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Investigating genetic, environmental risk factors for opioid use disorder

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A new study by VA Connecticut Healthcare System and Yale School of Medicine researchers assesses how the most up-to-date genetic and psychosocial predictors of opioid use disorder compare and combine

when predicting the risk of becoming dependent on opioids.

"We've made great progress in understanding some of the genetic and environmental factors that influence risk for opioid use disorder, but we know less about the complex interplay between them," said Joseph Deak, Ph.D., associate research scientist at Yale School of Medicine, and co-lead author of the study.

Other recent studies have assessed the biological, psychological, and social factors that influence risk for opioid use disorder. Recent advances in genetic discovery have led to personalized medicine applications for some medical traits that incorporate genetic risk estimates, which can be in the form of "polygenic risk scores." These scores aggregate genetic information across the genome to understand whether some people may be at higher genetic risk than others.

In the VA and Yale study, researchers analyzed data of 1,958 people who participated in a prior study by Yale and University of Pennsylvania researchers (called the Yale-Penn study) of substance use genetics.

In the new study, researchers examined the role of recently developed polygenic risk scores for opioid use disorder and environmental and psychosocial factors such as education level, adverse childhood experiences, and related psychiatric conditions.

The findings, published in *Psychological Medicine*, showed that environmental factors explained more risk for opioid dependence than did polygenic risk scores. Selected environmental factors, such as annual household income and education level, explained on average three-fold greater risk than the opioid use disorder polygenic risk scores alone.

Despite environmental factors playing a larger role, the authors did find that opioid polygenic risk scores explained 8% of the variance of opioid

dependence.

"This genetic prediction—based on the best-available full-genome data—is enough to show a solid statistical relationship, but not enough to bring into the clinic," said Joel Gelernter, MD, Foundations Fund Professor of Psychiatry at Yale and senior author of the study.

"While the field has made significant advances in understanding the genetic predictability of opioid use disorder, our results suggest that the current genetic predictors do not yet have the utility for a clinically meaningful prediction," said Peter Jongho Na, MD, MPH, an addiction psychiatrist at VA Connecticut Healthcare System, US Department of Veterans Affairs Career Development Investigator, assistant professor of psychiatry at Yale School of Medicine, and co-lead author of the study.

"But importantly, they suggest that interventions and policy measures that target modification of environmental factors may help mitigate the risk for opioid use disorder."

The study also found that among people with higher opioid use disorder polygenic risk scores, those with higher education level were less likely to have opioid dependence, whereas those with post-traumatic stress disorder (PTSD) were more likely to have opioid dependence than those without PTSD.

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