1. Past research work

When I began my graduate studies in epidemiology, I knew I wanted to use my work experience as a statistician in academia by applying new methods to existing public health problems. One way I accomplished this goal was to use innovative statistical approaches in my dissertation research, completed in 2018. To help me understand associations between early infant growth and lipid levels in adolescence, I assessed patterns of infant growth as an exposure through nonlinear mixed effects models and latent class growth mixture modeling. In turn, these new applications provided novel insights into infant growth before six months as exposure and its association with lipid biomarkers.

In my first dissertation aim, I found evidence of an association between lower socioeconomic position of an infant's family and slower and less favorable anthropometric growth profile even in the first five months[1]. Work from my second aim pointed towards a positive association between relatively faster growth in the first five months of life and a favorable lipid profile in adolescence[2]. These findings are not in line with most evidence to date. Replication of these results would confirm the first five months of growth, with its distinct growth profile, underpin associations with exposures and outcomes that differ from later age periods and warrant interventions targeting slower growth, not faster growth.

Following my doctoral work studying links between infant growth and lipid levels in adolescence, I continued my epidemiological research and the application of advanced methods as a postdoctoral fellow at the National Institute of Environmental Health Sciences. Within Dr. Clarice R. Weinberg's research group, I have focused on epidemiological methods in breast cancer epidemiology and continued to incorporate biomarkers in my research. This experience has challenged me as I learned best practices in breast cancer research, and it has been rewarding to have advanced training in cancer and cardiovascular disease outcomes – two of the most frequently occurring diseases in the United States with shared risk factors[3].

My recent work also brought a shift in my methodological focus from 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[4]. With my collaborators, I found evidence supporting an increase in risk around the age of the affected sister's diagnosis, and, if replicated, this original work offers the potential to use a sister's age at diagnosis in diagnostic screening of women with affected sisters.

A goal of my most recent research focusing on serum iron biomarkers is to find less invasive and more accessible measures to serve as surrogates for iron measures obtained through blood collection. Potential proxies for serum iron status include toenail measures and self-reported conditions derived from questionnaires and known to be related to iron levels. Preliminary findings, with one manuscript in review[5] and another in preparation, do not support using these proxy approaches to serum iron measures, showing the difficulty in replacing trace metal measures from blood collection with less invasive and better-scaling approaches.

These experiences in my doctoral and postdoctoral work enabled me to study biomarkers across the life span. My future research plans maintain my study of breast cancer outcomes and include a new direction to study modifiable lifestyle exposures. Given this research and future plans, 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.

2. Future plans

My future research plans include two research areas. One area will provide an opportunity for me to develop an independent body of research centered on modifiable lifestyle indicators unique to breast cancer risk factors after menopause. Another research area will extend my previous experience with biomarkers to a focus on microchimerism, an exciting and growing domain of research. Together, this scope of research will allow me to strengthen and grow my research in breast cancer epidemiology.

2a. Male-origin microchimerism and breast cancer and ovarian cancer

In my current position as a postdoctoral fellow in Dr. Weinberg's research group, we started a new project this year to investigate the association between male-origin microchimerism (MOM) and female cancers, including ovarian and breast cancer. We are in the initial phases of this project, and we expect completion of sample processing for this project by the end of the year.

Broadly speaking, microchimerism constitutes the existence of cells from one individual in another genetically distinct individual. With our research, we will investigate the presence of male cells in females, male-origin microchimerism, as an exposure related to breast cancer and ovarian cancer. MOM is surprisingly common, with one study detecting MOM in 70 percent of women[6]. Recent research has supported a strong inverse association between MOM and female cancers, and one recent study reported about half the risk of ovarian cancer in women with detected MOM[7]. In addition to assessing the association between MOM and these female cancers, we will also explore predictors of this exposure and persistence of MOM over time. Research on the impact and etiology of MOM in female cancers is sparse, and information from this research will provide a needed opportunity to expand our knowledge in this area.

2b. Lifestyle change over time and postmenopausal risk of breast cancer

In terms of my proposed second area of future research, I plan to continue my current focus on breast cancer incidence in an aging population alongside work to characterize concurrent patterns of change in lifestyle measures. Modifiable lifestyle risk factors are associated with breast cancer, the second most common cancer for women in the United States, who experience a 1 in 8 risk of being diagnosed across their lifetime. The postmenopausal period presents an interesting window of time for women in which certain lifestyle indicators figure more prominently in breast cancer incidence than for younger groups. Specifically, there are certain lifestyle indicators with strong levels of evidence supporting an association with postmenopausal breast cancer incidence, such as alcohol use, body fatness, and physical activity. Furthermore, these indicators count among the leading risk factors of mortality in the United States, yet less than ten percent of NIH-funded prevention research projects examine more than one of these indicators[8].

How correlated individual lifestyle indicators comprise a co-existing entity, i.e. a single healthy lifestyle measure, and if change in this healthy lifestyle construct is associated with breast cancer incidence, remains unclear in existing research. A health-promoting lifestyle construct may modify associations with known genetic risk factors. Furthermore, we can identify people with certain lifestyle characteristics who carry a disproportionate breast cancer burden, also considered a high-risk subset of the population eligible for interventions[9]. Defining risk distribution measures that involve modifiable behaviors remains an important and underdeveloped area of research in public health. With better knowledge of this association, we could improve efforts to identify subgroups as optimal targets for breast cancer prevention.

My overarching goal is to better understand the role of healthy lifestyle trajectories as they relate to breast cancer incidence and their interplay with genetic factors. To address this goal, I plan a three-pronged analytic approach using data from the Sister Study, a large contemporary large U.S. cohort of women founded by investigators at NIEHS. First, I will pursue an innovative analytic approach through confirmatory factor analysis to estimate a healthy lifestyle construct. During this process, I also plan to assess variation of this construct across age and racial/ethnic groups. Second, I plan to assess patterns of change over time in this construct that could influence breast cancer risk, through joint modeling of longitudinal and time-to-event models. Lastly, I will use risk inequality methods to characterize the concentration of disease burden across the range of lifestyle indicators and use this inequality assessment to determine if it modifies genetic risk of breast cancer through gene-environment models.

Postmenopausal women who have an unfavorable lifestyle profile and carry a disproportionate disease burden may demonstrate stronger genetic associations with breast cancer risk than those in lower disease-burden groups. It is vitally important to not only characterize a constellation of lifestyle indicators that impact cancer and all-cause mortality outcomes, but to understand how lifestyle factor changes over time influence these outcomes. This advance in our understanding would help clarify carcinogenic pathways and also highlight critical areas of intervention in midlife, providing important insights into avenues of prevention.

In sum, in considering future research directions, my goal is to include high-impact modifiable exposures relating to breast cancer incidence in women after menopause and to build upon the methodological work from my dissertation and postdoctoral work, namely longitudinal, latent growth mixture modeling alongside time-to-event methods. These targeted lifestyle exposures, which include BMI, physical activity, and alcohol use also present an excellent opportunity to teach students advanced epidemiologic methods related to common and modifiable exposures relevant to public health. In sum, I am motivated and enthusiastic about pursuing an independent research program in cancer epidemiology and advanced methods application to better understand the role of common modifiable lifestyle factors in the role of breast cancer risk. To follow this path and collaborate with faculty at the Department of Population Health Sciences at Duke University is a welcome opportunity.

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