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Protocol of the Prevent Anal Cancer Study of Self-Swabbing and Novel Biomarkers

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Introduction: Men who have sex with men (MSM), whether HIV-positive or HIV-negative, are at increased risk of developing anal cancer, a condition primarily caused by persistent HPV infection. Anal cancer screening in HIV-positive and HIV-negative MSM involves Digital Anal Rectal Exam (DARE) and/or Pap cytology, which may be followed by high-resolution anoscopy (HRA). It is possible that home-based self-sampling of anal canal exfoliated cells may increase compliance with screening compared to clinic-based screening.

Objective: Our study hypothesizes that there will be better compliance with home-based screening versus clinic-based screening among Milwaukee HIV-positive and HIV-negative MSM. In addition, we will use the specimens collected at home and in the clinic to test two novel biomarkers (persistent HPV infection and host DNA plus HPV DNA methylation) for detection of precancerous anal canal lesions among MSM.

Methods: Anal canal exfoliated cell specimens will be obtained from participating men by self-swab or by clinician swab at 0 and 12 months. All participants will then undergo HRA. Computer-assisted self-interviews at several time points will collect demographic and experiential data from study participants.

Significance: Study findings will increase knowledge about anal cancer screening among MSM and contribute to reduced morbidity and mortality from anal cancer.

Funding source: National Cancer Institute

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Increasing Mammography Uptake through Academic-Community Partnerships in Ethnic Minority Communities

Susan G. Komen Foundation

Introduction: Non-Caucasian women have a higher death rate from breast cancer, particularly African American and Hispanic women. Decreased knowledge and beliefs about breast cancer, poor social support, financial barriers, and reduced access to care contribute to delayed diagnosis in these patients. Immigrant women have lower utilization of screening practices compared to other groups of women. Community Based Academic Partnerships (CBAPs) appear to be an effective method of collaborating with communities to promote cancer awareness and screening efforts. Addressing these barriers is crucial to improving breast cancer mortality.

Objective: Part 1: Breast health education at faith-based community centers Develop community academic partnership with ethnic minority groups in the Milwaukee area (ex. Hmong Community, Muslim Health Community Center, Sikh Temple) Identifying barriers to breast cancer screening Provide culturally appropriate breast cancer education workshops Provide free clinical breast exams to all participants Provide mobile mammography for eligible participants through Wisconsin Well Women’s program Increased mammography uptake Part 2: Focus groups to evaluate effectiveness of breast health education workshops Contact trusted community leaders at the sites we held workshops Conduct focus group interviews with community leaders To understand success of the workshops To understand challenges of the workshops Assess how well the workshops aligned with community needs Understand barriers to breast cancer screening which provides a cultural context for the barriers to women

Methods: Select community partners Collect data concerning breast health education at faith-based community centers Conduct focus groups to evaluate effectiveness of breast health education workshops

Results: 493 women attended the workshops & 375 women were included in final analysis. 32.6% of women lacked medical insurance & 34.8% of women lack PCPs. 360 women were >40 years old and appropriate for mammography. 188 women had not received a mammogram. 75/188 were uninsured and qualified for free mammogram. 60/75 received mammogram. 113 women were privately insured and received screening mammogram through their PCP or the mobile mammography unit.

Conclusions: CBAPs with cultural sites are an effective method of increasing screening mammography and breast health cancer knowledge among immigrant and refugee women in Milwaukee.

Significance: Milwaukee has had a high influx of both refugees and immigrants in recent years. Ensuring these populations receive adequate screening care could decrease the breast cancer death rate.

Funding source: Susan G. Komen Foundation
### Introduction: Tobacco use is the leading preventable cause of cancer. To reduce the incidence of and mortality from smoking-related cancer, it is necessary to both prevent tobacco use and develop more effective smoking cessation interventions for current smokers. FDA-approved pharmacotherapies for smoking cessation, combined with smoking cessation counseling, have limited efficacy. In best case scenarios, 6-month abstinence rates are ~35%. Thus, there is a critical need to develop more effective smoking cessation interventions. Previous research in our lab using functional magnetic resonance imaging (fMRI), a non-invasive measure of human brain activity, found that smokers with larger brain responses to pleasant stimuli than to smoking cues were more likely to successfully quit. This neural biomarker, “relative cue reactivity”, was also predictive of medication success. This previous research was limited because 1) relative cue reactivity could only be quantified after the full study sample was collected and 2) the measure was developed in non-Hispanic white smokers, which does not represent the full population of smokers.

Objective: Identify a quantitative measure of relative cue reactivity that can be calculated in individual participants at the time of fMRI assessment.

Methods: We analyzed data from our previous trials using logistic regression with long-term smoking abstinence as the dependent variable and several candidate measures of relative cue reactivity from several anatomical regions of interest as predictors. We compared the predictive validity of each candidate quantitative measure of relative cue reactivity and each region of interest and identified the most accurate predictor of abstinence. We are currently using this measure of relative cue reactivity in studies about the relationship between brain activity and smoking behavior in a more diverse sample of smokers. We are also exploring whether the use of mentholated cigarettes, which is common among AA smokers, has an effect on relative cue reactivity.

Results: We found that quantifying relative cue reactivity in terms of the difference between cue reactivity (brain responses to smoking minus neutral cues) and reward sensitivity (brain responses to salient minus salient cues) to be the most reliable predictor of long-term abstinence. This metric had the strongest relationship with smoking abstinence when it was used to analyze brain responses from the bilateral caudate nucleus.

Conclusions: The caudate, part of ascending dopamine systems in the brain that influence motivated behavior such as addiction, will be used as an a priori region of interest in future studies of the predictive validity of relative cue reactivity. After extracting data from this region of interest, we will use the following contrast of parameter estimates to quantify relative cue reactivity: 

\[ RCR = \beta_{\text{SMO}} - \beta_{\text{NEU}} - \beta_{\text{PLE}} - \beta_{\text{UNP}} \]

where the beta values indicate the degree of brain activation to smoking-related (SMO), neutral (NEU), pleasant (PLE), and unpleasant (UNP) stimuli. Upon further validation, this neural biomarker will be used to predict cessation success and to inform intervention decisions in smoking cessation research.

Significance: Using neural biomarkers to predict smoking cessation success has the potential to 1) lead to the development of more effective interventions by identifying brain systems and processes that are most related to abstinence; 2) improve clinical practice by informing the development of assessment tools (e.g., questionnaires, behavioral tasks) that can be disseminated and used to predict abstinence risk, and 3) reduce smoking-related health disparities by providing insight into mechanisms that make it more difficult for African Americans to quit smoking.

### Methods: Patients with CML were recruited by their physicians, CML advocacy groups, and through social media. An online survey platform (Qualtrics®) was used for informed consent and to administer the questionnaire, which was anonymous in nature. As part of the survey, patient demographic and health characteristics were also collected.

Results: Of the 458 pts who completed the survey, the median age of respondents was 54 years (range 18-81); 88% of pts identified as non-Hispanic white, 2% as non-Hispanic black, 2% as non-Hispanic Asian, 4% as Hispanic, and 4% other. Patients rated their overall health as poor (4%), fair (18%), good (40%), very good (28%) and excellent (9%). All but one respondent said that more research was needed for CML, with pts indicating their preferences for where they considered the need was greatest (Table 1).

Overwhelmingly, 94% of respondents considered cure in CML as not taking any more pills. All but three respondents had received treatment with a TKI, with 26% (n=119) of pts having previously stopped their TKI medication for at least one month. When presented with the possibility of stopping all future treatment for CML with additional treatment, 97% of pts were willing to add another oral medication to their TKI while 89% of pts would accept intravenous treatment in addition to a TKI. Half of the pts had discussed treatment discontinuation with their physician, with 45% considering this option in an attempt at treatment-free remission. Of the pts that stopped taking their TKIs for at least one month, 65% did so because of side effects and another 10% because of cost.

Conclusions: Patients defined cure in CML as permanently stopping treatment. There was overwhelming support for more research into CML, both for cure and into complications of treatment.
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**Introduction:** Cancer disparities are a significant public health issue. Identifying underserved areas with high disparities and engaging communities will inform relevant efforts to reduce disparities.

**Objective:** To identify geographic areas in Southeastern Wisconsin with high cancer incidence and mortality; and to understand African Americans’ (AA) perceptions and experiences of cancer disparities.

**Methods:** Adaptive spatial filtering, a disease mapping method, was used to estimate spatial patterns of cancer incidence, late stage incidence, and mortality for breast, colorectal, lung and prostate cancer. We also conducted semi-structured focus group with AA women and men living in Milwaukee. Groups were stratified by gender and cancer diagnosis (breast or prostate). Inductive content analysis was used to examine perceptions of existing cancer disparities and how they can be addressed.

**Results:** Maps highlighted areas of significant disparities in Milwaukee zip codes representing predominantly African-American neighborhoods. Nine focus groups were conducted with 79 AA men and women (mean age 51 years). Themes related to reasons for disparities included: decrease in community investment, food deserts, medical mistrust, lack of AA health professionals, cancer myths, and fear. Potential solutions included: community-based cancer education, greater workforce diversity achieved through pipeline programming, better access to healthy foods and strategies to improve communication and build trust between patients and their doctors.

**Conclusions:** Future research interventions and programming should seek innovative strategies to build cancer awareness and education and improve access to trusted quality care.

**Introduction:** Despite advances in breast and lung cancer research, racial and geographic disparities in incidence, late-stage diagnosis, and mortality persist in Wisconsin. Root causes for cancer-related health disparities are complex and multifactorial, and require bold, innovative approaches.

**Objective:** The Advancing a Healthier Wisconsin Endowment’s Cross-Cutting Component is dedicated to reducing breast and lung cancer disparities in Wisconsin by integrating the strengths of research, education, and community and investing over $20M over a period of 8 years.

**Methods:** This initiative began with formation of a leadership team to collect data, share knowledge, and create guiding frameworks. This Design Team was comprised of basic scientists, population health experts, clinicians, and community leaders and worked to curate data from successful initiatives nationwide, and develop a structure to identify the molecular, genetic, socioeconomic, and behavioral factors that contribute to cancer disparities. The Design Team conducted literature reviews, created geospatial maps, and designed an interview process for stakeholders to share their expertise. This data was then used to inform research and implementation studies to reduce cancer disparities statewide.

**Results:** Our experiences with basic and clinical biomedical health professionals, statewide community-based Discussion Sessions and data from nationwide investigations reveal that groups acting alone do not feel that they have the capacity to significantly reduce cancer disparities through their efforts alone. Each sector offered unique perspective about contributors to cancer disparities and opportunities to create positive change.

**Conclusions:** Our results demonstrate that to significantly reduce breast and lung cancer disparities, multidisciplinary, cross-cutting teams are needed that will: 1) Encourage participants to think beyond their expertise, collaborate with experts from different fields, and refine their approach to their own work to increase their impact, 2) Facilitate the creation, adaptation, or adoption of strategies that address the complexity of cancer disparities, and 3) Develop, test, and evaluate initiatives to address breast and/or lung cancer disparities in incidence, late-stage diagnosis, and mortality.

**Significance:** Cancer disparities are complex and multifactorial, however many of the risk factors that contribute to cancer incidence and mortality have been identified across diverse communities and scientific disciplines. Mapping efforts reveal that single risk factors, such as access to mammography or radon exposure, do not correlate directly with geographic hot spots for cancer disparities. Literature reviews elucidate that research and community efforts that span across the translational spectrum contribute to reductions in cancer disparities. Discussion sessions reveal that all stakeholders had unique expertise and perspective that enhanced the teams collective understanding of cancer disparities.

**Funding source:** Advancing a Healthier Wisconsin Endowment
| Thalji, Samih, MD | Surgical Resident | Kong, Amanda, MD, M5 | Pop Sci | NIEhoff Foundation Grant | Introduction: Higher hospital volume has been shown to be associated with improved outcomes and increased overall survival following treatment for certain cancers. There remains a paucity of data examining treatment-related outcomes specifically in breast cancer patients age 80 or older. Objective: The primary aim of this study is to determine the association between hospital volume and mortality following surgery for breast cancer in patients 80 years of age or older. The secondary aim is to elucidate patient and treatment-related characteristics associated with high volume centers. Methods: The National Cancer Database was queried for women aged 80 years and over who underwent surgery for stage I-III invasive breast cancer between 2005 and 2014. Hospital volume was defined as the average number of cases over two years: the year of the patient’s index operation and the year prior. A Cox proportional hazards model with penalized cubic splines was used to examine the association between annual hospital volume and overall survival. Hospitals were categorized into high-volume and low-volume centers based on penalized cubic spline analysis. The log-rank test was used to examine survival difference between groups. Intergroup comparisons were made using X2 and analysis of variance. Results: The final cohort included 59,043 patients. Based on penalized cubic spline analysis, a cutoff of ≥270 cases/year was used to categorize patients as receiving their surgery at a high-volume center (9,110 patients) or a low-volume center (49,933 patients). High-volume centers were significantly associated with decreased risk of death (HR 0.814, CI 0.784-0.846, P<0.001). High-volume centers were associated with a slightly younger patient population (84.0 vs 84.1 years, P<0.001), proportionally more Black and Hispanic patient populations (8.2% vs 6.4% and 4.0% vs 2.5%, P<0.001), earlier stage disease (stage I: 56.6% vs 54.3%, P<0.001), performed more breast-conserving surgeries (68.6% vs 61.6%, P<0.001), and had a higher proportion of patients receiving adjuvant radiation (38.2% vs 36.6%, P<0.004). There were no significant differences in ER, PR, or HER2 status, tumor size, tumor grade, or receipt of adjuvant chemotherapy or hormone therapy between high and low-volume centers. Conclusion: Among elderly breast cancer patients age 80 or above, there is a significant association between undergoing surgery at a high-volume center (defined as ≥270 cases/year) and improved survival. Patients in this population who undergo surgery at high-volume centers are characterized by an earlier stage of disease and more commonly receive breast-conserving surgery, as well as subsequent adjuvant radiation. Significance: Elderly breast cancer patients age 80 or above may benefit from treatment at high-volume breast cancer centers. Systems in place at high-volume centers may result in more consistent and comprehensive multi-modal therapy for breast cancer. Funding source: Froedtert Foundation Grant |
| Zhou, Yuhong | Postdoctoral Fellow | Beyer, Kirsten, PhD | Pop Sci | NIH R01-CA214805-01 | Introduction: Access to quality housing is a key determinant of health. However, this access is known to be subject to discriminatory practices, with more limited access for specific population groups. It is essential to characterize the nature of discriminatory practices in order to identify policy interventions to reduce housing discrimination. Methods: The Home Mortgage Disclosure Act (HMDA) database is used to measure the odds of denial of a mortgage by applicant race (Black relative to White), applicant ethnicity (Hispanic relative to non-Hispanic White) and location of the property (census tract relative to MSA) for all census tracts in the 105 most populated US MSAs, using logistic regression modeling. First, continuous surface maps for each form of discrimination are created for each MSA to visualize spatial patterns of racial and ethnic bias and redlining. Then, these values are averaged for each census tract to produce tract level estimates of the odds of denial. The magnitude of each form of bias across MSAs and by census defined region are calculated and compared. Spatial clustering of each measure is evaluated using Moran’s I, and compared across regions. A set of decision rules guiding the calculation of estimates is presented, and estimates are provided at the census tract level for each MSA to support future work in this area. Results: Results indicate that race is the strongest predictor of denial of a mortgage application, comparing Black to non-Hispanic White applicants (median OR=2.61), followed by ethnicity of the applicant (median OR=2.01). Discrimination based on the location of the property, commonly referred to as “redlining,” had the smallest, albeit still significant, associated odds of denial (median OR=1.05). This pattern was similar across the four census regions examined. Results of spatial clustering analyses revealed, as expected, that redlining was most significantly clustered across MSAs (median Moran’s I=0.69), followed by racial bias (median Moran’s I=0.49), and then ethnic bias (median Moran’s I=0.40). Redlining and racial bias were highly clustered across each region. Ethnic bias was most clustered in the Midwest and least in the West. Conclusions: Housing discrimination continues to affect access to quality housing for specific population groups in the United States, with implications for health, well-being, employment, and socio-economic status, among other concerns. Despite the attention paid to the problem of place-based discrimination (redlining) and the implication of race in the valuation or devaluation of places, race-based and ethnicity-based discrimination appear to be more formidable obstacles in achieving housing equity. Of note, areas within metropolitan areas that have high values for race or ethnicity-based mortgage bias are generally located outside of the central city, whereas redlining is generally the highest in the central city. New attention should be paid to the discrimination faced by applicants of color who seek to purchase homes outside of urban cores, as rates of denial for these groups are of sizeable magnitude and may be preventing the migration of populations of color to semi-urban and suburban locales, with implication for patterns of racial segregation and associated health outcomes. Significance: This study provides the first available small scale estimates of contemporary mortgage lending bias by race, ethnicity and place across US MSAs. Decision rules are |