

Submitter Name: Kit Elam  
Submitted email: [kitelam@iu.edu](mailto:kitelam@iu.edu)

## **Functional Polygenic Risk for Aggression Indirectly Predicts Adult Substance Use Disorder Diagnoses via Substance Use Offending in Emerging Adulthood**

Kit K. Elam<sup>1</sup>, Jodi Kutzner<sup>1</sup>, Thao Ha<sup>2</sup>

<sup>1</sup>Department of Applied Health Science, School of Public Health, Indiana University;

<sup>2</sup>Department of Psychology, Arizona State University

A substance use offense, breaking an alcohol or drug related law, reflects antisocial behavior which can increase risk for substance use problems later in life. Individuals may also be at risk for substance use offending and substance use problems based on genetic predisposition. We examined whether polygenic risk for aggression increased risk for substance use offending in emerging adulthood and the subsequent influence on adult substance use disorder (SUD) diagnoses, and potential moderation of genetic influences by a family-based intervention, the Family Check-Up (FCU).

Participants were from a longitudinal randomized trial of the FCU (322 control, 309 intervention). Substance use offending was measured using court records from age 19-23 and SUD using diagnostic interviews at age 27. A functional polygenic risk score for aggression (fPRS) was created in a previous study by applying gene-set enrichment analysis to results from an aggression meta-GWAS (Elam et al., 2019), which we replicated in the current study. We hypothesized that substance use offending in emerging adulthood would mediate the influence of the fPRS on SUD in adulthood. The FCU was examined as a moderator of genetic effects.

An indirect effect was found: the fPRS increased risk for adult SUD via substance use offenses in emerging adulthood. Additionally, the fPRS was directly associated with SUD but only in the control group. Results imply that genetic predisposition for aggression may increase risk for problematic substance use later in life via antisocial behavior such as substance use offending, and that psychosocial interventions can buffer such genetic predispositions.