



## Current Projects

**Wallner L, Suwanabol A. Survivorship Care and Recurrence Risk Evaluation for Early-Onset Colorectal Cancer Patients: the SURVIVE-CRC Study.**

**Project Summary:** Over the past two decades, the incidence of early-onset colorectal cancer (CRC diagnoses among adults < 50 years of age) has increased by an alarming 22%. Younger adult survivors of CRC face unique challenges compared to their older counterparts, including persistent and burdensome symptoms affecting their ability to work and disrupting their family life. While evidence-based guidelines exist for addressing the ongoing physical and psychosocial care of cancer survivors broadly (i.e., survivorship care), they are largely based on evidence generated from older patients and remain poorly informed and of suboptimal quality. Furthermore, current CRC survivorship care guidelines, which include surveillance for recurrence, management of late- and long-term effects of cancer and its treatment, and general preventive care, are not sufficient or specific enough to address the complex challenges faced by survivors of early-onset CRC. This has resulted in surveillance under-use and missed opportunities for cure, surveillance over-use and substantial patient burden, and a wide range of unmet survivorship care needs within the rapidly growing population of working- and reproductive-age individuals with early-onset CRC. Thus, there is critical need to design a model of survivorship care that aligns: 1) the intensity of surveillance with actual risk of recurrence, and 2) the provision of care services with patient needs. **Objectives:** The overall goal of this study is to develop risk-stratified survivorship care pathways for patients with early-onset CRC. **Specific Aims:** 1) Identify patterns of recurrence among a diverse, population-based sample of patients with early-onset CRC. 2) Characterize surveillance intensity and survivorship care needs among patients with early-onset CRC. 3) Develop and evaluate risk-stratified survivorship care pathways for patients with early onset CRC that tailor surveillance intensity to recurrence risk and align survivorship care services with patients' needs using the RAND/UCLA appropriateness Method (RAM). **Study Design:** This study is a population-based, explanatory sequential mixed-methods study. For Aim 1, we will sample adults diagnosed with early-onset CRC from 2015 to 2018 across three SEER sites (Georgia, Los Angeles, Kentucky) and identify rates of recurrence within five years. We will then characterize patterns of recurrence across SEER characteristics, and externally validate our results in a sample of patients with early-onset CRC from the Veteran's Health Administration. For Aim 2, we will survey a sample of adults diagnosed with early-onset CRC from 2019 to 2023 across the three SEER sites to assess surveillance received (e.g., cross-sectional imaging, CEA testing, endoscopy) and to identify unmet survivorship care needs. Together, this information will be used to develop risk-stratified care pathways for adults diagnosed with early-onset CRC. We will then engage a stakeholder panel in Aim 3 consisting of clinicians, patients, and caregivers to refine the framework and pathways and assess their acceptability, appropriateness, and feasibility. Finally, we will generate a best-practice statement to directly inform clinical guidelines and policies, with the overall goal of improving the delivery of high-quality survivorship care for adults with early-onset CRC.

## **Veenstra, C. Targeted and Immunotherapies for MEtastatic cancers in Diverse populations.**

**Project Summary:** One of the most important cancer care advances in recent history is the rapid dissemination of targeted therapies (molecularly targeted kinase inhibitors and immune checkpoint inhibitors) into the care of patients with metastatic cancer. The marked expansion of indications for use of these novel therapies has been fueled by growing enthusiasm among medical oncologists regarding their potential impact on survival for patients with very poor prognosis. Although the survival benefit of these therapies is modest for most patients, a small proportion experience long-term remission and potentially even cure of previously incurable cancer. Despite the exciting promise of these therapies, they are very expensive – sometimes exceeding \$10,000 per month. Because of the high cost and high stakes of these therapies, it is critical to understand their patterns of use; yet very little is known about targeted therapy use across diverse populations. Moreover, the impact of clinician factors on variations in use is not known. In the absence of such knowledge, it is difficult to develop effective interventions to support equitable delivery of these therapies to the growing population of patients living with metastatic cancer. This will be the first population-based study to generate an understanding about patterns of and variation in use of targeted therapies in diverse patients with metastatic cancer. The findings of this study will provide targeted, actionable information; inform development of clinical policies to improve resources and educational opportunities for clinicians who care for underserved patients with metastatic cancer; and inform development of multilevel interventions to improve equitable receipt of targeted therapies across diverse patient populations and practice settings. **Objectives:** The goal of this study is to characterize patterns of use of targeted therapies in a diverse, population-based sample of patients with metastatic cancers in which these therapies are widely indicated: non-small cell lung cancer, genitourinary cancer (renal cell and bladder), and melanoma. **Specific Aims:** 1) to identify patient factors with non-receipt of targeted therapies. 2) To identify clinician factors (knowledge and attitudes, practice resources and treatment delivery barriers, sociodemographics) associated with tendency to prescribe targeted therapies. 3) To quantify and explain the influence of treating medical oncologists on variations and disparities in patient receipt of targeted therapies. **Study Design:** This project is a large-scale, population based, observational study of patients with metastatic non-small cell lung cancer (NSCLC), renal cell carcinoma or bladder cancer (GU cancer), and melanoma, and their treating medical oncologists (clinicians). We will identify a total of N=2,240 patients over the age of 21 with metastatic NSCLC, GU cancer, or melanoma and reported to the Georgia or Los Angeles County Surveillance, Epidemiology and End Results (SEER) registries. We will also survey N=1,025 treating clinicians about their experiences treating patients with targeted and immunotherapies.

**Kurian AW, Katz SJ. Genetic Testing, Treatment Use, and Mortality After Diagnosis of Breast And Ovarian Cancer: The Georgia-California GeneLINK Initiative. NCI R01CA225697.**

**Project Summary:** Genetic testing is essential to identify and manage hereditary breast and ovarian cancer syndrome (HBOC), enabling precision prevention and screening and potentially reducing morbidity, mortality, and cost. The most efficient way to find HBOC cases is among women already diagnosed with breast cancer or ovarian cancer, because they are more likely than cancer-free women to have inherited a cancer-predisposing mutation. Once a cancer patient tests positive, then her cancer-free relatives can undergo a cost-effective, definitive test for the identified gene mutation. Testing cancer patients is thus the gateway to population-wide improvements in HBOC care. Yet genetic testing is difficult to integrate into the complex care of a newly diagnosed cancer patient. This is especially true as technology advances, with multiple-gene sequencing panels (MGS) replacing limited tests of only 2 genes (BRCA1 and BRCA2, BRCA1/2). MGS offers more information, but its value is uncertain. This is because the proportion of patients reported to have an uninformative, often anxiety-producing “variant of uncertain significance” (VUS) is 2-5% when only BRCA1/2 are tested, versus >30% with MGS. A major concern is that the increasing volume, complexity and ambiguity of results may worsen gaps in testing use, treatment quality, and health outcomes. To advance precision prevention of HBOC, there is great need to understand deployment of genetic testing and results management. Concerns include potential disparities in test use and results among sociodemographic and clinical subgroups and the impact of results on cancer treatment and mortality. To address these concerns we will examine potential gaps in genetic testing use, test results and treatment (including surgery, radiation and chemotherapy) among newly diagnosed breast and ovarian cancer patients, according to pre-test HBOC risk and sociodemographics. We will study approximately 190,000 breast cancer patients and 15,000 ovarian cancer patients who were diagnosed in 2013-2017 and reported to the statewide Georgia and California SEER registries, and then accrued into a Georgia-California SEER Genetic Testing Linkage Initiative (GeneLINK). Our hypotheses are stated as follows. Compared to breast cancer patients with normal test results, those with VUS only will have more contralateral prophylactic mastectomy. Among breast cancer patients indicated for radiation, pathogenic mutation carriers less often receive it than other patients. Among breast cancer patients who are not indicated for chemotherapy, mutation carriers more often receive it than negative/VUS/untested patients do, suggesting over-treatment. We will examine whether more intensive regimens (e.g., anthracyclines or platinum) are more prevalent in mutation carriers than other chemotherapy recipients, controlling for tumor factors. Among ovarian cancer patients with BRCA1/2 mutations who are indicated for targeted therapy with a PARP inhibitor, those with sociodemographic vulnerability factors less often receive it. Among breast and ovarian cancer patients who received chemotherapy, mortality will be lower in pathogenic mutation carriers than in non-mutation carriers.

**Katz SJ. Gaps in Genetic Risk Prevention in Breast Cancer Patients and Their Family. American Cancer Society Research Scholars Grant.**

**Project Summary:** Breast cancer is the first common health condition to be subjected to widespread extensive genetic testing after diagnosis. Multigene panel tests - comprising sequencing of at least 20 genes - have become the standard in the US which has resulted in tectonic changes in the distribution of results and the implications for patients and families regarding cancer prevention and control. The broadening of criteria for genetic risk evaluation after diagnosis of cancer combined with the extensiveness of the genes tested has fomented enormous challenges for clinicians, patients, and their families. **Objective/Hypothesis:** We propose a population-based survey study of patient experiences with germline genetic testing and patient communication with family members about hereditary cancer risk and prevention. We suspect that there is growing mismatch between test results and patient’s attitudes and behaviors about hereditary cancer risk and prevention. We speculate that growing variability in the implications of test results on cancer threat may cause gaps and disparities in communication between patients and their relatives – especially in high-risk families. **Specific Aims:** 1) To examine potential gaps and disparities in patients’ attitudes and behaviors about cancer risk reduction strategies (preventive surgery and high-risk surveillance) in relation to their genetic test results; 2) To examine potential gaps and disparities in family communication about genetic test results reported by patients with abnormal test results; and 3) To examine barriers to genetic risk evaluation reported by relatives

of patients with pathogenic variants. **Study Design:** We propose a population-based survey of patients diagnosed with breast cancer in 2018 in the states of Georgia and California who received germline genetic testing (N=3,140) and their first-degree relatives (FDRs). Patients will be selected based on their genetic test results and race/ethnicity from our Georgia-California Genetic Testing Linkage Initiative data infrastructure. We will survey all FDRs (N= 620) with whom patients with pathogenic variants discussed test results. Survey information will be merged with SEER and genetic test data and a de-identified dataset will be constructed for analyses.

### **Wallner LP. Disparities in the Delivery and Quality of Breast Cancer Survivorship Care American Cancer Society Research Scholars Grant.**

**Project Summary: Background:** The care of breast cancer survivors is complex, as it requires coordination among many providers over time and encompasses cancer-related follow-up care, management of late-term effects of treatment and general preventive care. However, coordination among providers and implementation of shared care models where oncologists work together with primary care physicians (PCPs) to deliver survivorship care remain significantly challenging. In addition, many survivors do not receive guideline-concordant survivorship care and significant socioeconomic disparities in the quality of cancer care remain. Yet, whether or not these disparities persist throughout the survivorship period is less clear, particularly as it relates to the delivery and coordination of survivorship care, and the receipt services that reduce the risk of mortality from recurrence and second primary cancers, including genetic testing. **Objective:** The goal of this study is to further our understanding about the quality of survivorship care by assessing disparities in both the delivery and quality of breast cancer survivorship care and examining whether more PCP involvement in survivorship care results in improved quality, particularly among vulnerable populations. **Specific Aims:** The specific aims of this project are: 1) to characterize provider roles in the delivery of breast cancer survivorship care among vulnerable populations, 2) examine disparities in the quality and coordination of breast cancer survivorship care and 3) explore whether more PCP involvement in survivorship care improves the quality and coordination of breast cancer survivorship care, particularly among vulnerable populations. We hypothesize that oncologists will lead the delivery of survivorship care for most women, PCP involvement in survivorship care will be lower among vulnerable populations, and significant disparities in the coordination quality of survivorship care will exist across patient-reported sociodemographic factors. However, we hypothesize that these disparities will be reduced among women with high PCP involvement in their survivorship care. **Study Design:** We will accomplish this by conducting a follow-up survey study 5 years after diagnosis in women who participated in the iCanCare Study, a racially and economically diverse, population-based study of 2502 women with early-stage breast cancer in Los Angeles County and Georgia diagnosed in 2014-15. We will utilize rich patient-reported socioeconomic measures (race, ethnicity, acculturation, literacy, education, and insurance) as well as extensive clinical information collected during initial treatment. Findings from this study will directly inform future cancer care delivery strategies, address how survivorship care delivery patterns impact the quality of survivorship care, identify important disparities in the delivery and quality of survivorship care, and guide the development of culturally-tailored interventions to improve survivorship care.

**Hawley ST, Jagsi R. Improving Patient-Centered Communication in Breast Cancer: A RCT of a Shared Decision Engagement System (ShaDES). NCI 1R01CA237046.**

**Project Summary:** Improving Patient-Centered Communication in Breast Cancer: A RCT of a Shared Decision Engagement System (ShaDES). The diagnosis of breast cancer triggers a cascade of decisions as patients consider multiple treatment modalities navigated by different specialists. Precise evaluative treatment algorithms have better individualized treatment recommendations, yet sifting through the complexity of the test information and treatment options can be often challenging to patients and can often cause anxiety. Thus, the advances of precision medicine cannot be realized without parallel advances in patient-centered communication (PCC). This rapidly evolving decision context has fueled a pressing need for more patient-centered communication to address the full breadth of issues—both cognitive and emotional—faced by patients in making breast cancer treatment decisions. There is a critical need for tools that can engage the patient both emotionally and cognitively and be integrated into the breast oncology care clinical workflow. This project is a multi-level, factorial study that crosses a patient-level RCT of 700 newly-diagnosed breast cancer patients within 25 breast surgical oncology practices to evaluate a shared decision engagement system (ShaDES) to support PCC. The system links an emotional support-enhanced version of the research group's previously developed iCanDecide patient-facing decision tool with a clinic level trial of a Clinician Dashboard to help clinicians address remaining cognitive and emotional needs in their patients. In collaboration with the Alliance NCORP Research Base and its Statistics and Data Core, the trial will: 1) evaluate the impact of the emotional support enhancements to iCanDecide on primary and secondary outcomes measuring patient appraisal of PCC, 2) evaluate the impact of the Clinician Dashboard on patient appraisal of PCC, 3) examine potential mediators of the patient and clinic interventions, and 4) conduct a process evaluation of the two intervention components to inform revision and future widespread implementation of ShaDES. The results will lay the groundwork for broad implementation of a shared decision engagement system to improve patient-centered communication in breast cancer.

**Katz SJ, An L, Kurian AW. 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. NCI U01CA254822.**

**Project 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 world-wide 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 determine the independent effects of the two design features on 1) the cancer patient's appraisal of communication and their engagement with relatives about hereditary cancer and GRE; 2) the invited relative's appraisal of decision-making and receipt of genetic testing; and 3) on the enrolled relative's completion of formal GRE. We will also explore the effect of the features on the outcomes across patient SES subgroups. The findings of this study have enormous potential to improve cancer prevention and early detection in families at high risk of hereditary cancer syndromes in the US.

**Veenstra CM. Partner Engagement & Receipt of Surveillance in Colorectal Cancer Survivors. NCI K07CA196752.**

**Project Summary:** After curative treatment for colorectal cancer, ongoing surveillance is necessary to detect cancer recurrence. Limited recurrences in the liver, lung, and at the site of the primary cancer can be surgically resected with a cure rate as high as 50%. However, nearly half of the 1.2 million yearly survivors of colorectal cancer in the US fail to receive potentially life-saving surveillance. This gap between ideal care and actual care represents an opportunity to identify previously untapped sources of support to improve the likelihood of cure in a large group of patients. The under-use of surveillance in half of all colorectal cancer survivors requires that we consider novel methods to improve care. Engaging the partners of patients, who, according to the National Cancer Institute, is "part of the survivorship experience," may represent one approach to improving cancer surveillance. The majority of colorectal cancer patients are married or partnered. Partners serve as a potential resource that providers can engage to increase patients' receipt of surveillance. Our preliminary studies show that 80% of colorectal cancer patients want partners involved in treatment decisions; 85% report high levels of partner support. The aims of this mixed methods study are 1) To identify, through in-depth interviews, factors that influence the receipt of surveillance testing from the perspective of survivors of colorectal cancer and their partners; 2) To determine the partner-specific factors associated with a high level of partner engagement in the patient's surveillance care process. We hypothesize that engagement will be lowest among male and/or black partners; 3) to determine the relationship between level of partner engagement and patients' receipt of surveillance. We hypothesize that receipt of surveillance will be lowest among patients whose partners are least engaged in the surveillance care process. Analyses will account for the role of other factors, including age, comorbidity, socioeconomic status, race, and spirituality in receipt of surveillance. Aims 2 and 3 will be accomplished by surveying a large and diverse cohort of colorectal cancer survivors and their partners. Not only will the proposed project provide data to inform future interventions targeted at couples (colorectal cancer patient-partner dyads), it will also serve as a vehicle for the applicant's development into an independent researcher in health services research. The applicant already has a strong background in studies of the quality of colorectal cancer care and a clinical foundation in colorectal cancer. Through select coursework, mentorship from national experts in health services research and social sciences, and completion of a carefully designed project linking skill acquisition to research aims, the applicant will emerge as an expert and independent investigator in health services research as it pertains to cancer survivorship.

**Radhakrishnan A. Engaging PCPS to Optimize Active Surveillance of Low-Risk Prostate Cancer. NCI K08CA245237.**

**Project Summary:** The population of older and medically complex cancer patients is growing exponentially, calling for the involvement of primary care providers (PCPs) in team-based models to deliver high-quality care to cancer patients across the continuum. Team-based care is especially needed in light of the rapid growth in diagnoses of low-risk cancers (such as prostate, thyroid, and breast). Not only are these patients typically older and with more comorbidities, but treatment strategies are increasingly moving away from surgery and radiation to active surveillance. Because guidelines for low-risk prostate cancer now recommend active surveillance as the primary disease management strategy, it represents the ideal case for studying how to better engage PCPs. A key gap where PCP involvement can help is in improving adherence to active surveillance; though a growing number of men are choosing this strategy, adherence to active surveillance once chosen remains suboptimal. Thus, it is critical to understand how to support men with low-risk prostate cancer to maximize adherence to active surveillance and importantly, how to effectively engage PCPs in low-risk cancer

management. Dr. Radhakrishnan's long-term career goal is to become an independent clinician-investigator focused on optimizing the role of PCPs in team-based care delivery across the cancer continuum. She is focusing on low- risk cancer management given the timely and critical need to meet the demands of the growing number of low- risk cancer patients. Leveraging the Michigan Urological Surgery Improvement Collaborative (MUSIC), this project aims to: 1) characterize provider and patient perspectives on active surveillance adherence; 2) design a patient-centered intervention that enables providers to support men on active surveillance to maximize adherence; and 3) perform a pilot evaluation of the intervention on key outcomes at primary care and urology practices. Successful completion of this work, and subsequent R01 studies, will improve low-risk cancer management by developing a patient-centered intervention integrated into primary care delivery systems. Dr. Radhakrishnan seeks to build upon her clinical background as a PCP and her research fellowship training to acquire additional skills and experiences to achieve her long-term career goal. With her mentoring team, she has developed a comprehensive career development plan that will support her to: 1) accomplish her training aims and develop a strong skillset in qualitative methods and expertise in intervention design, evaluation, and implementation; and 2) engage in career development activities to enable her to transition to independence as a clinician-investigator. She will be supported by a multidisciplinary team of dedicated mentors and advisors, who will oversee a broad range of coursework and experiential learning, and are committed to ensuring her success. Additionally, the University of Michigan offers Dr. Radhakrishnan the ideal environment for this proposal, with its exceptional resources and an outstanding mentoring team with proven success in developing junior clinician-scientists.