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Investigating causal influences on alcohol consumption and major depression across middle and late adulthood – A genetically informative pseudo-longitudinal approach

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Despite numerous associations between alcohol use and major depression, there has been limited research on shared liability that addresses comorbidity in a genetically informed framework. Both problematic alcohol use and major depression are liable to change across the lifespan, are heritable, and show moderate genetic correlation. While genetic studies have discovered numerous common loci influencing each, few large-scale studies have repeated measures for both outcomes across adulthood. In the absence of such collections, GWAS of independent samples from discrete age tranches can be used within genomic structural equation modeling (gSEM) to perform pseudo-longitudinal investigations of genetic factors across age. GWAS of monthly alcohol consumption and major depression were performed on six independent age intervals between 40-73 years using BGENIE. The primary analysis included subjects of European ancestry with age tranche sizes of 13,272, 13,694, and 26,966 for male, female, and combined sex analyses, respectively, with a total of 284,784 subjects. Results will also be reported for participants of African and South East Asian descent. This approach demonstrated that changes in alcohol consumption across adulthood are, in aggregate, primarily influenced by a single genetic factor. Alcohol consumption showed positive genetic correlation with major depression. Using gSEM, we evaluated competing hypotheses regarding the stability of genetic effects in both single- and cross-trait models. Single-trait cross-age tranche analyses showed genetic variance in consumption at each age interval could not be explained by the accumulation of any age-specific genetic influences or autoregressive processes.