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# Demographics and genetic epidemiology of opioid use disorder in national-wide population-based biobanking cohorts

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Opioid epidemic is an on-going national crisis in the United States. This study leverages on two population-based cohorts (All of Us [AoU] and UK Biobank [UKB], total sample size > 800,000) with both genomic data and electronic health records (EHR). We aim to combine genetics and epidemiology to better understand and manage opioid use disorder (OUD). We adopted consistent EHR criterions to define OUD cases and opioid-exposed controls. The distribution of OUD case/control status were firstly linked with gender, age, and ancestry; and then with genomic markers by genome-wide association study (GWAS). We identified 12,492 OUD cases (4.2%) and 80,287 controls (26.8%) from ~300,000 AoU participants; but we only identified 2,881 cases (0.6%) and 66,895 controls (13.4%) from ~500,000 UKB participants. Both OUD and regular opioid use are more prevalent ($P < 0.001$) in US than in UK. When zooming into different demographical groups, OUD cases in AoU are significantly more enriched ($P < 0.001$) in male participants, younger age group, and Black populations than those opioid use controls. As a comparison, OUD cases are slightly more enriched ($P < 0.05$) in female participants and older age group in UKB participants. In the discovery GWAS with UKB white population only, we identified 2 genes (*PLXNC1* and *TBC1D16*) harboring suggestively significant signals in association with OUD ($P < 0.000001$). Epidemiology discrepancies between US and UK may be explained by population structure, genetic liability, and health policy difference on opioid. Multi-ethnic GWAS in AoU will provide more genomic evidence to better explain OUD development across ancestries.