Opioid dependence (OD) is a growing issue affecting public health and social and economic welfare. Understanding its biology to develop more effective preventive strategies and treatments is a priority. Genome-wide association studies (GWAS) demonstrated to be an exceptional tool to investigate the genetic architecture of complex traits. The Substance Use Disorder workgroup of the Psychiatric Genomic Consortium is working on a large-scale OD GWAS, analyzing samples from 15 cohorts. The analysis is conducted considering two different analytic designs: DSM-IV OD diagnosis and DSM-IV criterion count. Additional independent samples with information about frequency of opioid use are available to follow up genome-wide significant loci and to conduct polygenic risk score analysis. The findings expected from this ongoing analysis will permit to move opioid research toward large-scale genomic investigations.