Research statement

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My current research interests, focusing on capturing patterns of changing exposures over age and time, inform both the prevention and study of breast cancer outcomes. Although ample evidence supports the role of lifestyle in breast cancer outcomes, the study of changing and longitudinal exposures remains understudied. My goals moving forward are to shift from focusing on a single exposure at one time point to capturing multiple exposures across time to better understand the mechanisms by which breast cancer occurs and interventions to prevent the occurrence of disease.

After working as a statistician in academia for eight years, I knew I wanted to weave my statistical background into my epidemiologic research by applying newly developed methods to existing problems in public health. For example, in my dissertation work I applied latent growth mixture models to repeated anthropometric measures to examine the connection between early life growth characteristics and lipid biomarkers in adolescence, which are associated with cardiovascular disease in adulthood. Following my graduate training, I was excited to continue my work with both biomarkers and longitudinal data and to gain experience in breast cancer research under the mentorship of Dr. Clarice R. Weinberg at the National Institute of Environmental Health Science.

As a postdoctoral researcher at NIEHS, my focus has shifted to breast cancer outcomes in an older population. With this work I have leveraged my knowledge of longitudinal analyses to focus on survival analysis when assessing changing breast cancer risk over age and time in relation to risk factors such as body size and a relative's age at diagnosis. Through my doctoral and postdoctoral work, I have studied multiple biomarkers across different periods in the life span. My future research plans are to continue my current focus on breast cancer incidence and to better understand how patterns of change in modifiable lifestyle risk factors such as body fatness, alcohol use and physical activity jointly function

over time to influence breast cancer incidence and mortality in an aging population. My overarching goals are to capture patterns of changing exposures over age and time to inform both the prevention and study of underlying causes of breast cancer and mortality.

1. Doctoral work

In my dissertation research that I completed in 2018, I sought to better understand associations between early infant growth and lipid levels in adolescence. The "Developmental Origins of Health and Disease"[1] theoretical framework informed my aims involving lipid biomarkers of cardiovascular disease risk. To fund this dissertation work, I successfully applied for and received an individual two-year American Heart Association predoctoral fellowship (2016-2018). To determine the extent to which associations exist between infant growth before six months and lipid outcomes measured during adolescence, I assessed patterns of infant growth as an exposure through innovative statistical approaches. These approaches included nonlinear mixed effects models and latent class growth mixture modeling, which provided novel insights into infant growth as a factor associated with lipid biomarkers. There were unexpected findings from my second dissertation aim,[2] including the association between relatively faster growth in the first five months of life and a favorable lipid profile in adolescence. I also found in my first dissertation aim[3] that the socioeconomic position of an infant's family can play a role in anthropometric growth even in the first five months, with lower socioeconomic position linked with slower and less favorable growth. These findings are not in line with most evidence to date and could point towards windows of time before six months of age that have distinct growth profiles and unique associations that may not be consistent with other age periods.

Other formative work during my doctoral training included a required practicum. For this experience, I chose to participate in a systematic review led by Dr. Anthony J. Viera. This opportunity allowed me to observe best practices in conducting a systematic review from beginning to end from a large and experienced team of researchers. My participation included the creation of an online database to store information from multiple reviewers at the start of the review in 2016, subsequent abstract reviews, and the manuscript[4] review in the past year. The applied work in this practicum has taught me the clinical value of this type of research and the amount of team work required to produce it.

2. Postdoctoral research

Following my doctoral work studying links between infant growth and lipid levels in adolescence, I followed my passion for epidemiologic research and the application of advanced methods to a postdoctoral position in Dr. Clarice R. Weinberg's research group with a focus on epidemiologic methods in breast cancer research. In this group, I have continued to study biomarkers with an emphasis on breast cancer outcomes. This experience has challenged me as I learned best practices in breast cancer research, and it has been rewarding to now have advanced training in cancer and cardiovascular disease outcomes – two of the most frequently occurring diseases in the United States with shared risk factors[5]. My postdoctoral work also brought a shift in my methodological focus from the application of mixed effects and latent class models to survival models with time-dependent covariates. One example of this focus is a recent study in which I used age-dependent covariates to explore familial correlation of breast cancer age of onset[6]. My collaborators and I have identified evidence supporting an increase in risk around the age of the affected sister's diagnosis, and, if replicated, this original work offers the potential for use in diagnostic screening of women with affected sisters.

Current projects include a multi-pronged focus on serum iron biomarkers, which are considered both an outcome and risk factor for human health conditions such as iron deficiency anemia, iron overload, and cancer. Recently, we found little evidence of an association between serum iron biomarkers and a risk of breast cancer in a large U.S.-based case-cohort of women[7]. Our findings contradict prior studies that indicate a positive association between serum iron levels and the risk of breast cancer. Our exploratory findings suggest very low levels of ferritin may be protective against breast cancer, especially in women who are obese.

Some of my ongoing research involving iron biomarkers explores whether less invasive and more accessible iron measures could substitute for iron measures obtained through blood collection. These potential proxies for serum iron status in health research include toenail samples and self-report questionnaire responses associated with iron levels. I have presented preliminary findings in two poster presentations at the Society of Epidemiological Research (SER) this year, and our findings do not support using these proxy approaches to serum iron measures. This outcome highlights the difficulty in replacing trace metal measures from blood collection with less invasive and better-scaling approaches.

Another project near completion describes age- and time-varying body mass index (BMI) breast cancer hazard ratios (HRs) using data from the Premenopausal Breast Cancer Collaboration Group[8]. This descriptive study requires meta-analyses of the estimated HRs by cohort prior to pooling data. Our findings, to be submitted as an abstract for the SER conference in 2022, indicate no evidence for change in BMI HRs during the age range spanning most transitions to menopause. This evidence points towards other windows of time in which the postmenopausal BMI HRs could increase. In doing these analyses, I

now have experience with both the planning and analysis required for evidence synthesis, and this can inform my work as a faculty member at the CCTES.

3. Future research

I plan to leverage my past work on exposures that change over time, time-to-event analyses, and women's health during mid-life, so I can develop future research focusing on the impact of lifestyle change for women during menopause. Evidence supports lifestyle factors as important and modifiable causes of morbidity and mortality. Specifically, there are certain lifestyle factors with strong levels of evidence supporting an association with postmenopausal breast cancer incidence such as alcohol use, body fatness, and physical activity. Menopause presents an important window of time for women during which these factors begin to figure more prominently in breast cancer incidence. I plan to start this research by investigating these lifestyle factors in the Sister Study, a large U.S.-based prospective cohort that is ideally suited for this observational research. Less than 10 percent of federally-funded research projects consider more than one of the top ten risk factors for mortality at a time[9], including the aforementioned lifestyle factors. To address this gap, I plan to assess simultaneous change in lifestyle over age and time, and determine their relationship with breast cancer incidence and all-cause mortality. Addressing this research gap may provide evidence informing the prevention of diseases that burden large numbers of people in the United States.

To accomplish the research aims mentioned above, I propose to apply joint regression model methods, a growing area of research that allows simultaneous assessment of longitudinal and time-to-event data. This approach is also an exciting area of methodological application because it allows for better ways to capture variability over time -- missing from research that commonly focuses on cross-sectional

measures. In considering future research directions, my goal is to include high-impact modifiable exposures relating to breast cancer incidence and mortality in women after menopause. This work will build upon the methodological work from my dissertation and postdoctoral work, namely longitudinal, latent growth mixture modeling alongside time-to-event methods.

Targeted lifestyle exposures, including BMI, physical activity, alcohol use, and smoking, also present areas that are accessible to an individual's capacity for change. In turn, this research focus on change in common lifestyle factors that are accessible to individuals can be an opportunity to meet one of the CCTES track's goals to promote consumer involvement in health research. In sum, I am motivated and enthusiastic about pursuing an independent and innovative research program focusing on the role of common modifiable lifestyle factors during midlife in relation to breast cancer and mortality outcomes. Conducting evidence synthesis research within my area of proposed study presents a unique and exciting intersection of fields within epidemiology. To be able to follow this path and collaborate with faculty at the Center for Clinical Trials and Evidence Synthesis at the Johns Hopkins University, Bloomberg School of Public Health is a welcome opportunity.

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