

## **Exploring Rural-Urban Differences in Polygenic Associations for Health among Older Adults in the United States**

Jason D. Boardman, University of Colorado, Boulder

### **Project Summary**

This project will use information from the Health and Retirement Study to evaluate the extent to which genetic associations for health, health behaviors, and mortality are comparable among older adults residing in rural areas compared to those in urban areas. Specifically, we will interact individual polygenic scores for thirteen health outcomes with an indicator of rural status to expand upon previous work showing reduced heritability of health behaviors in rural areas. This project will add important information to the large and growing body of research on gene-environment interactions by focusing on the rural-urban distinction. The existing research on rural-urban moderation of genetic associations is important but it has at least three limitations: 1) it emphasizes alcohol use; 2) three of the four derived their estimates from twin study design; 3) the molecular analysis was limited to two candidate genes (e.g., FTO and MC4R); 4) most were limited to adolescents; and 5) there is no information about changes in residential contexts over time. Our proposal will add to this important but limited body of work by 1) broadening the range of health and health behaviors examined; 2) utilizing state of the art polygenic scores to assess genetic risk; 3) expanding the age range to older adults who have had greater exposure to different environments over time; and 4) examining changes in urban and rural residential status over time. In addition, our proposed study would be the first to characterize the average polygenic scores across rural and urban settings. This last point is important because we will evaluate the possibility of gene-environment correlation in determining the composition of rural environments as populations age. We will take advantage of the longitudinal component of the HRS to examine the average polygenic score for thirteen health outcomes among long term urban residents, urban to rural movers, rural to urban movers, and long-term rural residents. To date, this form of gene-environment correlation has not been assessed empirically and will contribute to the gene-environment literature, including recent work in the area of sociogenomics. We can also evaluate the changing sociogenomic composition of aging populations in rural vs. urban areas, a function of mortality. Finally, we will examine the role of social resources as a mediating and moderating mechanism for these associations. Social isolation is more prevalent among residents of rural communities. Social resources and connections to others have also been shown to moderate genetic associations for health outcomes with a specific emphasis on mental health. We will first examine the degree to which social resource disparities among rural-urban residents attenuate the hypothesized rural-urban differences in polygenic associations. We will then evaluate whether access to and utilization of social resources among rural residents differentially affects polygenic associations. Together, this aim will highlight the centrality of social interactions as a determinant of health and provide new evidence regarding specific mechanisms.