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Multi-Ancestry Genome-Wide Association Meta-Analysis of Buprenorphine Treatment Response

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Although increasing numbers of patients are being prescribed buprenorphine to treat opioid use disorder (OUD), individual response to the drug varies, with few known clinical and no genetic predictors of treatment response. Understanding the impact of clinical and genetic factors could enhance the effectiveness of buprenorphine therapy by tailoring treatment to the needs of individuals. To address this, we combined a cohort of buprenorphine-treated Veterans with OUD (nAFR = 751 and nEUR = 3,643) from the Million Veteran Program (MVP) with a cohort of subjects with OUD from a clinical trial of extended-release buprenorphine (nAFR = 130 and nEUR = 294) to identify clinical and genetic factors associated with treatment response. In the MVP cohort, individuals with chronic pain were more likely (OR = 1.16 [1.01-1.33]) to respond to buprenorphine, whereas in the clinical trial cohort, those who used tobacco (OR = 0.47 [0.23-0.97]) or had greater withdrawal severity (OR = 0.85 [0.732-0.969]) were less likely to do so. In the cross-ancestry meta-analysis across cohorts, we identified one genome-wide significant locus (rs149319538) that maps to SLC39A10, which encodes a zinc transporter. Phenome-wide association analyses of rs149319538 implicated connectivity of the uncinate fasciculus, a limbic white matter fiber tract. Clinical characteristics, including chronic pain, tobacco use, and withdrawal severity, may be useful in predicting buprenorphine treatment response. Although we identified the first genome-wide significant variant associated with buprenorphine treatment response, larger samples are needed to replicate these findings and identify additional clinical and genetic factors to predict buprenorphine treatment efficacy.