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**The Psychiatric Genomics Consortium Substance Use Disorders Working Group  
(PGC-SUD): An Update**

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The Psychiatric Genomics Consortium's Substance Use Disorders working group (PGC-SUD) conducts genome-wide association studies (GWAS) of SUD and examines genetic comorbidity between SUD and other medical disorders. The PGC-SUD published the first trans-ancestral meta-analytic GWAS of alcohol, opioid and cannabis use disorders.

These analyses highlighted genetic distinctions between earlier stages of substance use/exposure or typical intake and later pathological stages of problem use and SUD, and examined the genetic correlation between SUD and somatic and mental health traits (e.g., depression, schizophrenia, suicide, pain, cardiometabolic disease). Despite their genetic overlap, consumption and SUDs show partially differing associations with comorbid conditions, emphasizing the continued need to increase sample sizes for SUD. The results also support a high degree of polygenicity undergirding SUD. PGC-SUD has collaborated with other groups to enrich larger meta-analyses of SUD and problematic substance use. We have also explored commonalities among SUD, and recent analyses demonstrate the role of dopaminergic pathways in a shared liability. Ongoing analyses are investigating the impact of diagnostic definitions on gene identification for nicotine use disorder. We are also beginning to explore the epigenetics of SUD. Future directions include enhancing GWAS sample sizes for SUDs and improving our understanding of serious comorbidities with SUD, as well as incorporating analyses of structural variants.