Submitter Name: Bradley T. Webb Submitter Email: bwebb@rti.org

Deep ascertainment and genetic architecture of alcohol use disorder and related outcomes in All of Us.

Amanda E. Gentry[1], Amy Moore[2], Mohammed F. Hassan[1], Roseann E. Peterson[3,1], Julie D. White[2], Dana B. Hancock[2], Eric O. Johnson[2], Bradley T. Webb[2]

[1]Department of Psychiatry, Virginia Institute for Psychiatric and Behavioral Genetics, Virginia Commonwealth University, Richmond, Virginia, USA; [2]GenOmics and Translational Research Center, RTI International, RTI International, Research Triangle Park, North Carolina, USA; [3]Department of Psychiatry and Behavioral Sciences, Institute for Genomics in Health, SUNY Downstate Health Sciences University, Brooklyn, New York, USA

Alcohol use disorder (AUD) is moderately heritable with significant social and economic impacts. The All of Us (AoU) research program is a powerful resource for studies of AUD and related outcomes. The reported prevalence of AUD in AoU is 1.88% when using an EHR-based only ascertainment approach. In contrast, studies using structured interviews, such as NESARC, show lifetime AUD prevalences of ~29%. This discrepancy may create significant impact for genetics studies since misclassification reduces power. Fortunately, AoU has information beyond the core AUD F10 ICD code including procedures, prescriptions, laboratory values, surveys, and self-report. We hypothesized a more comprehensive assessment could identify additional cases, participants at increased risk, and screened controls. Cases were defined using self-report variables and alcohol specific prescriptions (acamprosate, disulfiram), ICD codes (alcoholic cirrhosis), and treatments (alcohol detoxification). Participants were defined as high-risk if they were heavy drinkers, regular binge drinkers, or had a family history of AUD. Controls were defined as not being a case, high-risk, or never-drinker. These definitions identified 25,988 (6.6%) cases, 19,288 (4.9%) high-risk, 307,139 (78.2%) controls, and 39,955 (10.2%) non-drinkers. The identification of additional cases is particularly important for genetic analyses in participants of non-European ancestry. For participants of admixed African ancestry with whole genome sequencing (WGS) data, 4,872 cases, 3,796 high-risk, 36,063 controls, and 10,034 non-drinkers were identified. Heritability and genetic correlations analyses are needed to provide empirical evidence to show the narrow and broad case definitions are similar and combining the broad and high-risk groups is justified.