TITLE: INTEGRATION OF MULTIMODAL CANCER PREDISPOSITION GENETIC COUNSELING PRACTICES WITHIN THE PEDIATRIC ONCOLOGY SETTING: VIDEO INTERVENTION FOR NEWLY DIAGNOSED FAMILIES UNDERGOING GENETIC TESTING

NCT NUMBER: NCT05472714

DATE: JULY 26, 2024

Title:	Integration of Multimodal Cancer Predisposition Genetic Counseling Practices Within the Pediatric Oncology Setting: Video Intervention for Newly Diagnosed Families Undergoing Genetic Testing
Short Title	Educational Video for Genetic Testing
Regulatory Sponsor:	
eIRB Number	
Protocol Date:	July 26, 2024

Version 1 Date: September 9, 2021

Amendment 1 Date: November 2, 2021 V2

Amendment 2 Date: December 22, 2021 V3

Amendment 3 Date: April 14, 2022 V4

Amendment 4 Date: July 22, 2022 V5

Amendment 5 Date: October 11, 2022 V6

Amendment 6 Date: November 17, 2023 V7

Amendment 7 Date: July 26, 2024 V8

Suzanne P. MacFarland, MD
The Children's Hospital of Philadelphia
3501 Civic Center Blvd, CTRB #3054
Philadelphia, PA, 19104
Phone 215-300-6428
email: macfarlands@chop.edu

TABLE OF CONTENTS

ABBREVIATIONS AND DEFINITIONS OF TERMS

AE	Adverse event
AYA	Adolescent/Young Adult
CHOP	Children's Hospital of Philadelphia
CPS	Cancer Predisposition Syndrome

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 establishing best practices to optimize delivery of care for patients undergoing testing and their families. Tumor/normal genetic testing (testing of both tumor tissue and a paired normal sample) at time of cancer diagnosis or relapse is now widespread in pediatric oncology to improve cancer diagnostics, prognostics, and treatment; this testing also has potential to uncover underlying cancer predisposition syndromes with lifelong implications. Disseminating information at the time of cancer diagnosis is difficult, and is best done by a provider with expertise in cancer genetics. Thus, we will develop an informational video for use prior to tumor/normal genetic testing to augment genetic counseling resources to support patients and families.

Objectives:

Develop and evaluate the acceptability, feasibility, and preliminary efficacy of an informational video on paired tumor/normal testing for children and adolescents with a new diagnosis of cancer, tumors or other diagnosis.

Study Design:

We will use a non randomized trial whereby a convenience sample of patients/families will be recrtuited to be controls in Year 1, followed by a convenience sample that will be allocated the video intervention In Year 2.

Setting/Participants:

This is a 2-year, single-site study that is being conducted at the Children's Hospital of Philadelphia (CHOP). We are enrolling up to 220 family units, including caregivers of pediatric probands (any age) and probands age 12-26, undergoing germline testing at CHOP. The families will receive standard physician-delivered education prior to testing (n=100; Yr 1) or will have also viewed the new video added to standard of care (n=110; Yr 2).

Study Interventions and Measures:

We will develop an informational video for use prior to tumor/normal genetic testing for families, which will be incorporated into standard of care by year 2. To evaluate the impact of the video intervention, we will compare assessments of two cohorts- an unexposed (no video intervention, Year 1) and exposed (video intervention, Year 2). Assessments will take place within 1-4 weeks of testing and again within 8 weeks of receiving results.

PROTOCOL SYNOPSIS

Study Title	Integration of Multimodal Cancer Predisposition Genetic Counseling Practices Within the Pediatric Oncology Setting: Video Intervention for Newly Diagnosed Families Undergoing Genetic Testing
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 to establish best practices to optimize delivery of care for patients undergoing testing and their families. Disseminating information at the time of cancer diagnosis is difficult, and is best done by a provider with expertise in cancer genetics. Thus, we will develop an informational video for use prior to tumor/normal genetic testing for families to augment genetic counseling resources to support patients and families.
Study Objective(s)	Develop and evaluate the acceptability, feasibility, and preliminary efficacy of an informational video on paired tumor/normal testing for children and adolescents with a new diagnosis of cancer, tumors or other diagnosis .
Test Article(s)	An informational video to be presented within one week of cancer diagnosis to those referred for genetic testing.
Study Design	Non randomized trial with controls recruited and followed in Year 1 and intervention group recruited in Year 2.
Subject Population key criteria for Inclusion and Exclusion:	**Inclusion Criteria** 1. Parent of child (any age) +/- proband if age 12-26 2. Receiving tumor/normal testing 3. Appropriate to approach per oncology team 4. English speaking **Exclusion Criteria** 1. Cognitive impairment limiting participation
Number Of Subjects	Anticipated total of 360 subjects will be evaluated at CHOP.
Study Duration	Each subject's participation will last approximatley 8 months, depending on the timing of their genetic testing results
Study Phases **Screening**	(1) Screening: screening for eligibility by record review (2) Year 1: obtaining consent and administering survey within 1-4 weeks of

Study Treatment Follow-Up	testing and (3) Repeat survey again within 8 weeks of results disclosure. (4) Year 2: same as Year 1 but with the addition of an informational video during physician delivered education
Efficacy Evaluations	Knowledge of genetic testing
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	The means and SD of this score will be calculated for control (no video) and intervention (video) groups separately, and compared using two sample t test and linear regression
DATA AND SAFETY MONITORING PLAN	PI will be responsible for data quality management and ongoing assessment of safety

TABLE 1: SCHEDULE OF STUDY PROCEDURES

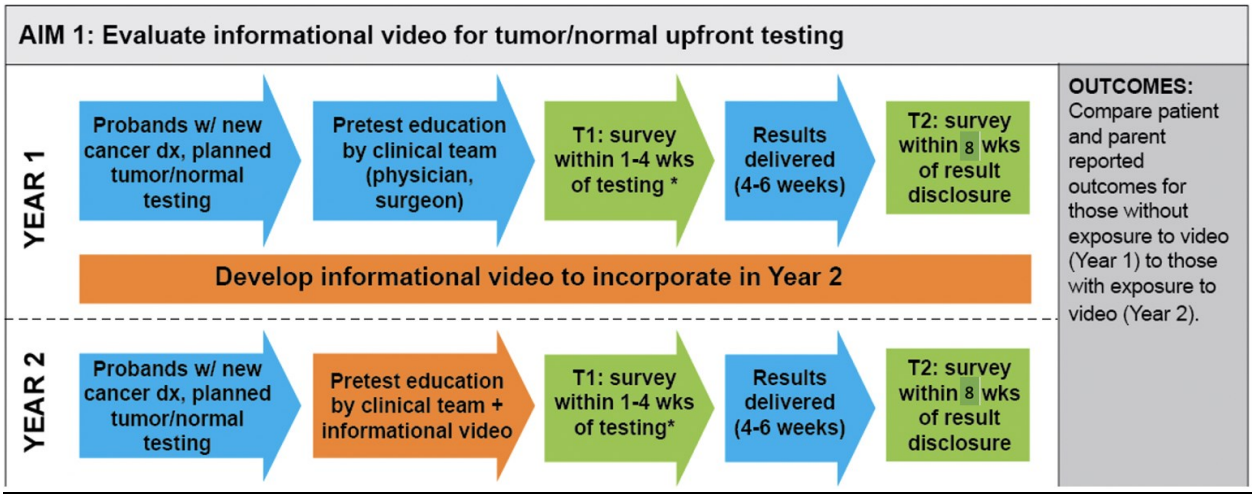

Table 1: Introduction of digital supports to clinical care, workflow Year 1 and 2. Blue indicates standard of care timepoints, orange indicates study interventions, and green indicates data gathering points. *No base 0

2 BACKGROUND INFORMATION AND RATIONALE

2.1 Introduction

The long-term goal of this research is to develop an intervention that will ultimately transform delivery of care for children and adolescents undergoing genetic testing associated with a cancer diagnosis, which may have implications for underlying CPS. This proposal will focus on the development and initial evaluation of a novel educational video intervention. We specifically propose a connected health approach whereby we will develop and test a technology-based tool that includes a video targeting patient informational needs around testing. This proposal is informed by our ongoing longitudinal study of children and their families undergoing genetic testing that has revealed less than optimal adjustment and need for more resources.

The successful completion of this study will create a novel, scalable, and generalizable digital support 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.

2.2 Name and Description of Investigational Product or Intervention

We will develop an informational video to be presented within one week of diagnosis to those referred for genetic testing. The video will combine multi-model features of animation, provider delivered information, and family testimonials. The production of the video will be led by CHOP Research Creative Services and will be submitted by amendment to IRB for review prior to use.

Name	Description
Tumor/Normal Sequencing Video Education	This 5 minute video will be developed with CHOP Research Institute Research Creative Services. It will include all information that is important to convey at time of tumor/normal paired sequencing including: 1) basic genetic principles, 2) process of genetic testing and return of results, 3) possible results including positive, negative, and variant of uncertain significance, 4) legal protections in place in event of a positive result, 5) possible familial cascade testing in event of a positive result, and 6) recommendations for managing the uncertainty and positive results. It will include engaging elements including animation, provider explanations, and family testimonials.

2.3 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 germline testing has exceeded the pace of deployment of genetic counseling resources. Prior to testing, it is important that families understand the risks and benefits of germline testing, legal protections, and possible outcomes of positive results that include cascade testing for family members. Unfortunately, there are not enough genetic counselors to meet the demand for counseling before and after germline testing. 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.

2.3.1 Process and Experience of Genetic Testing

There are many compelling reasons to determine whether an individual harbors a CPS, including the ability to conduct screening and surveillance that leads to early cancer detection and improved prognosis, the ability, in the setting of cancer, to modify therapy based on genetic susceptibility, and the need for familial testing to identify all at-risk individuals.[1] Receipt of genetic test results that warrant further familial testing or reveal a new threat to health can result in significant distress to patients and families, resulting in lower information retention.[3-6] Given these implications, it is recommended that genetic testing be undertaken by a trained genetic counselor.[7] However, given urgency of tumor/normal testing after detecting cancer,[8] genetic testing education is usually completed by a physician or surgeon during moments of high stress. Family understanding of the risks and benefits of genetic testing in this setting, and without a trained genetic counselor, have yet to be studied, including effects on stress and decisional satisfaction.

2.3.2 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.[9] Video-based education to supplement genetic counseling for a suspected cancer predisposition has been shown to be cost effective, acceptable, and feasible in adult settings[10,11] and non-inferior to pre-test genetic counseling in adults with cancer and/or with a CPS.[12,13] Interventions that leverage technology have promise to fill a gap in counseling services and to be modifiable for other settings.

2.4 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.

3 STUDY OBJECTIVES

The long-term goal of this research is to develop an intervention that will ultimately transform delivery of care for children and adolescents undergoing testing for CPS. This study will introduce a digital health support to facilitate access to genetic counseling knowledge in the pediatric oncology setting. It will evaluate and optimize a video-based intervention prior to tumor/normal testing in the setting of new childhood cancer diagnosis.

3.1 Primary Objective

The primary objective of this study is to develop and evaluate the preliminary efficacy of an informational video on paired tumor/normal testing for children and adolescents with a new diagnosis of cancer, tumors or other diagnosis. Knowledge of genetic testing will be assessed as the primary aim, measured after testing (before results) and then again after results are received. Decisional satisfaction and distress will also be measured.

3.2 Secondary Objectives

The secondary objective is to evaluate the acceptability and feasibility of the informational video. A survey of acceptability will be administered. Feasibility will be assessed with absence of technical difficulties of video delivery and timeliness of delivery of video after recommendation for testing.

4 INVESTIGATIONAL PLAN

4.1 General Schema of Study Design

4.1.1 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 identified through existing tracking systems within the Cancer Center as well as EPIC.

4.1.2 Study Treatment Phase (start of the study intervention)

In year 1, as the video is being developed, we will enroll up to 100 families of patients receiving the current standard-of-care approach to tumor-normal genetic testing with provider based education. In year 2, we will enroll an additional 120 families and incorporate the video into standard-of-care practices prior to tumor/normal genetic testing with provider based education.

4.2 Study Duration, Enrollment and Number of Sites

This is a 2-year, single-site study. We will enroll up to 220 family units with child proband(s) receiving germline testing for a CPS.

4.2.1 Duration of Subject Study Participation

Study participation is expected to last up to 8 months, beginning at the time of consent. Participants will complete electronic assessments either remotely or in clinic at least 1 week after cancer, tumors or other diagnosis and no more than 4 weeks after tumor/normal testing is sent (T1). Participants will also be asked to complete a repeat assessment (T2) within eight weeks after return of testing results (which can take up to 5 months). All assessments are expected to last approximately 30 minutes each.

4.2.2 Total Number of Subjects Projected

We will approach 220 family units of child proband(s) undergoing genetic testing at CHOP: n=100 with no video in Year 1; n=120 with video in Year 2. 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. It is expected that approximately 660 subjects (220 family units/triads which will consist of the proband subject and up to 2 caregivers) will be enrolled to produce approximately 392 evaluable subjects.

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 (under 18) to participate, and the proband under age 18 must provide assent.

4.3 Study Population

The study population will include up to 220 family units of child proband(s) undergoing genetic testing at CHOP and their parent(s).

4.3.1 Inclusion Criteria

<u>Parents</u>

1) Parent or Legal Guardian of a patient with a new diagnosis of cancer, tumor, or other diagnosis referred for tumor/normal sequencing (proband) in the Cancer Center at CHOP
2) Able to be approached within 1-4 weeks of tumor/normal sequencing
3) Appropriate to approach per oncology team
4) No cognitive impairment limiting ability to complete measures
5) Ability to read and speak English fluently

<u>AYA probands</u>

1) Child proband receiving germline testing in the Cancer Center at CHOP
2) Ages 12+
3) Able to be approached within 1-4 weeks of tumor/normal sequencing
4) Appropriate to approach per oncology team
5) No cognitive impairment limiting ability to complete measures
6) Ability to read and speak English fluently

4.3.2 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.

5 STUDY PROCEDURES

5.1 Participant Identification

Patients will be identified through collaboration between existing Cancer Center informatics systems that identify new cancer patients as well as partnership with the Division of Genomic Diagnostics to identify all patients undergoing paired tumor/normal sequencing. Patients will be recruited at least one week after cancer diagnosis (to avoid additional study consents during this stressful time), and no more than 4 weeks after tumor/normal testing is sent (to ensure data collection prior to return of results). Families will then be approached by phone or in clinic to confirm study eligibility and (if appropriate) obtain informed study consent.

5.2 Study Treatment Phase

5.2.1 Pre-Test Assesssment

Families will not be approached prior to genetic testing, as this a stressful time that involves multiple consent conversations (procedural and/or surgical consent, consent to begin upfront therapy, consent for other treatmentfocused studies). Additionally, given implications for cancer diagnosis and treatment, testing must not be delayed for study interventions. Thus, in order to evaluate the impact of the video intervention that takes place soon after cancer, tumor or other diagnosis and consent for cancer treatment, we will not be conducting pre-test/baseline assessments. Rather, we will compare assessments of two cohorts-- an unexposed (no video intervention, Year 1) and exposed (video intervention, Year 2). This avoids approaching patients at upfront time of diagnosis.

5.2.2 Initial Assessment (T1)

Following consent/assent, all participant(s) are asked to complete an electronic self-report assessment either remotely, in the inpatient setting, or in clinic via RedCAP. Assessment 1 (T1) must be completed prior to receipt of results or within 1-4 weeks after germline testing.

5.2.3 Follow-Up Assessment (T2)

Following receipt of germline test results (which may take up to 5 months), all participants are asked to complete an electronic self-report assessment either remotely or in clinic via RedCAP. The post-test assessment (T2) must be completed within 8-weeks after receiving germline test results.

5.2.4 Digital Intervention (Video)

In the first year of this study, we will develop the digital intervention, video counseling, to be implemented in year two. The production of the video will be led by CHOP Research Creative Services.

5.3 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.

6 STUDY EVALUATIONS AND MEASUREMENTS

6.1 Screening and Monitoring Evaluations and Measurements

6.1.1 Medical Record Review

EHR review will identify date of birth as well as diagnostic and treatment data, including underlying cancer diagnosis, treatment history (start, end, modalities), genetic testing results, and surveillance visits and appointments.

6.2 Efficacy Evaluations

6.2.1 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), genetic testing results, and appointments. 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).

Genetic Knowledge Scale[14] This is a 12-item true/false questionnaire that assesses basic genetic knowledge and knowledge of Tumor/Normal paired genetic testing in both adolescents and adults. This measure is scored by awarding one point for each item answered correctly and zero points for incorrect and unsure responses. Scores are summed, with higher scores indicating greater genetic knowledge.

Satisfaction with Decision Scale[15] 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)[16] 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 Distress Subscale (MICRA)[17] 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".

Acceptability Scale
This is a 15-item measure asking about satisfaction, perceived appropriateness, positive effect, demand, and potential for future use; adapted from our prior work.

*Timing: T1 = 1-3 weeks after testing, T2 = within 8 weeks after return of results.

Outcomes	Table 2: Efficacy Outcome Measures	*Timing:	Total time (min)
Genetic knowledge	Adapted items from TRACC study, from 1) 15 items of generic genetic knowledge[14]	T1, T2	8
Decision satisfaction	Satisfaction with Decision Scale: 6 item Likert Scale[15]	T1, T2	3
Distress	Impact of Events Scale: cancer-related anxiety per 2 subscales (intrusion and anxiety): 15 item Likert Scale[16]	T1, T2	10
Distress	Multidimensional Impact of Cancer Risk Assessment (MICRA) distress subscale: 6 item Likert Scale[17]	T2	8
Feasibility and Adherence	Absence of technical difficulties tracked by team and vendors; Video: delivery within 1 week of diagnosis.	T1, T2	1
Acceptability	This is a measure containing questions asking about satisfaction, perceived appropriateness, positive effect, demand, and potential for future use; adapted from prior studies	T2	8

7 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 much differences by sex based on data from similar studies.

7.1 Primary Endpoint

The primary outcome is the primary caregiver's knowledge score measured before receipt of genetic results. The means and SD of this score will be calculated for control (no video) and intervention (video) groups separately, and compared using two sample t test and linear regression. Baseline characteristics will be evaluated and compared using Wilcoxon test for continuous variables and Fisher's exact test for categorical variables.

7.2 Secondary Endpoints

The same analyses noted above will be performed for the secondary outcome, the knowledge score measured after receipt of genetic results, and further longitudinal analyses will be conducted to evaluate the scores measured before and after receipt of genetic results simultaneously, using mixed effects model to account for potential correlations among repeated measures. Another secondary analysis will include data from all caregivers' and probands' knowledge scores, and use mixed effects model to account for potential correlations within the same family. The same analyses will be performed for decisional satisfaction and distress scores, Secondary endpoints of acceptability ratings and feasibility will be documented with standard descriptive statistics such as means and frequencies.

7.3 Statistical Methods

7.3.1 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).

7.3.2 Efficacy Analysis

See description of primary endpoint above

7.4 Sample Size and Power

Based on expected enrollment of family members, the primary outcome of knowledge score, we will have 75 data points per group, and for the secondary analysis of all participants will have 133 data points per group. This sample size will provide 80% power to detect a moderate effect size of 0.46 (mean difference 0.46 SD) for the primary analysis assuming a two-sided type I error of 0.05, and the secondary analysis will have higher power while the

magnitude of the power gain will depend on the observed within-family correlation in the knowledge score.

8 STUDY INTERVENTION

8.1 Description

Digital Intervention (Video)

We will develop an informational video to be presented within one week of diagnosis to those referred for genetic testing. This will convey: 1) basic genetic principles, 2) process of genetic testing and return of results, 3) possible results including positive, negative, and variant(s) of uncertain significance, 4) legal protections, 5) possible familial cascade testing, and 6) recommendations for managing the uncertainty and positive results. The video will combine multi-model features of animation, provider delivered information, and family testimonials. The team will meet weekly to develop and review content. We will invite feedback from our patient/family advisory board and Patient Education Services in the Cancer Center. The production of the video will be led by CHOP Research Creative Services.

SAFETY MANAGEMENT

8.2 Clinical Adverse Events

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

8.3 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.

9 STUDY ADMINISTRATION

9.1 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 office 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.

9.2 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 investigators 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).

9.3 Regulatory and Ethical Considerations

9.3.1 Data and Safety Monitoring Plan

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

9.3.2 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 PI 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.

9.3.3 Potential Benefits of Trial Participation

Potential benefits for study participants include access to an infomational video that has the potential to support families in coping with a new diagnosis of cancer and related genetic

testing. There is potential for benefit to the population of individuals undergoing testing, who do not always have access to adequate genetic counseling. Tools to improve the process of upfront testing have the potential to improve understanding and decrease stress around testing and follow up. From Dr. Schwartz's prior experience, these types of interventions have been implemented in the past with little to no associated distress.

9.3.4 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.

9.4 Recruitment Strategy

Patients will be identified through collaboration between existing Cancer Center informatics systems (e.g., EPIC queries) that identify new cancer patients as well as partnership with the Division of Genomic Diagnostics to identify all patients undergoing paired tumor/normal sequencing. Recruitment and enrollment will be tracked using a password protected Excel spreadsheet.

The Cancer Center at CHOP, of which Dr. MacFarland is faculty, has a long track record engaging caregivers and adolescents/young adults in innovative descriptive and intervention research. Response and retention rates for our studies, often involving multiple reporters, are high (~75 to 95%), including studies with multiple assessments that last over an hour. In our ongoing study of genetic counseling outcomes, which involves probands and their caregivers undergoing genetic testing for CPS, over 90% of caregivers and over 60% of adolescents/young adults approached have been enrolled in study. The CHOP Cancer Center has approximately 500 new diagnoses of cancer per year, with over 200 of these individuals undergoing tumor/normal paired sequencing, and this number is expected to increase; thus, given prior experience we expect to meet our accrual goal.

9.5 Informed Consent/Assent and HIPAA Authorization

Eligible participants will be recruited either in person or by phone, 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. Potential participants will be reminded that participation is voluntary and will not affect their care. They will be informed that they can take as much time as

needed to decide about study participation, and that they may withdraw from the study at any time. If consent is obtained remotely, the coordinator will explain the study via phone and answer questions prior to emailing the participant a link to the electronic consent accessed through RedCap. 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. Participants must be consented within within 4 weeks after germline testing.

Ambivalent subjects will be informed of their timeline to make a decision and reminded that their decision is voluntary and will not affect their care.

After the potential participant successfully completes this process, written informed consent or verbal consent (if by phone) or electronic consent (if remote) will be obtained. A copy of the signed informed consent document is given to each participant for his/her records. 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.

9.5.1 Main Study

Eligible participants will be recruited either in person or by phone, with approval of treating oncology provider. Consent will be obtained by a member of the study team in a private location.

9.5.2 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.

9.5.3 Individuals with Limited English Proficiency

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

9.5.4 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 in a locked file cabinet in locked office. A copy of the signed informed consent document will be emailed or mailed to each participant for his/her records.

9.6 Payment to Subjects/Families

9.6.1 Reimbursement for travel, parking and meals

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

9.6.2 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 (T1 and T2).

9.6.3 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 (T1 and T2).

10 PUBLICATION

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

11 REFERENCES

1. Brodeur GM, Nichols KE, Plon SE, Schiffman JD, Malkin D. Pediatric Cancer Predisposition and Surveillance: An Overview, and a Tribute to Alfred G. Knudson Jr. *Clin Cancer Res.* 2017;23(11):e1-e5.
2. Kamihara J, Bourdeaut F, Foulkes WD, et al. Retinoblastoma and Neuroblastoma Predisposition and Surveillance. *Clin Cancer Res.* 2017;23(13):e98-e106.
3. Landier W, Ahern J, Barakat LP, et al. Patient/Family Education for Newly

Diagnosed Pediatric Oncology Patients. *J Pediatr Oncol Nurs.* 2016;33(6):422-431.
4. Frey MK, Lee SS, Gerber D, et al. Facilitated referral pathway for genetic testing at the time of ovarian cancer diagnosis: uptake of genetic counseling and testing and impact on patient-reported stress, anxiety and depression. *Gynecol Oncol.* 2020;157(1):280-286.
5. Wouters RH, Bijlsma RM, Ausems MG, van Delden JJ, Voest EE, Bredenoord AL. Am I My Family's Keeper? Disclosure Dilemmas in Next-Generation Sequencing. *Hum Mutat.* 2016;37(12):1257-1262.
6. Gopie JP, Vasen HF, Tibben A. Surveillance for hereditary cancer: does the benefit outweigh the psychological burden?--A systematic review. *Crit Rev Oncol Hematol.* 2012;83(3):329-340.
7. McGill BC, Wakefield CE, Vetsch J, et al. "I remember how I felt, but I don't remember the gene": Families' experiences of cancer-related genetic testing in childhood. *Pediatric blood & cancer.* 2019;66(8):e27762.
8. Surrey LF, MacFarland SP, Chang F, et al. Clinical utility of custom-designed NGS panel testing in pediatric tumors. *Genome Med.* 2019;11(1):32.
9. Caulfield BM, Donnelly SC. What is Connected Health and why will it change your practice? *QJM: An International Journal of Medicine.* 2013;106(8):703-707.
10. Jones GE, Singletary JH, Cashmore A, et al. Developing and assessing the utility of a You-Tube based clinical genetics video channel for families affected by inherited tumours. *Familial cancer.* 2016;15(2):351-355.
11. Axilbund JE, Hamby LA, Thompson DB, Olsen SJ, Griffin CA. Assessment of the use and feasibility of video to supplement the genetic counseling process: a cancer genetic counseling perspective. *J Genet Couns.* 2005;14(3):235-243.
12. Watson CH, Ulm M, Blackburn P, et al. Video-assisted genetic counseling in patients with ovarian, fallopian and peritoneal carcinoma. *Gynecol Oncol.* 2016;143(1):109-112.
13. Manchanda R, Burnell M, Loggenberg K, et al. Cluster-randomised non-inferiority trial comparing DVD-assisted and traditional genetic counselling in systematic population testing for BRCA1/2 mutations. *J Med Genet.* 2016;53(7):472-480.
14. Fitzgerald-Butt S, Bodine A, Fry K, et al. Measuring genetic knowledge: a brief survey instrument for adolescents and adults. *Clin Genet.* 2016;89(2):235-243.
15. Holmes-Rovner M, Kroll J, Schmitt N, et al. Patient Satisfaction with Healthcare Decision: The Satisfaction with Decision Scale *Medical Decision Making.* 1996;16(1):58-64.
16. Horowitz M, Wilner N, Alvarez W. Imact of Event Scale: A Measure of Subjective Stress. *Psychosomatic Medicine.* 1979;41(3):209-218.
17. Cella D, Hughes C, Peterman A, et al. A brief assessment of concerns associated with genetic testing for cancer: The multidimensional impact of cancer risk assessment (MICRA) questionnaire. *Health Psychology.* 2002;21(6):564-572.