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## **Dissecting the Etiology of Alcohol Use Disorder by an Integrative Heritable Component Approach**

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Alcohol Use Disorder (AUD) is a pervasive condition that exhibits a complex interplay of genetic, phenotypic, and environmental factors. While previous studies have identified genetic loci associated with alcohol consumption, these efforts fail to capture the genetic heterogeneity and gene-environment interactions in AUD pathogenesis. By employing a novel statistical methodology integrating phenotypic, genotypic, and environmental data, we aim to uncover the complex dynamics influencing AUD risk, thus addressing a critical gap in current research, and potentially informing more effective strategies for prevention, intervention, and treatment. We expect that the inclusion of environmental factors in analyses will uncover AUD-related traits with enhanced heritability, providing insights that are more accurate and directly applicable to clinical settings. Synthetic trials have demonstrated that traits derived using the environmentally modified Genetic Relationship Matrix (GRM) exhibited significantly higher estimated heritability and greater fidelity to ideal solutions than those obtained with unmodified genetic data. Initial trials utilizing Semi-Structured Assessment for Drug Dependence and Alcoholism (SSADDA) dataset indicate that by incorporating environmental data, the model more accurately captures the complex nature of AUD associated traits, yielding higher heritability compared to analyses based solely on unmodified genetic data. Future directions will include the creation of a clinical severity index through the application of constraints to the derived coefficients and the conduction of a Genome-Wide Association Study to identify genetic variants linked to this index.