PARTNERS HUMAN RESEARCH COMMITTEE
PROTOCOL SUMMARY

Answer all questions accurately and completely in order to provide the PHRC with the relevant information to assess the risk-benefit ratio for the study. Do not leave sections blank.

PRINCIPAL/OVERALL INVESTIGATOR
Daniel C. Chung

PROTOCOL TITLE
Development and Implementation of Electronic Decision Aids for Genetic Testing in Inherited Cancer Syndromes

FUNDING
NIH U01CA243695-01

VERSION DATE
11/3/2022 (V3.0)

SPECIFIC AIMS

Concisely state the objectives of the study and the hypothesis being tested.

We propose to implement an electronic decision aid to assist individuals in choosing a multi-gene panel with their medical oncologist instead of a genetic counselor. We will test the hypothesis that a decision aid without a genetic counselor can facilitate quality decisions around the selection of a specific multi-gene panel. In addition to positive changes in knowledge, shared decision making, and decisional conflict, we anticipate that the decision aid will increase access to genetic testing in a timely manner. Utilizing an effectiveness-implementation hybrid study design, we propose these specific aims:

1. To pilot electronic decision aids for selection of a multi-gene panel
   a) Implement our decision aid already completed for ovarian cancer patients
   b) Adapt the decision aid for pancreatic cancer patients
   c) Create standard operating procedures for implementation and pilot each tool at two institutions (MGH and BMC) to establish feasibility and acceptability

BACKGROUND AND SIGNIFICANCE

Provide a brief paragraph summarizing prior experience important for understanding the proposed study and procedures.

The indications and demand for genetic testing in cancer care are rapidly growing. Hereditary cancer syndromes are more common than previously appreciated, and genetic testing is standard of care to establish these diagnoses. In addition, genetic test results are now critical to guiding targeted therapies in patients with established tumors such as ovarian and pancreatic cancer, so timely access to genetic testing is essential. Genetic counselors have traditionally managed the testing process, but there is a critical shortage of counselors and they are not able to meet the demand for testing. Without a genetic counselor, effective communication of testing options, outcomes, and risks could be compromised. Oncologists are unable to offer testing by themselves due to lack of time and expertise in genetic testing. One of the most challenging decisions in the pre-test setting is the choice of gene panel. Multi-gene panels are now the norm, but panels can include as few as 5 or as many as 125 genes. This variation depends upon whether the panel includes genes associated with a single tumor type or multiple tumor types, and whether genes with low levels of evidence of pathogenicity are also included. There is no consensus on what constitutes an ideal panel, and the decision of which panel to select is highly individualized. Innovative strategies to support patients facing these time-sensitive and complex pre-test decisions are needed.

Decision aids are well-suited to address this challenge by providing education, facilitating the process of informed choice, clarifying personal preferences, and promoting shared decision making.

RESEARCH DESIGN AND METHODS

Briefly describe study design and anticipated enrollment, i.e., number of subjects to be enrolled by researchers study-wide and by Partners researchers. Provide a brief summary of the eligibility criteria (for example, age range, gender, medical condition). Include any local site restrictions, for example, "Enrollment at Partners will be limited to adults although the sponsor's protocol is open to both children and adults."

All adult patients diagnosed with malignant ovarian tumor or malignant pancreatic adenocarcinoma who are referred for genetic testing and who have not previously completed germline genetic testing will be invited to complete the Decision Aid at the start of their next clinic appointment. Patients who are unable to complete surveys will be excluded from this study.

We plan to enroll 100 patients in total (50 ovarian cancer patients; 50 pancreatic cancer patients) between MGH and BMC oncology clinics. MGH locations will include oncology clinics at MGH main campus, NSMC, NWH, and Waltham MGH.

There are no local site restrictions.

Briefly describe study procedures. Include any local site restrictions, for example, "Subjects enrolled at Partners will not participate in the pharmacokinetic portion of the study." Describe study endpoints.

After a recommendation is made for genetic testing during the initial consultation, a session to complete the DA will be scheduled at the start of the next appointment. At this appointment, the MA will escort the patient to a private area and provide the electronic tablet containing the Decision Aid (DA) and instructions for use. Upon completion of the DA, patients will be asked to indicate their decision about whether to pursue genetic testing and which specific multi-gene panel to pursue. Two copies of the DA summary will be printed out. The patient will keep one copy of the summary sheet and the second will be shared with their MD provider in clinic. No PHI will be entered or stored on the electronic device. The only identifier included will be a User ID. The provider will review the preferences, discuss any questions, document the discussion in the electronic medical record, and proceed with informed consent/genetic testing as per patient preference. The provider will collect the DA printout and store with the study staff. At any time in this process, the patient can elect to defer a decision and request a follow-up appointment with a genetic counselor.

For studies involving treatment or diagnosis, provide information about standard of care at Partners (e.g., BWH, MGH) and indicate how the study procedures differ from standard care. Provide information on available alternative treatments, procedures, or methods of diagnosis.

N/a

Describe how risks to subjects are minimized, for example, by using procedures which are consistent with sound research design and which do not unnecessarily expose subjects to risk or by using procedures already being performed on the subject for diagnostic or treatment purposes.

The risks of this study are expected to be minimal as the patients will be able to decline participation in the DA at any timepoint.

Describe explicitly the methods for ensuring the safety of subjects. Provide objective criteria for removing a subject from the study, for example, objective criteria for worsening disease/lack of improvement and/or unacceptable adverse events. The inclusion of objective drop criteria is especially important in studies designed with placebo control groups.

A patient can decline participation at any time.

FORESEEABLE RISKS AND DISCOMFORTS

Provide a brief description of any foreseeable risks and discomforts to subjects. Include those related to drugs/devices/procedures being studied and/or administered/performed solely for

research purposes. In addition, include psychosocial risks, and risks related to privacy and confidentiality. When applicable, describe risks to a developing fetus or nursing infant.

This is a low risk study. All participants will complete surveys at baseline and post-intervention that assess knowledge, shared decision making, and decisional conflict. There are no physical risks or medical/device side effects involved in the study. All efforts will be made to protect the confidentiality of protected health information. Identifiable information will be stored in a secure, password-protected database. Only authorized study personnel at Massachusetts General Hospital or Boston Medical Center will have access to this information. Further identifiable information may be revealed if necessary to protect the patient from risk or harm. Certain federal and state agencies may also have access if required by law. All staff have completed clinical investigation training that includes a focus on subject confidentiality.

It is possible that patients will feel upset by questions about their risk for an inherited cancer syndrome. We will monitor emotional distress. If this occurs, the clinical research coordinator will inform the PI or genetic counselor, who will provide potential referrals if it is determined that the participant requires and desires further psychological assistance. There are Psychiatry Services or Social Work Departments who provide clinical services to patients, or the genetic counselor can more thoroughly address concerns about inherited cancer risk.

EXPECTED BENEFITS

Describe both the expected benefits to individual subjects participating in the research and the importance of the knowledge that may reasonably be expected to result from the study. Provide a brief, realistic summary of potential benefits to subjects, for example, "It is hoped that the treatment will result in a partial reduction in tumor size in at least 25% of the enrolled subjects." Indicate how the results of the study will benefit future patients with the disease/condition being studied and/or society, e.g., through increased knowledge of human physiology or behavior, improved safety, or technological advances.

A potential benefit to participating in the study is the opportunity to learn more about inherited cancer risk and genetic testing options. In aggregate, the study will define the implementation process and role for decision aids in the pre-test counseling for genetic testing. This approach promises to increase access, communication, and quality decision making for genetic testing. The risks to participation are low. Genetic testing is already part of routine care, and the focus of this study is to develop a new strategy for effective education and decision-making prior to genetic testing.

EQUITABLE SELECTION OF SUBJECTS

The risks and benefits of the research must be fairly distributed among the populations that stand to benefit from it. No group of persons, for example, men, women, pregnant women, children, and minorities, should be categorically excluded from the research without a good scientific or ethical reason to do so. Please provide the basis for concluding that the study population is representative of the population that stands to potentially benefit from this research.

The study population is representative of the population seen in the MGH and BMC oncology clinics for treatment of ovarian cancer and pancreatic cancer.

When people who do not speak English are excluded from participation in the research, provide the scientific rationale for doing so. Individuals who do not speak English should not be denied participation in research simply because it is inconvenient to translate the consent form in different languages and to have an interpreter present.

Non-English speakers are not the targeted population of this study. If English is not the primary language for an eligible subject, we will use medical interpreters to guide patients through the decision aid or translate the decision aid into other languages.

For guidance, refer to the following Partners policy:
Obtaining and Documenting Informed Consent of Subjects who do not Speak English
https://www.partners.org/Assets/Documents/Medical-Research/Clinical-Research/Non-English-Speaking-Subjects.pdf

RECRUITMENT PROCEDURES

Explain in detail the specific methodology that will be used to recruit subjects. Specifically address how, when, where and by whom subjects will be identified and approached about participation. Include any specific recruitment methods used to enhance recruitment of women and minorities.

All patients seen in the MGH and BMC oncology clinics with ovarian or pancreatic cancer who are referred for genetic testing will be invited to participate by their oncologist. If the patient is interested in learning more about the decision aid at the end of their appointment, the oncologist will take them to another exam room where they can discuss the study with a study coordinator. If the patient agrees to participate, the study coordinator will schedule the DA for the beginning of the patient's next clinic appointment and provide the DA Study Fact Sheet for the patient to review.

Institutions will register eligible participants in the Clinical Trials Management System (CTMS) OnCore as per DF/HCC Policy REGIST-101

Provide details of remuneration, when applicable. Even when subjects may derive medical benefit from participation, it is often the case that extra hospital visits, meals at the hospital, parking fees or other inconveniences will result in additional out-of-pocket expenses related to study participation. Investigators may wish to consider providing reimbursement for such expenses when funding is available

A small monetary incentive ($10) will be offered to participants for completion of the post-decision aid study survey.

For guidance, refer to the following Partners policies:

Recruitment of Research Subjects
https://www.partners.org/Assets/Documents/Medical-Research/Clinical-Research/Recruitment-Of-Research-Subjects.pdf

Guidelines for Advertisements for Recruiting Subjects
https://www.partners.org/Assets/Documents/Medical-Research/Clinical-Research/Guidelines-for-Advertisements.pdf

Remuneration for Research Subjects
https://www.partners.org/Assets/Documents/Medical-Research/Clinical-Research/Remuneration-for-Research-Subjects.pdf

CONSENT PROCEDURES

Explain in detail how, when, where, and by whom consent is obtained, and the timing of consent (i.e., how long subjects will be given to consider participation). For most studies involving more than minimal risk and all studies involving investigational drugs/devices, a licensed physician investigator must obtain informed consent. When subjects are to be enrolled from among the investigators' own patients, describe how the potential for coercion will be avoided.

When eligible subjects come in for their next oncology clinic appointment, they will be met by a study coordinator at check-in. The coordinator will go over the DA Study Fact Sheet with them, giving ample time for subjects to ask questions. Subjects will then be provided with a tablet to complete the DA survey. Informed consent will be implied if the patient completes the survey.

NOTE: When subjects are unable to give consent due to age (minors) or impaired decision-making capacity, complete the forms for Research Involving Children as Subjects of Research and/or Research Involving Individuals with Impaired Decision-making Capacity, available on the New Submissions page on the PHRC website:
https://partnershealthcare.sharepoint.com/sites/phrmApply/aieipa/irb

For guidance, refer to the following Partners policy:
Informed Consent of Research Subjects:

https://www.partners.org/Assets/Documents/Medical-Research/Clinical-Research/Informed-Consent-of-Research-Subjects.pdf

DATA AND SAFETY MONITORING

Describe the plan for monitoring the data to ensure the safety of subjects. The plan should include a brief description of (1) the safety and/or efficacy data that will be reviewed; (2) the planned frequency of review; and (3) who will be responsible for this review and for determining whether the research should be altered or stopped. Include a brief description of any stopping rules for the study, when appropriate. Depending upon the risk, size and complexity of the study, the investigator, an expert group, an independent Data and Safety Monitoring Board (DSMB) or others might be assigned primary responsibility for this monitoring activity.

NOTE: Regardless of data and safety monitoring plans by the sponsor or others, the principal investigator is ultimately responsible for protecting the rights, safety, and welfare of subjects under his/her care.

The PI, Dr. Chung, will act as the chief Data and Safety Monitoring Officer for all proposed research. The potential risks are minimal as this is a survey study and there are no physical or medication interventions. Monthly reports on collected data will be generated by study staff, and any issues will be reported to the Principal Investigator (PI) and dealt with accordingly. The PI will supervise data and safety monitoring at all levels. He will determine when research needs to be altered or stopped.

Describe the plan to be followed by the Principal Investigator/study staff for review of adverse events experienced by subjects under his/her care, and when applicable, for review of sponsor safety reports and DSMB reports. Describe the plan for reporting adverse events to the sponsor and the Partners' IRB and, when applicable, for submitting sponsor safety reports and DSMB reports to the Partners' IRBs. When the investigator is also the sponsor of the IND/IDE, include the plan for reporting of adverse events to the FDA and, when applicable, to investigators at other sites.

NOTE: In addition to the adverse event reporting requirements of the sponsor, the principal investigator must follow the Partners Human Research Committee guidelines for Adverse Event Reporting

Dr. Chung will be responsible for reporting any unanticipated problems, including adverse events, to the PHRC. The PI will report any unanticipated problems within 5 working days/7 calendar days of the date at which the PI first becomes aware of the problem during the conduct of the study, after study completion, or after subject withdrawal or completion. Although this proposed project is perceived to be relatively low-risk, the study may be terminated by Dr. Chung if the frequency of serious or unexpected adverse events is higher than that anticipated. Once this determination is made, a

memo will be sent to the IRB and to NIH explaining the reasons for the determination.

MONITORING AND QUALITY ASSURANCE

Describe the plan to be followed by the principal investigator/study staff to monitor and assure the validity and integrity of the data and adherence to the IRB-approved protocol. Specify who will be responsible for monitoring, and the planned frequency of monitoring. For example, specify who will review the accuracy and completeness of case report form entries, source documents, and informed consent.

NOTE: Regardless of monitoring plans by the sponsor or others, the principal investigator is ultimately responsible for ensuring that the study is conducted at his/her investigative site in accordance with the IRB-approved protocol, and applicable regulations and requirements of the IRB.

Dr. Chung will oversee all data collection and ensure that it is stored in a confidential and secure manner consistent with all regulatory requirements. Formal monthly meetings focusing on data collection and storage will be held with all the research staff, and a Data Monitoring Committee (PI, Karen Sepucha (Co-Investigator), Kristen Shannon (Co-investigator), Steve Bartels (Co-Investigator)) will meet quarterly.

For guidance, refer to the following Partners policies:

Data and Safety Monitoring Plans and Quality Assurance
https://www.partners.org/Assets/Documents/Medical-Research/Clinical-Research/DSMP-in-Human-Subjects-Research.pdf

Reporting Unanticipated Problems (including Adverse Events)
https://www.partners.org/Assets/Documents/Medical-Research/Clinical-Research/Reporting-Unanticipated-Problems-including-Adverse-Events.pdf

PRIVACY AND CONFIDENTIALITY

Describe methods used to protect the privacy of subjects and maintain confidentiality of data collected. This typically includes such practices as substituting codes for names and/or medical record numbers; removing face sheets or other identifiers from completed surveys/questionnaires; proper disposal of printed computer data; limited access to study data; use of password-protected computer databases; training for research staff on the importance of confidentiality of data, and storing research records in a secure location.

NOTE: Additional measures, such as obtaining a Certificate of Confidentiality, should be considered and are strongly encouraged when the research involves the collection of sensitive data, such as sexual, criminal or illegal behaviors.

The privacy of all subjects will be protected and confidentiality maintained. After enrollment, all subjects will be identified by a unique identification

number. The code key connecting the name of the subject to the identification number will be kept in a separate secure location. No PHI will be entered or stored on the electronic decision aid device. The only identifier will be a User ID.

Personal information along with study data will be kept in REDCap, an online partners sponsored data storage site. Only investigators and study staff will have access to the data stored in password protected computer databases.

SENDING SPECIMENS/DATA TO RESEARCH COLLABORATORS OUTSIDE PARTNERS

Specimens or data collected by Partners investigators will be sent to research collaborators outside Partners, indicate to whom specimens/data will be sent, what information will be sent, and whether the specimens/data will contain identifiers that could be used by the outside collaborators to link the specimens/data to individual subjects.

No specimens or data will be shared with collaborators outside of Partners.

Specifically address whether specimens/data will be stored at collaborating sites outside Partners for future use not described in the protocol. Include whether subjects can withdraw their specimens/data, and how they would do so. When appropriate, submit documentation of IRB approval from the recipient institution.

No specimens or data will be shared with collaborators outside of Partners.

RECEIVING SPECIMENS/DATA FROM RESEARCH COLLABORATORS OUTSIDE PARTNERS

When specimens or data collected by research collaborators outside Partners will be sent to Partners investigators, indicate from where the specimens/data will be obtained and whether the specimens/data will contain identifiers that could be used by Partners investigators to link the specimens/data to individual subjects. When appropriate, submit documentation of IRB approval and a copy of the IRB-approved consent form from the institution where the specimens/data were collected.

Data collected at the BMC site will be de-identified and sent to Dr. Chung via Secure file transfer.