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PI: Alanna Rahm

Title: IMPULSS - Implementing universal lynch syndrome screening across multiple healthcare systems: Identifying strategies to facilitate and maintain programs in different organizational contexts

Grant#: R01CA211723
Project Period: 08/01/2017 – 07/31/2023

Project Summary/Abstract: Lynch syndrome (LS) is the most common form of inherited colorectal cancer risk. People with Lynch syndrome are also at increased risk for endometrial, ovarian, gastric, small bowel, and renal cancers. Importantly, well-established clinical guidelines with strong evidence exist for cancer treatment, screening, and prevention in individuals with LS. Identification of individuals with LS is accomplished through a variety of techniques, including family and medical history evaluation, computational models, or tumor testing. The systematic screening of all colorectal tumors for LS was first recommended by the Evaluation of Genetic Application in Practice and Prevention (EGAPP) working group in 2009 and has been designated high priority by the National Academies of Science, Engineering, and Medicine working group and by the Blue Ribbon Panel. The potential public health impact to reduce cancer morbidity and mortality of this intervention supports this priority, as effective implementation of LS screening will help meet the goals of the Cancer Moonshot as well as demonstrate the promise of precision medicine. Currently, implementation of LS screening in healthcare systems remains suboptimal for a variety of reasons. LS screening involves the coordination of multiple departments and individuals across an organization, which is often difficult in large, complex, healthcare systems. Therefore, the overarching goal of this project is to utilize tools from implementation science to describe, explain, and compare decision making and other variations in LS screening implementation across multiple healthcare systems to create and evaluate in a real world setting an organizational toolkit to facilitate implementation of LS screening.

Specific aims:
1. Describe variation in LS screening implementation across multiple healthcare systems
2. Explain practice variation and determine factors associated with optimal implementation
3. Determine the relative effectiveness, efficiency, and costs of different LS screening protocols by healthcare system
4. Develop and test in a natural environment an organizational toolkit for LS screening. This toolkit will enable effective implementation of LS screening programs; ultimately preventing needless suffering of patients and their family members from preventable cancers, decreasing waste in healthcare system costs, and informing strategies to facilitate the promise of precision medicine.

PI: Kimberly Kaphingst, Sandra Buys, & Meenakshi Siggireddi

Title: BRIDGE - Leveraging an electronic medical record infrastructure to identify primary care patients eligible for genetic testing for hereditary cancer and evaluate novel cancer genetics service delivery models

Grant#: U01CA232826
Project Period: 09/18/2018 – 08/31/2023

Project Summary/Abstract: Identifying individuals with inherited cancer susceptibility is critical for targeted cancer prevention, screening, and treatment. Strategies to assess the genetic risk of unaffected individuals are needed. Scalable and sustainable methods to automatically extract and analyze family history information routinely captured in the electronic health record (EHR) can identify primary care patients appropriate for cancer genetic services. Increased patient ascertainment needs to be paired with implementation studies to compare models of delivering genetic services, including patient-directed models. Because access to services continues to be a barrier for those from minority racial and ethnic groups and rural areas, examining responses to different delivery models across population subgroups is essential. This study will employ an implementation science framework to test a replicable EHR-based clinical decision support (CDS) infrastructure to: 1) automatically identify unaffected patients from 48 primary care clinics in two healthcare systems, University of Utah and New York University, who qualify for cancer genetic services (Aim 1); and 2) compare two models of genetic services delivery for 1,920 primary care patients using a randomized trial design with clinic-level randomization (Aims 2 and 3). Innovative features include implementation of population-based CDS assessment of family history information available in the EHR; comparison of outcomes of patient-directed and enhanced standard of care delivery models; and focus on impact of race/ethnicity and rurality. This highly impactful translational research builds on our unique strengths in cancer genetics, clinical informatics, and population sciences, and addresses issues of immediate clinical significance, including increasing hereditary cancer genetic testing in appropriate patients and improving access for underserved groups.

Specific Aims:

1. Evaluate whether the CDS approach identifies patients who have not previously been referred, and whether this varies by race/ethnicity and rurality.
2. Compare: a patient-directed model in which those identified by the CDS infrastructure as meeting testing criteria will be informed of their cancer risks, provided with educational resources, and offered the option to select genetic testing through a patient portal to an enhanced standard of care model in which providers and patients are notified through CDS when criteria are met and of the availability of standard of care genetic counseling. We will compare uptake of genetic testing by model and whether this differs by race/ethnicity and rurality.
3. Compare the effects of the two delivery models on adherence to recommendations 12 months after return of results, examining differences in effects by race/ethnicity and rurality.

PI: Elizabeth Swisher & Catherine Wang

Title: PICNIC - Implementing the moon: Getting genomic testing to the public

Grant#: U01CA232795
Project Period: 09/20/2019 – 08/31/2024

Project Summary/Abstract: Genetics reports on 22 areas of clinical practice guidelines on how to use genetic tests, based on data that clinical outcomes are enhanced or improved by regular use. Current practice guidelines from ACMG provide referral indications for cancer predisposition assessment. Identifying patients with high genetic risk for breast, ovary, colon, or other cancers has important clinical ramifications for an individual's healthcare, but genetic risk if often not identified because of testing barriers at several levels. Barriers at the provider level include inadequacies in risk recognition, patient referrals and availability of genetic professionals to provide counseling in a traditional testing paradigm. Barriers at the level of the patient include poor understanding of the availability and benefits of testing and inadequate access to testing services. How to best implement appropriate genomic testing and follow-up care into an operating healthcare system is not known. Issues of communication, clinical flow, reportable actions, and transmission of information and support are of critical importance and must change and grow to accommodate the new information contained within genomic testing. Studies to date of the implementation process have been conducted in high resourced facilities, under optimal conditions, often not at the system level.

Specific Aim:

1. Compare the efficacy and implementation of two strategies for identifying members of a primary care clinic's population who have a family or personal history of cancer and offering high-risk individuals to obtain genetic testing for cancer susceptibility mutations in a randomized trial.

The two methods are:

2. Point of Care (POC) approach: A tablet-based screening for family/personal history of cancer will be offered to all patients aged 25- 65 coming in for a routine appointment at the clinic.
3. Direct Patient Engagement (DPE): Letters will be sent to all individuals aged 25-65 in a clinic's population, inviting them to visit a web site for screening for family /personal history of cancer. In both strategies, those determined to be high-risk will receive online education about genetic testing and an invitation to obtain such testing through a web-based platform.

Outcomes will be the fraction of the active clinic patient population that completes screening and the fraction of the active clinic patient population that undergoes testing. 2. Identify changes, problems, and inefficiencies in clinical flow and interactions during and after the implementation of genomic testing for cancer risk across primary care clinics. 3. Evaluate the effects of two methods of implementation of genomic screening for cancer risk on patient, provider, and health system leader reports of benefits and harms, satisfaction, perceived quality of care, including across gender, racial/ethnic, socioeconomic, and genetic literacy divides. 4. Evaluate the value (cost-effectiveness) and affordability (budget impact) of each screening strategy.

PI: Katherine Nathanson & Steven Joffe

Title: GEN-Y: Randomized trial of universal vs guideline-directed germline testing among young adults with cancer

Grant#: U01CA232836
Project Period: 09/20/2019 – 08/31/2024

Project Summary/Abstract: Cancer is the leading nontraumatic cause of death among young adults. In individuals under age 40, cancer has a distinct biology and often has an underlying genetic etiology. However, consensus guidelines driven by phenotypic characteristics fail to identify many young adult patients with inherited genetic risk, in part due to their complexity and to lack of data on mutation frequency. We likely vastly underestimate the frequency and spectrum of germline susceptibility in young adults with cancer, knowledge of which would have far-reaching implications both for their treatment and follow-up care and for the diagnosis and management of relatives. Thus, better strategies for diagnosing inherited risk among young adults with cancer are needed. Further, genetic testing rates among relatives of those identified with inherited cancer risk range from 50-60%; interventions to overcome the barriers that patients and relatives face, so they can take appropriate screening and risk-reducing measures, must be developed and tested. Finally, there is a critical need to integrate genetic evaluation and test results into the electronic medical record (EMR) to facilitate tailored clinical decision support for both clinicians and patients.

Specific Aims:

1. Conduct a randomized controlled trial among 1421 young adults with cancer, one-third of whom will be members of racial or ethnic minorities or medically underserved groups, to compare rates of ascertainment of genetic risk between guideline-driven, phenotype- directed genetic testing (current standard of care) and universal cancer panel genetic testing. Working with the Penn Medicine Nudge Unit and Information Services, we will develop EMR-based algorithms for automatic patient referral and clinical decision support, driven by discrete genetic test results ported into the EMR via HL7, that will include 'active choice' nudges, direct-to-patient alerts, and physician dashboards that minimize physician burden. We will compare adherence to screening recommendations among participants to that among historical controls.
2. Compare the impact of the two up-front testing strategies among patients, enhanced by a novel strategy of direct team outreach to at-risk relatives, on ascertainment of genetic risk among family members. We also will conduct qualitative interviews with a diverse sample of patients, relatives, and family groups to describe the critical interactions that facilitate or impede communication about risk and cascade testing within families and to explore the acceptability of direct clinical team outreach to at- risk relatives.

PI: Georgia Wiesner & Lori Orlando

Title: Improving identification and healthcare for patients with inherited cancer syndromes: Evidence-based EMR implementation using a web-based computer platform

Grant#: U01CA232829
Project Period: 09/17/2019 – 08/31/2024

Project Summary/Abstract: From the earliest recognition of families with a high rate of cancer over 100 years ago, researchers have been focused on the genetic underpinnings of inherited cancers; however, identification remains a significant challenge due to persistent barriers across patient, provider and health system stakeholders, despite recent advances in the development of electronic medical records (EMR) and risk prediction tools that use family health history (FHH) information. Innovations in bioinformatic technology hold great promise in overcoming many of these barriers, particularly with the development of FHH applications that collect and analyze family data, and SMART-on-FHIR capabilities that can integrate third party apps with the EMR. MeTree, a patient facing risk assessment platform for 23 hereditary cancer syndromes with integrated education and evidence- based clinical decision support, is one such platform that served as the backbone of the Implementing Genomics in Practice (IGNITE) network's FHH clinical utility study, where it demonstrated improvements in the identification of those at risk, yet, also highlighted ongoing challenges particularly around undergoing genetic counseling and testing, and awareness of risk. We submit that these barriers can be overcome and that we can significantly improve identification and management of those at risk for hereditary cancer syndromes by bringing together a single clinical care platform that contains: a patient-facing risk assessment program integrated into the EMR, automated risk calculation with clinical decision support for patients and physicians for multiple hereditary cancer syndromes, systematic assessment of risk across a variety of clinic settings, guidance and education on family health history, genomics, risk management, and cascade screening, and an implementation sciences framework to allow us to build a novel and scalable clinical care paradigm for hereditary cancer risk assessment and risk management.

Specific Aims:

1. Deploy a care delivery model that will facilitate systematic risk assessment for hereditary cancers in diverse clinical environments (in primary care and cancer care clinics at two different medical centers) in a randomized controlled trial of 4000 patients
2. Improve access to genetic healthcare providers for participants at risk for hereditary cancer syndromes by deploying the care delivery model in the cancer genetic counseling clinics in a randomized controlled trial of 300 patients;
3. Explore the feasibility of our care delivery model to improve family engagement for cancer risk assessment for patients who are found to have cancer gene variants or strong family histories of cancer.

PI: Doug Corley, Ravi Sharaf, & Carmit McMullen

Title: The Family Study: Comparing three ways to identify and provide care to patients at risk for hereditary cancer

Grant#: NCT04145388 (PCORI)
Project Period: 07/01/2020 – 08/31/2025

Project Summary/Abstract: About one in ten people in the United States will develop cancer due to a hereditary predisposition. A hereditary predisposition means an increased risk of cancer due to presence of cancer in multiple family members or due to the inheritance of a cancer-causing gene mutation. People susceptible to hereditary cancer are at a very high risk of developing malignancy, often at an early age. Family history collection has been universally recommended as the best way to identify those at risk of hereditary cancer. Family history information consists of a patient's personal medical history as well as information about the health of relatives. However, doctors often do not adequately collect and act upon family history information such that as few as 5% of people at risk of hereditary cancer are identified, and as few as half of them receive the recommended preventative health care that can lower their chance of developing or dying from cancer. Our study aims to solve this problem and find the best approach for family-history collection (to identify individuals at risk of hereditary cancer) and for provision of follow-up care for those at risk. We propose a large (18,000 person), randomized trial to compare three methods to identify individuals at risk of hereditary cancer and provide them with the recommended follow up care. The trial will take place in a large health system with members who are diverse in their age, race, ethnicity, income, and urban-rural residence.
We will compare:

1. Physician collection of family history information and physician provision of follow-up care (usual care)
2. Patient completion of online prediction models that numerically estimate cancer risk based on select family history information, with follow up care that is coordinated by a genetic counselor and nurse practitioner team
3. Online patient-completion of a detailed three-generation family history (pedigree), along with follow up care that is coordinated by a genetic counselor and nurse practitioner team.

When the study ends (outcomes), we will better understand the strengths and weaknesses of each method and which is best in terms of benefits and harms that are important to patients. We will learn which method is best for identifying people at risk of hereditary cancer, what patients think about each method, how each method impacts follow up care that can reduce or prevent cancer mortality, how many health care resources are used in each method, and what is
needed to spread these interventions to other health systems.

PI: Paul Spellman & Jackie Shannon

Title: Evaluation of population-based testing for HBOC and Lynch Syndromes

Grant#: U01CA232819
Project Period: 06/10/2020 – 05/31/2025

Project Summary/Abstract: The standard of care for genetic testing of hereditary breast and ovarian cancer (HBOC) syndrome and Lynch syndrome is based on guidelines from the NCCN. The paradigm was developed based on the principle that genetic testing was expensive and that the incidence of these syndromes was low. Over the past twenty years the price of testing has fallen dramatically, and it is now recognized that both HBOC and Lynch syndrome are relatively common (joint incidence of about 1 in 200). Many individuals in the population are affected by HBOC or Lynch but come from small families with few female relatives. Given the decreases in family size that have occurred over the past 50 years this is becoming a common situation. It is estimated that only 20% of those affected by HBOC are aware of their condition. Overall, there is a significant unmet need for those with HBOC and Lynch syndrome to be identified so they can have the opportunity for appropriate medical care. What we need are approaches that can rapidly, accurately, and inexpensively identify those with inherited cancer syndromes. The costs of sequencing have fallen dramatically, and members of our team have QIAseq based targeted resequencing platforms for germline studies that dramatically lower the cost of panel-based sequencing while allowing easy, rapid multiplexing. The costs of testing will be near $90 per sample. We have taken the task of developing a strategy that can be applied to detect HBOC and Lynch syndromes in broader populations. We will study the effectiveness of population scale testing of these two syndromes by enrolling 27,500 individuals, who are:

1. eligible for inherited cancer syndrome testing (2,500)
2. have had cancer but are not covered by current screening guidelines to receive a low-cost genetic screen (7,500) or
3. healthy (17,500).

Those individuals identified to have Lynch or HBOC will be followed for outcomes and compared to a matched cohort identified following standard screening guidelines. Additionally, relatives of those identified will be enrolled in cascade screening. We will determine if testing either cancer patients or the general population represents a sustainable strategy for population screening based on QALY measurements.

PI: Elena Stoffel, Jennifer Griggs, & Ken Resnicow

Title: Innovative Approaches to Expand Cancer Genetic Screening & Testing for Patients & Families in a Statewide Oncology Network through Community, State, & Payer Partnerships

Grant#: U01CA232827
Project Period: 06/08/2020 – 05/31/2025

Project Summary/Abstract: Germline genetic variants that impact cancer risk, prevention, and treatment strategies are implicated in up to 20% of cancers; however, only a fraction of people at risk for hereditary cancer syndromes undergo diagnostic genetic testing. Barriers to testing, at both the patient and provider levels, include gaps in knowledge and poor access to specialty genetics services. This multiphase project seeks to employ practice-level and patient-level interventions to increase the proportion of patients in whom family history is documented and assessed for genetic risk and in whom guideline-concordant genetic evaluation is completed. This proposal leverages existing partnerships between a statewide oncology network, public health agencies, payers, and a multidisciplinary team at the University of Michigan to encourage systematic family history ascertainment and genetic risk assessment among newly diagnosed cancer patients cared for in 68 medical and gyn-oncology practices. In partnership with the Michigan Department of Health and Human Services and a network of nearly all oncology practices in Michigan, the Michigan Oncology Quality Consortium, we will deploy interventions to promote collection and assessment of family history and genetic evaluations for eligible patients with breast, colorectal, ovarian, prostate and endometrial cancer cared for in diverse clinical and geographic settings across the state.

Specific Aims:

1. Test the impact of innovative practice-based interventions on the proportion of patients who have a comprehensive family history documented in their medical record. In the first phase, using a stepped-wedge design, we will provide a tablet-based family health history survey tool to practices and evaluate the impact of the tool on quality measures of family history documentation and guideline concordant genetic referrals. In the second phase, at Year 4, we will test the impact of adding value-based reimbursement using family history ascertainment as the quality improvement metric.
2. Evaluate the impact of two behavioral interventions (tailored messaging via mobile optimized web interface vs genetic counseling using motivational interviewing) on uptake of genetic testing among patients with cancer who meet clinical criteria and disclosure of genetic test results to at-risk relatives.
3. Address longitudinal follow up of cancer patients, exploring uptake of cascade genetic testing in families with germline mutations.

PI: Jennifer Mack

Title: The AYA-RISE intervention: Risk information and screening education for adolescents and young adults with cancer predisposition syndromes

Grant#: U01CA243688
Project Period: 09/18/2019 – 08/31/2024

Project Summary/Abstract: Growing evidence shows that hereditary cancer predisposition syndromes affect 5-10% of cancer patients, with heightened risk among patients who develop cancer at a young age, especially adolescents and young adults (AYAs). Genetic counseling is therefore recommended for all AYAs with new cancer diagnoses, for whom results can lead to future cancer screening, risk-reducing surgeries, and reproductive counseling. Testing can also have a domino effect, identifying other affected relatives and reducing cancer risk in entire families. AYAs require unique considerations when communicating cancer risk due to wide variability in developmental and emotional maturity. Genetic counseling necessitates complex cognitive and affective processing from AYAs, ideally resulting in an active ownership of their condition and a commitment to life-long health behavior change. This tall order comes as AYAs are forming their identity, gaining parental independence, and considering future childbearing – often under the shadow of enormous personal or family losses from cancer. These factors complicate AYAs' ability to weigh tradeoffs of genetic testing and screening recommendations – sometimes with tragic consequences. Unfortunately, there have been few if any efforts to optimize cancer risk communication and decision-making for AYAs. The goal of this project is to develop, implement and test an AYA-specific intervention for cancer risk communication and decision-making. Our interdisciplinary team of experts in health communication, cancer genetics, oncology, and pediatric psychology from 4 major Cancer Risk Programs will develop AYA-RISE (Risk Information and Screening Education), a web-based intervention comprised of (1) an interactive chatbot designed to communicate genetic information to AYAs in developmentally appropriate ways; and (2) an individualized patient portal, serving as an educational resource and longitudinal repository for cancer risk and screening information. Iterative user testing with qualitative feedback from AYAs will be used to optimize the program prior to conducting a type I hybrid implementation effectiveness trial of AYA-RISE.

Specific Aims:

1. To refine and pilot AYA-RISE, adapting implementation to ensure feasibility and acceptability among AYAs with cancer risk syndromes, their family members, and providers.
2. To test AYA-RISE among AYAs with cancer predisposition syndromes at 4 centers to determine impact on (1) patient knowledge of cancer risk and recommended screening; (2) psychological distress; (3) patient ownership of information; and (4) follow-up for recommended care.
3. To evaluate implementation outcomes of AYA-RISE, including ways that AYAs use the chatbot and patient portal, and AYA, family, and provider experiences, to facilitate future dissemination.

PI: Angela Bradbury

Title: A randomized hybrid type 1 effectiveness-implementation study of an Ehealth delivery alternative for cancer genetic testing for hereditary cancer predisposition (eREACH)

Grant#: U01CA243702
Project Period: 09/17/2020 – 08/31/2025

Project Summary/Abstract: Germline cancer genetic testing has become a standard evidence-based practice, with established risk reduction and cancer screening guidelines for genetic carriers. Yet, access to genetic specialists is limited in many areas in the US, and <20% of eligible patients with a personal or family history of breast or ovarian cancer complete genetic testing. Thus, there is an urgent need to consider alternative delivery models to increase access and uptake of genetic testing, while maintaining adequate patient cognitive, affective and behavioral outcomes. Our research has shown that providing remote services increases uptake of genetic testing in community practices. Preliminary data from our ongoing NIH-funded RESPECT study has revealed high interest in a web-based eHealth alternative to traditional pre-test counseling and no significant differences in pre- and post-disclosure outcomes when the web-based eHealth intervention is utilized as compared to participants who received traditional pre-test genetic counselor. To address the clinically significant need for alternative delivery models to increase access and uptake of cancer genetic testing, while maintaining adequate patient cognitive, affective and behavioral outcomes, we propose to recruit a nationally diverse "real-world" sample of 1000 patient who have access barriers to genetic testing and to conduct a Hybrid Type 1 effectiveness-implementation study to evaluate web-based eHealth delivery alternatives for genetic education and testing. We will partner with several cancer advocacy groups (ASCO, breastcancer.org, Cancer Support Community, Pennsylvania Prostate Cancer Coalition) to recruit patients to this randomized non-inferiority study using a modified 2x2 design (Aims 1-2). In Arm 1, traditional pre-test (visit 1) and post-test (visit 2: disclosure) counseling will be provided remotely through the national Penn Telegenetics Program and compared to delivery arms where patients can complete pre-test and/or disclosure of results through a self-directed web-based eHealth intervention, either in place of, or as an adjunct to traditional genetic counseling. Concurrently, we will conduct a CFIR (Consolidated Framework for Implementation Research)-informed process evaluation to understand moderators of intervention usage and patient outcomes and facilitators and barriers to future implementation and sustainability of this novel eHealth alternative delivery model for genetic services both within and beyond cancer care (Aim 3).
Specific Aims:

1. Evaluate the effectiveness of offering web-based eHealth delivery alternatives of pre/post-test genetic counseling to provide equal or improved timely uptake of genetic services and testing, and short-term cognitive, affective and behavioral outcomes in patients with barriers to genetic testing as compared to the traditional two-visit delivery model with a genetic counselor.
2. Evaluate the effectiveness of web-based eHealth delivery alternatives to provide: a) equal or improved longitudinal understanding of, reactions to and use of genetic test results and b) reduced genetic counselor time as compared to the traditional two-visit delivery model with a genetic counselor.
3. To conduct a multi-stakeholder mixed-methods process evaluation, to understand a) potential moderators of short-term and longitudinal outcomes to understand who benefits more or less from eHealth delivery alternatives; and b) facilitators and barriers to implementation eHealth delivery alternatives for genetic services and recommendations for future adaptation and sustainability in clinical practice throughout, and beyond oncology.

PI: Steven Katz, Lawrence An, & Allison Kurian

Title: A population-based virtual solution to reduce gaps in genetic risk evaluation and management in families at high risk for hereditary cancer syndromes: The Georgia-California GeneLINK trial

Grant#: U01CA254822
Project Period: 09/15/2020 – 08/31/2025

Project Summary/Abstract: There is growing evidence that targeting genetic risk evaluation (GRE) in families where a cancer susceptibility gene pathogenic variant (PV) has been identified may be the most cost-effective approach to reduce the population burden of cancer through prevention. However, there are enormous challenges to implementing successful cascade genetic risk evaluation in families with hereditary cancer syndromes. The clinical context of GRE after cancer diagnosis is increasingly complex: As MGP testing has become the norm, guideline organizations have converged on a list of >40 cancer susceptibility genes in which PVs are clinically actionable, with wide variability in cancer threat and a myriad of strategies for prevention and early detection. A daunting challenge is that the cancer patient is responsible for communication and engagement of relatives for GRE. Despite the shared health threat among at risk relatives (ARRs), the social and contextual factors that affect family communication are complex. Furthermore, ARRs are dispersed worldwide and receive care in disparate health care practices. Importantly, there is little incentive and limited resources for clinicians to engage cancer patients' relatives and genetic counseling services are increasingly strained. Given the lack of guidance for families, it is not surprising that most ARRs of cancer patients with PVs do not undergo GRE. We are uniquely positioned to develop and optimize a direct-to-family virtual genetic risk evaluation and testing solution offered to all at risk relatives of a population-based sample of adults recently diagnosed with cancer in Georgia and California who tested positive for a clinically relevant PV. We will use a unique data infrastructure we pioneered to identify and invite a diverse cohort of cancer patients with clinically relevant PVs and their families to participate in our study. We propose a 2 x 3 factorial randomized trial of 900 patients diagnosed in 2018-2019 in the two states who had a clinically significant PV detected by genetic testing that will offer genetic risk evaluation and testing to all 1st and 2nd degree relatives. We will evaluate the effects of two intervention design features on patient- and relative-centered outcomes: 1) the level of personalized family genetic risk support (a technology assisted personally tailored patient and family member education and communication tool called the Family Genetic Health Program, FGHP) vs. the FGHP plus direct assistance from a human FGHP Navigator); and 2) the price offered to the relatives for the genetic test (standard $200 vs. $100 vs. $50 per test). We will also explore the effect of the features on the outcomes across patient SES subgroups.

Specific Aims:

1. Determine the independent effects of the two virtual platform design features on the cancer patient's appraisal of communication and their engagement with relatives about hereditary cancer and genetic risk evaluation.
2. Determine the independent effects of the two virtual platform design features on the invited relative's appraisal of decision-making and receipt of genetic testing.
3. Determine the independent effects of the two virtual platform design features on the enrolled relative's completion of formal genetic risk evaluation.

PI: Daniel Chung

Title: Development and implementation of electronic decision aids for genetic testing in inherited cancer syndromes

Grant#: U01CA243695
Project Period: 09/14/2020 – 08/31/2025

Project Summary/Abstract: 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. Genetic test results are also critical to guiding targeted therapies in patients with established tumors such as ovarian and pancreatic cancer. 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. One of the most challenging decisions 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. Panels can include genes associated with a single tumor type or multiple tumor types, and genes with weaker evidence for pathogenicity may also be included. There is no consensus on what constitutes an ideal panel, and the choice of panel is therefore 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. We propose to develop 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.

Specific Aims:

1. To develop and pilot electronic decision aids for selection of a multi-gene panel in ovarian and pancreatic cancer patients.
2. To evaluate the efficacy of the decision aid with an oncologist versus a traditional genetic counselor session for multi-gene panel testing in a randomized clinical trial at multiple institutions.
3. To evaluate the effectiveness of implementation of the decision aid in multiple, diverse populations.

PI: Tuya Pal & Deborah Cragun

Title: IMproving care after inherited cancer testing (IMPACT)

Grant#: U01CA254832
Project Period: 09/16/2020 – 08/31/2025

Project Summary/Abstract: Despite the tremendous advances in genetic testing for inherited cancer, the promise of this technology cannot be realized through testing alone. Rather, it is critical to access appropriate follow-up care that may include cancer risk management (CRM) options for individuals and their at-risk family members. Current gaps in implementation of guideline-adherent follow-up care based on inherited cancer genetic test results include both over and under treatment among those with pathogenic and likely pathogenic (P/LP) variants or a variant of uncertain significance (VUS). Furthermore, we are missing the opportunity to magnify the uptake and impact of testing among family members who are at high risk due to suboptimal family communication (FC) of genetic test results and cancer family history. Our highly innovative and practice-changing study is designed to shift the paradigm by which individuals with P/LP variants and VUS in inherited cancer genes are provided with information to enhance guideline-adherent CRM and FC of test results. Through our proposed type I effectiveness-implementation hybrid randomized control mixed methods study, we will test two interventions with a diverse group of 600 individuals with a P/LP variant or a VUS result in a variety of inherited cancer genes for which CRM guidelines are available. Intervention A is focused on increasing guideline- adherent CRM (LivingLabReport), and Intervention B is focused on increasing FC and subsequent family testing (GeneSHARE). Alongside developing, refining, and testing interventions to improve guideline-adherent CRM and FC, we will study the implementation of these interventions across racially, geographically, and socio- economically diverse populations and settings. The information gathered through testing effectiveness and implementation of the interventions will be used to develop, modify and pilot test adaptive stepped interventions with the potential to efficiently maximize effectiveness in improving guideline-adherent CRM and FC. This transdisciplinary effort, enriched for accrual of Blacks, rural dwellers, and other underserved populations, will inform policy and the development of scalable models for delivering evidence-based care. Ultimately, our study will help address the need for access to effective information to guide CRM and enhance FC in diverse populations across various genes and settings which is greatly needed if the population at large is to benefit from genomic advances in this era of personalized medicine.

Specific Aims:

1. Conduct a randomized control trial to assess the effectiveness of two interventions (LivingLabReport and GeneSHARE) among those tested for inherited cancer predisposition to improve cancer risk management (CRM) and family communication (FC).
2. Create and pilot an adaptive intervention to tailor resources to promote CRM and FC among those who have not achieved the primary outcomes after 12 months.
3. Document and compare multiple implementation outcomes across the different interventions.

PI: Jada Hamilton

Title: Prospective Trial of a Linguistically and Culturally Appropriate Mainstreaming Model for Hereditary Cancer Multigene Panel Testing Among Diverse Cancer Patients

Grant#: U01CA243644
Project Period: 09/16/2020 – 08/31/2025

Project Summary/Abstract: Efficient yet effective models for delivering genetic counseling and testing are sorely needed to meet increasing demands for timely genetic risk information. Traditional germline genetic testing models, which include in-depth genetic counseling both before and after testing, are time intensive and place substantial demands on the limited genetic counselor workforce. A "mainstreaming" model, which allows for non-genetics healthcare providers to order genetic testing without pre-test genetic counseling, with support from genetic counselors at the time of result disclosure, has shown promise. Yet, past evaluations of mainstreaming models were restricted to the context of BRCA1/2 testing, do not reflect the growing use of multigene panel testing (MGPT), rarely used rigorous experimental study designs or evaluated theoretically-relevant decision-making, psychosocial, and communication outcomes; have not capitalized on opportunities to improve post-test clinical and familial communication; and neither included nor addressed informational needs of minority and medically underserved patients The proposed study aims to develop, test, and evaluate a linguistically and culturally appropriate mainstreaming (LCAM) model for hereditary cancer MGPT among cancer patients diverse in race/ethnicity, language, and education. We will first use formative research methods to adapt existing pre-test educational materials and post-test clinical communication materials for use among the diverse population treated at our community hospital partnering sites (Kings County Hospital Center, Queens Cancer Center). Next, we will conduct an RCT involving English, Haitian Creole, or Spanish-speaking patients diagnosed with breast, ovarian, pancreatic, or prostate cancer (N=500). Patients will be randomized to obtain access to cancer MGPT through either: i) standard-of-care wherein in depth pre-test and post-test genetic counseling are provided via telegenetics (i.e., videoconferencing delivered at the site clinic) with standard post-test clinical communication materials, or ii) LCAM intervention wherein patients receive the adapted pre-test educational materials with testing ordered by their oncologist, followed by post-test genetic counseling provided via telephone with adapted clinical communication materials. Patients will complete assessments of decision-making, psychosocial, and behavioral outcomes at baseline, upon deciding whether to have MGPT, and at 1-week and 6-months following receipt of their test results. Long-term engagement among patients who receive a variant of uncertain significance (VUS) result will also be explored one year after result receipt through uptake of an offer to discuss any changes in cancer risk or variant reclassification and an additional assessment.
Specific Aims:

1. Adapt existing mainstreaming model pre-test educational materials (brochure and video) and post-test clinical communication materials (clinic visit summary and family dissemination messaging) to confirm relevance to and comprehension by the diverse patient population.
2. Test effects of the LCAM intervention on patient decision-making, psychosocial, and behavioral responses compared to standard-of-care.

2.1. Evaluate how effects of genetic testing model on decision-making, psychosocial, and behavioral responses may vary based on moderating characteristics of patient race, ethnicity, language, sex, health literacy, genetic literacy, or medical mistrust.

3. Describe long-term engagement among patients receiving variant of uncertain significance (VUS) results and possible variation across genetic testing models.

fPI: Anita Kinney

Title: Comparative Effectiveness of Interventions to Increase Guideline-based Genetic Counseling in Ethnically and Geographically Diverse Cancer Survivors

Grant#: 1 R01 CA211625
Project Period: 12/22/2016-11/30/2022

Project Summary/Abstract: Genetic counseling or Cancer Genetic Risk Assessment (CGRA) for hereditary breast and ovarian cancer (HBOC) is an evidence-based precision medicine strategy that facilitates informed decision making about effective health management options. Identification of individuals at increased risk of HBOC is crucial for cancer survivors and their families to benefit from biomedical advances in cancer prevention, early detection, treatment and survivorship. Although national guidelines for CGRA and genetic testing have been available for two decades, only one-third or less of high-risk women have accessed these services. The optimal risk assessment strategy starts with an individual with an HBOC-related cancer. Widespread dissemination and adoption of national guidelines for informed decision-making and promoting CGRA is needed to achieve a population-level reduction in cancer morbidity, mortality and disparities. Thus, it is important to promote access to CGRA, particularly in medically underserved populations. The proposed Genetic Risk Assessment for Cancer Education and Empowerment (GRACE) Project seeks to address this important translational gap by developing and implementing strategies to promote guideline-based care in the Rocky Mountain region where there are distinguishable disparities in CGRA utilization by ethnicity and geography. Remarkably, few intervention studies have been conducted to address the regional and national translational gap in CGRA utilization for these diverse populations, underscoring our study's high impact and innovative public health intervention delivery approach. The GRACE Project is guided by evidenced-based behavior change counseling strategies to promote risk-based care delivery and reduce disparities that consider individual, cultural, social and system-level factors. The study's primary aim is to test the comparative effectiveness of mailed targeted print (TP) vs. TP plus a telephone-based tailored counseling and navigation intervention (TCN) vs. usual care (UC) to increase guideline-based CGRA for HBOC. We will oversample Hispanics and rural dwellers and enroll 1206 high-risk female cancer survivors. Women will be recruited through the Colorado and New Mexico cancer registries and meet the criteria for a CGRA referral. Enrollees will be randomized to one of 3 study arms and complete baseline, 1-month, 6-month and 12-month surveys.

Specific Aims:

1. Compare the effectiveness of a targeted intervention (TP) vs. a tailored (TPC) intervention vs. usual care (UC) on CGRA utilization 6 months (primary outcome) after the intervention and at 12 months, after removal of key access barriers.
2. Compare the effectiveness of the interventions on genetic testing utilization.
3. Examine potential underlying theoretical mediating and moderating mechanisms that will further specify and elucidate significant intervention effects.
4. Compare the cost effectiveness of the interventions vs. usual care, for utilization of CGRA services. If effective, either or both interventions have the potential to reach a large number of high-risk families and reduce disparities through broad dissemination.

PI: Kevin Sweet & Mira Katz

Title: A Randomized Controlled Trial: Genetic counseling patient preference intervention via electronic health record portal vs conventional genetic counseling for women at elevated risk for breast cancer.

Grant#: 1 R01 CA248739
Project Period: 01/01/2021 – 12/31/2025

Project Summary / Abstract: Women at elevated risk for breast cancer should complete genetic counseling and may require more frequent screening or additional tests (e.g. breast magnetic resonance imaging [MRI]). Despite guidelines emphasizing the importance of genetic counseling as part of the genetic testing process, opportunities to provide genetic counseling for women at elevated breast cancer risk are often missed. Conventional genetic counseling, consisting of separate pre- and post-genetic test sessions, is not patient driven, and is labor and time intensive to meet increasing demand (workforce burden). Our overall goal is to improve the genetic counseling experience and adherence to the National Comprehensive Cancer Network (NCCN) recommendations for women at elevated breast cancer risk. The proposed randomized controlled trial (RCT) is our next step to reach our goal. A well-established interdisciplinary team will build on past work to test a novel genetic counseling patient preference (GCPP) intervention integrated within an electronic health record (EHR) portal that allows patients to indicate their preferences while directly receiving genetic test report information and post-genetic test counseling. The RCT will be conducted among 1,000 women at elevated risk for breast cancer who agree to participate in the study. Women will be randomized to: 1) GCPP via EHR patient portal; or 2) conventional genetic counseling. The proposed study is innovative because it will test a novel EHR-based genetic counseling intervention in a randomized controlled trial. The study is significant because it will determine the efficacy of the GCPP intervention in a clinical care setting to address many of the limitations of conventional genetic counseling (e.g. not patient driven). The proposed research is relevant to public health by determining the degree to which a novel genetic counseling approach influences medical outcomes for women at elevated breast cancer risk. The study results may change how genetic counseling is delivered to women with elevated breast cancer risk and address the increasing burden on the genetic counseling workforce.

Specific Aims:

1. Determine the efficacy of GCPP compared to conventional genetic counseling for adherence to NCCN guidelines for having: 1) a clinical encounter every 6-12 months; and 2) an annual mammogram (and breast MRI with contrast if recommended).
2. Determine the efficacy of the GCPP compared to conventional genetic counseling for adherence to other NCCN recommended cancer screening (e.g. colorectal cancer screening).
3. Determine the efficacy of the GCPP compared to conventional genetic counseling on breast cancer genetic knowledge, the accurate perception of breast cancer risk, breast cancer-specific worry, post-test/counseling distress, and satisfaction with counseling.
4. Exploratory Aim. Explore the genetic counseling preferences among the GCPP group.

PI: Ken Tercyak & Beth Peshkin

Title: Improving Genetic Counseling for BRCA+ Mothers

Grant#: 1 R01 CA246589
Project Period: 01/02/2020-12/31/2024

Project Summary/Abstract: Women carrying deleterious BRCA mutations are expected to notify their relatives about the family's inherited cancer susceptibility. This is important because relatives have a 50% chance of harboring the same cancer-causing genes and may themselves be at risk for breast and other cancers. Patients sometimes collaborate with a genetic counselor to follow this advice—disclosing their BRCA+ status to parents, adult siblings, and additional members of their kindred. Evidence suggests women with children also want to inform their daughters and sons about maternal BRCA+ genetic test results, but carrier mothers are often psychologically distressed after testing and have difficulty navigating the social and medical implications for their adolescent and young adult (AYA) offspring. It is common for these mothers to experience uncertainty over early notification of BRCA+ to AYAs, manage their own thoughts/feelings about familial cancer, and maintain open the lines of communication with relatives without 'keeping secrets' from their own children. Although genetic counseling assists with aspects of this decisional and psychosocial burden, there are no evidence-based resources specifically devoted to ameliorating mothers' anxiety/depression, worry, and self-blame and traverse complex questions surrounding BRCA+ status notification to their AYAs. In response to this gap, we developed and successfully piloted a new, fully manualized psychosocial support and family communication decision making protocol for BRCA+ mothers with AYA children. Our intervention is theoretically grounded, and deeply attends to self-management needs, hereditary cancer stresses, and age-appropriate AYA concerns. Following standard genetic counseling, it adds 3 sessions of brief telephone counseling delivered by well-trained peers (parent coaches) who are also BRCA+ mothers themselves. Coaching covers: a) maternal socioemotional support, b) communication decision making training, and c) coping skill-building. We will rigorously test for efficacy in a 2-arm RCT to determine improvements in maternal psychosocial functioning and parent-AYA child communication outcomes after standard genetic counseling. BRCA+ mothers with AYA daughters and sons will be recruited from cancer genetic testing centers in the greater DC and Hackensack, NJ areas, randomized to an intervention or usual care control condition, and monitored for up to 6 months posttreatment. Our results should provide evidence for favorably impacting this population's genetic counseling outcomes, with a disseminable intervention poised for adoption. Peer support may be conventional within the breast cancer community at-large, but it remains an unproven treatment ally in genetically informed oncology care. The proliferation of genetic tests, and the modest genetic counseling workforce, necessitate new healthcare delivery models that leverage these and other accessible resources. Targeted peer coaching with an empirical decision support aide could prove to be a viable extension of genetic counseling efforts with BRCA+ mothers, and a complementary approach to hereditary cancer prevention and control in public health settings.

Specific Aims:

1. To determine the impact of peer counseling (PC) vs. standard care (SC) on communication of maternal BRCA+ status to AYA children.
2. To evaluate the relative efficacy of PC vs. SC on informed decision making about disclosure, psychosocial distress, and parent-AYA child interaction.
3. To understand the mechanisms of intervention impact on these outcomes and changes.
4. To identify mothers most likely to benefit from intervention to inform intervention targeting.

PI: Suzanne O'Neill & Ken Tercyak

Title: Peer Support for Young Adult Women with High Breast Cancer Risk

Grant#: 1 R01 CA242750
Project Period: 01/01/2020-12/31/2024

Project Summary/Abstract: BRCA1/2 mutation carriers have highly elevated odds of developing hereditary breast and ovarian cancer, as may their first- and second-degree relatives. The National Academies of Sciences Engineering and Medicine's Genomics and Population Health Action Collaborative highlights the testing of carriers' relatives and their uptake of screening and risk-reducing surgeries as a primary way that genetics can contribute to the reduction of population cancer burden. Patterns of testing over the past decade have shifted to include more younger and cancer-unaffected women to capitalize on this cancer prevention opportunity. However, interventions have not kept pace with this changing landscape, as there are currently no funded trials that meet the unique clinical, developmental, and psychological needs of young adult relatives (YARs) of mutation carriers. Our pilot data suggests that YARs report high levels of distress and desire to seek HBOC risk information and emotional support beyond their healthcare providers and families—especially support from knowledgeable peers who can relate to their experiences and offer neutral grounding and objective guidance about coping strategies. Peer support is a promising psychosocial cancer care approach that could fill this void. However, few evidence-based standards inform its practice. In response to this cancer control challenge, we developed a new, fully manualized/scripted intervention for YARs called "Peers and Cancer Empowerment" (PeACE). PeACE is grounded in evidence-based psychosocial telephone counseling protocols for HBOC distress reduction. We adapted those protocols for our target population through a systematic approach without contradicting their core features. PeACE includes streamlined telephone counseling delivered by well-trained community peer coaches. Session content incorporates coping training for HBOC stress reduction, and decision making and problem-solving training about confronting and managing cancer risk. We will rigorously test PeACE's efficacy in an RCT to improve HBOC-related outcomes for YARs. Trial participants are randomized to an intervention or equated control condition and followed for up to 12 months. We hypothesize that PeACE better reduces cancer-specific and general distress, uncertainty, and decision conflict, as well as increased uptake of genetic counseling. This innovative project expands capacity to address psychological distress management and related outcomes in persons living with HBOC risk.

Specific Aims:

1. Assess intervention effects on YARs' distress and decision-making outcomes about HBOC risk management.
2. Identify YARs most likely to engage with and benefit from PeACE.
3. Understand mechanisms by which PeACE impacts outcomes and explains change among YARs.

PI: Alejandra Hurtado De Mendoza

Title: Testing a culturally targeted narrative video to reduce disparities in the use of genetic counseling and testing in Latina women at-risk of HBOC

Grant#: 1 R01 CA248543
Project Period: 01/01/2021-12/31/2025

Project Summary/Abstract: National guidelines recommend that women at increased risk for Hereditary Breast and Ovarian Cancer (HBOC) due to BRCA1/2 mutations be referred for genetic counseling and consider genetic testing. Awareness of a positive result can inform treatment decisions for cancer patients and risk management plans in both cancer survivors and women unaffected with cancer. The slow translation of guidelines into practice particularly impacts minority populations who receive services in community health clinics. Latina women have lower awareness and use of genetic counseling and testing (GCT) than non-Latina Whites. Latinas face multiple health care, pragmatic, and psychosocial barriers to GCT uptake. Latinas prefer culturally targeted interventions in Spanish with plain language, visual aids, and a narrative format. We developed a culturally targeted narrative video in Spanish for at-risk Latinas. Piloted in a single-arm trial (N=35), Latinas reported high satisfaction and exhibited a significant increase in knowledge from pre- to post-test. Nearly all participants (95%) reported an interest in GCT, and 62% completed genetic counseling. We will use an innovative hybrid research design that combines elements of traditional efficacy studies as well as best practices from implementation research to enhance the quality and speed of the translational process. Guided by an expanded Integrated Behavioral Model, we will conduct a RCT to evaluate the efficacy of our video vs. the FORCE fact sheet on enhancing GCT uptake and psychosocial outcomes. To maximize the potential for implementation in community clinics, we will train clinic staff to administer the Referral Screening Tool (RST), a validated tool to identify women at-risk of HBOC. Guided by the Consolidated Framework for Implementation Research, we will conduct an Implementation Focused Process Evaluation to gather data on clinic implementation outcomes for use of the Referral Screening Tool and the video. We will refer participants to free Spanish telephone genetic counseling. We will randomize 300 at-risk Latinas at three sites with large Latino populations. Our primary outcome is genetic counseling uptake.

Specific Aims:
1. Evaluate the impact of our video vs. fact sheet on genetic counseling uptake.
2. Evaluate the impact of our video vs. fact sheet on psychosocial and process evaluation outcomes.
    a. Exploratory aim: Evaluate mechanisms of the video's impact on genetic counseling uptake (knowledge, attitudes, norms, self-efficacy, anticipatory emotions). If counseling uptake does not differ by arm, then we will evaluate predictors of uptake.
3. Explore key implementation outcomes related to feasibility, acceptability, adoption, fidelity, and future sustainability of using the Referral Screening Tool and the video at the community clinics.

PI: Charite Ricker, Timothy Bickmore and Danielle Braun

Title: Increasing Access to Genetic Testing in Underserved Patients Using a Multilingual Conversational Agent

Grant#: 1 R01 CA263532
Project Period: 06/01/2022 – 05/31/2026

Project Summary/Abstract: The volume of patients who meet national criteria for germline genetic testing based on a cancer diagnosis alone, regardless of family history (i.e. ovarian, pancreatic, advanced prostate, etc.) is rapidly growing. Germline genetic test results can inform oncology and surgical treatment decisions, as well as early detection and prevention for the family. However, traditional pre- and post-test genetic counseling approaches may not be sufficient to meet the growing need. Additionally, traditional pre-test counseling may be a barrier, leading to decreased uptake, especially in those with advanced disease. Patients cared for in settings with limited or no genetic services, including low-literacy, non-English speaking, and rural community patients already face disparities in access. As such, these patients remain underrepresented in clinical and research cohorts, and innovative strategies to optimize genetic counseling approaches are understudied. Relational Agents (RAs) are an effective means of automating health education and counseling, as well as overcoming literacy barriers in the use of information technologies. RAs, animated computer characters simulate face-to-face conversation between a patient and a provider using verbal and nonverbal conversational behavior. This study will develop an English and Spanish RA to communicate personalized pre-test genetic education to a cohort of cancer patients who meet established cancer-based genetic testing criteria across two diverse clinical settings (including a low-resource, urban, safety-net hospital and a university medical center that serves a significant rural population). We hypothesize that the use of an RA will increase the proportion of patients who receive genetic test results within 90 days of initiating cancer care, compared to usual care. If successful, this would be a novel, effective, and scalable means of providing genetics education that could improve patient decisional preparedness, knowledge, and satisfaction, ultimately leading to increased access for patient populations who are traditionally underserved in genetics. Understanding the implementation context and identifying facilitators and barriers to integrating a RA will increase sustainability and generalizability.

Specific Aims:

1. Develop an English- and Spanish-language RA using a patient-driven approach.
2. Conduct a multisite randomized controlled trial of the RA to deliver pre-test education versus usual care in English- and Spanish-speaking patients to compare the proportion in each arm who receive genetic test results in 90 days at Los Angeles County+University of Southern California Medical Center and University of Rochester Medical Center.
3. Understand the implementation context and identify facilitators and barriers to utilizing the RA in these clinical settings.

PI: Kenneth Offit & Jada Hamilton

Title: Digital Technology to Enhance Access to and Effectiveness of Cancer Genetic Counseling

Grant#: 1 R01 HG011914
Project Period: 08/15/2022 – 05/31/2026

Project Summary/Abstract: A substantial number of people at hereditary risk for cancer could benefit from novel genetic counseling (GC) approaches that promote education, engagement, and outreach to at-risk relatives (ARR). When probands carrying pathogenic/likely pathogenic variants (PV) are asked to share medically actionable genetic results with their ARR, less than 30% of ARR complete predictive "cascade" testing, putting lives at risk. Provider -facilitated outreach to ARR leads to improved cascade testing uptake. Yet, rigorous experimental study designs have not been used to demonstrate comparative effectiveness of this approach for sustainably expanding ARR access to cancer GC and testing, or to investigate whether digital technology may enhance provider-facilitated outreach. Patients with a variant of uncertain significance (VUS) may also benefit from enhanced GC engagement; current standard of care leaves serious risks for misinterpretation by patients and non-genetics providers, and consequent medical mismanagement. Patients may experience negative responses to VUS, particularly when encountering discordant interpretations or recommendations between providers and confusion about how they will receive variant updates. In addition, best practices for follow-up and reassessment of a VUS would benefit from technology to support continuity of patient care with local primary care providers (PCPs). The proposed study addresses these needs by assessing the impact of a new GC model that leverages the increasing digitization of healthcare on psychosocial, behavioral, and implementation outcomes for probands with PV and their ARR, and for patients with a VUS result.

Specific aims:

1. Enhance an existing digital platform to increase patient access and sustained engagement with cancer GC services, as well as efficiency of care delivery. Through eliciting feedback from end-users, we will iterate on an existing digital platform to optimize it for facilitating cascade testing and follow-up of MSK genetics patients and ARR. This enhanced Digital Genetics Platform (eDGP) will include an interactive pedigree to engage ARR for cascade testing and those with VUS for family history updates, tailored educational materials for diverse patients and their PCPs, a communication mechanism for genetics providers and patients to exchange updates, a self -scheduling mechanism for improved follow-up, and telegenetics.
2. Evaluate uptake, outcomes, implementation readiness, and cost of a provider-facilitated cascade testing intervention supported by the eDGP. Provider-facilitated cascade testing will include outreach to ARR, partnerships with local PCPs, telegenetics pre- and post-test GC services, and mailed saliva kit genetic testing, all enabled by the eDGP. Via an RCT design, we will evaluate this model against standard of care proband-mediated cascade testing. We will also estimate intervention costs.
3. Evaluate uptake, outcomes, implementation readiness, and cost of a digitally-facilitated VUS follow-up intervention utilizing the eDGP. The eDGP will improve the delivery and quality of care through tailored educational materials and increased transparency of follow-up management plans for patients with a VUS and their PCPs. Via an RCT design, we will compare this model to standard of care patient-led periodic re-contact with the GC care team. and explore PCPs' use and evaluation of provider-directed VUS education and will estimate intervention costs.

PI: Suzanne MacFarland & Lisa Schwartz

Title: Integration of multimodal cancer predisposition genetic counseling practices within the pediatric oncology setting

Grant#: 1 R21 HG011912
Project Period: 09/01/2021 – 08/31/2023

Project Summary/Abstract: Recent advances have led to a rapid increase in the testing and identification of cancer predisposition in children. There is growing evidence that ≥15% of childhood cancer patients harbor a germline (heritable) cancer predisposition, some of which are associated with a 10,000-fold increased cancer risk. Prior to testing for cancer predisposition, it is important that families understand the risks and benefits, legal protections, and possible outcomes of positive results. Moreover, positive results usually indicate the need for lifelong follow-up, including complex cancer surveillance, which can be difficult for families to understand and implement. Unfortunately, there are not enough genetic counselors to meet the demand for counseling before and after genetic testing and, in positive cases, to support cancer surveillance. Thus, there is a critical need for innovative and scalable interventions that efficiently allocate resources and optimize care for pediatric patients receiving testing for cancer predisposition and their families. The long-term goal of this research is to develop interventions that will transform care for children and adolescents undergoing testing for, and living with, cancer predisposition syndromes (CPS) by increasing access to effective genetic counseling resources. Leveraging our existing digital health research, this study will develop and evaluate novel technology-based tools to be incorporated into standard care. The successful completion of this study will create novel, scalable, and generalizable digital supports for families to augment genetic counseling services, inform best practices for genetic counseling, and inform a future multisite trial to further evaluate the impact of the new tools.

Specific Aims:

1. Develop and evaluate the acceptability, feasibility, and preliminary efficacy of a video that targets patient informational needs at the time of genetic testing. Participants will be families of children or adolescents with a new cancer diagnosis receiving paired tumor/normal sequencing (n=150), including caregivers of pediatric probands (any age) and probands age 12+. Participants will receive standard physician- delivered education prior to testing (n=75; Yr 1) or will have also viewed the newly created video added to standard of care (n=75; Yr 2) and will complete survey measures before and after receipt of genetic testing results. The cohorts will be compared on outcome measures.
2. Develop and evaluate the acceptability, feasibility, and preliminary efficacy of PrePARE (Predisposition Planning, Adjustment, Recommendations, and Education) an open access, individualized, digital care plan and accompanying text messages of appointment reminders necessary for cancer surveillance, among children and adolescents with a known CPS. Probands (n=88) with a CPS will receive a PrePARE care plan and accompanying text message reminders. Caregivers of pediatric probands (any age) and probands age 12+ will complete measures pre- and post-delivery of PrePARE. The participant scores will be compared pre and post intervention. In addition to indices of acceptability and feasibility, outcomes measures for both aims include knowledge of genetic testing and surveillance, distress, and decisional satisfaction.

PI: Anita Kinney and Marc Schwartz

Title: Integration of multimodal cancer predisposition genetic counseling practices within the pediatric oncology setting

Grant#: 1 R01CA277599
Project Period: 2/1/2023 – 01/31/2028

Project Summary/Abstract: Genetic testing (GT) for hereditary cancer and related health services do not reach all segments of the population equitably. Racial disparities in genomic care are profound, persistent, and growing. Less than 30% of high-risk cancer patients are referred for germline GT, with appreciably lower referral and testing rates among racial minorities, especially among Blacks. GT of cancer survivors can directly inform treatment following progression or treatment resistance and can facilitate primary and secondary prevention of cancers in their unaffected relatives. Demand for GC (genetic counseling) and GT continues to increase with expanding GT indications and decreasing sequencing costs yet supply of genetic counselors remains limited. The conventional approach of referral to pretest genetic counseling is a common barrier to receiving GT. Further, evidence suggests that traditional comprehensive, pre-test GC does not meet the needs of many survivors, especially underserved minorities. Thus, new models of genome-based care are needed that are responsive to community needs, improve access, do not overburden scarce genetic counseling resources, and do not widen existing disparities. Some health care systems and commercial GT laboratories use digital interventions, including videos and relational agents (RAs), instead of traditional pre-test GC sessions, without providing specifics about community engagement development, acceptability, or efficacy in oncology settings through a rigorous methodologic strategy as we propose. Given the life-saving benefits of GT, understanding how to effectively educate, empower and test high-risk patients in a culturally acceptable way can move the field forward and reduce persistent racial disparities. This study will address this translational gap. In response to community identified needs and enthusiastic support from cancer patients, relatives and community advocates while also building on our pilot work, we will enroll 428 Black cancer patients meeting national guidelines for GT into a 2-arm randomized controlled trial. This approach may be of particular benefit to hundreds of thousands Black patients and their relatives because they are often unaware of their risks, less likely to have a provider discuss their risk and refer them for GT at the time of diagnosis and are not equably garnering the potentially lifesaving benefits of personalized prevention, screening, and treatment.

Specific Aims:
1) Compare the efficacy of a culturally tailored RA vs. Enhanced Usual Care (EUC) on engagement in genetic education and GT uptake.
2) Evaluate the impact of the RA vs. EUC on informed decision-making and psychosocial outcomes.
3) Explore potential mechanisms by assessing mediators and moderations of effectiveness.

PI: Allison Kurian and Steven Katz

Title: Personalized genetic test results management and outcomes after diagnosis of cancer: the Georgia-California SEER Genelink Study

Grant#: 1 R01CA283207
Project Period: 03/05/2024 – 02/28/2029

Project Summary/Abstract: The rapid diffusion of genetic testing across adult cancer diagnoses is a unique opportunity to personalize cancer treatment and prevention at the population level. Germline genetic testing guidelines have broadened to encompass nearly all patients with breast, ovarian and pancreatic cancer; all patients with advanced prostate cancer; and many patients with colorectal, endometrial, and other cancer types. The growing use of genetic testing is driving the development of precision oncology: a new paradigm for personalizing prevention and treatment based on genetic testing results in addition to or instead of traditionally- measured tumor features. Increasingly, an inherited pathogenic variant in a specific gene serves as an essential common thread that connects diverse cancer diagnoses and enables genetically targeted cancer therapy. However, we know virtually nothing about how genetic test results are managed across cancer types. We pioneered the Georgia-California (GACA) Genetic Testing Linkage Initiative, linking industry-provided genetic testing data to SEER registry records for all adults diagnosed with cancer in Georgia and California from 2013-19. We found that genetic testing across cancer conditions has increased but rates are too low relative to clinical recommendations. Our foundational work underscores the urgent need for research about how well genetic testing results are broadly integrated into the management of cancer. We are now completing the next phase of the GACA Genetic Testing Linkage Initiative: merging SEER data for all adults diagnosed with cancer in Georgia or California from 2013-21 (N=1,826,000), with an update planned for cancers diagnosed in 2022-23 (N=456,000), to genetic results through 2025. We will use this unique, population-based data infrastructure to determine whether genetic testing results management is effectively personalized across common cancers with high testing rates. We will also examine cancer mortality by genetic testing results to inform communication about prognosis and personalized treatment.

Specific Aims:

1. To examine the extent to which locoregional and systemic therapies are well-personalized according to clinical indications derived from actionable genetic results and tumor features across common cancers with high testing rates: male and female breast, colorectal, endometrial, ovarian, pancreatic, and prostate cancers.
2. To examine the extent to which immunotherapy is well-personalized according to clinical indications derived from actionable genetic results and tumor features across the selected cancer types described in Aim 1.
3. To examine the extent to which genetically targeted, curative therapy of early-stage breast cancer is well-personalized according to clinical indications derived from actionable genetic results and tumor features.
4. To examine the association of germline pathogenic variants with mortality across the selected cancer types described in Aim 1.