Identifying heterogeneous treatment effects on health outcomes among children with prenatal cannabis exposure via causal inference analysis with the ABCD dataset

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Researchers who study drug use in adolescence typically seek to answer causal research questions like, what effect does a drug have on adolescent brain circuitry or behavioral measures? While causal questions like these are best answered with randomized controlled trials (RCTs), it is unethical and impossible to conduct experiments that randomize vulnerable populations like adolescents or pregnant individuals to use cannabis. If such an experiment were even hypothetically feasible or conducted in animals, these experimental studies often report average treatment effects and ignores individual differences that might explain *why* or *how* outcomes vary among different subgroups of individuals. One way to estimate causal processes in the absence of performing an experimental design is to apply causal inference methods to large observational datasets. In this study, a causal random forest model was applied to baseline and year 1 follow up (age 10-11) data of the very large Adolescent Brain and Cognitive Development (ABCD) study (N=9,826), to test if prenatal cannabis exposure (n=605) moderates a causal pathway between sleep and internalizing symptoms. A causal random forest model was selected to flexibly model interaction terms from a set of covariates (including prenatal cannabis, alcohol, and tobacco exposure, and other sociodemographic measures) that might uncover individual differences in the effect of sleep on internalizing symptoms. Results indicated that, on average, an increase in sleep hours from baseline to year one was related to a decrease in internalizing symptoms (average treatment effect =-0.36, Std.Err.=.08). Moreover, this effect was moderated by prenatal cannabis exposure (heterogeneous treatment effect=0.13, Std.Err.=27), but not for prenatal alcohol or cigarette exposure (or other measures). These findings suggest that children with prenatal cannabis exposure are unique and will likely require a different approach to lowering internalizing symptoms in adolescence beyond interventions targeting sleep behaviors. Additionally, these results highlight the utility of applying causal inference models to uncover individual differences in treatment effects. Similar approaches will be applied to future ABCD data releases when the participants advance through adolescence and cannabis initiation becomes prevalent, allowing for the exploration of child cannabis use as an exposure or outcome measure of interest.

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