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## **Genome-wide association studies of substance use in people living with HIV across the US**

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The prevalence of hazardous alcohol use and smoking in people living with HIV (PLWH) in the US is much higher than in the general population. Genome-wide association studies (GWAS) may provide insights into new mechanisms that confer increased substance use patterns among PLWH. To identify novel genetic loci associated with substance use, we performed GWAS of five alcohol and smoking phenotypes in a multi-ethnic population of 7,825 PLWH from the Center for AIDS Research Network of Integrated Clinical Systems (CNICS) population. We performed GWAS of five self-reported alcohol consumption and smoking history phenotypes, using either logistic or linear regression models adjusted for age, sex, CNICS site, self-reported race, and the first 10 principal components. We additionally conducted stratified analyses by self-reported race. We imputed genome-wide genotype data to the Haplotype Reference Consortium (HRC) panel and removed variants with imputation quality score <0.3 or minor allele frequency <0.05, leaving approximately 7M SNPs for analyses. No individual genetic variant reached genome-wide significance at  $p=5 \times 10^{-8}$  for any of the phenotypes. We observed suggestive variants at  $p < 10^{-6}$  that warrant replication using additional data. Suggestive variants will be validated in an independent set of 2,000 CNICS participants currently being genotyped for replication analyses. Identifying novel variants associated with substance use in ethnically and racially diverse PLWH with a high rate of smoking and alcohol consumption will help better understand the underlying mechanisms of these harmful behaviors.