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Bipolar disorder in the All of Us database

Bipolar disorder (BD) is a mental illness that is characterized by episodes of mania and/or depression and is associated with adverse comorbidities such as cognitive impairment and suicidal behavior. BD is split into type I and II in the DSM-5, the former necessitating a manic episode. In 2015, the NIH began the All of Us Research Program (AoU), which sought to build a diverse database for health conditions and help identify disease risk factors and best treatments for people of different backgrounds. The purpose of this study was to utilize the AoU data to perform a Genome-Wide Association Study for a combined BD I and II cohort, and compare findings with those of the Psychiatric Genomics Consortium (PGC) and Million Veterans Program (MVP).
Using AoU, phenotypes of BD I and II were created leveraging electronic health records. Participants were then assessed for criteria indicative of BD I, BD II, or schizophrenia (SCZ), given the considerable overlap between SCZ and BD in existing literature. Patients meeting criteria for SCZ and BD were further distinguished by the dominance of SCZ or BD in their most recent health records. Control patients were never prescribed a mood stabilizer or antipsychotic, did not have a diagnosis of BD on the questionnaire, and had no codes for BD, SCZ, or depressive disorders.
There were 6,862 total cases of BD of multiple ancestries: 1,640 African, 1,014 Latino, 40 East Asian, 4,112 European, 15 Middle Eastern, and 41 South Asian. After removing patients with missing genomic data, a GWAS was run with 3,297 cases and 13,188 age-matched controls of European ancestry. Although there were no genome-wide significant loci, the results are correlated with the PGC and MVP studies. This analysis will be repeated for patients of African and Latino ancestry. GWAS results will be meta-analyzed with PGC and MVP, representing a significant addition to cross-ancestry genetic results.