TITLE: ENGaging and Activating cancer survivors in GEnetic services (ENGAGE) Study
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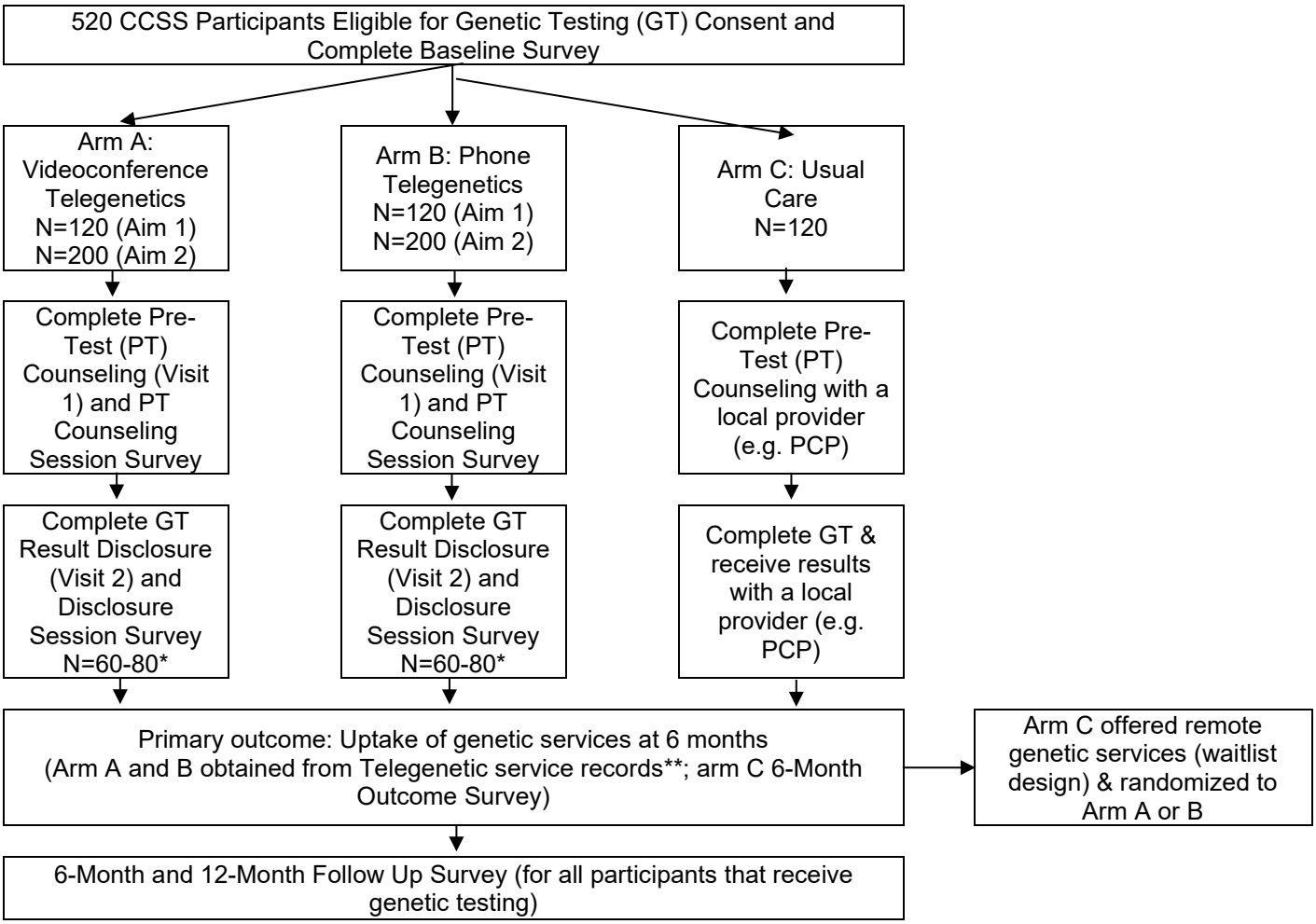
SCHEMA



*N=60-80 includes participants from Arm C who have services via the waitlist.
**6-Month Outcome Survey also given to participants on Arms A and B that have lost contact with Penn Telegenetics before receiving genetic services

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List of Abbreviations

ENGAGE	ENGaging and Activating cancer survivors in GEnetic services
CCSS	Childhood Cancer Survivor Study
myLTFU	A HIPAA-compliant interface between participants, study investigators, and the CCSS Coordinating Center which allows direct messaging and web portal-based data collection
PCP	Primary Care Provider
SMN	Secondary Malignant Neoplasm
NCCN	National Comprehensive Cancer Network
GC	Genetic Counselor
FH	Family History
RCT	Randomized Controlled Trial

1.0 Background

Germline cancer genetic testing has become a standard evidence-based practice, with established risk reduction and screening guidelines for genetic carriers (1-4). Yet, many at-risk patients do not have access to genetic services, leaving numerous genetic carriers unidentified and at increased risk of late diagnosis of cancers and inferior outcomes (5-9). Access to genetic specialists is limited in many areas in the U.S., requiring patients to travel long distances to referral centers or to work with primary care providers (PCPs) to order testing, presenting significant barriers to testing (9-12). Thus, innovative delivery models to increase uptake of genetic services and adherence to guidelines for genetic testing are needed to realize the benefits of Precision Medicine (8, 12-15).

Suboptimal access to genetic services is an acute problem for adolescent and young adult (AYA) cancer survivors, many of whom are at high risk for subsequent malignant neoplasms (SMN) because of cancer therapy or an inherited cancer predisposition (16, 17). A recent study revealed that 12% of survivors had a germline mutation in a cancer susceptibility gene (e.g. TP53, BRCA1/2) (18). National Comprehensive Cancer Network(NCCN) and Children's Oncology Group (COG) guidelines recommend survivors with personal (e.g. sarcoma) and/or family history of cancer be referred for genetic testing to implement appropriate surveillance or preventive measures (e.g. breast cancer surveillance or prophylactic mastectomy in women with TP53 or BRCA 1/2) (19,20). Yet, <15% of survivors have access to genetic services (21). Further, survivors and their PCPs are largely unaware of survivors' health risks and adherence to surveillance guidelines is low (22-26).

To address the gap in access to genetic services, this study will evaluate the effectiveness of an adapted model of remote delivery of genetic services to increase the uptake of recommended genetic assessment and testing in childhood cancer survivors. In a randomized study of remote telegenetic services delivered on-site at community oncology practices compared to usual care options for genetic services (e.g. travel to regional cancer program for counseling or testing) in adult patients who meet NCCN criteria for cancer genetic testing (PI:Bradbury, clinicaltrials.gov NCT02517554), 77% of patients randomized to remote services had genetic counseling and 61% had genetic testing, as compared to 6% ($p<0.001$) and 17% ($p<0.001$) in the usual care arm (27). These data establish that providing remote genetic services can significantly increase uptake of genetic testing in patients in community practices. Yet, this on-site model requires collaboration with oncology practices and multi-level support within practices, which limits scalability for a nationally distributed population.

Remote telemedicine services by phone or videoconference could address gaps in access to recommended genetic testing. Genetic services are geographically limited, with the majority located in urban and/or academic centers. Some patients proceed with testing without a genetic provider (i.e. with their PCP). This has been shown to be associated with lower genetic knowledge and satisfaction, (28) and many at-risk patients do not proceed with testing at all (29-31). Remotely providing genetic services, as an alternative to in-person delivery, could address access barriers. Remote videoconference has been shown to be a highly effective alternative to in-person services in some areas (e.g. education, psychiatric services), (32, 33) but in areas such as cancer genetics data has been more limited, with no data reporting on extending services in the home, across a national population or in specifically childhood cancer survivors (34-45).

2.0 Purpose of Study

As childhood cancer survivors receive care locally from PCPs, the ***in-home, collaborative PCP model*** is designed to increase access to genetic services and uptake of genetic testing in childhood cancer survivors. In this model, individual survivors can access remote telegenetic services and genetic counselors will partner with PCPs to order genetic testing. This approach of partnering with PCPs to increase compliance with guidelines has been successful in the North American cohort of childhood cancer survivors, the Childhood Cancer Survivor Study (CCSS). In the CCSS EMPOWER study (PI:Oeffinger, clinical trials.gov NCT01579552), 92% of survivors had a PCP who enrolled with their patient and women in the PCP-engaged intervention group were more likely (33.1% v. 17.6%, p=0.018) than controls to report a surveillance mammogram ordered by the PCP, providing support for our collaborative PCP model (46).

ENGAGE (**ENG**aging and **A**ctivating cancer survivors in **GE**netic services) is a 3-arm randomized Hybrid 1 Effectiveness and Implementation study in 520 CCSS survivors to evaluate the effectiveness of our ***in-home, collaborative PCP model*** of remote telegenetic services to increase uptake of cancer genetic testing in childhood cancer survivors compared to usual care options for genetic testing.

Specific Aim 1: To evaluate the effectiveness of our ***in-home, collaborative PCP model*** of remote telegenetic services to increase uptake of genetic testing at 6 months as compared to usual care among childhood cancer survivors who meet criteria for cancer genetic testing. Our primary outcome will be a composite variable indicating whether a person had pre-test counseling or genetic testing.

Specific Aim 2: To evaluate the effectiveness of remote videoconferencing to provide greater increase in knowledge and decrease in distress and depression as compared to remote phone services (Aim 2a), to examine the moderators of patient outcomes with remote telegenetic services (Aim 2b), and to estimate intervention costs and incremental cost-effectiveness of the three study arms (Aim 2c).

Specific Aim 3: To conduct a multi-stakeholder, mixed-methods process evaluation to understand patient, provider and system factors associated with uptake of counseling and testing in our adapted ***in-home, collaborative PCP model*** and facilitators and barriers to uptake to provide recommendations for future implementation.

3.0 Methods

3.1 Subject Selection / Participant Characteristics

All potential participants will be identified through the CCSS Coordinating Center. The CCSS Coordinating Center at St. Jude Children's Research Hospital is a multi-institutional cohort established in 1994 to evaluate the outcomes of childhood cancer survivors, and follows the outcomes of 24,335 childhood cancer survivors across the US (47). The CCSS Coordinating Center will use a combination of electronic (email/text), mailed, and phone-based recruitment methods to contact all potential participants. Recruitment materials will be sent to living CCSS participants to identify those who meet criteria for cancer genetic testing.

Potential subjects will include individuals who are:

- 18 years of age or older

- Able to understand and communicate in English
- Currently reside in the US
- CCSS survivors of the following primary cancers:
    - CNS tumor
    - Sarcoma (except Ewing sarcoma)
- CCSS participant with one or more subsequent malignant neoplasm (SMN)
- CCSS participant with any primary childhood cancer and a family history (FH) that meets NCCN criteria for genetic testing

Family history (FH) information will be assessed using existing CCSS data on the types of cancer the participant has reported in their family members, as well as the number of affected family members. The FH data was previously collected as part of the standard dataset for the CCSS Coordinating Center.

Exclusion criteria for this study include:

- Uncorrected or uncompensated speech defects that would lead to the participant being unable to communicate effectively with a medical provider
- Uncontrolled psychiatric/mental condition or severe physical, neurological or cognitive deficits rendering individual unable to understand study goals and tasks
- Participants who have already completed and received a clinically appropriate multi-gene panel genetic testing, or participants in the process of receiving genetic testing for hereditary cancer risk genes.

3.2 Enrollment Procedures

The CCSS Coordinating Center will send an initial recruitment email (**Appendix A**) to all eligible CCSS participants. The CCSS Coordinating Center will then send a reminder email and text message via the myLTFU DatStat Connect portal to these participants that links the participant to the study's informational web page. Interested participants that follow this link will then be asked to log in and sign electronic informed consent (**Appendix B**) to enter the main home page on the myLTFU portal and join the study. Immediately following the informed consent, participants will be directed to complete an Eligibility Survey (**Appendix C**). Eligible participants will be directed to complete the Baseline Survey (T0) (**Appendix D**) through the myLTFU platform (see below in Section 3.3). Once eligible participants complete this Baseline Survey, they will be randomized to one of three arms (usual care control, remote telegenetic services by phone or by videoconferencing).

Mailed recruitment materials will also be used for participants that do not respond to the email recruitment methods. The CCSS Coordinating Center will complete follow-up phone calls for all participants that do not respond to email and mail recruitment materials.

3.3 Study Procedures and Measures

STUDY PROCEDURES

This intervention will utilize a participant portal called myLTFU, a HIPAA-compliant interface between participants, study investigators, and the CCSS Coordinating Center. It allows direct and interactive messaging and web portal-based data collection, complementing already

established communication methods. The participant portal is accessible by computer, tablet, or smartphone. The application will allow participants to complete their assigned surveys, track their self-reported outcomes, view customized educational content, upload and download documents and pictures, and interact through secure chat with the study team.

Communication with participants will mostly take place via the DatStat Connect Platform, which allows pre-programmed messages and workflows to be activated by situational triggers.

RANDOMIZED STUDY PROCEDURES:

Once individuals have successfully completed the informed consent process, Eligibility Survey and Baseline (T0) Survey, the study steps will commence as follows:

1. Randomization

Upon successful completion of informed consent and baseline (T0) survey, participants will be randomized into one of three potential study arms. Randomization assignments will be determined by a permuted block design and stratified by male/female/other. Study arms will consist of variations of methods of delivery for genetic counseling.

Once enrollment goals for Aim 1 are reached (120 completed baseline survey and sent randomization flyer), we will halt enrollment ot Arm C. We will continue to enroll to Arms A and B to meet enrollment goals for Aim 2.

ARM	**COUNSELING METHOD**
ARM A	Remote Videoconference Telegenetics
ARM B	Remote Phone Telegenetics
ARM C	Usual Care

After randomization, participants will be sent information flyers (**Appendix E**) via the myLTFU app that correspond to the appropriate arm to which they have been randomized. Flyers will include instructions for how to contact the Penn Telegenetics team to schedule their appointment (Arms A and B) or usual care options (Arm C) for obtaining genetic services (e.g. ask PCP or providers, use the National Society of Genetic Counselors website www.nsgc.org).

Participants will be followed up with by a member of the research team to ensure they have received the flyers with the randomization assignment and information. Participants in all arms will be fully informed of how to initiate genetic services, and that it is their responsibility to do so.

2. Pre-Test Counseling, Visit 1 (Remote Telegenetics Arms A and B)

Those who contact the Penn Telegenetics will be registered with the Penn Telegenetics Program, consistent with routine clinical care. They will be scheduled with a Penn Telegenetics Genetic Counselor according to their study arm. Participants in Arms A and B will be asked to complete a study survey following their pre-test counseling sessions, Visit 1 (T1) (**Appendix F**).

ARM A: Remote telegenetic counseling by videoconference: Those who contact Penn Telegenetics in Arm A will complete their pre-test counseling session (Visit 1) by videoconference, utilizing communication protocols and checklists adapted from related studies

(**Appendix G**) (50). Penn GCs are licensed in all U.S. states that require licensure to provide remote telegenetic services (49). Consistent with standard clinical practice, GCs will review personal and FH, the risks, benefits and limitations of genetic testing, testing options based on their personal and FH (e.g. *TP53* testing or a panel of cancer susceptibility genes) and the costs associated with genetic testing. If the participant consents, this session will be recorded for research and training purposes.

Videoconferencing Technology platforms: Participants will be provided links to download secure, HIPAA compliant, videoconferencing software on their home computer or device. The Penn Telegenetics team provides back-up systems if one platform is not able to launch or fails to maintain connectivity. In our communication protocols, if videoconference technology fails, GCs will convert the session to phone.

ARM B: Remote telegenetic counseling by phone: Participants will complete their pre-test counseling (Visit 1) session by phone with a Penn Telegenetic Counselor (GC) utilizing communication protocols and checklists adapated from related studies (Appendix G) (48). The remainder of procedures for pre-test counseling are as described above for Arm A. If the participant consents, this session will be recorded for research and training purposes.

ARM C: Usual Care Arm: Participants in the usual care arm will receive usual care services depending on which referral method they choose and if they initiate services. As below, after the 6-Month Outcome Survey, if they have not had genetic services through usual care they will be offered services and re-randomized to Arm A/B in a waitlist design.

3. Genetic Testing

ARMS A and B: If patients on Arms A and B elect to proceed with genetic testing, they will be asked to provide their PCP's/ or other provider's (usual source of care or a local health care provider of their choice) contact information A licensed physician is required to order genetic testing in most states. If Dr. Bradbury or Dr. Henderson has licensure in the residing state, they will be the ordering physician if no PCP/ provider has been identified. The Penn Telegenetics Team will contact the patient's PCP/provider and their practice to inform them that their patient is a candidate for remote genetic services and the Penn Telegenetic counselors can provide counseling and facilitate testing through a collaborative relationship with the patient's provider. The PCP/provider would need to agree to be the ordering provider for the genetic testing and register with the Penn Telegenetics Program, a model that has been successful in our current clinical program. PCPs/providers will provide their credentials and contact information, so that the GC can collaborate with the provider to facilitate testing. Practice staff will be permitted to complete the PCP/provider registration on behalf of the provider. Once the PCP/provider has registered and agreed to support testing in their patient, the Penn GC will collaborate with the patient and provider/practice to arrange for sample collection, and provide support for insurance coverage. The registered PCP/provider will receive a chart note summarizing the pre-test counseling visit and testing ordered.

ARM C: Participants in the usual care arm will receive usual care services depending on which referral method they choose and if they initiate services. As below, after the 6-Month Outcome Survey, if they have not had genetic services through usual care they will be offered services and re-randomized to Arm A/B in a waitlist design.

Genetic Testing in all arms will be clinical cancer genetic testing through standard clinical commercial labs, consistent with real-world practice and as indicated based on their personal

and family history. Most testing will be covered by insurance. Consistent with our experience in community patients in the Penn Telegenetics Program, we expect the majority of participants to have coverage. For those who do not, GCs can use commercial lab financial assistance programs or identify the lowest possible self-pay options, consistent with their current practice. For example, there are currently several labs that offer genetic testing or panels for ≤ $250. This information will be provided in the study flyers, so that it accessible to all participants regardless of arm.

4. Genetic Testing Result Disclosure, Visit 2 (Remote Telegenetics Arms)

ARM A: Remote telegenetic counseling by videoconference: The Penn GC will share results with the patient by videoconference at a scheduled visit. The Penn GC will provide the patient's provider with a chart note, summarizing the results and associated implications and cancer risk estimates, as well as standard risk reducing or screening strategies and implications for relatives. Penn GCs will be available to answer PCP/provider questions (by email or phone) and facilitate referral to regional clinical expertise centers as indicated. Patients will be recommended to follow-up with their PCP/provider to implement any screening and medical (including risk reduction) recommendations. If the participant consents, this session will be recorded for research and training purposes.

ARM B: Remote telegenetic counseling by phone: The Penn GC will share results with the patient by phone at a scheduled visit. The remainder of procedures for post-test counseling are as described above for Arm A. If the participant consents, this session will be recorded for research and training purposes.

Following the completion of the disclosure session, participants on Arms A and B will also be asked to complete a study survey (T2) (**Appendix H**).

5. Completion of Primary Outcome 6-Month Status Survey (Usual Care Arm & Certain Remote Telegenetics Arms Participants, **Appendix I1**)

Participants on the usual care arm will be contacted at the 6-month timepoint (6-months post randomization) to assess uptake of genetic services. Participants on Arms A and B that have not completed genetic counseling or testing will also be contacted at the 6-month timepoint to assess uptake of genetic services through the 6-Month Status Survey. Those who have had genetic testing will be asked to provide authorization for the study team to obtain a copy of their genetic test result for the purpose of research (**Appendix I2**).

Participants on Arm C that have not had genetic testing at 6 months will be offered telegenetic services (waitlist design, see **Study Schema**). This option will not be shared at enrollment. Rather, they will be told that after they complete the 6-Month Status Survey, we will review again genetic testing options with them.

6. Completion of 6-Month Follow Up Survey (T3)

All participants who have genetic testing will be asked to complete a T3 survey 6 months after the genetic testing result disclosure session (**Appendix J**).

7. Completion of 12-Month Follow Up Survey (T4)

All participants who have had genetic testing will be asked to complete a T4 survey 12 months after the genetic testing result disclosure session (**Appendix J**).

OUTCOMES AND MEASURES

Table 1. Effectiveness outcomes and measures			
CONSTRUCT	**T0**	**T1**	**T2-T4**
Moderators of patient outcomes			
Sociodemographics	X		
Cancer history	X		
Family history	X		
Health literacy	X		
Comfort with technology	X		
Self-efficacy	X		
Financial Wellness	X		
COVID Impact	X		X
Outcomes			
Uptake counsling, testing, identification carriers at 6 months* (Telegenetics records for Arms A/B & the 6-Month Status Survey in Arm C)			
Understanding of Genetic Information			
Test result recall			X
Knowledge of genetic disease	X	X	X
Perceived risk	X	X	X
Reactions to genetic information			
Anxiety and Depression	X	X	X
Cancer specific distress	X	X	X
Satisfaction with genetic services and telemedicine		X	X
Behavioral use of genetic information			
Performance of behaviors	X		X
Cost (patient and system)**		X	X
*Aim 1; **Aim 2; T0=baseline (within 30 days of visit 1, can accept within 45 days. beyond that it needs to be updated), waitlist usual care particiants will need to complete a new baseline, T0b; T1=survey post pre-test counseling, Visit 1 (ideally collect 1-3 days and up to 7 days. accept up to 14 days but from 7-14 days we may elect to drop and impute). T2=survey immediately post genetic testing disclosure (same timing as T1); T3/T4 survey=6/12-month post genetic testing disclosure (idealy get within 14 days of 6/12 month mark but accept within 60 days of 6 month or 12 month mark)			

The T0-T4 patient surveys for the RCT will be completed through a secure website, linked through the myLTFU platform. The 6-Month Outcome Survey will be administered by phone. If the phone survey cannot be completed, the survey will be offered self-administed through the myLTFU platform.

Effectiveness Outcomes (Aims 1 and 2):

1) **Uptake of counseling, testing and identification of carriers at 6 months** (Aim 1): This information will be obtained through study records for Arms A and B (intervention arms) and the 6-Month Outcome Survey among nonresponders in Arm A and B (e.g. those who did not contact Penn Telegenetics or did not complete visit 1 or visit 2) and in Arm C (usual care). The outcome survey will query completion of each outcome, date, and provider and will explore barriers and reasons for no uptake (Appendix I).

2) **Understanding of genetic information** will be assessed at baseline (T0, all Arms), post genetic pre-test counseling session (T1), post genetic test (T2), 6 months post genetic testing (T3), and 12 months post genetic testing (T4) for those in Telegenetic Arms A and B. *Knowledge of genetic disease* will be evaluated using The KnowGene Scale, a 16-item scale administered to patients after genetic testing and/or genetic counseling to measure their understanding of the health implications of genetic testing results. It includes health implications to oneself as well as relatives. This measure covers penetrance, actionability, limitations of current technology, and monogenic inheritance patterns (51).

Perception of genetic disease will include three items (T0-T4), utilized in related research and evaluating perceived risk of developing a second cancer on a verbal scale and perceived numerical risk, as well as a single item evaluating perceived timeline. (52, 53, 54, 55) .

3) Reactions to genetic information will be assessed at baseline (T0, all Arms), post genetic pre-test counseling session (T1), post genetic test (T2), 6 months post genetic testing (T3), and 12 months post genetic testing (T4) for those in Telegenetic Arms A and B).

a) *General anxiety and Depression* will be assessed by the 4-item each short Patient Reported Outcomes Measurement Information System (PROMIS), a system of highly reliable, precise measures of patient-reported health status for physical, mental, and social well-being (56, 57).
b) *Disease-specific distress* will be measured using the 8 –item Impact of Events Scale (IES) (58-61), also with strong internal consistency (alpha = 0.82-0.90) in genetic delivery studies (62-64).
c) *Satisfaction with genetic services* will be assessed with 9-items evaluating satisfaction with genetic services (T1 and T2). These items have been utilized in our related studies evaluating alternative and traditional genetic delivery models (alpha = 0.73-0.85) (62, 63, 65-69) and adapted for web-based delivery and this study design.
d) *Satisfaction with telemedicine* will be assessed with 8-items adapted for genetic counseling sessions and utilized in our preliminary studies.(70)
e) *Multidimensional responses to genetic testing*, including positive responses and uncertainty will be assessed using the Multi-dimensional Impact of Cancer Risk Assessment Questionnaire (MICRA) at T2-T4. The MICRA is a 21-items scale that has been utilized in many genetic studies to evaluate distress, uncertainty and positive

responses to receipt of genetic test results (71). The final item was excluded as it is not included in the three subscales and assessed regret which will be assessed in a separate scale.

f) Decisional regret (T2-T4) will be assessed with the 5-item validated Decision Regret Scale used frequently in related genetic studies (72, 73).

4) Use of genetic information will include performance of behavior items utilized in the CCSS and related studies (T0, T3, T4). Behaviors will include cancer specific (screening, prophylactic surgery, chemoprevention) and general risk modifying behaviors (e.g. diet, exercise, tobacco and alcohol use). Communication with providers and relatives following disclosure will be measured as well.

5) Cost of remote services and usual care: Estimation of intervention costs will adopt a societal perspective, including relevant direct medical and nonmedical costs borne by providers, payers and patients. These include print materials, postage, telecommunication services and personnel time required to deliver each intervention, as well as patient time and travel costs associated with genetic counseling sessions. Information to estimate intervention costs will be collected from study billing and payment records (e.g. print materials, postage) and telegenetic staff logs (personnel time). The cost of personnel time will be based on institution-specific salaries, including fringe benefits, for the personnel delivering the study interventions. In sensitivity analysis, we will substitute site-specific salary information with national average wage rates for the relevant occupational categories (e.g. physician, genetic counselor, office assistant). Intervention cost estimates will not include the cost of resources used solely for research purposes. Information about patient time and travel and other out-of-pocket costs (e.g. co- payments), will be obtained through the participant surveys. If patients report utilizing other health care services as a result of their study participation (e.g. additional medical or counseling visits) within the 6-month follow-up period, these services will also be included as immediate downstream costs of the interventions. Service unit cost values will be based on values reported in the literature or Medicare fee schedules. Medicare's reimbursement methodology was developed to approximate true resource costs. Thus, Medicare reimbursement amounts are appropriate for this purpose, even though we expect few participants will be covered by Medicare. Cost/service use will be assessed at T1, T2, T3 and T4 timepoints.

Moderators of patient outcomes with remote telegenetic services (Aim 2b): Moderators (T0 only) include sociodemographics, health literacy and comfort with technology.

a) Sociodemographic data will include race/ethnicity, education, marital status, gender, age, employment status, household income, health insurance (yes/no) and a usual source of medical care (yes/no) which will be collected in the Baseline Survey (T0)
b) History of cancer will be collected in the Baseline Survey (T0).
c) Genetic test result (positive, negative, true negative and test/genes included) will be obtained from Telegenetic Service records and the 6-Month Outcome Survey.
d) Health literacy will be assessed at baseline (T0) with 3 health literacy Brief Literacy Screen (BHLS) screening items which have been validated to detect inadequate health literacy in clinical medical populations (74).
e) Computer literacy will be assessed at baseline (T0) with selected items from the NCI Health Information National Trends Survey (HINTS), including internet and social media use (8 items), electronic medical record use and perceptions of privacy (14

items).(78)

f) Self-Efficacy will be measured at baseline (T0) with the 4-item PROMIS Self-efficacy short form for managing chronic conditions, which has been validated in adults with medical conditions (including cancer) and has good internal consistency (alpha= 0.85-0.92).(77)
g) Financial wellness will be measure at baseline (T0) with 2 items from the Personal Financial Wellness Scale. (91)
h) Psychological impacts due to COVID-19 will be assessed using 15-16 items previously utilized in the CCSS to assess the impact of the COVID-19 pandemic on CCSs. The final item asking about number of individuals in the household is excluded at T2. While this protocol is independent of COVID-19, there is potential for COVID-19 events and impact on psychosocial outcomes to impact other primary and secondary outcomes. The measure is included to allow for analyses to evaluate the impact of these on study outcomes (78)

Implementation outcomes (Aim 3): CFIR informed constructs have been selected to evaluate factors related to uptake of remote telegenetic services, implementation facilitators and barriers and adaptations. We will collect quantitative and qualitative data from multiple key informants (e.g. patients, PCPs, office staff, PCP advisory board and research staff.) Additional methods and analyses included in **Appendix K:** Reporting and analysis plan for implementation outcomes.

3.4 Duration of Protocol

We anticipate the total enrollment for this protocol will last no longer than 5 years.

3.5 Location where research will be conducted

This research will be conducted at the University of Pennsylvania, the University of Chicago and at the CCSS Coordinating Center at St Jude.

3.6 Number of experimental subjects

An approximate 520 participants are anticipated to enroll to meet enrollment goals for the randomized trial (both Aims 1 and 2). As outlined above, once enrollment goals for Aim 1 are reached (120 completed baseline survey and sent randomization flyer), we will halt enrollment ot Arm C. We will continue to enroll to Arms A and B to meet enrollment goals for Aim 2.

An approximate 15-30 patients, 15-30 primary providers and 15-30 primary care provider office staff participants are anticipated to enroll for aim 3, for a total of up to 90 additional participants (**Appendix K).**

4.0 Statistical Considerations and Analyses

Analyses for Aim 1: *We hypothesize that patients randomized to remote telegenetic services will have significantly higher uptake of the composite variable denoting genetic testing or genetic counseling at 6 months.* Our primary outcome will be a composite variable of whether the person had genetic testing or genetic counseling by 6 months (1 if either is true, 0 if neither is true). Uptake of separate genetic testing or genetic counseling decisions (as some patients will make informed decisions to defer testing) and identification of genetic carriers will be three secondary outcomes. We will use Fisher's Exact tests to compare uptake of our primary composite variable and secondary outcomes between the arms. The primary comparison groups will be the usual care/waitlist group vs. the combined remote telegenetics groups (phone

plus videoconference) prior to rerandomization of the waitlist group. For the primary analyses, we will use an intention to treat approach whereby comparisons are made between randomization arms. In secondary analyses, we will compare the randomization arms to investigate if potential confounders (e.g. age) are balanced among the randomization arms. We will do this via pairwise Wilcoxon-rank sum tests and Chi-squared tests as appropriate. If any potential confounders are not found to be balanced among the randomization arms (i.e. $p<0.10$ for any potential confounders in pairwise comparisons), we will use multiple logistic regressions of uptake to investigate the randomization arm effect. In these models, we will include randomization arms as binary (0/1) indicator covariates (leaving one out as the reference); we will also include the potential confounders as covariates in the regressions. These regression models will be akin to sensitivity analyses, designed to study if our inferences are robust after accounting for potential confounders.

Missing data: We do not expect substantial missing data, although there may be loss to follow-up over time. For the primary outcomes, we will assume that those lost to follow-up did not have pre-test counseling or testing (i.e. failures under the intention-to-treat paradigm). Data from our community practice stakeholder interviews suggests this is reasonable since many patients do not get genetic services even when referred. In secondary analyses, we will account for missing data using the multiple imputation technique of Raghunathan with 25 imputed datasets.(81) We will contrast the results obtained through imputation and those obtained from complete case analyses to study if missing data bias could be substantially affecting our inferences.

Sample Size Justification for Aim 1: We chose our sample size to have sufficient power for both Aims 1 and 2. For Aim 1, the sample size was selected to detect average differences in the primary endpoint (a composite variable indicating either genetic testing or genetic counseling) between the primary randomization arms of interest. The primary comparison groups will be the usual care/waitlist group versus the combined remote telegenetics groups (phone or video conference as one group); the primary analysis will consider the groups prior to the waitlist rerandomization. Preliminary data demonstrated that uptake of genetic testing from an ongoing registered randomized trial of remote telegenetic services vs. usual care for cancer genetic testing in community practices was at least 53% (29/55 with uptake) in the intervention arm, but only 17% (4/24 with uptake) in the control arm. With 120 patients in the usual care/waitlist group and 240 patients in the combined telegenetics groups with complete data (after accounting for loss to follow up), we will have >99% power to detect a similar difference in uptake of genetic testing. This assumes a 1% Type I error rate (2-sided) and the use of Fisher's Exact Test. We set the Type I error rate to a conservative 1% to partially account for multiple hypothesis testing when including secondary outcomes and potential moderators in Aim 3. Given the magnitude of the pilot data differences, we anticipate excellent power for the moderator/subgroup analyses. The comparison of the usual care/waitlist group to the combined telegenetics group will be the comparison used to determine if the study accomplishes its primary objective. The uptake of pre-test counseling (Aim 1 secondary objective) and comparison between the phone and videoconference groups (see Aim 2a) are secondary objectives.

Analyses for Aim 2: *We hypothesize that remote telegenetic services by videoconferencing will be associated with greater decreases in cancer related distress and depression and increases in knowledge when compared to phone services.* Our primary outcomes for Aim 2a include changes in 1) cancer related distress; 2) depression; and 3) knowledge. We will compare the usual care at baseline group to the combined arms receiving remote services at baseline. For

comparisons between the remote videoconferencing versus phone groups, we will assign participants to the remote group assigned at baseline, or after rerandomization for the waitlist group. Our primary change scores for the first three variables will be change between baseline and immediately post genetic testing. For the waitlist group, there will be a second baseline measurement after the usual care period has ended. For the 3 primary analyses in Aim 2, we will use T-tests. We will assess balance of potential confounders (e.g. age, race, study site, waitlist assignment) between arms using T-tests or Fisher's exact tests as appropriate. Waitlist group will be considered a confounder in these secondary regression analyses. We will use multiple linear regression models to control for potential confounders inadequately balanced. We will include in the models the confounding variables and indicator (binary 0/1 variables) to indicate randomization arms (leaving one group out as the reference). For longitudinal analyses, we will examine time trajectories using regressions estimated by Generalized Estimating Equations (GEE) to account for within subject temporal correlation. Panel time will be included via indicator variables. We will also include interaction terms between randomization arm and time indicators to investigate temporal effects.(82) We will repeat analyses, but assign participants to per-protocol (i.e. restricting sample to those who properly used the assigned method of disclosure) or as-treated groups (e.g. assigning all participants to a group based on the method of disclosure used, regardless of assignment). For Aim 2 secondary outcomes, we will use multiple linear regressions for continuous outcomes and multiple logistic regressions for binary outcomes using GEE-estimation as described.

To evaluate moderators of patient cognitive, affective and behavioral outcomes (Aim 2b), we will use logistic regressions in which we include variables of interest as covariates. For moderation (i.e. effect modifier analyses), we will include indicator variables for randomization arms in the GEE-estimated multiple linear (for continuous outcomes) or logistic regressions (for uptake); we will also include panel time indicators, the potential moderator variables, and all two-way and three-way interactions among the arm/time/moderator variables. Interactions are created by multiplying two variables together.(82) To maintain power, we will examine non-time moderators separately. We will also examine multiple regression models with potential confounding variables. We will repeat the analyses but assign participants to per-protocol (i.e. restricting sample to those who properly used the method of disclosure as assigned) or as-treated groups (e.g. assigning all participants to a group based on the method of disclosure used, regardless of group assignment).

The economic impact of remote telegenetic services (Aim 2c) will be assessed by performing: 1) cost analysis and 2) cost-effectiveness analysis. The goal of the cost analysis is to estimate the cost of delivering remote telegenetic services, by phone and videoconference, compared to usual care. As above, the cost analysis will take a societal perspective, including the costs of all resources consumed for the implementation and delivery of remote genetic services. Separately, we will examine costs from the health system perspective that can inform decisions about the provision and reimbursement of services, and ultimately will influence the effective dissemination and implementation of remote telegenetic services beyond the study. Cost-effectiveness will be estimated as the incremental cost per (1) additional survivor who receives genetic testing, and (2) additional mutations detected. The numerator of the incremental cost-effectiveness ratio (ICER) will include intervention costs and patient time and travel costs, estimated as described above. In the first analysis, the denominator will be defined by the primary trial endpoint of genetic testing received within 6 months. Because receipt of genetic testing is the measure of effectiveness in this case (i.e. the denominator of the ICER), neither the cost of testing nor the cost of related services provided after genetic testing will be included in the numerator. For the second analysis, the numerator of the ICER will include both genetic test costs and any related health care service costs (additional tests, visits, counseling)

associated with genetic testing at 6 months. Incremental cost effectiveness will be estimated using standard methods, and sensitivity analysis will be used to assess the impact of assumptions and uncertainty on results and conclusions.(83, 84) Although estimation of lifetime costs and outcomes associated with remote telegenetic testing is beyond the scope of this proposal, our results could serve as preliminary data for future grants that explore the long-term cost-effectiveness of increasing genetic testing among cancer survivors.

Sample Size Justification for Aim 2: We further chose our sample size such that we would have sufficient power for Aim 2 comparisons of the videoconference versus phone arms. After rerandomization of the waitlist group, we anticipate potentially having 180 people/arm randomized to the videoconference or phone arms. Based on prior experience, we anticipate that loss to follow-up will be less than 28% in each arm, leaving us with 130 evaluable participants with follow-up data in each group (180-180*28%= approximately 130). Some of the loss to follow-up will occur prior to the waitlist group being rerandomized. We used our pilot data to determine power for this aim (see Table 2 for estimates). We assumed 85% power and a 1.67% Type I error rate. We used a 1.67% Type 1 error rate (2-sided) by applying a Bonferroni correction for the three outcomes of interest to the typical 5% Type I error rate (5%/3=1.67%). We see in Table 2 that we have excellent power for all three arms with at least 95/arm, which is well below our expected 130/arm anticipated sample size. Table 2 also demonstrates that we have sufficient power for subgroup analyses, with a sample size of just 22/arm needed for knowledge comparisons between arms.

Table 2. Sample size calculations for Aim 2

Variable	Change scores[+] (SD) of phone vs. videoconferencing	Number needed*
Knowledge	+5.7 (11.2) vs. +18.6 (12.6)	22/arm
Cancer specific distress**	+3.6 (12.4) v. -2.6 (12.3)	95/arm
Depression	-0.2 (2.0) vs. -1.6 (2.0)	50/arm

[+]Baseline to post genetic testing *85% Power, 1.67% alpha; **intrusive subscale

Amendment note added June 5, 2023: Our anticipated visit 2 completion sample size for the phone and videoconferencing arms will be 60 to 80 per arm, which is below are initial goal of 180/arm. With 60 to 80 per arm, we will still have adequate power for the knowledge and depression endpoints.

Analyses for Aim 3 included in **Appendix K.**

5.0 Informed Consent and Patient Safety

The potential risks associated with participating in this research study are low. These include:

- loss of confidentiality or breach of genetic test information

- distress related to re-opening previous discussions and experiences regarding a personal history of cancer, family history of cancer and/or learning of one's own or one's family member(s)'s potential risk for developing cancer

Attempts will be made to minimize these risks and their possible occurrence will be explained to all participants at the time of consent. Study staff, including genetic counselors, will also be available to discuss these risks with participants over the telephone or in person at any point during the study. Should a participant express the need for a mental health referral, a genetic provider indicates a concern or other data collection reveals significant distress, research staff will identify local social services for assistance and referral.

5.1 Payment to subjects:

Participants will receive a gift card code in the defined amount for the completion of the following surveys in the randomized trial:

- Baseline (T0) Survey: $25
- Pre-Test Counseling Session Session (T1) Survey (Arms A & B): $25
- Disclosure Counseling Session (T2) Survey (Arms A & B): $25
- 6-Month Follow Up (T3) Survey (Arms A & B): $30
- 6-Month Outcome Survey (Arm C only): $75
- 12-Month Follow Up (T4)Ssurvey (Arms A & B): $30

5.2 Informed consent:

The CCSS Coordinating Center will send a letter of invitation, study consent, and a Baseline Survey via the myLTFU app to all eligible CCSS participants. The Project PIs and research staff, as well as the staff at the CCSS Coordinating Center, will be available to respond to questions or concerns of the survivor. Survivors will be informed that participation is voluntary and will not affect their continued participation in other aspects of the CCSS. The purpose of the study and potential risks and benefits will be explained during the informed consent process. All data gathered will be kept in a secured location and available only to members of the research study team. The key elements of the informed consent procedure which will be explained to participants are: (1) the research status of the study; (2) the potential risk and the provisions for it; (3) the lack of guarantee of benefit from participation; (4) the voluntary nature of the study; (5) the lack of consequence to medical care of the decision to consent or refuse to participate; and (6) the freedom to withdraw from the study or to refuse to answer specific questions or to participate in any aspect of the study at any time.

After a participant consents to the study, he or she will complete an eligibility form to confirm eligibility. Eligible participants will then be randomized to one of the three groups and sent the baseline questionnaires via the myLTFU app.

5.3 Confidentiality:

Due to the sensitive nature of the information stored in study databases, we will take extensive precautions to protect the confidentiality of participants. A series of security procedures will be undertaken to ensure subject privacy and HIPAA compliance. Several steps will be taken to mitigate the risk of breach of confidentiality. All clinical data will be stored in a locked file or password protected database. Study data will be password protected, with the password known only to the study coordinator, analyst, and the principal investigators.

DatStat's systems are securely housed on Microsoft Azure Cloud Computing Platform. The system is HIPAA compliant and fully validated for 21 CFR Part 11.

Once a patient contacts Penn Telegenetics, all information that they provide is part of routine clinical care. Patients will give Penn Telegenetics permission to share the clinical outcomes of testing with the research team for the purposes of the research study. This will include clinical documentation and genetic testing information.

Any recordings of genetic counseling sessions will be kept on secure servers at the University of Pennsylvania and the video conference provider. Only the study staff and the video conference providers will have access to the recordings. We have a Business Associate Agreement with our video conferencing providers. Recordings will be saved using the participants study ID number. All recordings will be deleted after the study ends.

APPENDICES

APPENDIX	TITLE
A	ENGAGE DATSTAT CONNECT Messaging Plan
B	Informed consent
C	Eligibility screener
D	Baseline (T0) survey
E	Randomization assignment flyers
F	Pre-Test Counseling Session (T1) Survey
G	Counseling checklists
H	Disclosure Session (T2) Survey
I1	6-Month Outcome Survey
I2	HIPAA authorization to use and disclose Individual health information for research
J	6- and 12-Month Follow Up (T3/T4) Survey
K	Reporting and analysis plan for implementation outcomes
L	Event Monitoring Committee Summary
M	ENGAGE Invitation Letters

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University of Pennsylvania School of Medicine
Research Participant
Informed Consent and HIPPA Authorization Form

Protocol Title:	**ENGaging and Activating cancer survivors in GEnetic services (ENGAGE) Study**
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Research Study Summary for Potential Subjects

You are being invited to participate in a research study. Your participation is voluntary, and you should only participate if you completely understand what the study requires and what the risks of participation are. You should ask the study team any questions you have related to participating before agreeing to join the study. If you have any questions about your rights as a human research participant at any time before, during or after participation, please contact the Institutional Review Board (IRB) at (215) 898-2614 for assistance.

The research study is being conducted to develop the best method for helping survivors of childhood cancer and other serious illnesses get genetic testing and counseling. We have learned that some childhood cancer survivors are more likely to develop cancer as an adult compared with the general population. In some cases, this is due to a gene mutation. Genetic testing can help identify childhood cancer survivors who need additional cancer screening or prevention.

If you agree to join the study, you will be asked to complete the following research procedures:

- Tell us about your health history and your family history of cancer
- Sign a release form allowing the genetic counselor, Penn, and UChicago research staff to see your medical records
- Provide a copy of your insurance card
- Complete up to 5 surveys, at different time points
- Be assigned to one of three study groups

Your participation will last for about 12-18 months, if you proceed to have genetic testing.

Genetic counseling and testing could help you and your provider better understand your risk for additional cancers. The most common risks of participation are:

- There may be a loss of your privacy if your information is accidently released to someone that is not involved in the study. We will do everything we can to make sure this does not happen.
- You may feel upset when answering questions about your personal or family history of cancer. You may also feel upset when learning information about your risk of cancer or your genetic test results.
- Some genetic and health information can be hard to understand. The genetic counselor will help you understand the information being provided.

Please note that there are other factors to consider before agreeing to participate such as additional procedures, use of your personal information, costs, and other possible risks not discussed here. If you are interested in participating, a member of the study team will review the full information with you. You are free to decline or stop participation at any time during or after the initial consenting process.

Why am I being asked to volunteer?
You are being invited to participate in a research study because your personal cancer history or the history of cancer in your family shows that you are likely to be eligible for genetic testing

If you decide to participate, you will be asked to sign this form.

What is the purpose of this research study?
The purpose of the study is to learn if remote genetic counseling services are an effective way to offer genetic counseling and testing to childhood cancer survivors. Remote genetic services means using video conferencing or the telephone to provide counseling from a genetic counselor about cancer genes. We will compare remote genetic services to usual care options

for genetic testing in your local area. Usual care means genetic services from genetic counselors or programs nearest to your local area or testing with one of your current health care providers. Knowing whether or not remote genetic services is effective will help both cancer survivors and their providers learn more about better accessing genetic testing and counseling. The University of Pennsylvania School of Medicine, the University of Chicago Comer Children's Hospital, and the St. Jude Childhood Cancer Survivor Study team are working together on this study.

Why was I asked to participate in this study?
You are being asked to join this study because your personal cancer history, or the history of cancer in your family, shows that you are likely to be eligible for genetic testing.

How long will I be in the study? How many other people will be in the study?
You will be in the study for about 12-18 months, if you proceed to have genetic testing. There will be about 360 people in the study.

What am I being asked to do?
As a part of your participation in the study, you will need to:

- Tell us about your health history and your family history of cancer
- Sign a release form allowing the genetic counselor, Penn, and UChicago research staff to see your medical records
- Provide a copy of your insurance card
- Complete up to 5 surveys, at different time points
- Be assigned to one of three study groups

Randomization

The first two groups involve **remote genetic services** in your home

Group 1: You will have genetic counseling with a University of Pennsylvania genetic counselor by **videoconferencing** in your home or private place you prefer. This means you and the genetic counselor will be able to talk to each other by using a computer. If you are eligible for, and choose genetic testing, you will also receive your results from the genetic counselor by videoconferencing. Or,

Group 2: you will have genetic counseling with a University of Pennsylvania genetic counselor by **telephone** in your home or private place you prefer. This means you and the genetic counselor will be able to talk and see each other over telephone. If you are eligible for, and choose genetic testing, you will also receive your results from the genetic counselor by telephone. Or,

Group 3: You will receive information about how to get genetic counseling and testing in your area (Usual Care). We will provide information on how to find local genetic services in your area. Alternatively, you can talk with your local primary care provider about how to get genetic testing in your area. We will contact you again in six months to see if you have had genetic services. If you have not, we will talk to you about your options for genetic services.

One of these groups will be assigned to you by random. That means you have an equal chance of being in any group.

Depending on the group you are randomized to, you may receive text messages, emails, and notifications, links to short videos, and other materials relevant to your participation on this study through the myLTFU app. Regardless of what group you are randomized to, you may be contacted by a research team member to follow up on survey responses you might give.

Surveys
The surveys will ask you about your thoughts and feelings about cancer risk and genetic testing and actions you have taken. The number of surveys will also depend on which group you are in.

If you are in Group 1 or Group 2 (remote genetic services), you will complete surveys at these time points:

- After you agree to participate in this study (baseline survey).
- After your first appointment with a Penn genetic counselor. This is called the pre-test genetic counseling session.
- After you receive your test results with a genetic counselor (if you choose genetic testing).
- Six months after you receive your test results (if you choose genetic testing).
- 12 months after you receive your test results (if you choose genetic testing).

If you are in Group 3 (usual care), you will complete surveys at these time points.

- After you agree to participate in this study (baseline survey).
- Six months after you finish your first survey (uptake of testing survey).
- If you have completed genetic testing, you will complete a survey six and twelve months after receiving your results.

You may fill out the surveys online, on paper, or by phone with a research staff member. Online surveys use a secure website to ensure security and privacy. These surveys will tell us about your thoughts and feelings about your cancer risk and your genetic counseling and testing experience. Each of these surveys will take you about 30 to 45 minutes to complete.

You do not have to answer any questions that make you feel uneasy. You may stop the surveys at any time. We will give you a unique ID number to use on your surveys. Your ID number will only be linked to your name in a password-protected database kept on secure computer servers. All paper copies of surveys will be kept in a locked room to protect your privacy.

We also may reach out to you once you finish the study for a brief interview. We will ask you to complete a separate consent for this interview, and the completion of this interview is completely optional. You do not have to consent to the interview if you do not want to.

Video or Audio taping
We will videotape or audiotape the counseling sessions so we can review them. This is for quality control and research purposes. The recordings may also be used for future research. You will not be identified by name in any future research. You may choose to not have your session video or audio taped.

What are the possible risks or discomforts?
There are few known risks for this research study. There may be a loss of your privacy if your information is accidently released to someone that is not involved in the study. We will do everything we can to make sure this does not happen.

You may feel upset when answering questions about your personal or family history of cancer. You may also feel upset when learning information about your risk of cancer or your genetic test results.

Some genetic and health information can be hard to understand. The genetic counselor will help you understand the information being provided.

What are the possible benefits of the study?

Genetic counseling and testing could help you and your provider better understand your risk for additional cancers.

What other choices do I have?

If you decide not to participate in this study, no other steps are necessary. Your site can provide you with information about genetic services in your area.

What happens if I do not choose to join the research study?
Nothing happens. You will still receive the same care you would normally receive.

Will I be paid for being in this study?
You will not get paid for taking part in this research study. You will receive a gift card when you complete each study survey, which depends on your group and if you proceed with testing.

- Baseline surveys: $25 gift card
- Pre-test genetic counseling session: $25 gift card
- After you receive your test results: $25 gift card
- 6-months and 12 months after you receive your results: $30 each
- 6-month uptake of testing survey: $50

Will I have to pay for anything?
Genetic counseling and testing itself is not research, but a part of your clinical care. Genetic counseling and testing services will be billed to you and your health insurer. In most cases, genetic testing and counseling are covered by insurance, but in some cases patients may have co-pays or out-of-pocket costs. If you have questions, please ask your genetic counselor or usual care provider to review the cost of these services with you.

When is the Study over? Can I leave the Study before it ends?
This study will end after all participants have completed all study steps, and all information has been collected.

The study staff or your doctor may stop you from taking part in this research study at any time, especially if any of the following occur:

- They feel it is in your best interest
- You do not follow the research study steps
- The research study is stopped.

You are free to leave the study at any time. Leaving will not interfere with your future care. Tell the study staff if you are thinking about stopping or decide to stop. The staff will tell you what follow-up care and counseling could be most helpful for you.

Who can see or use my information? How will my personal information be protected?
We will do our best to make sure that the personal information we collect is kept private. However, we cannot guarantee total privacy. Your personal information may be given out if required by law. Information from this study may be published or presented at scientific meetings. If this happens, your name and personal information will not be used.

Recordings will be kept on secure servers at the University of Pennsylvania and the video conference provider. Only the study staff and the video conference providers will be able to see the recordings. The research staff and video conferencing providers are trained in research participant privacy. We have a business Associate Agreement with our video conferencing providers. This means they must take the same care we take to protect your privacy. Your recordings and survey data will be saved using a unique ID number. It will not include names or other information that would link the information to you directly.

Organizations that may look at and/or copy your medical records for research, quality assurance and data analysis include:

- Your Local Community Site
- The research team at the University of Pennsylvania
- The research team at the University of Chicago
- The National Cancer Institute (NCI) and other government agencies involved in keeping research safe for people, like the Food and Drug Administration (FDA)

Electronic Medical Records and Release of Study Related Information

What is an Electronic Medical Record?

An Electronic Medical Record (EMR) is a computer version of your paper medical record within a health system. As genetic counseling and testing in this study are all clinical services, information about these counseling sessions and your test results will be included in the University of Pennsylvania Health System EMR (Groups 1 & 2) or your usual care provider's EMR or medical records (Group 3). As a part of this study, you are agreeing to let your local care provider share your records with the genetic counselor and research staff at the University of Pennsylvania.

Once placed in the EMR, these clinical records can be read by your local health care provider staff members that are not part of the research team. Information from your EMR may also be shared with others who need access to your EMR (for example, your health insurance company or disability provider). Your health care provider site will decide who gets to see your EMR.

What may be placed in the EMR?
Information related to your participation in the research (e.g., laboratory tests, notes from your physician, imaging studies, and clinical procedures, etc.) will be placed in your EMR maintained by Penn Medicine.

Once placed in your EMR your information may be accessible to appropriate Penn Medicine workforce members that are not part of the research team. Information within your EMR may also be shared with others who are determined by Penn Medicine to be appropriate to have access to your EMR (e.g. Health Insurance Company, disability provider, etc.).

Penn Medicine also participates in automated information sharing through Health Information Exchanges (HIEs). HIEs securely share parts of your electronic health record, including research information, with other healthcare organizations involved in your care. This information is shared to improve the quality, safety and efficiency of your healthcare. To request that your health information not be shared through HIEs, please call 215-662-4484.

Will I, as a subject, have access to research related clinical information within the EMR?
The 21st Century Cures Act requires healthcare institutions to allow patients increased access to their electronic medical record. As part of your participation in this research, if you receive remote genetic services from Penn Medicine, you will have the option to access research related clinical information within your EMR through Penn Medicine's patient portal – called MyPennMedicine (MPM).

What are my rights if I take part in this study? Who can I call about my rights?
Taking part in this study is your choice. If you decide to take part in this study, you may leave the study at any time. If you leave the study, you will not lose any of your regular benefits. Your medical care will not be affected, and you can still get your medical care from our institution.

We will tell you about new information or changes in the study that may affect your health or your willingness to continue in the study.

If you are injured because of this study, you do not lose any of your legal rights to seek payment by signing this form.

You may have questions about your participation in this research study or your rights as a research subject. If you do, please speak with the Principal Investigator listed on page one of this form. You may also contact the Office of Regulatory Affairs at the University of Pennsylvania by calling (215) 898-2614. They will provide more information about your rights as a research subject.

You can visit the National Cancer Institute's Web site (*http://cancer.gov/clinicaltrials/understanding/insurance-coverage*) for more information. You can print a copy of the "Clinical Trials and Insurance Coverage" information from this website.

You can also view more information about this study at ClinicalTrials.gov

Another way to get the information is to call 1-800-4-CANCER (1-800-422-6237) and ask them to send you a free copy

What information about me may be collected, used or shared with others?
The following information will be collected and may be used or shared with others:

- Name, address, telephone number, email address, date of birth
- Copy of your insurance card
- Personal and family medical/cancer history
- Results from genetic testing (if deciding to test)

- Medical record number
- Health plan ID
- Biometric identifiers, including finger and voice prints.

Why is my information being used?
Your information is used by the research team to contact you during the study. Your information and results of genetic testing are used to:

- Do the research
- Oversee the research
- See if the research was done right

Where may my information be stored?
Information related to your participation in clinical research will be contained in a clinical trial management system (CTMS). A clinical trial management system (CTMS) is used to register your information as a participant in a study. This allows for your research data to be entered and stored for the purposes of study operational and financial applications and other activities required as part of the conduct of the research. Once placed in the CTMS your information may be accessible to other authorized personnel at Penn Medicine that support research operations. Your information may be held in other research databases.

Who may use and share information about me?
The following people may use or share your information for this research study:

- Dr. Angela Bradbury (Principal Investigator)
- University of Pennsylvania research study staff
- Other authorized personnel at Penn Medicine and the University of Pennsylvania, including offices that support research operations
- Other research personnel with access to the databases for research and/or study coordination and as otherwise approved by the IRB

Who, outside of Penn Medicine, might receive my information?

- Those working under the direction of the investigator for the study, (for example the videoconference providers).
- Dr. Henderson and other oncology team members are the University of Chicago Comer Children's Hospital
- University of Chicago Comer Children's Hospital research study staff
- All research centers participating in this study, even if they are not part of the School of Medicine
- The funding sponsor and organizations supporting the sponsor
- St. Jude research study staff

<u>Oversight organizations</u>

- The Office of Human Research Protections

Once your personal health information is disclosed to others outside the School of Medicine, it may no longer be covered by federal privacy protection regulations.

The Principal Investigator or study staff will inform you if there are any additions to the list above during your active participation in the trial. Any additions will be subject to University of Pennsylvania privacy procedures.

How long may Penn Medicine use or disclose my personal health information?
Your authorization for use of your personal health information for this specific study does not expire.

Your information may be held in a research database. However, the School of Medicine may not use or share information collected in this study for any other purpose unless:

- You give written permission
- The University of Pennsylvania's Institutional Review Board grants permission
- As permitted by law

Can I change my mind about giving permission for use of my information?
Yes. You may take away your permission to use and disclose your health information at any time. You do this by sending written notice to Angela R. Bradbury, M.D., the investigator for the study (see page 1). If you withdraw your permission, you will not be able to stay in this study.

Future Use of Data
Your research information, including information collected about you through the study, your survey responses, and recordings will be de-identified. De-identified means that all identifiers have been removed. The information could be stored and shared for future research in this de-identified fashion. It would not be possible for future researchers to identify you as we would not share any identifiable information about you with future researchers. This can be done without again seeking your consent in the future, as permitted by law. The future use of your information only applies to the information collected on this study. Information obtained as part of the clinical counseling and genetic testing services through the University of Pennsylvania Telegenetics Program will be considered as research data.

What if I decide not to give permission to use and give out my health information?
Then you will not be able to be in this research study.

By signing this document, you are permitting the School of Medicine to use and disclose personal health information collected about you for research purposes as described above.

Who can I call with questions, complaints or if I'm concerned about my rights as a research subject?
If you have questions, concerns or complaints regarding your participation in this research study or if you have any questions about your rights as a research subject, you should speak with the Principal Investigator listed on page one of this form. If a member of the research team cannot be reached or you want to talk to someone other than those working on the study, you may contact the IRB at the number on page one of this form.

A copy of this consent and HIPPA authorization form will be given to you.

When you sign this form, you are agreeing to take part in this research study. This means that you have read the consent and HIPPA authorization form, your questions have been answered, and you have decided to volunteer. Your signature also means that you are permitting the University of Pennsylvania to use your personal health information collected about you for research purposes within our institution. You are also allowing the University of Pennsylvania to disclose that personal health information to outside organizations or people involved with the operations of this study.

As described on Page 3, we will videotape or audiotape the counseling sessions so we can review them.

Agree to have disclosure session recorded: [ ] YES
[ ] NO

_____	_____	_____	___: ___ AM/PM
Name of Subject (Please Print)	Signature of Subject	Date	Time

_____	_____	_____	___: ___ AM/PM
Name of Person Obtaining Consent (Please Print)	Signature	Date	Time