OMB No. 0925-0001 and 0925-0002 (Rev. 12/2020 Approved Through 02/28/2023)

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.

Follow this format for each person. DO NOT EXCEED FIVE PAGES.

|  |
| --- |
| NAME: Von Holle, Ann |
| eRA COMMONS USER NAME (credential, e.g., agency login): ANNVONHOLLE |
| POSITION TITLE: Postdoctoral Intramural Research Training Awardee |

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

|  |  |  |  |
| --- | --- | --- | --- |
| INSTITUTION AND LOCATION | DEGREE (if applicable) | END DATE MM/YYYY | FIELD OF STUDY |
| University of California, San Diego, San Diego, CA | BA | 06/1993 | Applied Mathematics |
| Johns Hopkins School of Public Health, Baltimore, Maryland | MHS | 05/1995 | Population Dynamics |
| University of North Carolina, Chapel Hill, North Carolina | MS | 05/2003 | Biostatistics |
| University of Pennsylvania, Philadelphia, PA | MA | 05/2005 | Demography |
| University of North Carolina, Chapel Hill, Chapel Hill, NC | PHD | 06/2018 | Epidemiology |
| National Institute of Environmental Health Sciences, Research Triangle Park, NC | Postdoctoral Fellow | present | Epidemiological methods |

### A. Personal Statement

My long-term career goals are to investigate modifiable risk factors of postmenopausal women as they relate to breast cancer prevention and mortality reduction. My past work as a biostatistician and more recent training in epidemiology motivated my proposed aims and further training to achieve my goals. Prior to my doctoral training in epidemiology, I was able to learn new analytical skills when applying them to population health studies and in this time developed an appreciation for structural equation modeling. I took that knowledge and transformed that as a doctoral student preparing my dissertation to focus on longitudinal patterns of infant anthropometric growth and their associations with lipids commonly used as biomarkers for cardiovascular disease. Among our findings, we discovered that lower socioeconomic position is associated with adverse growth characteristics, and faster growth in early infancy is associated with a favorable profile. As a postdoctoral fellow at the National Institute of Environmental Health Sciences in the past three years, I have continued work with biomarkers with an emphasis on time-to-event analyses to investigate breast cancer incidence outcomes and their association with iron biomarkers. In a recent publication, we found little evidence of an association between breast cancer and markers of circulating and stored iron, but a possible protective relationship with very low iron levels. While starting my postdoctoral work, I also completed an analysis that found a relative increase in risk as a woman nears the age of her sibling’s breast cancer diagnosis, i.e. correlated timing of onset within families. In conducting studies of breast cancer incidence outcomes with time-to-event methods during my postdoctoral fellowship, accompanied by the focus on the relationship between longitudinal anthropometric measures and chronic disease biomarkers, I will be well positioned to enter a new phase of research and study the role of lifestyle risk factors in the occurrence of breast cancer. This proposed K99/R00 research focuses on lifestyle risk factors that are associated with chronic disease, mortality, and postmenopausal breast cancer risk, providing a unique platform upon which I can expand my research expertise while meaningfully contributing to public health. The additional training in advanced joint modeling techniques and in-depth knowledge of the epidemiologic study of lifestyle factors creates a path for me to successfully complete the proposed research and move toward an overarching goal to inform public health prevention measures to reduce breast cancer incidence and mortality.

1. Von Holle A, O'Brien KM, Sandler DP, Weinberg CR. Evidence for familial clustering in breast cancer age of onset. Int J Epidemiol. 2021 Mar 3;50(1):97-104. PubMed Central PMCID: PMC7938508.
2. Von Holle A, O'Brien KM, Sandler DP, Janicek R, Weinberg CR. Association Between Serum Iron Biomarkers and Breast Cancer. Cancer Epidemiol Biomarkers Prev. 2021 Feb;30(2):422-425. PubMed Central PMCID: PMC7867615.
3. Von Holle A, North KE, Gahagan S, Burrows RA, Blanco E, Lozoff B, Howard AG, Justice A, Graff M, Voruganti VS. Sociodemographic predictors of early postnatal growth: evidence from a Chilean infancy cohort. BMJ Open. 2020 Jun 3;10(6):e033695. PubMed Central PMCID: PMC7282289.
4. Von Holle A, North KE, Tao R, Gahagan S. The perils of standardizing infant weight to assess weight change differences across exposure groups. Ann Epidemiol. 2018 Aug;28(8):515-520. PubMed PMID: 29936050.

### B. Positions, Scientific Appointments and Honors

Positions and Scientific Appointments

|  |  |
| --- | --- |
| 2005 - 2013 | Biostatistician, University of North Carolina, Chapel Hill, Department of Psychiatry, Chapel Hill, NC |
| 1999 - 2000 | Research Analyst, Maryland Health Care Commission, Baltimore, MD |
| 1997 - 1998 | Public Health Specialist, Peace Corps |

Honors

|  |  |
| --- | --- |
| 2021 - 2021 | Intramural Paper of the Month, Environmental Factor, NIEHS newsletter |
| 2016 - 2018 | Individual Predoctoral Fellowship Award (Award: 16PRE29200008), American Heart Association |
| 2014 - 2016 | Summer travel scholarship award, Summer Institute in Statistical Genetics |
| 2001 - 2005 | T32 predoctoral training fellowship in population studies, NICHD |

### C. Contribution to Science

1. **Biostatistician at the Center of Excellence for Eating Disorders (CEED)**

As a biostatistician at the CEED I had the privilege and opportunity to work on eating disorder research with an eminent group of clinical researchers. Of the 42 papers I worked on at CEED, 20 of them centered on the Norwegian Mother and Child Cohort Study (MoBa), a contemporary birth cohort of more than 100,000 pregnancies. My role as a biostatistician allowed me to successfully collaborate with lead authors in designing and conducting analyses. Of the 20 MoBa publications in which I was a co-author, I had the privilege to be the lead statistician on 15 of them. My role was to ensure that analyses accurately reflected the hypotheses posited by the researchers. In turn, this body of work can support researchers seeking well quantified research on children and mothers with eating disorders in areas such as basic epidemiologic information, postpartum weight change and child growth trajectories.

* 1. Perrin EM, Von Holle A, Zerwas S, Skinner AC, Reba-Harrelson L, Hamer RM, Stoltenberg C, Torgersen L, Reichborn-Kjennerud T, Bulik CM. Weight-for-length trajectories in the first year of life in children of mothers with eating disorders in a large Norwegian Cohort. Int J Eat Disord. 2015 May;48(4):406-14. PubMed Central PMCID: PMC4482472.
  2. Zerwas SC, Von Holle A, Perrin EM, Cockrell Skinner A, Reba-Harrelson L, Hamer RM, Stoltenberg C, Torgersen L, Reichborn-Kjennerud T, Bulik CM. Gestational and postpartum weight change patterns in mothers with eating disorders. Eur Eat Disord Rev. 2014 Nov;22(6):397-404. PubMed Central PMCID: PMC4205262.
  3. Von Holle A, Pinheiro AP, Thornton LM, Klump KL, Berrettini WH, Brandt H, Crawford S, Crow S, Fichter MM, Halmi KA, Johnson C, Kaplan AS, Keel P, La Via M, Mitchell J, Strober M, Woodside DB, Kaye WH, Bulik CM. Temporal patterns of recovery across eating disorder subtypes. Aust N Z J Psychiatry. 2008 Feb;42(2):108-17. PubMed PMID: 18197505.
  4. Bulik CM, Von Holle A, Hamer R, Knoph Berg C, Torgersen L, Magnus P, Stoltenberg C, Siega-Riz AM, Sullivan P, Reichborn-Kjennerud T. Patterns of remission, continuation and incidence of broadly defined eating disorders during early pregnancy in the Norwegian Mother and Child Cohort Study (MoBa). Psychol Med. 2007 Aug;37(8):1109-18. PubMed Central PMCID: PMC2657803.

1. **Doctoral work at the Department of Epidemiology at the University of North Carolina, Chapel Hill**

In my dissertation research, I wanted to better understand associations between early infant growth and lipid levels in adolescence. The “Developmental Origins of Health and Disease” theoretical framework informed my three aims, which, similar to my postdoctoral work, centered on a set of biomarker outcomes -- in this case the lipid biomarkers related to cardiovascular disease risk. To fund my dissertation work, I was fortunate to get an individual two-year American Heart Association predoctoral fellowship (2016-2018). When determining the extent to which associations exist between infant growth and lipid outcomes, I used nonlinear mixed effects models and latent class growth mixture modeling to characterize growth as an exposure. Through the three years I spent developing the ideas and plans, analyzing the data, and interpreting the results, I had some unexpected findings that included the association between relatively faster growth and a favorable lipid profile in the first five months of life. I also found in my first aim that the socioeconomic position of an infant’s family can play a role in growth even at the earliest times of life, 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 that have distinct growth profiles and unique associations that may not be consistent over age.

* 1. Von Holle A, North KE, Gahagan S, Burrows RA, Blanco E, Lozoff B, Howard AG, Justice A, Graff M, Voruganti VS. Sociodemographic predictors of early postnatal growth: evidence from a Chilean infancy cohort. BMJ Open. 2020 Jun 3;10(6):e033695. PubMed Central PMCID: PMC7282289.
  2. Von Holle A, North KE, Tao R, Gahagan S. The perils of standardizing infant weight to assess weight change differences across exposure groups. Ann Epidemiol. 2018 Aug;28(8):515-520. PubMed PMID: 29936050.

1. **Postdoctoral training at the National Institute of Environmental Health Sciences**

I have transitioned to a research focus in my postdoctoral work on a breast cancer cohort, a rewarding research domain that has allowed me to develop productive research spanning both cardiovascular disease and cancer outcomes. These outcomes are two of the most frequently occurring diseases for women in the United States and share common modifiable risk factors. My methodological focus on longitudinal changes shifted from mixed effects and latent class models to survival models with time-dependent covariates. The first manuscript from my postdoctoral work addresses familial correlation of breast cancer ages of onset. Our goal was to determine if a woman currently without a breast cancer diagnosis who had a sister diagnosed with cancer has higher relative breast cancer risk when closer to the age at diagnosis of the previously affected sister. We found evidence supporting such an increase, and this original work offers the potential for use in diagnostic screening of women a first-degree family history. Another line of research includes the study of circulating and stored iron levels as a biomarker. When assessing association between iron and breast cancer incidence, we found little evidence that higher iron levels increase breast cancer risk but did find evidence that very low levels of iron could be protective. If replicated, these findings can support new perspectives on this active area of research on associations between iron and cancer.

* 1. Von Holle A, O'Brien KM, Sandler DP, Weinberg CR. Evidence for familial clustering in breast cancer age of onset. Int J Epidemiol. 2021 Mar 3;50(1):97-104. PubMed Central PMCID: PMC7938508.
  2. Von Holle A, O'Brien KM, Sandler DP, Janicek R, Weinberg CR. Association Between Serum Iron Biomarkers and Breast Cancer. Cancer Epidemiol Biomarkers Prev. 2021 Feb;30(2):422-425. PubMed Central PMCID: PMC7867615.