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Largest GWAS of lifetime cannabis use (N = 184,765) reveals new genetics risks and overlap with psychiatric traits, and a causal influence of schizophrenia.

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Cannabis use is a heritable trait associated with adverse mental health outcomes. In the largest genome-wide association study (GWAS) for lifetime cannabis use to date (N = 184,765), we identified eight genome-wide significant independent single nucleotide polymorphisms in six regions. All measured genetic variants explained 11% of the total variance. Gene-based tests revealed 35 significant genes in 16 regions. A total of 21 genes had different expression levels for cannabis users versus nonusers. The strongest association with lifetime cannabis use was CADM2, which has been associated with substance use and risk-taking. Significant genetic correlations were found with 14 of 25 tested substance use and mental health-related traits, including smoking, alcohol use, schizophrenia and risk-taking. Mendelian randomization analysis showed evidence for a causal positive influence of schizophrenia risk on cannabis use. Our study provides new insights into the etiology of cannabis use and its relation to mental health.