

## Abstract

**Objective:** Elucidation of the interaction of biological and psychosocial/environmental factors on opioid dependence (OD) risk can inform our understanding of the etiology of OD. We examined the role of psychosocial/environmental factors in moderating polygenic risk for opioid use disorder (OUD).

**Methods:** Data from 1,958 European ancestry adults who participated in the Yale-Penn 3 study were analyzed. Polygenic risk scores (PRS) were based on a large-scale multi-trait analysis of genome-wide association studies (MTAG) of OUD.

**Results:** A total of 420 (21.5%) individuals had a lifetime OD diagnosis. OUD PRS were positively associated with OD (odds ratio [OR]=1.42, 95% confidence interval [CI]=1.21-1.66). Household income and education explained almost 50% of the variance in OD risk. Among individuals in the highest quartile of OUD PRS, those with less than high school education had a 7.4-fold greater probability of OD than those with a Bachelor's degree or higher; those with posttraumatic stress disorder (PTSD) were 1.8-times as likely to have OD as those without PTSD; and those who reported early substance use in the household were 1.9-times as likely to have OD as those without early exposure.

**Conclusions:** Our results show the interplay between genetics and psychosocial environment contributing to OD risk. PRS alone do not yet have useful predictive power clinically, but other factors enhance prediction. These findings could inform more targeted clinical and policy interventions.

## Bio

Dr. Peter J. Na is an addiction psychiatrist at the VA Connecticut Healthcare System and an assistant professor of psychiatry at Yale School of Medicine. Dr. Na's research interests are in the intersection of substance use disorders and suicidal behavior. His research focuses on the psychosocial and environmental factors that contribute to the development of addiction and suicidal behavior as well as treatment of individuals with co-occurring substance use disorders and psychiatric disorders.