Contributions to Science

1. Much of my early work as a cancer epidemiologist was focused on characterizing risk factors for molecular subtypes of breast cancer, particularly triple-negative breast cancer. Characterized by the absence of estrogen receptor, progesterone receptor, and HER2/neu expression, triple-negative breast cancer accounts for only 10-25% of all breast cancers; however, this disease subtype has emerged as being of particular clinical and public health significance due to its typically poor prognosis and the fact that no targeted cancer therapies exist for the treatment of this disease. At the time I began research into risk factors for triple-negative breast cancer, exceptionally little was known about the epidemiology of this aggressive disease. Through my work, I demonstrated that nulliparity and late age at first birth – both established risk factors for estrogen receptor-positive breast cancer – are, if anything, inversely associated with risk of triple-negative breast cancer, whereas other traditional breast cancer risk factors, such as lack of breastfeeding and postmenopausal obesity, are more consistently associated with disease risk across molecular subtypes. My work in this area utilized several existing data resources, including the Women's Health Initiative and the Breast Cancer Surveillance Consortium. I was responsible for the conception, design, implementation, and interpretation of all secondary data analyses I conducted in this area.
    a. **Phipps AI**, Chlebowski RT, Prentice R, McTiernan A, Wactawski-Wende J, Kuller LH, Adams-Campbell LL, Lane D, Stefanick ML, Vitolins M, Kabat G, Rohan TE, Li CI. Reproductive history and oral contraceptive use in relation to risk of triple-negative breast cancer. *J Natl Cancer Inst* 2011;103:470-7. (PMCID: PMC3057984)
    b. **Phipps AI**, Chlebowski RT, Prentice R, McTiernan A, Stefanick ML, Wactawski-Wende J, Kuller LH, Adams-Campbell LL, Lane D, Vitolins M, Kabat G, Rohan TE, Li CI. Body size, physical activity, and risk of triple-negative and estrogen receptor-positive breast cancer. *Cancer Epidemiol Biomarkers Prev* 2011;20:454-63. (PMCID: PMC3064558)
    c. **Phipps AI**, Buist DSM, Malone KE, Barlow WE, Porter PL, Kerlikowske K, Li CI. Reproductive history and risk of three breast cancer subtypes defined by three biomarkers. *Cancer Causes Control* 2011;22:399-405. (PMCID: PMC3042513)
    d. **Phipps AI**, Malone KE, Porter PL, Daling JR, Li CI. Body size and risk of luminal, HER2-overexpressing, and triple-negative breast cancer in postmenopausal women. *Cancer Epidemiol Biomarkers Prev* 2008;17:2078-86. (PMCID: PMC2561180)

2. In recent years, I have shifted the focus of my research from the impact of molecular heterogeneity on cancer risk factors to the impact of such heterogeneity on cancer outcomes. In this regard, I have conducted multiple secondary data analyses leveraging data from the Colon Cancer Family Registry characterizing the relationship of somatic mutations and tumor attributes with colorectal cancer outcomes. Unlike with breast cancer, the implications of molecular heterogeneity in colorectal cancer have been poorly studied, and molecular subtypes of colorectal cancer remain poorly understood. Through my work, I have contributed to this gap in knowledge – conducting and publishing several studies into the relationship between individual tumor characteristics and colorectal survival, and one of the first studies characterizing differences in survival across molecular subtypes of colorectal cancer defined by tumor marker combinations reflecting distinct etiologic pathways. With respect to this latter publication, we found that colorectal cancers with molecular attributes believed to reflect an origin in sessile serrated polyps exhibit a significantly poorer prognosis than those likely derived from the traditional adenoma-carcinoma pathway. I was responsible for the conception, design, implementation, and interpretation of all secondary data analyses I conducted in this area.
    a. **Phipps AI**, Limburg PJ, Baron JA, Burnett-Hartman AN, Weisenberger DJ, Laird PW, Sinicrope FA, Rosty C, Buchanan DD, Potter JD, Newcomb PA. Association between

molecular subtypes of colorectal cancer and patient survival. *Gastroenterology* 2015;148:77-87.e2. (PMCID: PMC4274235)

b. **Phipps AI**, Makar KW, Newcomb PA. Descriptive profile of PIK3CA-mutated colorectal cancer in postmenopausal women. *Int J Colorectal Dis* 2013;28:1637-42. (PMCID: PMC3830592)

c. **Phipps AI**, Buchanan DD, Makar KW, Win AK, Baron JA, Lindor NM, Potter JD, Newcomb PA. *KRAS*-mutation status in relation to colorectal cancer survival: The joint impact of correlated tumor markers. *British J Cancer* 2013;108:1757-64. (PMCID: PMC3668469)

d. **Phipps AI**, Buchanan DD, Makar KW, Burnett-Hartman AN, Coghill AE, Passarelli MN, Baron JA, Ahnen DJ, Win AK, Potter JD, Newcomb PA. *BRAF* mutation status and survival after colorectal cancer diagnosis according to patient and tumor characteristics. *Cancer Epidemiol Biomarkers Prev* 2012; 21:1792-8. (PMCID: PMC3467328)

3. Building on my research into the relationship between colorectal tumor biology and disease outcomes, and my research into the heterogeneity in risk factor associations across tumor subtypes, I have also conducted multiple studies exploring the relationship between modifiable lifestyle factors and colorectal cancer survival according to tumor attributes. Although much is known about the relationship between lifestyle factors and colorectal cancer risk, relatively few studies have considered the possible impact of lifestyle factors on colorectal cancer outcomes. I have conducted multiple secondary data analyses articulating the impact of pre-diagnostic smoking, alcohol consumption, physical activity, and NSAID use on post-diagnostic colorectal cancer outcomes. In particular, my work has demonstrated that cigarette smokers experience significantly poorer disease-specific survival after colorectal cancer than do their non-smoking counterparts, particularly among individuals with tumors that exhibit microsatellite instability or a somatic *KRAS* mutation. These findings, and additional research in this area, may ultimately provide clinicians with targeted messages for empowering colorectal cancer patients with ways to impact their prognosis.

   a. **Phipps AI**, Shi Q, Newcomb PA, Nelson GD, Sargent DJ, Alberts SR, Limburg PJ. Associations between cigarette smoking and colon cancer prognosis among participants in a North Central Cancer Treatment Group Phase III Trial N0147 (Alliance). *J Clinical Oncol* 2013;108:1757-64. (PMCID: PMC3661936)

   b. **Phipps AI**, Baron J, Newcomb PA. Prediagnostic smoking history, alcohol consumption, and colorectal cancer survival: the Seattle Colon Cancer Family Registry. *Cancer* 2011;117:4948-57. (PMCID: PMC3138819)

   c. Hardikar S, Newcomb PA, Campbell PT, Win AK, Lindor NM, Buchanan DD, Makar KW, Jenkins MA, Potter JD, **Phipps AI**. Prediagnostic physical activity and colorectal cancer survival: Overall and stratified by tumor characteristics. *Cancer Epidemiol Biomarkers Prev* 2015;24:1130-7. (PMCID: PMC4491038)

   d. Kuiper JG, **Phipps AI**, Neuhouser ML, Chlebowski RT, Thomson CA, Irwin ML, Lane DS, Wactawski-Wende J, Hou L, Kampman E, Newcomb PA. Recreational physical activity, body mass index and survival in women with colorectal cancer. *Cancer Causes Control* 2012;23:1939-48. (PMCID: PMC3499635)