Title: Integration of Multimodal Cancer Predisposition Genetic Counseling Practices Within the Pediatric Oncology Setting: Digital Care Plans for Patients With CPS

NCT Number: NCT05736497

Date: June 18, 2024

Title:	Integration of Multimodal Cancer Predisposition Genetic Counseling Practices Within the Pediatric Oncology Setting: Digital Care Plans for Patients With CPS
Short Title	Care Plans for Cancer Predisposition
eIRB Number:	21-019151
Protocol Date:	June 18, 2024

Amendment 1 Date: December 1, 2022

Amendment 2 Date: May 12, 2023

Amendment 3 Date: September 28, 2023

Amendment 4 Date: November 17, 2023

Amendment 5 Date: May 9, 2024

Amendment 6 Date: June 18, 2024

Amendment 7 Date: November 7, 2024

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Abbreviations and Definitions of Terms

AE	Adverse event
AYA	Adolescent/Young Adult
CHOP	Children's Hospital of Philadelphia
CPS	Cancer Predisposition Syndrome
PrePARE	Predisposition Planning, Adjustment, Recommendations, and Education

Abstract

Context:

As over 15% of pediatric cancers are associated with a cancer predisposition, it is increasingly becoming standard of care for children with cancer, as well as those with suspected hereditary risk, to be evaluated for germline cancer predisposition. Unfortunately, the increase in pediatric genetic testing has exceeded the pace of research supporting effective cancer surveillance in positive cases. Additionally, guidelines for cancer predisposition management are not easily accessed or understood by families; thus, there is often a disconnect between the understanding and retention of such information relayed to families. Thus, we will develop innovative, scalable digital health solutions to augment genetic counseling resources to support patients and families, including a digital care plan and targeted text-message alerts for families with an existing Cancer Predisposition Syndrome (CPS).

Objectives:

Develop and evaluate acceptability, feasibility, and preliminary efficacy of digital care plan and accompanying text message reminders for children and adolescents with a known CPS.

Study Design:

Quasi-experimental design with pre- post- testing of same cohort.

Setting/Participants:

This is a 2-year, single-site study that is being conducted at the Children's Hospital of Philadelphia (CHOP). A total of 100 families with a child with a CPS (diagnosis for five years or less) will be approached in the Cancer Predisposition Clinic at CHOP.

Study Interventions and Measures:

We will develop and implement a digital care plan and targeted text-message alerts with pre- and post-test evaluation of understanding of existing cancer predisposition guidelines, decisional satisfaction, and distress. Data will be collected at 3 time points: T0: prior to digital care plan; T1: 3 months after implementation; T2: 6 months follow up.

Protocol Synopsis

Study Title	Integration of Multimodal Cancer Predisposition Genetic Counseling Practices Within the Pediatric Oncology Setting: Digital Care Plans for Patients With CPS
Funder	National Institute of Health
Study Rationale	As over 15% of pediatric cancers are associated with a cancer predisposition, it is increasingly becoming standard of care for children with cancer, as well as those with suspected hereditary risk, to be evaluated for germline cancer predisposition. Unfortunately, the increase in pediatric genetic testing has exceeded the pace of research supporting effective cancer surveillance in positive cases. Additionally, guidelines for cancer predisposition management are not easily accessed or understood by families; thus, there is often a disconnect between the understanding and retention of such information relayed to families. Thus, we will develop innovative, scalable digital health solutions to augment genetic counseling resources to support patients and families, including a digital care plan and targeted text-message alerts for families with an existing Cancer Predisposition Syndrome (CPS).
Study Objective(s)	Develop and evaluate acceptability, feasibility, and preliminary efficacy of PrePARE and accompanying text message reminders for children and adolescents with a known CPS.
Test Article(s)	Digital care plans and text message reminders for families with a known CPS
Study Design	Quasi-experimental design with pre- post- testing of same cohort, before and after delivery of care plan and accompanying messages.
Subject Population key criteria for Inclusion and Exclusion:	**Inclusion Criteria** 1. Parent of child with CPS diagnosed within 5 years +/- proband if age 12-26 2. Proband received care at CHOP Cancer Predisposition clinic 3. If proband history of cancer, appropriate per oncologist

	4. English speaking **Exclusion Criteria** 1. Cognitive impairment limiting participation
Number Of Subjects	Anticipated total of 180 subjects will be recruited at CHOP.
Study Duration	Each subject's participation will last approximately 6 months.
Study Phases **Screening** **Study Treatment** **Follow-Up**	(1) Screening: screening for eligibility by record review and consultation with medical team (2) Obtaining consent and baseline survey (3) Receipt of PrePARE Care Plan and enrollment in text message system (4) Repeat survey 3 months after implementation and (5) Repeat survey at 6 months after implementation
Efficacy Evaluations	Understanding of existing cancer predisposition guidelines
Safety Evaluations	The PI will monitor the safety of the subjects and data and determine the need for additional psychosocial support.
Statistical And Analytic Plan	Mean and SD for the pre- and post-test (measured at 3 and 6 months) scores and the change scores will be calculated, and paired t test will be used
DATA AND SAFETY MONITORING PLAN	PIs will be responsible for data quality management and ongoing assessment of safety

Table 1: Schedule of Study Procedures

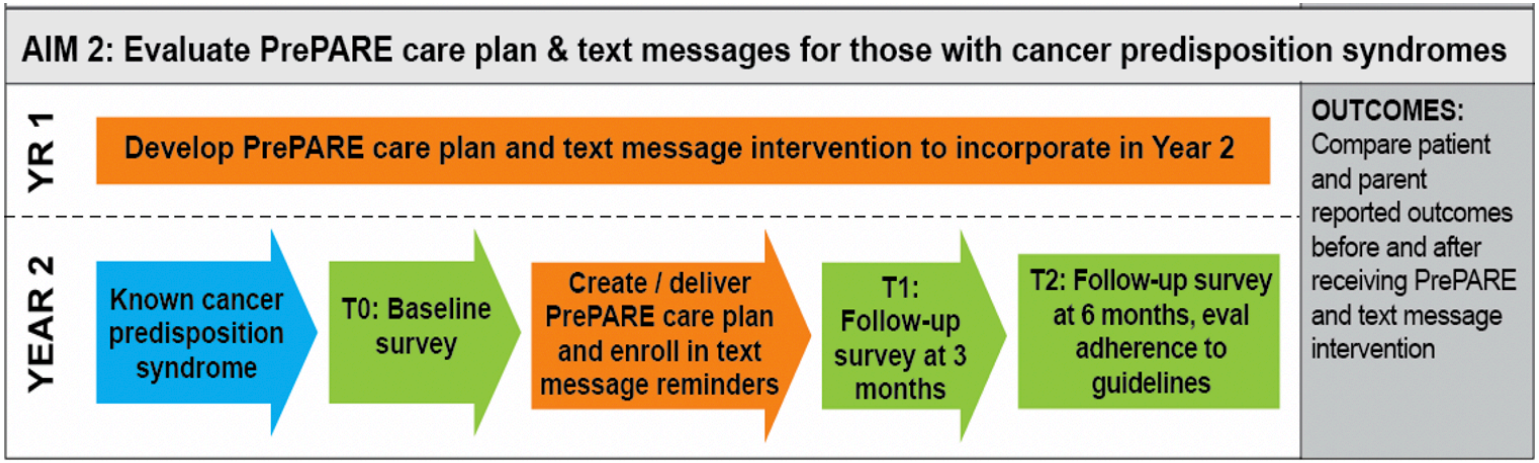

Table 1: Introduction of digital supports to clinical care, workflow Year 1 and 2. Blue indicates standard of care timepoints, orange indicates study interventions, and green indicates data gathering points.

Table 2: Cancer Prediposition SYNDROMES

Cancer Predisposition Syndrome (CPS)
Li-Fraumeni Syndrome
PTEN Hamartoma Tumor Syndrome
Beckwith-Wiedemann Syndrome
Familial Adenomatous Polyposis
Juvenile Polyposis Syndrome
Hereditary Pheochromocytoma & Paraganglioma
Peutz-Jegher Syndrome
Noonan Syndrome
DICER1 Syndrome
Gorlin Syndrome

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Background Information and Rationale

Introduction

The long-term goal of this research is to develop interventions that will ultimately transform delivery of care for children and adolescents undergoing testing for, and living with, cancer predisposition syndromes (CPS). This proposal will focus on the development and initial evaluation of novel interventions. We specifically propose a connected health approach whereby we will develop and test technology-based tools that include an open access individualized digital care plan system for those with a CPS known as PrePARE (Predisposition Planning, Adjustment, Recommendations, and Education), and accompanying text messages to support individualized surveillance. This proposal represents a novel extension of our digital health program of research, which has included the adaptation of UPenn's OncoLife care plan system for childhood survivors (https://smartalacc.oncolink.org/).

The successful completion of this study will create novel, scalable, and generalizable digital supports for families to augment genetic counseling services, inform best practices for genetic counseling, and inform a future multisite trial to further evaluate the impact of the new tools.

Name and Description of Investigational Intervention

We will develop individualized digital care plan system for those with a CPS known as PrePARE, and accompanying text messages to support individualized CPS surveillance.

Name	Description
PrePARE Care Plans	Using the digital platform of OncoLife, PrePARE will be a care plan to incorporate recommendations that are patient-specific. Content will reflect surveillance recommendations including imaging, laboratory studies, physical exam, endoscopy recommendations, and lifestyle modifications. It will be personalized to the diagnosis, and in the case of cancer history, will also include survivorship guidelines.
Text Message Intervention	Text messages will be sent to caregivers (and probands 12+ if they opt in) with information reinforcing content from their individual care plans such as healthy lifestyle tips and coping resources. Text messages will also prompt caregivers (and probands 12+ if they opt in) to make appointments based on individualized recommendations and will send appointment reminders confirmation requests. Additional text messages reminding participants to schedule and attend medical appointments will be sent by study team via CHOP issued device.

Relevant Literature and Data

There is growing evidence that ≥15% of childhood cancer patients harbor a germline (heritable) cancer predisposition, some of which are associated with a 10,000-fold increased cancer risk.[1,2] The increase in combined somatic and germline (tumor/normal) sequencing conducted at cancer diagnosis, as well as increased referral for testing in children with suspected cancer predisposition who have not yet developed cancer, has led to a rapid increase in identification of cancer predisposition in children. Many of these cases would not have been identified just a few years ago, prior to testing advances and changes in referral guidelines. However, the increase in pediatric genetic testing has exceeded the pace of deployment of genetic counseling resources. Moreover, positive results usually indicate the need for lifelong follow-up, including complex cancer surveillance, which can be difficult to understand and implement. Unfortunately, there are not enough genetic counselors to support cancer surveillance in patients who test positive for CPS. Thus, there is a critical need for innovative and scalable interventions that efficiently allocate resources and optimize care for pediatric patients and their families receiving testing for cancer predisposition.

Lifelong Impact of Cancer Predisposition

Results of genetic testing may reveal findings that are essential for long term health, requiring preventative and/or intervention measures. Despite the increase in pediatric genetic testing, and consensus on recommendations for those with significant findings,[3] there has not been a standardized approach to disseminating information about findings and implications for long term health and well-being. Guidelines for cancer predisposition management are not easily accessed or understood by families; thus, there is often a disconnect between the understanding and retention of such information relayed to families.[4] The delivery of digital interventions to enhance self-management of cancer survivors, as we have tested in our robust research program serves as a comparable framework for next steps in delivery of resources for families with cancer predisposition to address these limitations of care and fill research gaps of this burgeoning area. These resources will also be modifiable for other genetic syndromes requiring lifestyle modifications and surveillance.

Technology-Based Interventions

Digital health interventions are critical for "connected health", which leverages technology to meet a patient's needs in a proactive and efficient manner.[5] Texting interventions have demonstrated significant improvements in knowledge, health-related behaviors and clinic attendance of adolescents and adults with other chronic health conditions,[6-11] and in lifestyle modifications including adherence to pediatric health maintenance guidelines.[12] Texting is low-cost, highly available, brief, and can be written informally at a low reading level, making it applicable across diverse populations.[13-16] Care plans, used in cancer survivorship and created using algorithm-based digital platforms, are personalized documents that describe diagnoses, screening and prevention, and health maintenance, and have been shown to improve knowledge, engagement, and confidence.[17,18] Care plans for cancer predisposition have not been used and tested. Taken together, interventions that leverage technology have promise to fill a gap in counseling services and to be modifiable for other settings.

Compliance Statement

This study will be conducted in full accordance all applicable Children's Hospital of Philadelphia Research Policies and Procedures and all applicable Federal and state laws and regulations including 45 CFR 46. All episodes of noncompliance will be documented.

The investigators will perform the study in accordance with this protocol, will obtain consent and assent, and will report unanticipated problems involving risks to subjects or others in accordance with The Children's Hospital of Philadelphia IRB Policies and Procedures and all federal requirements. Collection, recording, and reporting of data will be accurate and will ensure the privacy, health, and welfare of research subjects during and after the study.

Study Objectives

The long-term goal of this research is to develop interventions that will ultimately transform delivery of care for children and adolescents living with CPS. In individuals with an existing cancer predisposition syndrome, it will evaluate the use of a digital care plan and text message intervention to improve knowledge of and adherence to surveillance guidelines.

Primary Objective

The primary objective of this study is to develop and evaluate preliminary efficacy of PrePARE care plans and accompanying text message reminders for families with a known CPS with pre- and post-test evaluation at two times points after baseline [3 months and 6-months]. Knowledge of existing cancer predisposition guidelines will be assessed. Decisional satisfaction and distress will also be measured.

Secondary Objectives

The secondary objective is to evaluate acceptability and feasibility of the care plans and text message reminders. A survey of acceptability will be administered. Feasibility will be assessed with absence of technical difficulties and CRC ability to create care plan in under 15 minutes.

Investigational plan

General Schema of Study Design

Screening Phase

Potential subjects will be screened using the protocol inclusion and exclusion criteria. Parental/guardian permission (informed consent) and, if applicable, child assent, will be obtained prior to any study related procedures being performed. Patients will be approached in the in person in the Cancer Center or by phone.

Study Treatment Phase (start of the study intervention)

During year 1, we will develop the digital interventions- PrePARE care plans and text message reminders. We will begin participant recruitment and implementation of the digital interventions in year 2.

Study Duration, Enrollment and Number of Sites

This is a 2-year, single-site study with recruitment and study related procedures developed in collaboration with the Cancer Predisposition Program at CHOP. Development of the PrePARE care plans and targeted text messages takes place during year 1. We will then enroll 100 family units with child proband(s) with a known CPS (diagnosed within 5 years) beginning in year 2.

Duration of Subject Study Participation

Study participation is expected to last approximately 6 months, beginning at the time of consent. Participants will complete electronic assessments either remotely or in clinic (T0). The patient/family will then receive the PrePARE care plan and will be enrolled in the text-message alert system. They will complete repeat surveys at 3 (T1) and 6 months (T2) after implementation. All assessments are expected to last approximately 30 minutes each.

Total Number of Subjects Projected

We will approach a total of 100 families of a child with a CPS in the Cancer Predisposition Clinic. Patients will be eligible if they have had a diagnosis of a CPS for five years or less. Eligible participants of the families include up to two primary caregivers of each proband, and probands, themselves, if at least 12 years or older up to age 26. The families will designate the primary caregiver to represent the family or up to two caregivers can participate. We expect participation from all 100 primary caregivers who consent. Based on prior studies, we expect 60 secondary caregivers will participate. The age of the child proband(s) in the family unit determines whether the child proband(s) are eligible to enroll. We expect 20 total AYA will participate.

We aim for a caregiver to participate from each family unit. But, we will not exclude any eligible probands that choose to participate even if a caregiver wishes not to. In these cases, a parent must provide consent for the child(ren) (under 18) to participate, and the probands under age 18 must provide assent.

Study Population

The study population will include 100 family units with child proband(s) with a known CPS diagnosed within 5 years.

Inclusion Criteria

<u>Parents</u>

1) Parent or Legal Guardian of a patient with a known cancer predisposition syndrome diagnosed within the last 5 years (see table 2 for list of common CPS)
2) Their child has received care at CHOP or other medical institutions (does not need to be receiving follow-up care at CHOP)
3) Appropriate to approach per oncology team/cancer predisposition team

4) No cognitive impairment limiting ability to complete measures
5) Ability to read and speak English fluently

AYA probands

1) Child proband with a known cancer predisposition syndrome diagnosed within the last 5 years
2) Ages 12+
3) Received care at CHOP or other medical institutions (does not need to be receiving follow-up care at CHOP)
4) Appropriate to approach per oncology team/cancer predisposition team
5) No cognitive impairment limiting ability to complete measures
6) Ability to read and speak English fluently

Exclusion Criteria

1) Not meeting any of inclusion criteria

Subjects that do not meet all of the enrollment criteria may not be enrolled. Any violations of these criteria must be reported in accordance with IRB Policies and Procedures.

Study Procedures

Patient Identification

Eligible families will be identified by patient information found in clinic rosters of the Cancer Predisposition Program and electronic health records. Team members of the clinic are co-investigators on this study and will be readily available to identify eligible families. Families will then be approached by phone, email or in clinic to confirm study eligibility and (if appropriate) obtain informed study consent.

Study Treatment Phase

Pre-Test Assessment (T0)

Following consent/assent, all participant(s) are asked to complete an electronic self-report assessment either remotely or in clinic via REDCap. The pre-test will take place prior to receipt of the PrePARE care plans and enrollment in the text message alert system. MyCHOP may be utilized for communication with enrolled participants. MyCHOP is a secure, online portal in which physicians and patients can communicate.

PrePARE Care Plans and Text Messages

Upon consent to study, families will receive their PREPARE care plan and will be enrolled in the text message alert system. A trained CRC will create the care plans and enroll families in the text message system.

Post-Test Assessment (T1)

Three months after implementation of the PrePARE care plan and text message alerts, all participants are asked to complete an electronic self-report assessment either remotely or in clinic via REDCap. MyCHOP may be utilized for communication with enrolled participants. MyCHOP is a secure, online portal in which physicians and patients can communicate.

Follow-Up Assessment (T2)

Six months after implementation of the PrePARE care plan and text message alerts, all participants are asked to complete an electronic self-report assessment either remotely or in clinic via REDCap. MyCHOP may be utilized for communication with enrolled participants. MyCHOP is a secure, online portal in which physicians and patients can communicate.

Subject Completion/Withdrawal

Subjects may withdraw from the study at any time without prejudice to their care. It will be documented whether or not each subject completes the study.

Study Evaluations and Measurements

Screening and Monitoring Evaluations and Measurements

Medical Record Review

Descriptive measures to be obtained from electronic health record (EHR) to include date of birth, genetic testing results, surveillance visits and appointments and, where applicable, cancer diagnoses and treatment history (start, end, modalities).

Efficacy Evaluations

Measures (Parent and AYA Self-Report)

Demographic and Disease-related Information A self-report measure will request the following information on both the primary parent, second parent, and child proband(s): date of birth, race/ethnicity, education level, family income, gender, and sex. Diagnostic and treatment data to be evaluated will include underlying cancer diagnosis, treatment history (start, end, modalities), and genetic testing results. In the event that there is missing data on the demographic and disease-related information self-report measure, the study team will extract the aforementioned medical information about the child proband(s) and primary/second parent(s) via the child proband's Electronic Health Record (EHR).

Satisfaction with Decision Scale[19] This is a 6-item scale that measures satisfaction with decision to have germline testing. Items are rated on a 5-point Likert scale ranging from 1 ("Strongly Disagree") to 5 ("Strongly Agree").

Impact of Events Scale (IES)[20] This 15-item measure assesses cancer-related anxiety through two subscales (intrusive thinking and avoidance). Responses are measured on a 4-point Likert scale with the following anchors: 0 "not at all", 1 "rarely", 3 "sometimes", and 5 "often". Scores range from 0 to 35 for intrusion, 0 to 40 for avoidance, and 0 to 75 for the total IES. Higher scores indicate greater cancer-related anxiety.

Multidimensional Impact of Cancer Risk Assessment (MICRA)[21] This 6-item measure assesses the specific impact of result disclosure after genetic testing. The Distress subscale (Items 1-4, 7, and 8) will be used to assesses the amount of cancer-specific distress after receiving genetic test results. Items are rated on a 4-point Likert scale with the following anchors: 0 "Never", 1 "Rarely", 3 "Sometimes", and 5 "Often".

Survey of Acceptability[22] Respondents provide ratings on a 5-point Likert scale asking about satisfaction, perceived appropriateness, positive effect, demand, and potential for future use; adapted from prior studies.

Knowledge Measure This measure will assess participant knowledge of the content within the care plans.

Outcomes	Table 3: Efficacy Outcome Measures	*Timing:	Total time (min)
Cancer risk/surveillance knowledge	Knowledge measure itemized to reflect content in care plan (per AYA STEPS study, PI Schwartz and Hill-Kayser)[23,24] We have a track record of developing knowledge measures for prior digital health interventions, which have been shown to be responsive to intervention (see prelim).	T0, T1, T2	8
Decision satisfaction	Satisfaction with Decision Scale: 6 item Likert Scale[19]	T0, T1, T2	3
Distress	Impact of Events Scale: cancer-related anxiety per 2 subscales (intrusion and anxiety): 15 item Likert Scale;[20] Multidimensional Impact of Cancer Risk Assessment (MICRA) distress subscale: 6 item Likert Scale[21]	T0, T1, T2	10
Acceptability	Rating on 5-point Likert scale to assess satisfaction, perceived appropriateness, positive effect, demand, and potential for future use; adapted from prior studies[22]	T1, T2 (only if missed in T1)	8
Feasibility and Adherence	Absence of technical difficulties tracked by team and vendors; PrePARE and texts: CRC ability to create care plan in under 15 min	T0, T1, T2	NA

*Timing: T0 = pre-test measure, T1 = 3 months post-intervention, T2 = 6 months post-intervention

STATISTICAL CONSIDERATIONS

Descriptive statistics will be calculated for all variables for each subsample (single/paired caregivers, probands).Where possible, total scores will be calculated based on scoring instructions of established questionnaires or at an item-level, where applicable. Acceptability and feasibility of the digital tools will be summarized using descriptive statistics. The biological variable sex will be assessed as a potential confounder and effect modifier in all analyses, although we don't expect many differences by sex based on data from similar studies.

Primary Endpoint

The primary outcome is change in knowledge score for all participating family members. Mean and SD for the pre- and post-test (measured at 3 and 6 months) scores and the change scores will be calculated, and paired t test will be used to test if there is significant change in the knowledge score. The post-test score measured at 6 months, and further longitudinal analyses will be conducted to evaluate the change scores at 3 and 6 months simultaneously using mixed effects model. Other secondary analyses will evaluate change scores from all family members, and mixed effects model will be used to account for within-family correlations. Covariates will be evaluated as noted in Aim 1. We will enroll 100 families. We also estimate 10 to 15% attrition from T0 to T1, leaving ~75 families with evaluable participants. Primary analyses of 75 participants (almost all primary caregivers) with post-test measures will provide 80% power to detect a moderate effect size of 0.33 (mean change is 0.33 SD), assuming a two-sided type I error of 0.05. The secondary analysis including all family members (n=180) will have higher power while the magnitude of the power gain will depend on the observed within-family correlation in the knowledge score. Percent of appointments attended will be calculated.

Secondary Endpoints

Secondary endpoints include greater decisional satisfaction, and reduced distress at 3 and 6 months compared to baseline and will be assessed via the same methods and the primary endpoint of knowledge. Additionally, acceptability ratings and feasibility will be documented with standard descriptive statistics such as means and frequencies.

Statistical Methods

Baseline Data

Baseline and demographic characteristics will be summarized by standard descriptive summaries (e.g. means and standard deviations for continuous variables such as age and percentages for categorical variables such as gender).

Efficacy Analysis

Mean and SD for the pre- and post-test (measured at 3 and 6 months) scores and the change scores will be calculated, and paired t test will be used to test if there is significant change in the knowledge score. The post-test score measured at 6 months, and further longitudinal analyses will be conducted to evaluate the change scores at 3 and 6 months simultaneously using mixed effects model. Other secondary analyses will evaluate change scores from all family members, and mixed effects model will be used to account for within-family correlations. Covariates will be evaluated as noted in Aim 1.

Sample Size and Power

We will enroll 100 families. We also estimate 10 to 15% attrition from T0 to T1, leaving ~75 families with evaluable participants. Primary analyses of 75 participants (almost all primary caregivers) with post-test measures will provide 80% power to detect a moderate effect size of 0.33 (mean change is 0.33 SD), assuming a two-sided type I error of 0.05. The secondary analysis including all family members will have higher power while the magnitude of the power gain will depend on the observed within-family correlation in the knowledge score. Percent of appointments attended will be calculated.

Study INTERVENTION

Description

PrePARE Care Plan Development

In 2007, Dr. Hill-Kayser (Penn Site PI) co-launched OncoLife—an internet-based tool for the creation of adult survivorship care plans (SCPs).[23] OncoLink, is freely accessible online with over 80,000 users. The OncoLife tool requires input of demographics, diagnosis, and treatments received to create a comprehensive, individualized SCP addressing surveillance recommendations, late effects, and lifestyle recommendations.[25] Smart-ALACC (Smart Adult Living After Childhood Cancer) was created as a version for AYA survivors of childhood cancer.[24]

The creation of PrePARE, a care plan tool for cancer predisposition, will use the digital platform of OncoLife, and will follow the development procedures that were used to adapt OncoLife to create Smart-ALACC. Adapting Smart-ALACC to create a care plan tool for pediatric cancer predisposition will require three steps: 1) Content will be developed to reflect recommendations for surveillance (imaging, laboratory, and physical exam as required up to every 3 months), follow-up care, family testing, cancer prevention, adjustment and well-being. The content will reflect published guidelines and existing literature, clinical experience, and data from our related studies. 2) The user interface will be modified to include specific data entry options to facilitate individualized care plans. 3) The additions to the interface will be mapped using PHP and Symfony to the content within the eZ CMS so that care plans can be seamlessly developed. Care plans will be created with the ability to combine PrePARE with SCPs if the proband has a history of cancer.

The genetic counselor will train the clinical research coordinator to create the care plans and review them with families. PrePARE care plans will incorporate age-based surveillance recommendations and, where applicable, cancer survivorship recommendations.

Text Messaging Intervention

Text messages will be sent using Twilio via REDCap. Twilio is a third-party web service that acts as a conduit between the caregivers and the associated REDCap project. Twilio SMS text messages will be routed through Twilio's servers and REDCap goes to great lengths to ensure that SMS transcriptions do not stay in Twilio's logs, but are removed shortly after being completed. This is done for security and privacy concerns (e.g., HIPAA), in which the participant’s phone number and their response do not get permanently logged on Twilio's servers, but instead remain securely in REDCap.

SAFETY MANAGEMENT

Clinical Adverse Events

Clinical adverse events (AEs) will be monitored throughout the study.

Adverse Event Reporting

Since the study procedures are not greater than minimal risk, SAEs are not expected. If any unanticipated problems related to the research involving risks to subjects or others happen during the course of this study (including SAEs) they will be reported to the IRB in accordance with CHOP IRB SOP 408.

STUDY ADMINISTRATION

Data Collection and Management

The data collection and management plan is consistent with CHOP Policy A-3-6: Acceptable Use of Technology Resources that defines the requirements for encryption and security of computer systems.

- Identifiable data will be collected as part of this study. This data includes full names/initials, dates of birth, addresses, telephone numbers, and e-mail addresses. Any missing demographic data (i.e., not completed in subjects' surveys) about the child proband(s) and primary/second parent(s) will be extracted from the child proband's Electronic Health Record, if available. However, participants will be identified by alphanumeric code only. This precautionary step allows for the electronic transfer of data without using data encryption techniques. At each stage of data collection and maintenance, measures are taken to ensure that all identifying information is taken out of data archives, and any hard copies of data that could identify participants are stored in locked file cabinets with restricted access, and that data files are password protected. Participant identification numbers are used that do not reveal the identity of participants (e.g., no use of birth dates, initials, social security numbers, etc). Identifiable data will be stored in a locked cabinet at CHOP in the offices of the PI, Dr. MacFarland. Only members of the research team will have access to the data. If the results of this study are presented at scientific meetings or published in professional journals, they will not contain information that could be used to identify patients, parents, or family members.

- Electronic data will be collected and stored using REDCap (Research Electronic Data Capture) database, a secure web-based software database supporting clinical and translational research databases. The database will be password-protected, stored, and backed up on a daily basis by CHOP's Research Institute. REDCap provides data management functionality; including automated export procedures for seamless data downloads to Excel and commonly used statistical packages (SPSS, SAS, Stata, R). The database will incorporate range checks and between-variables consistency checks to ensure quality control. The system will signal the presence of questionable or potentially incorrect items. After data cleaning and quality assurance procedures are completed, pertinent sets of data will be exported into SPSS for statistical analysis.

Confidentiality

All data and records generated during this study will be kept confidential in accordance with CHOP's Institutional policies and HIPAA on subject privacy. Neither the Investigator nor other site personnel will use records and/or data collected for any purpose other than conducting the study.

The following steps will be taken to maintain confidentiality: (1) a Certificate of Confidentiality (CoC) will be obtained; (2) subject identity will be coded using numbers keyed to a master list; (3) coded data will be entered directly into files that will be password protected; (4) all project staff will be trained in the importance of confidentiality, and will certify in writing to protect subject confidentiality; and (5) if the results of the study are published, data which might reveal the identity of any particular subject will be disguised. Subjects will be informed about

the limits of confidentiality (e.g., in cases in which a subject is in danger to themselves or others). No identifiable data will be retained or used for future studies. The investigator will obtain a data use agreement between the provider (the PI) of the data and any recipient researchers (including others at CHOP) before sharing a limited dataset (PHI limited to dates and zip codes).

Regulatory and Ethical Considerations

Data and Safety Monitoring Plan

The CHOP PIs will monitor and review the study progress, subject safety, and the accuracy and security of the emerging data.

Risk Assessment

This is a low risk study. Participants will complete self-report demographic and patient reported outcomes. Given the potentially personal nature of cancer and genetic testing and predisposition, some questions may potentially cause some distress for some respondents. All participants will be informed of this risk and the nature of the questions prior to participation and will be informed of the right to skip questions or discontinue participation if they become uncomfortable with the study. If participants become upset, they will be referred to the site PIs or a psychosocial professional (site will determine best referral source), who will assess the level of distress of the patient and determine the need for additional psychosocial support.

Breach of confidentiality and loss of autonomy for minors are additional potential risks of participation. To minimize these risks, during the consent process, participants will be informed of the voluntary and confidential nature of the research. Minors will be told they do not have to participate even if their parent wants them to, and their answers will not be shared with anyone outside the study team, including their guardian, unless required by law. All participants will be informed of their right to withdraw from participation in the study at any time and the freedom to decline answering any question.

Potential Benefits of Trial Participation

Potential benefits for study participants include access to digital interventions that have the potential to support families in coping with the lifelong burden of a cancer predisposition syndrome. For patients with a CPS, there is potential that the PrePARE and text message interventions will improve understanding of, and adherence with, ongoing surveillance guidelines. From Dr. Schwartz's prior experience, these interventions have been implemented in the past with little to no associated distress.

At least 15% of patients with a diagnosis of cancer have an underlying cancer predisposition syndrome, and many families live with the long-term risk of cancer related to a known familial cancer predisposition syndrome. Ongoing cancer surveillance according to accepted guidelines significantly improves outcomes for these individuals. Tools to improve the implementation of cancer predisposition guidelines have the potential not only to improve understanding and decrease stress around testing and follow up, but also to have survival benefit for patients.

Risk-Benefit Assessment

As the risks of the research are appropriately characterized as "minimal risk", they are reasonable in spite of the anticipated lack of direct medical or psychological benefit to subjects. The potential benefits from knowledge gained through this study and the indirect benefits of helping parents and children in the future outweigh the minimal risks associated with participation.

Recruitment Strategy

Eligible families will be identified by patient information found in clinic rosters of the Cancer Predisposition Program and electronic health records. Team members of the clinic are co-investigators on this study and will be readily available to identify eligible families. Families will then be approached by phone or in clinic to confirm study eligibility and (if appropriate) obtain informed study consent.

Our Cancer Predisposition Program is among one of the few national well-established programs of its kind and is growing at a rate of 50% more patients per year, with 360 new patients in the last year. In the near future, as we move toward germline testing for all new pediatric cancer patients, it is expected that more than 600 patients will be seen each year. Referrals come internally and externally. As per Table 1, of the current eligible patients, we expect 140 individuals available for recruitment (and growing). Thus, we believe our recruitment and retention goals are extremely feasible given precedent and number of eligible patients.

Informed Consent/Assent and HIPAA Authorization

Participants will be identified through existing patient tracking mechanisms within the Cancer Center. Eligible participants will be recruited either in person or by phone, facilitated by email contact, with approval of treating oncologist if applicable. Consent will be obtained by a member of the study team in a private location in the hospital, by phone, or electronically. Consent will be documented via signature on IRB-approved consent documents. In some cases, a family may prefer to sign the consent form through our secure RedCap database by accessing a link provided by the study team if consenting remotely, or a study provided IPAD if in person. If completing the REDCap electronic consent form, subjects will be asked to provide an electronic signature as a part of their consent. There will also be an option for assent to be provided via electronic signature.

Every potential participant will go through a detailed and careful consenting process, with frequent prompts and structured questions asked throughout to ensure they understand the procedures and risks. The subjects will be reminded that participation is voluntary and will not affect their care. Potential participants will be informed that they can take as much time as needed to decide about study participation, and they will be informed that they may withdrawal from the study at any time. As per 45 CFR 46.608, any patient 12 years or older will be required to give assent prior to participation, if able. If a potential participant is unable to understand the study protocol, they will not participate in the study.

After the potential participant successfully completes this process, written informed consent or verbal consent (if by phone) or electronic consent will be obtained. A copy of the signed informed consent document is given to each participant for his/her records. If consent is obtained verbally, participants will receive a copy of their completed consent form by email. After signing the electronic consent form, subjects will have the options to have the signed consent form emailed to their email address or download a PDF of their signed consent form for future reference.

Main Study

Eligible participants will be recruited either in person or by phone, facilitated by email contact, with approval of treating oncologist if applicable. Consent will be obtained by a member of the study team in a private location.

Consent/HIPAA Authorization Plan for Subjects Who Reach Age of Majority

If a participant turns 18 before the next scheduled assessment, he/she will be asked to sign a new consent form.

Individuals with Limited English Proficiency

LEP subjects will not be included in the study as the questionnaires and care plans are only available and validated in English.

Waiver of Documentation of Consent

The Investigator requests a Waiver of Documentation of Consent and Assent (verbal consent/assent) for subjects recruited over the telephone. If the prospective participant chooses to enroll in the study, a member of the study team will complete the entire consent document, which will be stored in a regulatory binder by the study coordinator. A copy of the signed informed consent document will be emailed or mailed to each participant for his/her records.

Payment to Subjects/Families

Reimbursement for travel, parking and meals

Participants will not be reimbursed for travel, parking, or meals.

Payments to parent for time and inconvenience (i.e. compensation)

To compensate for their time and effort, participants will be paid via a pre-loaded bank card (hereafter referred to as a ClinCard). Per Clinical Trials Financial Management policy, the ClinCard will be given in person or mailed to participants after they are enrolled in the study. If the ClinCard is sent via mail, participants will be instructed to email the study coordinator to confirm receipt of the ClinCard before funds are disbursed. If the ClinCard is delivered in person, participants will be asked to provide their signature as confirmation of Payments to subject for time, effort and inconvenience (i.e. compensation) receipt. Both confirmation of ClinCard receipt and stipend payments will be tracked for all study participants in an Excel file (managed by the study coordinator).

Payments may also be made via amazon e-gift card. The amazon e-gift card will be emailed and participants will be instructed to confirm receipt of gift card with study coordinator.

Stipend amounts are as follows:

Parent(s) of child proband(s) will receive $20/time point (T0, T1, and T2). Parent(s) of additional child proband(s) will receive an additional $10/time point (T0, T1, and T2).

Payments to AYA subject for time, effort and inconvenience (i.e. compensation)

To compensate for their time and effort, participants will be paid via a pre-loaded bank card (hereafter referred to as a ClinCard). Per Clinical Trials Financial Management policy, the ClinCard will be given in person or mailed to participants after they are enrolled in the study. If the ClinCard is sent via mail, participants will be instructed to email the study coordinator to confirm receipt of the ClinCard before funds are disbursed. If the ClinCard is delivered in person, participants will be asked to provide their signature as confirmation of Payments to subject for time, effort and inconvenience (i.e. compensation) receipt. Both confirmation of ClinCard receipt and stipend payments will be tracked for all study participants in an Excel file (managed by the study coordinator).

Payments may also be made via amazon e-gift card. The amazon e-gift card will be emailed and participants will be instructed to confirm receipt of gift card with study coordinator.

Stipend amounts are as follows:

AYA proband(s) will receive $20/time point (T0, T1, and T2).

Gifts

N/A

PUBLICATION

Results of the study will be disseminated via conference abstracts and peer reviewed journal publications. No individually identifiable PHI will be published.

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