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Alcohol consumption and misuse have a distinct genetic basis

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Alcohol consumption and misuse are core traits associated with development alcohol use disorders (**AUD**). In a first study, we obtained quantitative measures using the Alcohol Use Disorder Identification Test (**AUDIT**), which is a 10-item screening questionnaire that measures aspects of alcohol consumption (items 1-3, **AUDIT-C**) and problematic use (items 4-10, **AUDIT-P**), from UK Biobank (N=121,630), and performed two genome-wide association analyses (**GWAS**). Genetic correlation analyses revealed that the genetic overlap between AUDIT-C and alcohol dependence was positive but relatively modest (rg=0.38), suggesting that, although the use of alcohol is necessary to develop AUD, alcohol consumption alone may not be a good proxy for AUD. Furthermore, AUDIT-P and AUDIT-C showed different patterns of association across several traits. For example, AUDIT-P was positively genetically correlated with schizophrenia (rg=0.22), major depressive disorder (**MDD**, rg=0.26), and attention-deficit/hyperactivity disorder (**ADHD**, rg=0.23), whereas AUDIT-C was negatively genetically correlated with MDD (rg=-0.24) and ADHD (rg=-0.10). In a second study, we examined the extent to which polygenic risk scores (**PRS**) derived from AUDIT-C and AUDIT-P predicted variance in a range of alcohol use behaviors across samples that were variously ascertained. We identified that PRS for AUDIT-P were superior predictors of a range of alcohol-related phenotypes, particularly the domains of misuse and dependence. These studies suggest that alcohol consumption and misuse have a distinct genetic basis. These findings also reveal that the genetic architecture of alcohol consumption only partially overlaps with the genetics of clinically defined AUD.