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Polygenic risk scores analysis of alcohol use disorder

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Current polygenic risk scores (PRS) of alcohol use disorder (AUD) only explained a small portion of the overall genetic risk and cannot be used to evaluate the AUD risk. In this study, using genome-wide association studies (GWAS) of AUD from the Million Veteran Program and alcohol use problem scores of the Alcohol Use Disorder Identification Test from the UK Biobank, we proposed a novel framework to derive PRS by using variants having the same directions of effects in both GWAS to exclude study-specific findings and findings due to random variations. Using European ancestry samples from the Collaborative Study on the Genetics of Alcoholism (COGA; N=7900), we found that PRS was significantly associated with AUD (P-value=2.66E-16). Those in the top decile of PRS had odds ratios of 1.96 (95%CI: 1.54-2.51, P-value=7.57E-08) to develop AUD, comparable to previously reported odds ratios for the first-degree family history (1.91 to 2.38) estimated from national surveys. PRS did not interact with family history (P-value=0.60) and PRS remained significantly associated with AUD after adjusting for family history (P-values=6.8E-10). Individuals having high PRS had earlier ages of first drinking, cigarette and drug use, higher self-rating of effects of alcohol scores and maximum drinks, larger number of DSM-5 AUD criterion endorsed, and higher rates of nicotine and drug use disorders than those having low PRS (P-values≤3.28E-03). In conclusion, PRS could potentially be used to evaluate the risk for AUD, and characteristics of individuals having high and low PRS can help the development of novel prevention and treatment strategies.