-profit entities and requires full board review. For additional information, see the **IRB fees section of the IRB web site**.

- ◉ Duke PI initiated
- ○ Commercial / Industry (for-profit entity) initiated
- ○ Federal Government initiated
- ○ Cooperative Group Initiated
- ○ Foundation (non-profit group) initiated
- ○ Other

Sponsor and Funding Source

Add all funding sources for this study: (Select 'Duke University' if you do not have funding or a sponsor for your study).

View Details	Sponsor Name	Sponsor Type	Contract Type:	Project Number	Award Number
⊟	National Institutes of Health (NIH)	Externally Peer-Reviewed	Grant		

Sponsor Name:	National Institutes of Health (NIH)
Sponsor Type:	Externally Peer-Reviewed
Sponsor Role:	Funding
Grant/Contract Number:	GRANT12789558
Project Period:	From: to:
Is Institution the Primary Grant	

Holder:	Yes
Contract Type:	Grant
Project Number:	
Award Number:	
Grant Title:	
PI Name: (If PI is not the same as identified on the study.)	
Explain Any Significant Discrepancy:	

Is this a federally funded study?

(•) Yes ( ) No

Does this study have any of the following?

- Industry sponsored protocol
- Industry funded Duke protocol
- Industry funded sub-contract from another institution
- Industry provided drug/device/biologic
- SBIR/STTR funded protocol

( ) Yes (•) No

As part of this study, will any samples or PHI be transferred to/from Duke to/from anyone other than the Sponsor, a Sponsor subcontractor, or a Funding Source?

( ) Yes (•) No

Is the Department of Defense (DOD) a funding source?

( ) Yes (•) No

For Federally funded studies:

Is your funding subject to, and does it comply with, the funding agency's policy for data sharing?

(•) Yes ( ) No

Check all that apply:

- [ ] NIH Genome Sharing - dbGaP
- [ ] NIH Genome Sharing - GWAS
- [ ] NIH Genome Sharing - NCI databases
- [ ] NIH Genome Sharing - other
- [ ] Non-NIH Genomic
- [x] General Data Sharing

Enter the Grant Number or Other Federal Agency Proposal or Application Number:

K08 CA245107-01; GRANT12789558

Note: The Federal Funding Agency ID Number is the Sponsor's grant number assigned to your project and available on your Notice of Award (example: R01HL012345).

If known, enter the SPS (Sponsored Projects System) number if applicable:

247086

In the Initial Submission Packet, attach the following:
(1) The entire grant, or an explanation of why a grant is not needed.
(2) NIH institutional Certificate form related to data sharing (if applicable).

Mobile Devices and Software

Does this study involve the use of a software or a mobile application?

(•) Yes ( ) No

Please describe the following:

- The developer of the mobile app and how the app will be obtained.
- What PHI will be collected via the app.
- Where the data will be stored and who will have access to it.

Intervention Mobile App Development. The study team responsible for mobile app development has worked together for several years and completed application development. The app includes: 1) audio and video files and brief textbased
educational content reviewing strategies; 2) the ability to self-monitor symptom (pain, fatigue, distress) severity; 3) the ability to connect with group members via a social networking platform. This platform will be monitored and moderated by the study team; and 4) activity tracking synchronization, which allows participants to monitor their activity in the application and provides study staff with real-time data. We have used feedback from the focus groups and user testing to make revisions to the mobile app as indicated.

Pattern Health (Durham, NC) is a digital health company specializing in patient-centered web and mobile products for clinical and medical research and apps for health data tracking and analysis; they also have expertise in working with wireless devices. Pattern Health has an established relationship with researchers at Duke and are contracted for the development of a mobile app for use in the current study. The investigators worked with expert technicians at Pattern Health to design and develop the study app.

App data is stored in a MySQL database. This is a standard security feature, which allows the database to be kept separate from the web server to protect access to the database. In addition, the hard drive of the database machine is encrypted, which will provide security in case the hard drive is physically compromised.

Garmin vvofit 4 (activity tracker) will be worn by participants and data will be shared via the Pattern Health Mobile Application.

Only key study personnel will have access to mobile app data (e.g., PI, mentors, CRC, data manager, etc.).

Zoom will be used to deliver the user testing sessions, study intervention, and exit interviews.

List all software, including third party (non-Duke) and mobile apps, that will be utilized for ascertainment,

recruitment, or conduct of the research/project: (eg, MaestroCare, DEDUCE):

Software: MaestroCare, Deduce, RedCap, Microsoft Office programs (e.g., word, excel), SPSS, SAS, R, NVivo, Twilio

Are you using FCAP (Federated Clinical Analytics Platform) for this study?

○ Yes ◉ No

Multi-site Research

Is this a multi-site study?

○ Yes ◉ No

Complete for each site if Duke is the Primary grant awardee or coordinating center:

Entry 1

Site Name:	
City:	
State/Province:	
Country:	
	Site Contact Information
Primary Contact Name:	
Primary Contact Phone:	
Primary Contact Email:	
	Site Details
Does the site have an IRB?	○ Yes ○ No
Site IRB approval expiration date:	
If date not provided, explanation of why:	
Has the site granted permission for the research to be conducted?	○ Yes ○ No
Does the site plan to rely on the DUHS IRB for review?	○ Yes ○ No
What is the status of the study at this site?	○ Open ○ Closed
Site approval letters or site	

personnel lists:	Attach site approval letters, site closure letters (if applicable), or site personnel lists in the Initial Submission Packet.

Research Abstract

Please type your Research Abstract here:

The Research Abstract should summarize the main points of your study in one paragraph. The following guidelines may help you:

1. Purpose and objective (1-2 sentences)
2. Study activities and population group (2-4 sentences)
3. Data analysis and risk/safety issues (1-2 sentences)

More than 60,000 young adults (YAs) aged 18-39 are diagnosed with cancer in the US each year. Advances in treatment have yielded five year survival rates >70% suggesting that the majority of YAs will become long-term cancer survivors. Symptom (e.g., pain, fatigue, distress) interference is common for YA cancer survivors and impacts their abilities to achieve normative life goals (e.g., returning to work/school, achieving autonomy, pursuing social/romantic relationships) and adhere to recommended follow-up care. Symptom management has been identified as a significant issue in the transition to survivorship for YAs by the Institute of Medicine and National Cancer Institute, and assistance with symptom management is rated as an important and unmet need by YA survivors. Yet, behavioral symptom management interventions have not targeted the needs of those diagnosed as YAs. The proposed study aims to develop a novel behavioral symptom management intervention with associated, study-specific mobile application designed for survivors of YA cancer (cancer types: hematologic, breast, endocrine, or gastrointestinal cancers, melanoma, or germ cell tumors).

Intervention Development (Phase 1):

The preliminary version of the intervention will be guided by the research team's prior work developing and testing symptom management interventions for cancer survivors, national guidelines for YA oncology, consultation with experts in the field, and input from patient (N=35) and provider (individual interviews with N=15) stakeholders. Primary areas to be discussed during focus groups and individual interviews are patients' experiences with and providers' experiences treating pain, fatigue, and psychological distress and the impact of these symptoms on patients' lives. The intervention will be further refined following review by a new sample of patient user testers (n=10).

Randomized Controlled Trial (Phase 2):

In the proposed randomized clinical trial, YA cancer survivors will be randomly assigned to one of two conditions: 1) the Symptom Managment Program or 2) the waitlist group who will receive the Symptom Mangement Program in approximately six months. Five cohorts of YA survivors (n=12/cohort) will receive the hybrid intervention, including remote group sessions and the integrated mobile application. Participants (N=60) will complete 5 assessments over 12 months, the first occurring upon enrollment and subsequent assessments occurring every 3 months. Assessments will include measures of treatment acceptability, intervention component utilization, use of the mobile application (e.g., frequency of use, content visited), support received from group members, and open-ended questions of their perceptions of the intervention and mobile application and the benefits and costs of study participation The proposed study has the potential to make several significant contributions by targeting an underserved group of cancer survivors, addressing a critical gap in care, and addressing variables consistently linked to social, economic, and health burden for YAs. It will also provide important information about approaches to identify, recruit, and retain YA cancer survivors in research and provide pilot data for a larger trial. The final 30 participants consenting to participate will be asked to complete exit interviews following their final intervention session to learn more about users' experiences with the intervention.

Research Summary

State your primary study objectives

Intervention Development (Phase 1):

Develop a group-based behavioral symptom management intervention for YA cancer survivors (aged 18-39 at diagnosis). Preliminary intervention content will be guided by our prior work, consultation with experts in the field, and national guidelines for YA oncology and will be further informed by focus groups with YA survivors (three groups, N=35) and oncology providers (1-2 groups, N=15). Qualitative information will be used to develop and refine the intervention.

Randomized Controlled Trial (Phase 2):

The primary aim is to to investigate the impact of the symptom management intervention to enhance participants'' self-efficacy for managing symptoms and perceived support.

The symptom management intervention is a group-based behavioral symptom management intervention for YA cancer survivors (aged 18- 39 at diagnosis) with associated, study-specific mobile application (N = 60). Content is guided by our prior work, consultation with experts in the field, and national guidelines for YA oncology and will be further informed by focus groups or individual interviews with YA survivors (N=35) and individual interviews with oncology providers (N=15). Qualitative information was used to develop and refine the intervention. User testing of the prototype intervention and mobile application was conducted with a second set of YA survivors (N=10) who independently reviewed materials. Qualitative information was used to further refine the intervention.

State your secondary study objectives

Please select your research summary form:

Standard Research Summary Template

This is the regular (generic) research summary template which is required for all regular applications (unless your protocol fits under the other research summary templates in this category). Use of these instructions is helpful for ensuring that the research summary contains all necessary elements.

Standard Research Summary

Purpose of the Study

- Objectives & hypotheses to be tested

We seek to develop a novel, skill-based behavioral symptom management intervention designed to meet the unique needs of Young Adult (YA) cancer survivors. Despite high symptom burden, symptom interference, and risk for late effects, YA survivors are quite underrepresented in research. There is an urgent need to develop interventions appropriate for the cognitive, emotional, physical, and social needs of this population. We aim to create the first developmentally appropriate behavioral symptom management intervention for YA cancer survivors to target physical and psychological symptoms.

Symptom Management Intervention Development (Phase 1):

Aim 1: Develop a group-based behavioral symptom management intervention for YA cancer survivors (aged 18-39 at diagnosis) with associated, study-specific mobile application. Preliminary intervention content will be guided by our prior work, consultation with experts in the field, and national guidelines for YA oncology and will be further informed by focus groups and individual interviews with YA survivors (N=35) and individual interviews with oncology providers (N=15). Quantitative and qualitative information obtained from participants will be used to develop and refine the intervention. User testing of the prototype intervention and mobile application will be conducted with a second set of YA survivors (N=10) who will independently review materials. Qualitative information will be used to further refine the intervention.

Randomized Controlled Trial (Phase 2): In the proposed randomized controlled trial, YA cancer survivors will be randomly assigned to one of two conditions: 1) the Symptom Management Program or 2)

the waitlist group who will receive the Symptom Management Program in approximately six months. Six cohorts of YA survivors (n=10/cohort) will receive the hybrid intervention, including remote group sessions and the integrated mobile application. Participants (N=60) will complete 5 assessments over 12 months, the first occurring upon enrollment and subsequent assessments occurring every 3 months. Assessments will include measures of treatment acceptability, intervention component utilization, use of the mobile application (e.g., frequency of use, content visited), support received from group members, and open-ended questions of their perceptions of the intervention and mobile application and the benefits and costs of study participation. The proposed study has the potential to make several significant contributions by targeting an underserved group of cancer survivors, addressing a critical gap in care, and addressing variables consistently linked to social, economic, and health burden for YAs. It will also provide important information about approaches to identify, recruit, and retain YA cancer survivors in research and provide pilot data for a larger trial.

The final 30 participants will be asked to complete an exit interview after completing the final intervention session to better understand the experiences of individuals receiving the intervention.

Background & Significance

- Should support the scientific aims of the research

1. Scope of the problem. In the United States, there are approximately 600,000 survivors of young adult (YA) cancer, aged 18-39 at diagnosis.[24] The incidence of cancer in this age group has grown over the last four decades,[25,26] and for some forms of cancer (e.g., colorectal cancer), has increased more rapidly than for any other age group.[27,28] Advances in treatment have yielded five year survival rates of >70% suggesting that the majority of YAs will become long-term cancer survivors.[26,29-31] However, YAs have been identified as understudied and underserved[2] and are the least represented group of cancer survivors in clinical research.[32]

Treatments for YA cancer survivors can result in physical symptoms (e.g., pain, fatigue)[33-35] and emotional distress (e.g., anxiety, depression).[35-39] For many YAs, these symptoms are persistent.[40-42] YA cancer survivors are diagnosed during a critical developmental period when they are working to achieve complex, age-related goals like completing their educations, achieving autonomy and independence, building their careers, fostering successful peer and romantic relationships, and building their families.[43-46] Physical symptoms and emotional distress disrupt YA survivors' abilities to achieve life goals and plan for the future[33,40,47-52] and contribute to significant social, economic, and health burden.[53-56] YAs who report more symptoms and greater distress experience lower social functioning, in part from decreased social engagement due to symptoms.[54] When compared to peers without a history of cancer, YA survivors report more illness- or injury-related missed work days and significantly greater annual productivity losses ($4,564 vs. $2,314).[55] YA survivors also experience greater medical expenditures when compared to peers ($7,417 vs. $4,247), which result from medical care required to treat long-term and late effects of cancer treatment, including persistent symptoms.[55] Thus, YA survivors are likely to avoid medical care due to cost, reducing adherence to follow-up care during survivorship.[56]

2. Assistance with symptom management has been rated by survivors of YA cancer as a critical and unmet healthcare need[33,57,58] and has been listed as a significant issue in the transition to survivorship.[59,60] YAs lack confidence in their abilities to manage physical symptoms and distress, and have more difficulty coping with these challenges than older or younger cancer survivors.[26,61] In 2006, to develop a research agenda for adolescents and young adults (AYA) with cancer, the NCI, in collaboration with LiveStrong, convened a Progress Review Group (PRG).[2] This effort was supplemented by two recent workshops and subsequent reports from the National Cancer Policy Forum/Institute of Medicine (IOM)[3] and NCI.[31] Each of these seminal meetings highlighted the critical need for developing and testing interventions to reduce symptom burden as well as promote and target self-efficacy and self-management of symptoms for YA cancer survivors.

To date, there remains a serious paucity of evidence-based symptom management interventions that have been tested in this population. In a search of the NIH Research Portfolio Online Reporting Tools (RePORT; **https://projectreporter.nih.gov**; January 31, 2019) for studies funded in the last five years, we identified a single R01-supported study testing an intervention promoting resilience among AYAs

undergoing a hematopoietic stem cell transplant and one K-type award focused on promoting resiliency and stress management among AYA survivors. While both of these important studies aim to improve psychological symptoms, they do not target physical symptoms, which often co-occur and are interrelated with psychological symptoms for YAs.[33,62] In fact, the co-occurrence of physical and psychological symptoms is associated with greater symptom intensity and interference.[63] Meta-analytic data and reviews of studies conducted with primarily older adult (*M*>40) cancer survivors suggest that behavioral symptom management interventions result in significant reductions in physical and psychological symptoms, improved self-efficacy for symptom management, and decreased symptom interference.[64-69] However, few YAs have participated in these studies and represent only a small portion of overall study samples.[69-72] The efficacy of these interventions for YA survivors is largely unknown, and because of the wide age range of participants, these interventions have not been considerate of the developmental stage and associated needs of YA survivors. It is our goal to begin to fill this gap. To our knowledge, the proposed study will be the first to develop a behavioral symptom management intervention for YA survivors targeting both physical and psychological symptoms.

3. Significance of the proposed project to field. We aim to develop a novel, skill-based behavioral symptom management intervention designed to meet the unique needs of YA cancer survivors (aged 18-39 at diagnosis). The intervention has the potential to produce significant public health benefit by targeting an underserved and vulnerable group of cancer survivors and by addressing variables consistently linked to poor quality of life and adverse social, economic, and health outcomes. The proposed study addresses the following gaps in the literature. 1) YA cancer survivors have identified symptom management as an unmet healthcare need. It is our hope we will develop an intervention that will provide participants with skills to improve the severity of physical symptoms and emotional distress. By targeting multiple symptoms, which often occur in clusters, the developed intervention may result in reduced symptom interference.

In sum, the Scientific Premise of this application is responsive to the call for symptom management interventions, both from YA cancer survivors and the authors of the NCI PRG and the IOM and NCI workshops. The proposed project aims to address this gap by developing the **first** behavioral symptom management intervention tailored to the unique needs of YA survivors that targets both physical and psychological symptoms.

Design & Procedures

- Describe the study, providing details regarding the study intervention (drug, device, physical procedures, manipulation of the subject or the subject's environment, etc.). Discuss justifications for placebo control, discontinuation or delay of standard therapies, and washout periods if applicable. Identify procedures, tests and interventions performed exclusively for research purposes or more frequently than standard of care. Include alternative therapies, concurrent therapies discontinued per protocol, risk benefit ratio, and use of tissue/specimens. Discuss monitoring during washout periods if applicable. Include brief description of follow-up, if any.

Intervention Development (Phase 1): Preliminary intervention content was guided by the research team's prior work developing and testing symptom management interventions for cancer survivors that target multiple symptoms (i.e., pain, fatigue, distress), national guidelines for young adult (YA) oncology, and discussions with the study team. Intervention content was informed by quantitative and qualitative data from YA cancer survivors (N=35) through focus groups of individual phone interviews and individual interviews with oncology providers (e.g., oncologists, advanced practice providers) who treat YA cancer survivors (N=15). Providers will also be asked to complete a brief questionnaire, which asks about their sociodemographic characteristics and clinical practice as well as answer questions about their patients' needs. Survivors were asked to complete a brief questionnaire, which asks about their sociodemographic characteristics, symptom severity, and symptom self-efficacy. The group leader/interviewer made field notes following each group or interview to track emergent content areas. Focus groups and interviews were audio recorded and transcribed verbatim. The goal is to better understand the needs and preferences of the target audience and tailor the developed intervention to address these needs.

From the YA survivors, we hope to expand our understanding of their symptom experience, the interference of symptoms with important life goals and achievement of developmental milestones, self-efficacy for managing symptoms and knowledge of behavioral symptom management skills. YA survivors will also be asked to provide information about their preferences for the format of the intervention (e.g., session length, length of mobile application content) and barriers to session attendance and homework completion. This information was used to guide the content, structure, and format of the intervention and mobile application. Oncology providers were asked to provide information specific to the experiences of their YA patients such as common treatments and side effects, risks for persistent symptoms and side-

effects, symptom management interventions (medical and non-medical) and their efficacy, and recommendations for patients for communicating with providers about symptoms. Groups were 90 minutes in length and audio recorded. Individual interviews were 30-60 minutes in length and audio recorded. The company Sure Types A Lot transcribed audio files of the focus groups and individual interviews. The computer software NVivo was used to analyze transcripts of the audio files. Our team has extensive experience conducting focus groups and individual interviews and using qualitative data from participants to inform intervention development. The qualitative information provided by focus group participants was discussed with the study team and used to inform a prototype of the intervention and mobile application.

A new sample of YA cancer survivors (N=10) independently reviewed the prototype materials (e.g., printed patient manuals, mobile application) and provided feedback (e.g., content, content presentation, usability of the application) to better understand the experience of intervention users and refine materials. The prototypes of the intervention and mobile application were revised after review by each user tester to incorporate feedback. User testing sessions were delivered remotely using videoconferencing technology (Zoom). The first five participants recruited will review the printed patient manuals while the next five participants recruited will review the mobile application. Participants reviewing the printed patient manuals will be sent the manuals via mail prior to the user testing sessions. Prior to the start of user testing sessions for the mobile application, participants were provided with instructions for downloading the study mobile application on their personal mobile device. In the event that a participant did not have a mobile device, they were provided via mail with a study-specific Ipad. Participants were sent a unique invite code to use to register themselves in the application. Upon completion of the user testing session, participants' access to the application will be removed. The user testing session leader will make field notes following each session to track participants' comments and thoughts about intervention content and format. User testing sessions will be recorded in Zoom, and recordings were reviewed by the study team. The goal is to better understand participants' opinions of the intervention, intervention content, and presentation of information as well as their ability to interface with the content and mobile application. Participants were asked to complete a brief questionnaire, which asks about their sociodemographic characteristics, symptom severity, and symptom self-efficacy. Video recordings were transcribed by the company Sure Types A Lot, which is a Duke approved transcription service. The computer software NVivo was used to analyze transcripts. The qualitative information provided by user testers was discussed with the study team and used to refine the intervention and mobile application.

Randomized Controlled Trial (Phase 2): In the proposed randomized clinical trial, YA cancer survivors will be randomly assigned to one of two conditions: 1) the Symptom Managment Program or 2) the waitlist group who will receive the Symptom Mangement Program in approximately six months. Six cohorts of YA survivors (n=10/cohort) will receive the hybrid intervention, including remote group sessions and the integrated mobile application with medical provider-approved participation in a home-based exercise program. Participants will be given a Garmin vvofit 4 (activity tracker) to wear which will synch with the mobile application. Participants will be provided with instructions for downloading the study mobile application on their personal mobile device. In the event that a participant does not have a mobile device, they will be provided via mail with a study-specific Ipad. Participants will be sent a unique invite code to use to register themselves in the application. Participants will also be sent a secure Zoom link for group video sessions. Zoom sessions will be recorded and reviewed for training purposes and to assess intervention fidelity. We will provide instruction and remediation in the event of low fidelity.

Participants (N=60) will complete 5 assessments over 12 months, the first occurring upon enrollment and subsequent assessments occurring every 3 months. Assessments will include measures of treatment acceptability, intervention component utilization, use of the mobile application (e.g., frequency of use, content visited), support received from group members, and open-ended questions of their perceptions of the intervention and mobile application and the benefits and costs of study participation The proposed study has the potential to make several significant contributions by targeting an underserved group of cancer survivors, addressing a critical gap in care, and addressing variables consistently linked to social, economic, and health burden for YAs. It will also provide important information about approaches to identify, recruit, and retain YA cancer survivors in research and provide pilot data for a larger trial.

Assessment Schedule

1. Intervention Arm (receiving intervention upon enrollment)

	Baseline	3-months	6-months	9-months	12-months
Sociodemographics	X				
Diagnosis and treatment information	X				
Treatment Acceptability Questionnaire		X			
Intervention Satisfaction: SSTS-R		X			
Open ended questions about the program (mobile application and group sessions)		X			
Self-reported use of intervention skills		X	X	X	X
Self-reported use of mobile app		X	X	X	X

Brief Pain Inventory (9-item)	X	X	X	X	X
PROMIS Fatigue Scale (6-item)	X	X	X	X	X
PROMIS Depression Short Form (8-item)	X	X	X	X	X
PROMIS Anxiety Short Form (8-item)	X	X	X	X	X
Illness Intrusiveness Rating Scale	X	X	X	X	X
Self-Efficacy for Managing Chronic Disease Scale	X	X	X	X	X
PROMIS Self-efficacy for Managing Chronic Conditions Short Form (4a)	X	X	X	X	X
PROMIS Emotional Support Short Form (6-item)	X	X	X	X	X
PROMIS Instrumental Support Short Form (6-item)	X	X	X	X	X
PROMIS Informational Support Short Form (6-item)	X	X	X	X	X
PROMIS Social Isolation Scale (6-item)	X	X	X	X	X
Group Therapy Experiences Scale		X			
International Physical Activity Questionnaire	X	X	X	X	X
Stanford LCAT	X	X	X	X	X
Functional Assessment of Chronic Illness Therapy (FACIT)- Spiritual Wellbeing 12 Item Scale	X	X	X	X	X
Acceptance and Action Questionnaire for Cancer	X	X	X	X	X
Valuing Questionnaire	X	X	X	X	X

2. Waitlist Control Group (receiving intervention 6 months after enrollment)

	Baseline	3-months	6-months	9-months	12-months
Sociodemographics	X				
Diagnosis and treatment information	X				
Treatment Acceptability Questionnaire				X	
SSTS-R				X	
Open ended questions about the program (mobile application and group sessions)				X	
Self-reported use of intervention skills				X	X
Self-reported use of mobile app				X	X
Brief Pain Inventory (9-item)	X	X	X	X	X
PROMIS Fatigue Scale (6-item)	X	X	X	X	X
PROMIS Depression Short Form (8-item)	X	X	X	X	X
PROMIS Anxiety Short Form (8-item)	X	X	X	X	X
Illness Intrusiveness Rating Scale	X	X	X	X	X
Self-Efficacy for Managing Chronic Disease Scale	X	X	X	X	X
PROMIS Self-efficacy for Managing Chronic Conditions Short Form (4a)	X	X	X	X	X
PROMIS Emotional Support Short Form (6-item)	X	X	X	X	X
PROMIS Instrumental Support Short Form (6-item)	X	X	X	X	X
PROMIS Informational Support Short Form (6-item)	X	X	X	X	X
PROMIS Social Isolation Scale (6-item)	X	X	X	X	X
Group Therapy Experiences Scale				X	
International Physical Activity Questionnaire	X	X	X	X	X
Stanford LCAT	X	X	X	X	X
Functional Assessment of Chronic Illness Therapy (FACIT)- Spiritual Wellbeing 12 Item Scale	X	X	X	X	X
Acceptance and Action Questionnaire for Cancer	X	X	X	X	X
Valuing Questionniare	X	X	X	X	X

Measures

Sociodemographics:

1. Age, race/ethnicity, relationship status, employment status, occupation, income, and years fo education [Time Frame: Baseline]

Disease Characterics:

1. Diagnosis and treatment information [Time Frame: Baseline]

Primary Outcome Measures :

1. Intervention Satisfaction: SSTS-R [Time Frame: Following completion of the intervention, up to 12 months] Intervention satisfaction will be assessed using the SSTS-R, a 13-item measure with the first 12-items on a five-point scale ranging from 1 "strongly disagree" to 5 "strongly disagree." The 13th item asks, "How much did the intervention help with your sypmtoms?" with 5 answer choices ranging from "made things a lot better" to made things a lot worse."

2. Open Ended Questions About the Program [Time Frame: Following completion of the intervention, up to 12 months] Intervention will be evaluated using 3 open-ended questions, including the following: "1) What was the most helpful part of the program?," "2) What was the least helpful part of the program?", and "3) What suggestions do you have for us to help improve the program?"

3. Session attendance [Time Frame: Following completion of the intervention, up to 12 months] Treatment feasibility will be assessed by measuring the session attendance rate for each participant.

4. Treatment Acceptability Questionnaire [Time Frame: Following completion of the intervention, up to 12 months]
   The Treatment Acceptability Questionnaire is a six-item scale assessing participants' views of an intervention as acceptable, ethical, and effective.
   Items are rated on a 7-point Likert scale (e.g., 1 "very unacceptable" to 7 "very acceptable).

5. Use of Intervention Strategies [Time Frame: Following completion of the intervention, up to 12 months]Participants' use of intervention strategies will be assessed using a measure developed specific to components of the proposed intervention. Participants will be asked about how frequently treatment strategies discussed in session have been used outside of session since the previous session or last assessment depending on the timing of the questionnaire. A scale ranging from 0 "not at all" to 5 "2 or more times a day" will be used.
6. Self-reported use of the Mobile Application [Time Frame: Following completion of the intervention, up to 12 months]
   Participants' use of the mobile application will be assessed using a measure developed specific to components of the proposed mobile application.Participants will be asked about how frequently they have used components of the mobile application outside of session since the previous session or last assessment depending on the timing of the questionnaire. A scale ranging from 0 "not at all" to 5 "2 or more times a day" will be used.

Secondary Outcome Measures:

1. Change in Depressive Symptoms: PROMIS Depression Short Form [Time Frame: Baseline and again 3, 6, 9, and 12 months following the baseline assessment]Depressive Symptoms will be assessed using the PROMIS Depression Short Form, an 8-item measure assessing symptoms of depression in the last week. Participants are asked to respond to items (e.g., "I felt sad," "I felt helpless") using a five-point scale ranging from 1 "never" to 5 "always."

2. Change in Anxiety: PROMIS Anxiety Short Form [Time Frame: Baseline and again 3, 6, 9, and 12 months following the baseline assessment]Symptoms of Anxiety will be assessed using the PROMIS Anxiety Short Form, an 8-item measure assessing symptoms of anxiety in the last week. Participants are asked to respond to items (e.g., "I felt nervous," "I felt tense") using a five-point scale ranging from 1 "never" to 5 "always".

3. Change in Symptom Interference: Illness intrusiveness rating scale [Time Frame: Baseline and again 3, 6, 9, and 12 months following the baseline assessment]Symptom interference will be assessed using the Illness Intrusiveness Rating Scale (IIRS). The IIRS assesses the extent to which an illness and/ or its treatments interfere with 13 quality of life domains (e.g., health, diet, work, sex life, active recreation). Items are rated on a 7-point scale from 1 "not very much" to 7 "very much."
4. Change in Pain: Brief Pain Inventory [Time Frame: Baseline and again 3, 6, 9, and 12 months following the baseline assessment]The Brief Pain Inventory is a 9-item, self-report measure assessing pain severity and interference from pain across important life domains (e.g., general activity, work, relations with others). Participants rate their pain on a scale from 0 "no pain" to 10 "pain as bad as you can imagine."

5. Change in Fatigue: PROMIS Fatigue Short Form [Time Frame: Baseline and again 3, 6, 9, and 12 months following the baseline assessment]Fatigue will be assessed using the PROMIS Fatigue Scale, a 6-item self-report measure of fatigue. Participants are asked to think about the last week when responding to each item (e.g., "In the past 7 days, how run-down did you feel, on average?").

Exploratory Outcome Measures :

1. Group Therapy Experiences Scale [Time Frame: Following completion of the intervention, up to 12 months]The 17-item Group Therapy Experiences Scale will be used to assess the level of cohesion among group members (e.g., development of positive relationships, comfort level with other group members). Items 1-16 are rated on a 5-point scale with 1 = "strongly agree" to 5 = "strongly disagree." Item 17 is an open-ended question, "was there something in the group today that helped or hindered you?"

2. Change in Social Isolation: PROMIS Social Isolation Scale [Time Frame: Baseline and again 3, 6, 9, and 12 months following the baseline assessment]The PROMIS Social Isolation Scale is a 6-item measure is used to assess social isolation. Participants are asked to rate each item (e.g., "I felt left out," "I feel that people avoid talking to me") on a scale from 1= "never" to 5= "always."

3. Change in Self-Efficacy: The Self-Efficacy for Managing Chronic Disease Scale [Time Frame: Baseline and again 3, 6, 9, and 12 months following the baseline assessment]The Self-Efficacy for Managing Chronic Disease Scale is a 6-item scale. Participants rate their confidence in keeping pain, fatigue, emotional distress, and other symptoms from interfering with things they want to do on a scale from 1 "not at all confident" to 10 "totally confident."

4. Change in Self-Efficacy: PROMIS Self-Efficacy for Managing Chronic Conditions - Managing Symptoms - Short Form 4a [Time Frame: Baseline and again 3, 6, 9, and 12 months following the baseline assessment] The PROMIS Self-Efficacy for Managing Chronic Conditions - Managing Symptoms - Short Form 4a is a 4-item scale. Participants rate their confidence in managing their symptoms during daily activities, with relationships with friends and family, in a public place, and working with their doctor to manage these symptoms on a scale from 1 = "I am not at all confident" to 5 "I am very confident."

5. Change in Emotional Support: PROMIS Emotional Support-Short Form [Time Frame: Baseline and again 3, 6, 9, and 12 months following the baseline assessment]The PROMIS Emotional Support Short Form is a 6-item measure used to assess emotional support. Participants are asked to rate each item ("I have someone who will listen to me when I need to talk," "I have someone to talk with when I have a bad day") on a scale from 1= "never" to 5= "always."

6. Change in Instrumental Support: PROMIS Instrumental Support-Short Form [Time Frame: Baseline and again 3, 6, 9, and 12 months following the baseline assessment]The PROMIS Instrumental Support Short Form is a 6-item measure used to assess instrumental support. Participants are asked to rate each item (e.g., "Do you have someone to take you to the doctor if you needed it?," "Do you have someone to prepare your meals if you are unable to do it yourself?") on a scale from 1= "never" to 5= "always."

7. Change in Informational Support: PROMIS Informational Support-Short Form [Time Frame: Baseline and again 3, 6, 9, and 12 months following the baseline assessment]The PROMIS Informational Support Short Form is a 6-item measure used to assess informational support. Participants are asked to rate each item (e.g., "I have someone to turn to for suggestions about how to deal with a problem," "I have someone to give me information if I need it") on a scale from 1= "never" to 5= "always."

Other Outcome Measures:

1. Change in Activity: International Physical Activity Questionnaire [Time Frame: Baseline and again 3, 6, 9, and 12 months following the baseline assessment]The International Physical Activity Questionnaire is a seven-item questionnaire that assesses the amount of time participants have spent doing physical activity (e.g., moderate physical activities, vigorous physical activities, walking) in the last seven days.

2. Change in Activity: Stanford LCAT [Time Frame: Baseline and again 3, 6, 9, and 12 months following the baseline assessment] The Stanford LCAT is a categorical item that asseses the type of physical activities participants do.

3. Change in Spiritual Wellbeing: Functional Assessment of Chronic Illness Therapy (FACIT) [Time Frame: Baseline and again 3, 6, 9, and 12 months following the baseline assessment] The FACIT assesses the spiritual wellbeing of participants with 12-item questionnaire on a scale from 0 = "not at all" to 4 = "very much."

4. Changes in Cancer Experience: Acceptance and Action Questionnaires for Cancer (AAQ) [Time Frame: Baseline and again 3, 6, 9, and 12 months following the baseline assessment] The AAQ is an 18-item questionnaire to track phsychological flexibility related to coping with cancer and cancer

treatment. The scale ranges from 1 = "never true" to 7 "always true." Item is scored by adding all of the responses together.

5. Changes in Living in Alignment with Values: The Valuing Questionnaire (VQ) [Time Frame: Baseline and again 3, 6, 9, and 12 months following the baseline assessment]. The VQ is a 10-item self-report questionnaire with a scale 0 = "not true at all" to 6 "completely true.

Each participant will also receive 4 study newsletters over the course of the 12 months of their participation in the study. Study newsletters will be sent to participants via email or postal mail in the time between the intervention start and each follow-up assessment. The newsletters will provide educational information and tips for managing common problems experienced by young adult cancer survivors. The specific newsletter topics are: nutrition, sleep, finances, and cognitive problems.

Text message reminders will be sent out to all study participants automatically using Twilio, with REDCap as the backend. The messages will include reminders to complete study assessments and a link to their unique assessment in RedCap. Content of the messages will include:

- Thank you for participating in the Improving Symptom Management Study! It is time for your next set of surveys. [survey-queue-url] At any point you wish to stop receiving texts about this study, please opt-out at the link below: [survey-url:optout]
- At any point you wish to stop receiving texts about this study, please opt-out at the link below: [survey-url:optout]

Participant phone numbers will be provided to Twilio to facilitate the sending of text messages, and Twilio may store metadata about the delivery of the messages, such as successful or failure, and time and date stamps, but no other content will be stored. Messages for this study are one-way only and cannot be replied to.

The final 30 participants will be asked to complete an exit interview to obtain information about their experiences participating in the intervention (see exit interview guide). The exit interviews will occur following the 3 month assessment (intervention arm) or 9 month assessment (waitlist control arm). The exit interviews will be approximately 30 minutes and occur via Zoom. Exit interviews will be audio/video recorded. Participants will complete a consent addendum indicating their consent to participate in the exit interviews prior to their participation. Participants will be offered $15 via clincard in appreciation for their time.

Selection of Subjects

- List inclusion/exclusion criteria and how subjects will be identified.

Inclusion/Exclusion Criteria

Intervention Development (Phase 1):

Eligibility criteria for young adult (YA) survivors: diagnosed with cancer as a YA (aged 18-39); diagnosis of hematologic, breast, endocrine, or gastrointestinal cancer, melanoma, or germ cell tumor; receiving care at the DCI; completed curative treatment involving multimodal therapy within the last 5 years; able to speak/read English; and able to give informed consent. Exclusion criteria: non-ambulatory; major mental illness (i.e., schizophrenia); untreated or uncontrolled mental illness (i.e., bipolar disorder).

Eligibility criteria for oncology providers (e.g., oncologists, physician assistants): provide care to YA survivors at the DCI.

Subject Identification
Potential survivor participants will be identified via the following avenues:

a) Duke Teen and Young Adult (TYA) Oncology Database. Supported by a grant from the St. Baldrick's Foundation (IRB protcol: 00100124), the Duke TYA Oncology program has established a database of teens and young adults (aged 15-29) treated at Duke. Individuals consenting to be included in the database are asked if they would be willing to be participate in future research studies. Those interested and eligible, will be approached to participate in the proposed study.

b) Electronic Health Records under a HIPPA Waiver. Since the TYA database will only include potential participants who were diagnosed between the ages of 18 and 29 years, we will use additional approaches to recruit additional YA cancer survivors. Using procedures implemented in our prior studies, participants will be identified through electronic health records under a HIPPA waiver. Participants will be recruited in the following ways:

a) A letter and study brochure including a description of the study will be mailed at least two weeks prior to a scheduled oncology appointment informing potentially eligible participants of the study. The letter will state that the PI or member of the study staff may approach them in clinic at their next appointment; survivors wishing not to be approached can call a number to opt out of the study. The letter will also state that they will be called via phone in the event that we are unable to make contact during the scheduled clinic appointment.

b) Survivors may be referred to the study by their providers. The medical team will introduce the study, provide participants with the study brochure, and, if interested, the PI or study staff member will contact the survivor to assess eligibility, further describe the study, and discuss questions and concerns.

Potential provider participants will be identified by reviewing the staff directory of the Duke Cancer Institute to identify providers who treat hematologic, breast, and gastrointetinal cancers, melanoma, and germ cell tumors.

Randomized Controlled Trial (Phase 2):

Eligibility criteria for young adult (YA) survivors: diagnosed with cancer as a YA (aged 18-39); diagnosis of hematologic, breast, endocrine, or gastrointestinal cancer, melanoma, or germ cell tumor; receiving care at the DCI; completed curative treatment involving multimodal therapy within the last 2 years; able to speak/read English; and able to give informed consent. Exclusion criteria: non-ambulatory; major mental illness (i.e., schizophrenia); untreated or uncontrolled mental illness (i.e., bipolar disorder).

Subject Identification
Potential survivor participants will be identified via the following avenues:

a) Duke Teen and Young Adult (TYA) Oncology Database. Supported by a grant from the St. Baldrick's Foundation (IRB protcol: 00100124), the Duke TYA Oncology program has established a database of teens and young adults (aged 15-29) treated at Duke. Individuals consenting to be included in the database are asked if they would be willing to be participate in future research studies. Those interested and eligible, will be approached to participate in the proposed study.

b) Electronic Health Records under a HIPPA Waiver. Since the TYA database will only include potential participants who were diagnosed between the ages of 18 and 29 years, we will use additional approaches to recruit additional YA cancer survivors. Using procedures implemented in our prior studies, participants will be identified through electronic health records under a HIPPA waiver. Participants will be recruited in the following ways:

a) A letter and study brochure including a description of the study will be mailed at least two weeks prior to a scheduled oncology appointment informing potentially eligible participants of the study. The letter will state that the PI or member of the study staff may approach them in clinic at their next appointment; survivors wishing not to be approached can call a number to opt out of the study. The letter will also state that they will be called via phone in the event that we are unable to make contact during the scheduled clinic appointment.

b) Survivors may be referred to the study by their providers. The medical team will introduce the study, provide participants with the study brochure, and, if interested, the PI or study staff member will contact the survivor to assess eligibility, further describe the study, and discuss questions and concerns.

Potential provider participants will be identified by reviewing the staff directory of the Duke Cancer Institute to identify providers who treat hematologic, breast, and gastrointetinal cancers, melanoma, and germ cell tumors.

Subject Recruitment and Compensation

- Describe recruitment procedures, including what method(s) will be used, when the study will be introduced to potential participants and by whom. If any follow-up contact is planned, describe the proposed method and timing. Describe how you will ensure that subject selection is equitable and all relevant demographic groups have access to study participation (per 45 CFR 46.111(a) (3)). Include information about how many DUHS participants will be recruited. If participants are to be compensated and/or reimbursed, provide specific prorated amounts to be provided for expenses such as travel and /or lost wages, and/or for inducement to participate.

Subject Recruitment:

Survivor Participants will be recruited in the following ways:

a) A letter and study brochure including a description of the study will be mailed at least two weeks prior to a scheduled oncology appointment informing potentially eligible participants of the study. The letter will state that the PI or member of the study staff may approach them in clinic at their next appointment; survivors wishing not to be approached can call a number to opt out of the study. The letter will also state that they will be called via phone in the event that we are unable to make contact during the scheduled clinic appointment.

b) Survivors may be referred to the study by their providers. The medical team will introduce the study, provide participants with the study brochure, and, if interested, the PI or study staff member will contact the survivor to assess eligibility, further describe the study, and discuss questions and concerns.

c) A message sent through the electronic health record patient portal (MyChart) describing the study and requesting participation in the phone screening. The message will state that the PI or member of the study staff may approach them in clinic at their next appointment; survivors wishing not to be approached can call a number to opt out of the study. The message will also state that they will be called via phone in the event that we are unable to make contact during the scheduled clinic appointment.

If a survivor expresses interest and is eligible to participate, he or she will be scheduled for an in-person appointment during which informed consent will be conducted. Alternatively, informed consent may occur at the first face-to-face contact. In order to reduce the duration of in-person contacts, survivors will also be given the option to complete informed consent process at home online via REDCap or via phone. These participants will have the opportunity to complete their questionnaire set at home (online via REDCap) as well. If a participant is unable to attend a focus group, face-to-face, they will be offered the option of completing an individual interview, which may occur in person or via phone. Participants completing individual interviews may be consented in-person or online.

Subject Compensation

Phase 1:

Each participant will receive $30 for his/her time. There will be no cost to the subjects as a result of participation in the study.

Phase 2:

Each survivor participant will receive $30 for his/her time after each of the five assessments with a total of $150.

Survivor participants completing the exit interviews will receive $15 for his/her time after completion of the interview.

There will be no cost to the subjects as a result of participation in the study.

Consent Process

- Complete the consent section in the iRIS Submission Form.

Subject's Capacity to Give Legally Effective Consent

- If subjects who do not have the capacity to give legally effective consent are included, describe how diminished capacity will be assessed. Will a periodic reassessment occur? If so, when? Will the subject be consented if the decisional capacity improves?

Only individuals without evidence of cognitive impairment that would preclude informed consent will be consented.

Study Interventions

- If not already presented in the Design & Procedures section, describe study-related treatment or use of an investigational drug or biologic (with dosages), or device, or use of another form of intervention (i. e., either physical procedures or manipulation of the subject or the subject's environment) for research purposes.

Intervention Development (Phase 1): The study focuses on intervention development. Focus groups and individual interviews were held to obtain quantitative and qualitative data from young adult cancer survivors and oncology providers to inform the development of a behavioral symptom management intervention and associated mobile application. A prototype of the intervention and associated mobile application were developed and reviewed independently by user testers (YA cancer survivors, N=10).

The proposed group-based intervention sessions will provide skills training in cognitive and behavioral techniques that have been successfully used in symptom management interventions developed by members of the study team. The intervention will be tailored and refined based on qualitative data from focus group participants and user testers (e.g., session order, YA-specific examples, length of intervention content), the proposed intervention will provide systematic training in cognitive and behavioral coping skills (e.g., activity-rest cycling, cognitive restructuring, relaxation training). By employing these strategies, participants learn to adjust their thoughts, behaviors, and emotions in the service of better managing symptoms. The intervention aims to enhance participants' self-efficacy for managing symptoms and perceived support. According to Social Cognitive Theory (SCT), self-efficacy can influence an individual' s ability and willingness to initiate and sustain coping behaviors. Intervention sessions will use techniques based on SCT (e.g., modeling and role play, opportunities to receive feedback and for self-evaluation, self-monitoring, goal setting) to assist with improving participants' confidence in their abilities to apply skills to their own lives and symptoms. The inclusion of strategies based on SCT in psychosocial interventions developed by the research team and others has been associated with positive intervention effects. Additionally, SCT posits that the social environment can facilitate behavior change. We propose a group-based format for the intervention, and survivor focus group participants and user testers will be asked about their preferences forthis format. We believe interactions with other YA survivors will help to improve feelings of support and self-efficacy as well as promote skill use to ultimately improve outcomes . The proposed session format is: 1) group socialization (15 minutes); 2) review homework, mobile application use, and session outline (25 minutes); 3) education, skills training, and skills application (30 minutes); and 4) assign homework (5 minutes).

The intervention will include a mobile application. A prototype of the application was provided to user testers, who were asked to provide feedback based on their preferences. User testers received secure access to the study-specific mobile application developed by Pattern Health. Pattern Health has created a fully functional application platform that will be customized by the study team to deliver content consistent with the goals of the study. The mobile application content was refined based on input from focus groups and user testers and will include: 1) audio and video files and brief text-based educational content reviewing strategies; 2) the ability to self-monitor symptom (pain, fatigue, distress) severity; 3) the ability to connect with group members via a social networking platform. This platform will be monitored and

moderated by the study team; and 4) activity tracking synchronization, which allows participants to monitor their activity in the application and provides study staff with real-time data. Participants will receive push notifications with skill use suggestions based on their input of symptom severity ratings; suggestions will reflect intervention strategies discussed during previous sessions. The research team will also have real-time access to participants' symptom ratings, and participants will be given the option for phone coaching around skill use.

Randomized Controlled Trial (Phase 2): In the proposed randomized clinical trial, YA cancer survivors will be randomly assigned to one of two conditions: 1) the Symptom Managment Program or 2) the waitlist group who will receive the Symptom Mangement Program in approximately six months. Six cohorts of YA survivors (n=10/cohort) will receive the hybrid intervention, including remote group sessions and the integrated mobile application with medical provider-approved participation in a home-based exercise program. Participants (N=60) will complete 5 assessments over 12 months, the first occurring upon enrollment and subsequent assessments occurring every 3 months. Assessments will include measures of treatment acceptability, intervention component utilization, use of the mobile application (e.g., frequency of use, content visited), support received from group members, and open-ended questions of their perceptions of the intervention and mobile application and the benefits and costs of study participation. The proposed study has the potential to make several significant contributions by targeting an underserved group of cancer survivors, addressing a critical gap in care, and addressing variables consistently linked to social, economic, and health burden for YAs. It will also provide important information about approaches to identify, recruit, and retain YA cancer survivors in research and provide pilot data for a larger trial.

All participants will also receive 4 study newsletters over the course of the 12 months of their participation in the study. Study newsletters will be sent to participants via email or postal mail in the time between the intervention start and each follow-up assessment. The newsletters will provide educational information and tips for managing common problems experienced by young adult cancer survivors. The specific newsletter topics are: nutrition, sleep, finances, and cognitive problems. The newsletters are intended to assist with keeping participants engaged with the study in the time between assessments.

Risk/Benefit Assessment

- Include a thorough description of how risks and discomforts will be minimized (per 45 CFR 46.111(a) (1 and 2)). Consider physical, psychological, legal, economic and social risks as applicable. If vulnerable populations are to be included (such as children, pregnant individuals, imprisoned persons or cognitively impaired adults), what special precautions will be used to minimize risks to these subjects? Also identify what available alternatives the person has if he/she chooses not to participate in the study. Describe the possible benefits to the subject. What is the importance of the knowledge expected to result from the research?

Potential Risks. No adverse events are anticipated. Participation in this study is voluntary and participants can withdraw at any time. The risks associated with this study are minimal and rare. Participation in focus groups, individual interviews, or user testing are associated with few negative side effects. The focus groups, interviews, self-report measures, and user testing will cover topics including physical health (e.g., cancer diagnosis and treatments), physical symptoms (e.g., pain, fatigue), psychological distress, symptom interference, confidence in their ability to manage symptoms, and social support, all of which may request participants to provide sensitive and personal information. Participants may feel embarrassed or uncomfortable with disclosing this information. There is also the possibility of breach of confidentiality. For example, in a group setting, such as a focus group, there is risk of disclosure of personal information by another participant. All efforts will be made to remain sensitive to participant's needs, HIPAA requirements, and confidentiality procedures.

Protection Against Risk. If a participant endorses psychological distress due to study participation, the PI will consult with members of the study team (Kevin Oeffinger, MD and Rebecca Shelby, PhD). Dr. Oeffinger is a family physician and directs the DCI Supportive Care and Survivorship Center as well as the DCI Center for Onco-Primary Care. Dr. Oeffinger has extensive clinical and research experience with YA cancer survivors. Dr. Shelby is a licensed clinical psychologist. Drs. Oeffinger and Shelby will provide guidance regarding the appropriate course of action. The PI is also a licensed clinical psychologist and member of the Duke Cancer Patient Support Program and Cancer Symptom Management and Support Program. Her involvement in these programs will allow her to readily facilitate appropriate referrals to psychosocial services offered through the DCI (e.g., clinical psychologists and medical family therapists affiliated with the Duke Cancer Patient Support Program). Contact information for the PI is provided should participants have any questions or concerns. Additionally, the clinical research coordinator will be trained to monitor participants' psychological status and report to the PI if a participant shows signs of experiencing high levels of physical and emotional distress that need to be addressed outside the context

of the study. If this is determined to be the case, the clinical research coordinator will work directly with the PI and the participant to move forward in a way that is in the best interest of the participant. No participant will be kept in the study if he or she is experiencing increased or extreme distress.

Individuals receiving the group-based intervention will be provided with a home-based exercise protocol. Participating in physical activity poses minimal risks for cancer survivors, and may help to improve symptoms (e.g., fatigue, distress); however

precautions will be taken to ensure safety of research participants. Upon study enrollment, participants' health care providers will be asked to provide a written statement of medical clearance for home-based physical activity. Providers will also be asked to contact members of the study team if a change in a participant's health indicates that it would no longer be advisable for him or her to continue in the home-based exercise program. The exercise protocol has been developed and reviewed by experienced exercise physiologists and providers with expertise in this area, and the recommendations are consistent with those provided by the aforementioned national organizations. Participants will be given specific instructions (i.e., verbal, written, and with demonstration) regarding safe exercise and special consideration for exercising with side effects (e.g., lymphedema, neuropathy). In the event that a participant has concerns that require exercise modifications, the cancer center exercise physiologist and the participant's medical provider will be consulted to develop an appropriate plan.

Second, there is the possibility of a breach of confidentiality, which will be addressed in the consent form and expressed to participants upon accrual. All efforts will be made to maintain confidentiality. For example, in a group setting, such as in a focus group, there is risk of disclosure of personal information by another participant. Individuals participating in focus groups will be instructed to maintain participants' confidentiality at the onset of the group, and participants will be asked not talk about other participants' comments outside of the group.

Additional efforts will be employed to maintain confidentiality. Two password-protected databases will be used to ensure confidentiality of participant information and data by keeping identifying information separate from research records. A tracking database will be used for recruitment and follow-up. This database will house information related to the participants in the study, such as phone numbers and addresses. No medically sensitive or outcome data will be stored in this database. This database will also track nonparticipants (i.e., those who have declined participation), only to the barest minimum, to ensure that they are not contacted again about participation. At the end of the study, all identifiable data of non-participants such as their names will be deleted. All study data (data abstracted from medical records, focus group record) will be stored in a separate, password-protected database without any personal identifiers. The databases will be created in Research Electronic Data Capture (REDCap), a secure, web-based application designed to support data capture. Data stored in REDCap is HIPAA-compliant and secure and stored on the Duke Heath Technology Services' servers behind the Duke Firewall.

Electronic files (e.g., audio files, video recordings and deidentified transcripts of focus groups) will be stored in separate password protected files on an Office of Information Technology (OIT) secured DUMC network drive. This drive will be backed to tape and secured by the OIT department on a daily basis. Access to the Duke network requires a password protected, 128-bit encrypted virtual private network connection provided by Cisco systems. Only the PI and individuals affiliated with the project will have access to these records.

Additional steps have been taken to maintain the security of information entered by participants into the mobile application and to ensure participants' safety. First, Patten Health's platform is engineered to keep PHI safe and secure. The platform is HIPAA compliant and third-party certified under the HITRUST Common Security Framework. Second, participants will be able to engage with group members through chat style forums on the mobile application. These forums will be set up and moderated by the PI and members of the research team. The PI and research team will receive real-time notification of and subsequently approve every message before it goes live. In the event that a participant attempts to post an inappropriate or concerning message (e.g., suicidal ideation), steps will be taken to contact the participant and provide appropriate intervention (e.g., referral to services provided within the DCI including clinical psychologists and medical family therapists affiliated with the Duke Cancer Patient Support Program, recommendations to access emergency care). The PI and members of the research team are licensed clinical psychologists who provide outpatient psychotherapy. They have received extensive training in recognizing and managing acute psychological crises and are well equipped to assist patients in the event significant distress or suicidal ideation is endorsed in the forum. Finally, the PI will use the Pattern Health web console to manage and monitor information input by participants (e.g., symptom severity ratings). Participants will be contacted in the event of a change in symptom severity and provided with appropriate intervention.

To ensure security while using Zoom, the following recommended steps will be taken:

Prior to Meetings:

- **Generate meeting ID automatically** – Unique meeting IDs expire 30 days after the meeting has occurred, and provide protection if a meeting ID was shared accidentally to a public audience.
- **Require meeting password** – Don't share your meeting password.
- **Enable waiting room** – Review attendees before admitting them to the meeting.

During Meetings:

- **Lock meeting** – Prevents any additional participants from joining.
- **Screen sharing is host only** – By default, only hosts can share their screens. Hosts can grant individuals the ability to share in the participant panel.
- **Remove unwanted participants** - Beside the participants name (in the Participant pane) select **M ore,** and then select **Remove.**
- **Report participant** - If a user made attempts to disrupt your meeting either by speaking, chatting, or showing offensive video, select the option **Report** which is available under the **Security** icon or on each participant's name. This will alert Zoom Support.

Recording Meetings:

- Attendees will be advised that they are being recorded.
- 'Display participants' names will be unchecked so that their name is not included in the recording.
- Only the meeting host will have permission to record the session.

Potential Benefits of the Proposed Research to Participants and Others. YA cancer survivors participating in the study will have the opportunity to discuss their experiences with pain, fatigue, psychological distress, and symptom interference as well as changes to their support system since their diagnosis and treatment with an interested interviewer (the PI) and/or peer survivors. Provider participants will have the opportunity to share their knowledge and expertise with the PI, who has an interest in improving the health and wellbeing of their patients. The possible benefits to society could include increased knowledge of the experience of YA cancer survivors as well as development of a behavioral symptom management intervention. Additionally, the proposed study may provide important information about approaches to identify, recruit and retain YA cancer survivors in research.

Importance of the Knowledge to be Gained. First, YA cancer survivors are an underserved and underrepresented population of survivors in clinical research. Second, physical symptoms and emotional distress are often persistent for YA cancer survivors and significantly interfere with important life areas and the achievement of normative life goals. Third, assistance with symptom management has been rated by YA cancer survivors, the Institute of Medicine, and The National Cancer Institute as a critical and unmet need; however, the majority of behavioral symptom management interventions designed for cancer survivors have been tested with older adult survivors (e.g., mean age $\geq$40) and have not been tailored to meet the unique developmental needs of YA survivors. Thus, the efficacy of these interventions among YA cancer survivors is largely unknown. Fourth, behavioral symptom management interventions rarely concurrently target physical and psychological symptoms. By developing an intervention to target multiple symptoms, which often occur in clusters, the developed intervention may result in reduced symptom interference. and have the potential to result in public health benefit by addressing variables consistently linked to significant social, economic, and health burden for YA cancer survivors.

Costs to the Subject

- Describe and justify any costs that the subject will incur as a result of participation; ordinarily, subjects should not be expected to pay for research without receiving direct benefit.

There are no costs to the subjects.

Data Analysis & Statistical Considerations

- Describe endpoints and power calculations. Provide a detailed description of how study data will be analyzed, including statistical methods used, and how ineligible subjects will be handled and which subjects will be included for analysis. Include planned sample size justification. Provide estimated time to target accrual and accrual rate. Describe interim analysis including plans to stop accrual during monitoring. Phase I studies, include dose escalation schema and criteria for dose escalation with definition of MTD and DLT.

Intervention Development (Phase 1):

Individual and focus group interviews will be transcribed verbatim by Sure Types A Lot. Sure Types a Lot is a transcription service with a business associate agreement with Duke Heath that covers PHI. Qualitative Description[115-117] using thematic analysis[118,119] will be used to analyze data from focus group participants, individual interviews, and user testers. Qualitative Description has been recommended for use by health researchers particularly in the context of intervention development because it stays close to the data and does not attempt to manipulate it from its original state.[115-117] This information can then be used to influence the development and/or refinement of an intervention.[115] Qualitative Description is especially useful for obtaining information about participants' experiences, opinions, and barriers/facilitators to a proposed intervention[117] and has been recommended for obtaining information to improve care.[115] Ultimately, qualitative description assists with providing a better understanding of the target audience's perspective rather than providing evidence of an existing theory or relying on high level interpretation, as is the case with other qualitative approaches.[131]

Open ended questions will be used to obtain information on areas that are poorly understood [e. g., symptom experience of young adult (YA) survivors] and amenable to intervention.[115-117] The questions will be developed from the research team's general knowledge of the symptom experience of cancer survivors, the team's prior work developing and testing interventions for cancer survivors that target multiple symptoms (i.e., pain, fatigue, distress; e.g.,[12,23,75]), published literature, national guidelines for YA oncology,[60] and discussions with experts in the field. The group leader /interviewer (Dorfman) will make field notes following each group to track emergent content areas. The goals of the groups and individual interviews areto better understand the needs/preferences of the YA target audience and to tailor the intervention to address these needs. From survivor focus group participants, we will obtain information on the symptom experience of YA cancer survivors, the interference of symptoms with important life areas specific to the developmental stage of YAs, and barriers to communicating about symptoms. YA survivors will also be asked to provide information about their preferences for the proposed structure and format of the intervention (e.g., number and frequency or in-person sessions, barriers to session attendance and homework completion) and their attitudes towards proposed intervention content. Oncology providers will be asked to provide information specific to the experiences of their YA cancer patients, including common treatments and treatment side effects and risks for and common late effects of treatments. Additionally, they will be asked about medical and non-medical interventions recommended to patients to assist with symptom management as well as the efficacy of these interventions.

Focus groups and individual interviews will be audio recorded and transcribed verbatim. Thematic analysis[120,121] will be used. Thematic analysis aims to identify, analyze and report common themes and trends across data.[121] Prior to analysis, we will develop a preliminary code book derived from major content areas. The code book will include a description of the codes as well as exemplar quotations and topics. Codes will be applied to focus group transcripts using NVivo.[122] Two independent individuals will code each transcript to ensure similar understanding of the codes and consistency in judgment.[120] Discrepancies in interpretation of the data or application of codes will be resolved as needed. The codebook will be updated throughout the coding process to add data-driven codes; as new codes emerge, they will be applied to previously coded text.[121] Next, the codes will be sorted into potential themes and subthemes using an iterative process as recommended.[121] A descriptive summary of the themes will be produced and used to inform development of the prototype intervention.[117]

A new sample of YA cancer survivors (N=10) will independently review the prototype materials (printed patient manuals, mobile application) and provide feedback on areas including intervention content, content presentation, and usability and functionality of the mobile application to help the research team better understand the experience of potential users of the intervention and refine the materials. The PI will be present during the user testing sessions, and a semi-structured interview guide will be used to guide the sessions. As with the focus groups, user testing sessions will be transcribed verbatim and analyzed using techniques from thematic analysis, as described above, and the final descriptive summary will be used to finalize the intervention.

Randomized Clinical Trial (Phase 2):

Participants (N=60) will complete 5 assessments over 12 months, the first occurring upon enrollment and subsequent assessments occurring every 3 months. Assessments will include measures of treatment acceptability, intervention component utilization, use of the mobile application (e.g., frequency of use, content visited), support received from group members, and open-ended questions of their perceptions of the intervention and mobile application and the benefits and costs of study participation.

Feasibility and Acceptability. Descriptive statistics (mean, standard deviation, percent, etc.) will be used to examine feasibility and acceptability data.

Patterns of change and relationships between key outcome variables. Using an intent to treat sample, multilevel models will be used to examine the rate and trajectory of change in intervention targets (i.e., symptoms, symptom interference) for the wait-list period (months 0-6; N=30, control arm only) and the intervention period (pre- and post-intervention, 3-month follow-up; N=60). Observations will be nested within individuals and individuals will be nested within clusters. Unconditional models will be used to determine fixed and random effects for the variables of interest. Time will be coded as months since baseline. Determination of linear versus quadratic change will be made by comparing the fit of the two models using the likelihood ratio test.[123-125]

Exploratory Aim. Self-efficacy and Support as Mediators. Bootstrap mediation will be used to examine the hypothesis that change in self-efficacy from baseline to post-treatment will mediate group differences in outcomes (i.e., symptoms, symptom interference) over time.[126-128] Bootstrap mediation analyses can be applied even when the sample size is small or moderate (e.g., N=20-60).[129,130]

Exit Interviews: A semi-structured interview guide will be used to guide the exit interviews. As with the focus groups and user testing sessions, exit interviews will be transcribed verbatim and analyzed using techniques from thematic analysis, as described above, and the final descriptive summary will be used to better understand subjects' experiences participating in the intervention.

Data & Safety Monitoring

- Summarize safety concerns, and describe the methods to monitor research subjects and their data to ensure their safety, including who will monitor the data, and the frequency of such monitoring. If a data monitoring committee will be used, describe its operation, including stopping rules and frequency of review, and if it is independent of the sponsor (per 45 CFR 46.111(a) (6)).

The proposed study carries minimal risk. Data obtained from participants will include information from medical chart review, participant interviews/focus groups, and self-reported information related to sociodemographic/medical characteristics, symptoms, and seymptom self-efficacy. All participants in the study will continue their usual care during the course of the study and be informed that choosing to participate in the study will in no way impact the treatment they receive at Duke University Medical Center (DUMC), and for Duke employees, their job at Duke. All survivors will continue to be monitored by their physicians at the Duke Cancer Institute (DCI) throughout the course of the study; thus participants' doctors will provide monitoring of their overall medical status. If a health concern is identified during contact with study staff, the survivors' treating oncologist will be contacted, and appropriate referrals for medical treatment will be provided to survivors. All research personnel who have direct contact with patients will be trained to observe and report any adverse events. The PI will report any adverse event to Duke's Institutional Review Board in real time. An adverse event is defined as any untoward medical event occurring during the clinical evaluation, which is causally related to the study protocol. A serious adverse event is defined as any event which results in death, is immediately life threatening, results in persistent or significant disability/incapacity, results in patient hospitalization, or is serious for any other reason representing significant hazard. All adverse events will be reported to Duke's IRB in real time.

All data will be stored on a secure server with multiple backups created regularly. All interactions with study participants will be under the direction of two licensed clinical psychologists (Dr. Caroline Dorfman, Dr. Rebecca Shelby). As a practicing clinical psychologist, the PI has experience with distressed patients with chronic disease. If a participant shows signs of experiencing high levels of physical or emotional distress that need to be addressed outside the context of this study, the PI will work directly with the participant to move forward in a way that is in the participant's best interest. No participant will be kept in the study if they are experiencing increased extreme distress. Study staff will be carefully trained to monitor participants' psychological status and report to Dr. Dorfman or Dr. Shelby when emotional distress

is identified in a participant. Drs. Dorfman and Shelby work directly with Cancer Patient Support Program at Duke as practicing licensed psychologists; they are integrated into the psychosocial care program at the DCI and have experience referring cancer patients who are distressed to appropriate psychosocial or psychiatric care within this large team of mental health professionals. They will use the same resources when making referrals for distressed participants in this study.

Video recordings will be recorded directly onto a Duke computer using a Duke laptop camera. The video files will be only temporarily stored on the local Duke computer and will be moved to Department of Psychiatry & Behavioral Sciences protected folder. The recordings will kept no longer than 6 years after the study completion date and at that time, will be destroyed.

Privacy, Data Storage & Confidentiality

- Complete the Privacy and Confidentiality section of the iRIS submission form.

Study Scope

Does this study have a cancer focus? Cancer focus includes studies that enroll >50% oncology or malignant hematology patients; or, preventing, detecting, and diagnosing cancer or understanding the impact of cancer on patients and their caretakers.

(•) Yes ( ) No

Does this study involve the use of a drug, biologic, food, or dietary supplement?

( ) Yes (•) No

Does this study involve the use of a medical device, an algorithm (whether computer based or not), an in vitro diagnostic test, or samples to look for biomarkers?

( ) Yes (•) No

Does this study employ magnetic resonance, including imaging (MRI), spectroscopy (MRS), angiography (MRA) or elastography (MRE) beyond the standard of care?

( ) Yes (•) No

Does this study specify or require the performance of diagnostic procedures using ionizing radiation (x-rays, DEXA, CT scans, nuclear medicine scans, etc.) that are beyond the standard of care?

( ) Yes (•) No

Does this study specify or require the performance of therapeutic procedures using ionizing radiation (accelerator, brachytherapy or systemic radionuclide therapy) that are beyond the standard of care?

( ) Yes (•) No

Does this study specify or require the use of a laser system for diagnosis or therapy that is beyond the standard of care (excludes the use of lasers as a standard surgical instrument)?

( ) Yes (•) No

Will the participant be subjected to increased or decreased ambient pressure?

○ Yes ◉ No

Do you plan to recruit subjects from Duke Regional Hospital (DRH)?

○ Yes ◉ No

Do you plan to recruit subjects from Duke Raleigh Hospital (DRAH)?

◉ Yes ○ No

Does this study include using the Duke logo in any advertisements?

◉ Yes ○ No

Is this study retrospective, prospective, or both?

"Retrospective" means that data or samples already in existence (collected prior to the study submission) will be used.
"Prospective" means there will be data or samples collected in this study for research purposes.

○ Retrospective
◉ Prospective
○ Retrospective and Prospective

If the study is both retrospective and prospective: Is this a review solely of information collected for non-research purposes (i.e. a review of medical records)?

○ Yes ○ No

Does this protocol include any research using botulinum toxin, including the FDA-approved clinical product (Botox)?

○ Yes ◉ No

Does this protocol involve the administration of any of the following materials to humans?

Category of Investigational Product	Examples
Any mRNA	Pfizer or Moderna COVID-19 vaccines
Any viral vector	AAV vector, adenoviral vector (e.g., J&J or Astrazeneca COVID-19 vaccine)
Any genetically-modified cells	CAR-T cells (e.g., Kymriah, or other autologous cells)
Any genetically-modified organisms (virus, bacterium, or other agents)	Oncolytic viruses (Imlygic, others), certain live attenuated vaccines, challenge viruses or challenge bacteria

Any plasmid DNA	DNA vaccines
Any other recombinant or synthetic nucleic acid (DNA, RNA, others)	

○ Yes ◉ No

Protocol Review and Monitoring Committee Section

Is this trial:

○ Interventional
◉ Observational
○ Other

A. Select one: (see Appendix A in help icon to the right for definitions)

☑ Cohort
☐ Case-Control
☐ Case-Only
☐ Case-Crossover
☐ Ecologic or community study
☐ Family-based
☐ Other:

B. Select the time perspective(s): (see Appendix A in help icon to the right for definitions)

☑ Prospective
☐ Retrospective
☐ Cross-sectional
☐ Other:

Provide the NCT number in clinicaltrials.gov (if this is an applicable clinical trial) for this submission:

NCT04035447

Supply the *estimated primary completion date* :

12/01/2023

Supply the *estimated study completion date* :

02/15/2024

Is there an independent Data Monitoring Committee (DMC/DSMB) for this protocol?

○ Yes ◉ No

Is this a Duke investigator-initiated multi-site trial?

○ Yes ◉ No

PROJECTED ACCRUAL **Projected accrual should be based on PI input, Disease Group Leader input, protocol priority, and availability of the subject population. Future PRMC decisions on renewal or termination will be based primarily on accrual projections provided below.**

Time from IRB Initial Review Date (Total number of subjects will calculate once you save section)

Projected # of subjects who are not screen failures	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6	Year 7	Year 8	Total
At DUHS	60		15	30	15				

Projected # of subjects who are not screen failures	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6	Year 7	Year 8	Total
At non-DUHS sites:	0	0	0	0	0	0	0	0	**0.00**

COMPETING STUDIES **List all studies that compete for the subject population being recruited for this study.**

eIRB #	Principal Investigator	Protocol Title
No records have been added		

Which oncology CRU disease group would this protocol belong to?

Multi

Will you use the services of the DCI Monitoring Team? All cancer focused Duke investigator initiated trials must use DCI Monitoring unless you have discussed an alternative with the Monitoring team.

○ Yes ◉ No

Will this protocol require the services of the DCI-IT team to help develop a study database?

○ Yes ◉ No

Duke Raleigh Hospital (Site Specific)

Study involves:

☐ Research data collection only
☐ Drug(s)

☐ Device(s)
☑ Therapy/treatment

Should you have questions regarding this form or approval process, please call Tracy Killette (Duke Raleigh) at telephone number (919) 862-5965.

Subject Population Groups and Enrollment

Population Groups (Select targeted population groups only):

☑ Adults
☐ Minors who are Wards of State
☐ Minors
☑ Duke Patients
☐ Pregnant individuals
☐ Fetuses
☐ Imprisoned Persons
☐ Adults incapable of giving consent
☐ Adults with diminished capacity
☐ Disabled subjects
☐ Students
☑ Employees
☐ Healthy Controls
☐ Deceased subjects
☐ Blanket Protocol

Students and employees over whom Key Personnel have a supervisory role may not be enrolled in this study.

Please select any population groups excluded from participation in this study:

☐ Pregnant individuals

Maximum number of subjects to be consented at Duke:

Enter a single number. If you anticipate consenting a range of subjects, enter the **upper** limit of the range. The number should represent the maximum number of subjects for the life of the study.

120

Maximum number of subjects to be consented at all sites:

Enter a single number. If you anticipate consenting a range of subjects, enter the **upper** limit of the range. The number should represent the maximum number of subjects for the life of the study.

120

Subject Procedures and Costs

Biobank - Does this study involve the collection, use, tracking, banking (storage) or distribution of human biological specimens?

Human biological specimens include blood or its components, healthy or diseased tissue, bodily fluids, DNA /RNA or human stem cells.

○ Yes ◉ No

Procedures

Check all that apply:

- [ ] Genetic Testing
- [ ] Gene Transfer
- [ ] DNA Banking
- [ ] Testing for Reportable Infectious Diseases
- [ ] Human Cell Banking
- [ ] *Use of Human Embryonic Stem Cells
- [ ] *Use of Human-induced Pluripotent Stem Cells
- [ ] *Use of Other Cells Derived from Human Embryos
- [ ] *Use of Human/Animal Chimeric Cells
- [ ] *Specialized Cell Populations for Cell Therapy
- [ ] Use of Human Tissue
- [ ] Use of Bodily Fluids
- [ ] Use of Blood (or its components)
- [x] Not Applicable

Will blood be drawn in this study for research purposes?

○ Yes ◉ No

Will the Operating Room be used in this study?

Include only research time, not clinical care time.

○ Yes ◉ No

Will there be extra costs to subjects or insurance as a result of the research (e.g. tests, hospitalization)?

○ Yes ◉ No

Will there be Subject Compensation?

◉ Yes ○ No

Compensation for Travel / Lost Income (in USD):

150

Other Subject Compensation:

Participants will be reimbursed up to a total of $150 for expenses related to participation (parking, gas, and time). This reimbursement will consist of $30 for completing each of the five study assessments. Participants completing the exit interviews will be compensated $15 for their time.

Subject Recruitment Materials

For each document to be reviewed, use the table below to provide the following information:

Attach a copy of each advertisement to be used with this study in the Initial Submission Packet. If any advertisement will have multiple wording variations, attach a copy of each version of the advertisement. For media materials (i.e., videos, radio ads, commercials), include transcripts and links.

If an advertisement includes the Duke logo, be sure to indicate "yes" in Study Scope section.

The IRB must approve all study advertisements used to recruit.

Types of subject recruitment materials include, but are not limited to, the following:

Direct Advertising
Posters
Billboards
Flyers
Brochures

Media Advertising
Newspaper Ads
Magazine Ads
Radio Ads
TV commericals / Video
Internet website
Social Media

Other Types of Advertising
Newsletter
Email
Postcards / Letters

(Note: Doctor-to-Doctor letters do not require IRB approval)

Document name	Material category	Location material displayed	Has this material previously been approved by the IRB?
Survivor Brochure	○ Billboard / Flyer / Poster ◉ Brochure ○ Internet website / Email ○ Letter / Postcard ○ Phonescript ○ Radio ○ Television / Video ○ Newsletter / Newspaper / Magazine ○ Other	Please be specific. For example, "Duke" would not be an appropriate location. "Duke Hospital Television" would be an appropriate response. Mailed to potential survivor participants with invitation letter	◉ Yes ○ No
Letter to potential survivor participants	○ Billboard / Flyer / Poster ○ Brochure ○ Internet website / Email ◉ Letter / Postcard ○ Phonescript ○ Radio ○ Television / Video ○ Newsletter / Newspaper / Magazine	Please be specific. For example, "Duke" would not be an appropriate location. "Duke Hospital Television" would be an appropriate response. Letter mailed to potential participants	◉ Yes ○ No

	○ Other		
Email to potential provider participants	○ Billboard / Flyer / Poster ○ Brochure ○ Internet website / Email ○ Letter / Postcard ○ Phonescript ○ Radio ○ Television / Video ○ Newsletter / Newspaper / Magazine ○ Other	Please be specific. For example, "Duke" would not be an appropriate location. "Duke Hospital Television" would be an appropriate response. Letter will be emailed to potential provider participants inviting them to participate in the study	◉ Yes ○ No
Phone Script to Recruit Survivors	○ Billboard / Flyer / Poster ○ Brochure ○ Internet website / Email ○ Letter / Postcard ◉ Phonescript ○ Radio ○ Television / Video ○ Newsletter / Newspaper / Magazine ○ Other	Please be specific. For example, "Duke" would not be an appropriate location. "Duke Hospital Television" would be an appropriate response. Phone Script to Recruit Survivors	◉ Yes ○ No
Phone Script to recruit Providers	○ Billboard / Flyer / Poster ○ Brochure ○ Internet website / Email ○ Letter / Postcard ◉ Phonescript ○ Radio ○ Television / Video ○ Newsletter / Newspaper / Magazine ○ Other	Please be specific. For example, "Duke" would not be an appropriate location. "Duke Hospital Television" would be an appropriate response. Phone Script to recruit Providers	◉ Yes ○ No
Phone script to recruit user testers	○ Billboard / Flyer / Poster ○ Brochure ○ Internet website / Email ○ Letter / Postcard ◉ Phonescript ○ Radio ○ Television / Video ○ Newsletter / Newspaper / Magazine	Please be specific. For example, "Duke" would not be an appropriate location. "Duke Hospital Television" would be an appropriate response. Phone script to recruit user testers.	◉ Yes ○ No

	○ Other		
Letter to potential user testers	○ Billboard / Flyer / Poster ○ Brochure ○ Internet website / Email ◉ Letter / Postcard ○ Phonescript ○ Radio ○ Television / Video ○ Newsletter / Newspaper / Magazine ○ Other	Please be specific. For example, "Duke" would not be an appropriate location. "Duke Hospital Television" would be an appropriate response. Letter to recruit user testers	◉ Yes ○ No
Brochure for user testing	○ Billboard / Flyer / Poster ◉ Brochure ○ Internet website / Email ○ Letter / Postcard ○ Phonescript ○ Radio ○ Television / Video ○ Newsletter / Newspaper / Magazine ○ Other	Please be specific. For example, "Duke" would not be an appropriate location. "Duke Hospital Television" would be an appropriate response. Mailed to potential survivor participants with invitation letter	◉ Yes ○ No
RCT Survivor Brochure	○ Billboard / Flyer / Poster ◉ Brochure ○ Internet website / Email ○ Letter / Postcard ○ Phonescript ○ Radio ○ Television / Video ○ Newsletter / Newspaper / Magazine ○ Other	Please be specific. For example, "Duke" would not be an appropriate location. "Duke Hospital Television" would be an appropriate response. Mailed to potential survivor RCT participants with invitation letter	○ Yes ◉ No
RCT Letter to Potential Survivor Participants	○ Billboard / Flyer / Poster ○ Brochure ○ Internet website / Email ◉ Letter / Postcard ○ Phonescript ○ Radio ○ Television / Video ○ Newsletter / Newspaper / Magazine ○ Other	Please be specific. For example, "Duke" would not be an appropriate location. "Duke Hospital Television" would be an appropriate response. Letter mailed to potential RCT participants	○ Yes ◉ No

RCT Phone Script to Recruit Survivors	○ Billboard / Flyer / Poster ○ Brochure ○ Internet website / Email ○ Letter / Postcard ◉ Phonescript ○ Radio ○ Television / Video ○ Newsletter / Newspaper / Magazine ○ Other	Please be specific. For example, "Duke" would not be an appropriate location. "Duke Hospital Television" would be an appropriate response. Phone script to recruit potential RCT participants	○ Yes ◉ No
Mychart recruitment letter	○ Billboard / Flyer / Poster ○ Brochure ○ Internet website / Email ○ Letter / Postcard ○ Phonescript ○ Radio ○ Television / Video ○ Newsletter / Newspaper / Magazine ◉ Other	Please be specific. For example, "Duke" would not be an appropriate location. "Duke Hospital Television" would be an appropriate response. Mychart recruitment letter	○ Yes ◉ No

Consent Process

Attach draft consent forms in the Initial Review Submission Packet.

Consent forms must be MS Word documents and follow the specific format outlined by the IRB. **Click here** to download a copy of the consent form template.

Note: Please do not edit the section of the footer that contains the Protocol ID, Continuing Review and Reference Date fields. Those fields will be used to stamp the final consent form when it is approved by the IRB. If you want to add an internal version date, please put it in the header.

Who will conduct the consent process with prospective participants?

Provide their role(s) in this study (PI, Study Coordinator, etc.):

Caroline Dorfman, PI
Juliann Stalls, Collaborator
Michael Willis, Study Coordinator
Smrithi Divakaran, Study Coordinator

Who will provide consent or permission?

(Select all that apply):

- [x] Participant
- [ ] Parent(s) or Legal Guardian(s)
- [ ] Legally Authorized Representative (LAR)

How much time will the prospective participant (or legally authorized representative) have between being approached about participating in the study and needing to decide whether or not to participate?

If you are not giving the person overnight to consider whether or not to participate, please justify.

As much time as needed.

Where will the consent process occur?

The consent process may occur in the Duke Oncology Clinics or in the offices of the Pain Prevention Research and Treatment Program where the PI is housed.
Survivor participants will also have the opportunity to complete the consent process online. For online consent, interested survivors will receive a secure email directing them to a unique REDCap link and code to an online informed consent document. There is evidence that informed consent provided online does not differ from that obtained in person. For phone consent, interested patients will be mailed a copy of the consent form to review and fill out with a witness.

What steps will be taken in that location to protect the privacy of the prospective participant?

The consent process will take place in a private room to protect the privacy of the prospective participant.

For online consent, interested survivors will receive a secure email directing them to a unique REDCap link and code to an online informed consent document. there is evidence that informed consent provided online does not differ from that obtained in person. Participants will be instructed to complete the online consent in a private location of their choosing. For the phone consent, participants will be in the privacy of their own homes.

How much time will be allocated for conducting the initial consent discussion, including presenting the information in the consent document and answering questions, with each prospective participant?

As much time as needed.

What arrangements will be in place for answering participant questions before and after the consent is signed?

For the in-person consent process, participants will be asked numerous times throughout the process if they have questions and/or understand what they have been told. For the online and phone consent process, study staff will be available over the phone and by email to answer questions before, during and after the consent is reviewed and signed.

Describe the steps taken to minimize the possibility of coercion or undue influence.

Participants will be encouraged to take their time making their decision about whether or not to participate. Participants will be reminded that participation in the study is voluntary and they can withdraw at anytime. They will also be told that their decision whether or not to participate will in no way affect their healthcare at DUMC or the DCI. If a participant is a Duke employee, they will be informed that their decision whether or not to participate will in no way affect their job status at DUMC or the DCI.

What provisions will be in place to obtain consent from participants who do not read, are blind or who do not read/understand English?

Due to the nature of the study, participants who are blind or do not read/understand English will not be included in the study.

Do you plan to obtain written consent for the conduct of research?

(●) Yes ( ) No

Protected Health Information (PHI)

Indicate how you intend to use potential subjects' Protected Health Information (PHI):

( ) I will review, but not record, PHI prior to consent.
(●) I will record PHI prior to consent.
( ) I do not intend to use PHI prior to consent.
( ) I will record PHI without consent. (decedent research, database repository, chart review)

Request for Waiver or Alteration of Consent and/or HIPAA Authorization

Will the population include deceased individuals?

( ) Yes (●) No

This waiver request applies to the following research activity or activities:

☑ Scheduling of research activities in MaestroCare and/or the recording of PHI via telephone for screening purposes prior to obtaining written consent for the research. Scheduling of research activities in MaestroCare and/or the recording of PHI via telephone for screening purposes prior to obtaining written consent for the research.
☑ Ascertainment (identification, selection) and/or recruitment of potential subjects while recording identifiable private information, such as protected health information (PHI), prior to obtaining the subject's consent.
☐ Conduct of the research project without obtaining verbal or written consent and authorization.

Note: Answer the questions below as they pertain solely to PHI collected prior to consent.

Provide the following information:

List the elements of informed consent and/or HIPAA authorization for which waiver or alteration is requested:

- Provide the rationale for each.

Information necessary to recruit patients will be used for this study. Additional information will also be collected to allow us to describe patients who consent verse those who do not. Identifying information will only be kept for patients who decline consent to prevent future efforts to recruit a patient into the study who has already declined consent. A waiver is being requested for all elements of consent and HIPAA authorization.

List the specific protected health information (PHI) to be collected and its source(s):

- (Note: PHI = health information + identifiers)

The PHI will be gathered from electronic medical records and includes patient's name, address, telephone number, email address, oncologist's name, recruitment site, MRN, date of birth, race, and ethnicity. To determine eligibility, we will record cancer treatment status (surgery, chemotherapy, radiation, and/or medication), cancer type, and cognitive and hearing impairments recorded in medical records.

Criteria for Waiver: The DUHS IRB may waive the requirement for informed consent and authorization if all of the following criteria are met:

- Please respond to each item in the space below using protocol-specific language to provide justification:

a) The research or clinical investigation involves no more than minimal risk to subjects:

The research presents no more than minimal risk to subjects and involves to procedure in which written consent is normally required outside the research setting.

b) The waiver or alteration will not adversely affect the rights and welfare of the subjects. Include a description of any measures to be taken to ensure that the rights and welfare of subjects will be protected:

All subjects who agree to participate will participate in the informed consent process, which will include the authorization and detail their rights to the study. PHI for potential subjects who do not consent will be destroyed.

c) Whenever appropriate, the subjects will be provided with additional pertinent information after participation:

All subjects who agree to participate will participate in the informed consent process, which will include the authorization and detail their rights to the study. PHI for potential subjects who do not consent will be destroyed.

d) If this research activity relates to research involving deception, explain how subjects will be provided with additional pertinent information after study participation and what information will be provided. Otherwise indicate "not applicable":

Not applicable.

e) The use or disclosure of protected health information involves no more than minimal risk to the privacy of individuals, based on, at least, the presence of the following elements (e1. and e2.)

Demonstrate that the use or disclosure of PHI involves no more than minimal risk to the privacy of subjects by describing the plans requested below:

e1) An adequate plan to protect the identifiers from improper use and disclosure. Describe the plan (how protection will be accomplished) and indicate where the PHI will be stored and who will have access:

The identifiers will only be used by minimal study staff who will select eligible recruits for this study. This information will be kept in two places: (1) a password-protected spreadsheet in electronic files housed behind the Duke University Medical Center (DUMC) firewall, and (2) a REDCap database. Both will contain patients' name, MRN, and date of birth. The spreadsheet will contain information relevant to initial eligibility screening (patients' cancer treatment status variables, cancer stage, cancer type, diagnosis date, treatments, date of treatment completion). The REDCap database will be used to track study staff's contact with patients approved for approach by the patients' medical oncologists (if applicable) and, therefore, will include patients' contact information (phone number, address, email address), race, ethnicity, oncologist name, recruitment site, and non-PHI internal tracking information (e.g., when a patient was contacted, the study the patient was approached for, the date their oncologist provided permission for the study team to contact them when applicable, study status).

e2) An adequate plan to destroy the identifiers at the earliest opportunity consistent with conduct of the research, unless there is a health or research justification for retaining the identifiers or such retention is otherwise required by law.

Describe the plan (how and when identifiers will be destroyed and by whom). If there is a health or research justification for retaining the identifiers or such retention is otherwise required by law, provide the reason to retain identifiers:

For patients who enroll this information will be retained for the research record and will be subject to appropriate safeguards and destroyed with the research record. For those who decline, all identifying information will be deleted from the eligibility screening spreadsheet. We are requesting permission to retain information stored in the REDCap database so that we do not contact a person who has already declined for the study. This will allow us to respect the wishes of the patients who do not want to be involved. This will also allow us to retain demographic information and basic medical information on patients who are eligible but decline to see if our data is systematically under including certain subgroups of the study population that would limit our ability to generalize findings.

e3) Adequate written assurances that the protected health information will not be reused or disclosed to any other person or entity except (i) as required by law, (ii) for authorized oversight of the research study, or (iii) for other research for which the use or disclosure of PHI would be permitted by the HIPAA Privacy Rule. By electronically signing this submission, the PI provides this written assurance:

I agree.

f) The research could not practicably be conducted or carried out without the waiver or alteration:

- Explain why informed consent/authorization can not be obtained from subjects.

This waiver is necessary to be able to determine patients' eligibility for the study and to be able to contact the patient to inquire about interest in the study.

g) The research could not practicably be conducted or carried out without access to and use of the protected health information:

This waiver is necessary to be able to determine patients' eligibility for the study and to be able to contact the patient to inquire about interest in the study.

h) For research using biospecimens or identifiable information, the research could not practicably be carried out without access to and use of the protected health information:

This waiver is necessary to be able to determine patients' eligibility for the study and to be able to contact the patient to inquire about interest in the study.

Waiver of Documentation of Consent and HIPAA Authorization for Scheduling in MaestroCare and/or the recording of PHI via telephone for screening purposes:

These research activities prior to obtaining written consent for the study presents no more than minimal risk of harm to subjects:

- (●) True
- ( ) False

These are procedures for which written consent is normally not required outside of the research context:

- (●) True
- ( ) False

An IRB-approved phone script will be used to obtain verbal consent from subjects for scheduling and/or screening prior to obtaining written consent for the study:

- (●) True
- ( ) False

Privacy and Confidentiality

Explain how you will ensure that the subject's privacy will be protected:

Consider privacy interests regarding time and place where subjects provide information, the nature of the information they provide, and the type of experience they will be asked to participate in during the research.

All recruitment procedures will comply with HIPAA guidelines, and all protocols and procedures are subject to Institutional Review. All participants will be informed that participation is voluntary and will in no way affect their medical treatment at the DCI or DUMC. The recruitment procedures for survivor participants will be as follows:

a) Duke Teen and Young Adult (TYA) Oncology Database. Supported by a grant from the St. Baldrick's Foundation (IRB protocol: Pro00100124), the Duke TYA Oncology program has established a database of teens and young adults (aged 15-29) treated at Duke. Individuals consenting to be included in the database are asked if they would be willing to be participate in future research studies. Those interested, will be approached to participate in the proposed study.

b) Electronic Health Records of the DCI. Once a potential participant has been identified, his/her medical provider will be notified that study staff would like to attempt to recruit him/her for this study. Potential participants will be mailed a letter signed by the PI informing them about the study, describing the study, and requesting participation in the study. Potential participants will be informed that they will be contacted in the clinic at their next scheduled appointment. Potential participants will be given the phone number of the PI to call if they have questions or to request not to be contacted. The study staff will describe the study purpose, procedures, risks and benefits, and provide potential participants with an opportunity to discuss their questions and concerns as well as assess for participants' eligibility. Informed consent will be documented by signature on forms approved by the appropriate IRB for eligible and interested survivors. In the event that the study team is unable to make contact with the participant during the scheduled clinic appointment (e.g., due to time constraints), the participant will be informed that we would like to contact him/her by telephone to further discuss the study and set up a time to complete informed consent procedures. Survivors may also be referred to the study by their providers. The medical team will introduce the study, provide participants with the study brochure, and, if interested, the PI or study staff member will contact the survivor to assess eligibility, further describe the study, and discuss questions and concerns.

If a cancer survivor is not eligible for the study, or if he/she decides he/she is not/no longer interested in participating in the study, the participant will be provided with the names and contact information of resources offered at through the DCI or in the community, as appropriate. All participants will be told that they can discontinue study participation at any time with no penalty or impact to their medical care.

If a patient agrees to be approached or has received a letter but not opted out of being contacted, then study staff will approach the patient and the study will be described in a private area of the clinic or during a private telephone call.

Participants will be reminded that they can decline to respond questions (qualitative or quantitative) during the focus group, individual interviews or user testing session that make them feel embarrassed or uncomfortable without consequence. If a participant endorses psychological distress due to study participation, the PI, a clinical psychologist, will determine appropriate course of action. The PI will facilitate appropriate referrals to services provided within the DCI (e.g., clinical psychologists and medical family therapists affiliated with the Duke Cancer Patient Support Program) and the Duke Department of Psychiatry and Behavioral Sciences. Contact information for the PI is provided should participants have any questions or concerns.

The data obtained will be collected specifically for the proposed research project. Research material obtained from human subjects will include information from medical chart review and patient/provider interviews (i.e., focus groups). Medical chart review will be used to confirm survivor eligibility. Focus groups and individual interviews will be audio recorded to allow for transcription and analysis of qualitative data. Participants will be identified by subject number in the transcripts. The audio of the focus groups will be stored separately from the transcripts and other study data in electronic files housed behind the Duke University Medical Center (DUMC) firewall.

Mobile App Data Storage and Security. App data is stored in a MySQL database. This is a standard security feature, which allows the database to be kept separate from the web server to protect access to the database. In addition, the hard drive of the database machine will be encrypted, which will provide security in case the hard drive is physically compromised.

Magazine Article Feature.
Duke Cancer Institute's Breakthroughs magazine plans to highlight this research study. The magazine story author would interview a research participant (or participants) who had participated in the study intervention. The magazine article may also include photos of the featured participant(s) taken or provided specifically for purposes of the magazine feature. Only participants who have completed participation in the study will be approached; research participants who are approached for will be reminded that agreeing to participate in the magazine article is voluntary and will have no bearing on their involvement in this research or any aspect of their care at Duke Health. Any research participant who agrees to be included in this magazine article will sign a HIPAA release form and a photo release form consistent with institutional policy.

Describe how research data will be stored and secured to ensure confidentiality:

How will the research records and data be protected against inappropriate use or disclosure, or malicious or accidental loss or destruction? Records and data include, for example, informed consent documents, case report forms or study flow sheets, survey instruments, database or spreadsheets, screening logs or telephone eligibility sheets, web based information gathering tools, audio/video/photo recordings of subjects, labeled specimens, data about subjects, and subject identifiers such as social security number.

Two password-protected databases will be used to ensure confidentiality of participant information and data by keeping identifying information separate from research records. The first database, used for

tracking and recruitment, will house the contact information of individuals who may be eligible for the study as well as participants who have agreed and those who have declined to participate. No medically sensitive or outcome data will be stored in this database, and all identifiable data of non-participants (e.g., names) will be deleted. The second password-protected database will store study data. Participants' data and research records will be identified using subject identification numbers. A document linking participant names to subject id numbers will be stored separately from data and research records in a password-protected database. Deidentified transcripts of focus groups and interviews will be stored in separate password protected, electronic files. All electronic research records and files will be stored in password protected computer files on an Office of Information Technology (OIT) secured DUMC network drive. This drive will be backed to tape and secured by the OIT department on a daily basis. Only the PI, sponsors, and study staff affiliated with the project will have access to the research records. Additionally, individuals participating in focus groups will be instructed to maintain participants' confidentiality at the onset of the group. Participants will be asked not to talk about other participants' comments outside of the group.

Mobile App Data Storage and Security. App data is stored in a MySQL database. This is a standard security feature, which allows the database to be kept separate from the web server to protect access to the database. In addition, the hard drive of the database machine will be encrypted, which will provide security in case the hard drive is physically compromised.

Application Questions Complete

Please click Save & Continue to proceed to the Initial Submission Packet.

The Initial Submission Packet is a short form filled out after the protocol application has been completed. This is an area to attach protocol-related documents, consent forms, and review the application.