Submitter Name: Amy Moore
PI Name: Eric O. Johnson

Submitter Email: almoore@rti.org
PI Email: ejohnson@rti.org

Leveraging the *All of Us* Research Program to Better Understand the Genetic Architecture of Opioid Use Disorder Spectrum Behaviors

Amy Moore[1], Bradley T. Webb[1], Sandra Sanchez-Roige[2,3], Vanessa Troiani[4], Eric O. Johnson[1]

[1]RTI International, RTI International, Research Triangle Park, North Carolina, USA;
[2]Department of Psychiatry, University of California San Diego, La Jolla, California, USA;
[3]Department of Medicine, Vanderbilt University Medical Center, Nashville, Tennessee, USA;
[4]Geisinger Clinic, Geisinger, Danville, Pennsylvania, USA.

Attempts to understand the genetic underpinnings of opioid use disorder have had limited success compared to other diseases. These difficulties have been attributed to limited sample size, insufficient genetic diversity, difficulty identifying appropriate control groups, and challenges characterizing the spectrum of opioid use behaviors. The *All of Us* (AoU) Research Program contains extensive behavioral and clinical data coupled with genotype information from over one million Americans, with targeted recruitment of individuals traditionally underrepresented in biomedical research. We used diagnostic codes (ICD9/10) for opioid abuse or dependence from electronic health records and survey self-report indicating lifetime opioid misuse to identify opioid misuse cases. After requiring high-quality genotyping data and genetically predicted ancestry determinations, we calculated autosomal SNP-heritability for each of three ancestry groups from AoU: African (AFR) (n_{cases}=5,647), American (AMR) (n_{cases}=3,680), and European (EUR) (n_{cases}=15,761) using genotype data from the Global Diversity Array. Heritability calculations were performed using Bolt-REML and adjusted for sex at birth, year of birth, and 16 principal components of ancestry. Preliminary results comparing opioid misuse to unscreened controls within genetically predicted ancestries in AoU yield SNP-heritabilities of 0.0295 (SE=0.0099) for AFR, 0.165 (0.0112) for AMR, and 0.0625 (0.00383) for EUR ancestry, respectively. Ongoing work will define optimal control groups and conduct genome-wide association testing in the full WGS cohort (up to N = 245,394). We anticipate additional work leveraging the extensive data present in AoU to consider further examination of the genetic architecture of opioid misuse, including sex differences, comorbid conditions, and patterns of recovery.