Overlap among substances used by youths is a well-described phenomenon, and understanding the pathways across substances has been a subject of research for at least several decades, with the framework of understanding gateway models of progression from use of tobacco (as well as alcohol and cannabis) to use of other substances. Sun and colleagues examined a new type of early use of tobacco in the form of electronic cigarettes (e-cigarettes), and they have examined whether its use is a risk factor for the subsequent onset of cannabis use. The authors use data from the landmark Population Assessment of Tobacco and Health (PATH) Study, which provided nationally representative household population data on 9828 cannabis-naive youths aged 12 to 17 years, to study the longitudinal association between e-cigarette use and subsequent cannabis initiation. Particularly noteworthy is the inclusion of data from the recent era of high nicotine potency e-cigarette products (ie, the “Juul” era) that have been remarkably popular among youths. With these data, the authors document strong associations between prior e-cigarette use and the onset of cannabis use. After adjustment for sociodemographic characteristics, family and peer tobacco use, other substance use, and sensation seeking, e-cigarette use at baseline was associated with an adjusted relative risk for the onset of cannabis use of 2.19 to 3.41 (with the variation depending on the specific cannabis and e-cigarette measurements). However, the authors also show that although the pathways from e-cigarette use to cannabis use are clear, they are unlikely to explain a major portion of cannabis use among youths. Thus, their findings help to explain a paradox of high rates of e-cigarette use in the face of generally stable prevalence of cannabis use in the overall youth population. The authors suggest that an explanation for this apparent paradox is that, even though the adjusted risk ratio for the onset of cannabis use after e-cigarette use is robust, because only a relatively modest subgroup of youths use e-cigarettes, the fraction of youths who use cannabis that might be explained by this pathway from e-cigarettes to cannabis is not large.

One reason that understanding the correlates and outcomes of e-cigarette use is important is because e-cigarettes have rapidly increased in popularity to become a predominant substance of misuse among US youths. E-cigarettes are a recent substance that has not been included in the decades of evidence available on the outcomes of other kinds of drug use. Furthermore, unlike the clear negative health implications of many other substances (eg, injection drug use), e-cigarette use is complicated by very different risks for different populations. A switch to vaped nicotine from combustible cigarettes may reduce harms for an adult smoker who is unable to cease smoking using other means. In contrast, exposure of the adolescent brain to nicotine may affect brain development and may increase the risk of addiction. It is also noteworthy that bright packaging, use of certain flavorings in e-cigarettes, the relative ease of surreptitious use, and the comparatively high rates of peer use may contribute to reduced adolescent concern over the possible risks of e-cigarette use. Although perception of the risk of e-cigarettes has begun to increase among adolescents, they may not realize that most e-cigarettes contain nicotine, or they may not understand the effect that nicotine has on the developing brain.

With results documenting an association of e-cigarette vaping with subsequent onset of cannabis use, a key topic to explore is the explanation for the association. Nicotine has been shown to potentiate the rewarding properties of other substances, potentially including cannabis, which
could be one mechanism by which e-cigarettes could increase subsequent cannabis use, and Sun et al. discuss possible causal pathways. They demonstrate that even with a fully causal link, the resulting effect on the onset of cannabis use would be modest. The other plausible explanation is that common factors may explain the onset of use of both substances, with no specific causal pathway from e-cigarettes to cannabis. In this case, the order of onset may be random rather than predictable in the direction tested in this study, and future work might include examining the alternative pathways from cannabis use to e-cigarettes. Although inclusion of multiple, potentially confounding variables diminishes the possibility of confounding, it also remains possible that nonmeasured factors could explain the association. Regardless, even with the contribution of potential biological mechanisms, the "gateway" properties of any drug are intensely driven by social and environmental factors that may lead to the initiation and progression to further drug use, which may be successfully targeted by existing evidence-based prevention interventions.

Finally, although the authors are focused on the primary question of the entire sample of underage youths (ie, <18 years), the age range covered includes 12 to 17 years, a time of major increases in substance use. Results for the risk ratios are adjusted for age, but studies may need to be conducted to understand the differences across these trajectories from e-cigarettes to cannabis among different age groups. Such future research may even be able to use the same PATH Study data to explore these and other important issues related to overlap among the substances of misuse. For instance, the prevention interventions targeting 12- to 14-year-old youths may differ from the interventions for 15- to 17-year-old youths, so understanding whether or not the associations are consistent across these ages could be important for policy makers.

The findings from this study illuminate the increased risk of future cannabis use as a possible consequence for adolescents who vape nicotine. This risk further highlights the compounding benefits of the primary prevention of vaping among adolescents in reducing the risk of exposure of the adolescent brain to nicotine, as well as reducing the risk of potential future exposure to cannabis and other negative outcomes.

ARTICLE INFORMATION
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Corresponding Author: Wilson M. Compton, MD, MPE, National Institute on Drug Abuse, National Institutes of Health, 301 N Stonestreet Ave, 3WFM Room 09020, MSC 6025, Bethesda, MD 20892 (wccompton@nida.nih.gov).

Author Affiliations: National Institute on Drug Abuse, National Institutes of Health, Bethesda, Maryland.

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