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Clinical Perspective: Treatment of adolescent e-cigarette use – limitations of existing nicotine use disorder treatment and future directions for e-cigarette use cessation

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Electronic cigarette use ("vaping") has surged in the U.S. since mid-2010s. From 2011 to 2018, current e-cigarette use among high school students escalated from 1.5% to 20.8% (~3.05 million youth), countering downward trends in combustible nicotine product use (21.8% in 2011 to 13.9% in 2018). While preventing the initial uptake of vaping is crucial, for the millions of adolescents who have taken up this behavior—many of whom express interest in quitting (e.g., 44.5% of current, adolescent non-light e-cigarette users in one U.S. national representative sample), it is critically important to help them to quit vaping to curtail future substance use disorders and other health consequences. Here, we discuss several challenges around adolescent vaping treatment and highlight research areas in urgent need of attention.

Challenges related to perceptions of e-cigarette use safety

One contributor to the proliferation of e-cigarette use is the widespread misperception that e-cigarettes are safe.³ Evidence supports the idea that e-cigarettes are associated with lower levels of exposure to many toxicants than combustible tobacco products.³ Unfortunately, youth may conflate "safer" with "safe" (i.e. they may not distinguish "less harmful" from "harmless"), which makes tobacco control communication strategies difficult and might lower youths' intrinsic motivation to cut back or quit. E-cigarette use can lead to detrimental health consequences. E-cigarettes contain toxic chemical compounds including aldehydes, metals, and volatile organic compounds that can cause cancer and potentially severe lung damage (e.g., e-cigarette, or vaping, product use-associated lung injury (EVALI)).⁴ Further, e-cigarette use increases the risk of subsequent initiation of combustible cigarette smoking (odds ratios range: 1.4–8.3) and nicotine use disorder among youth and young adults.^{4, 5}

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Adolescent e-cigarette use is also associated with potentially harmful polysubstance use via vaping devices, including the widespread practice of vaping cannabis—adding tetrahydrocannabinol (THC) wax or oil, or dried cannabis buds or leaves in the e-cigarette device—and a range of other unregulated solutions. According to the 2016 NYTS data, 1.7 million high school students and 425,000 middle school students reported ever using cannabis in e-cigarettes.⁶ Additionally, among EVALI patients whose data were available on substance use (n = 2,022), 82% (1,650) reported THC-containing product use.⁷ It was also found that 94% of EVALI patients aged 13–17 years who used THC containing products acquired the products via informal sources such as friends, family, or online dealers.⁸ There is evidence that such use of informally sourced THC containing products can be dangerous as they tend to contain vitamin E acetate which is associated with EVALI.⁸

Challenges with adapting treatments developed for adults to treat adolescent vaping

Despite the potential gravity of adolescent e-cigarette use, there have been no randomized controlled trials (RCTs) for treatment of vaping in adolescents. One intuitive approach to treating adolescent vaping would be to apply interventions developed for tobacco cessation, although most of the existing research has been conducted in adults. Common treatment approaches to cigarette smoking or nicotine use disorders (NUDs) include pharmacological interventions such as nicotine replacement therapy (NRT), bupropion, and varenicline. Evidence supported behavioral interventions include cognitive behavioral therapy, motivational therapy, and contingency management. More recent approaches include text messaging, app-based cessation programs, and social media sites.

However, research on the effectiveness of these existing NUD treatments has been inconclusive when applied to adolescents. A recent Cochrane review examined the longterm effectiveness of behavioral (psychotherapy, counseling) interventions on adolescent smoking cessation, concluding there was not clear evidence to support these interventions for adolescents. Moreover, although the review found group-based behavioral interventions for adolescent smokers to be most promising, the quality of existing research was rated low or very low. Other studies have found mobile phone-based interventions for smoking cessation (e.g., automated text messaging, smartphone apps) to be superior to minimal support, but very few studies have actually tested effectiveness for smokers younger than 20 years old. ¹⁰ As for pharmacological interventions, a recent meta-analysis found that medication, especially bupropion, was effective in short-term smoking cessation (4 weeks) but not long-term (up to 24 weeks) for adolescents who smoke. 11 A lack of empirical support for long-term effects of pharmacological intervention has also been found in other studies. 9 Moreover, more adverse events such as nausea, muscle pain, cough, and headache were reported in relation to some pharmacological interventions (e.g., NRT, bupropion) in youth compared to placebo or control. Thus, although pharmacological interventions originally tested in adults may be tolerated by adolescents, caution is needed when implementing them for youth vaping in light of inconclusive efficacy findings coupled with limited data on predictors of adverse effects.

Challenges with monitoring progress in adolescent vaping treatment

Substance use disorder treatment typically includes monitoring of substance use intensity (frequency, amount) over time, including during treatment. For combustible cigarettes, this often entails tracking the number of cigarettes or packs smoked per day. The absence of standardized measures for nicotine intake via e-cigarettes complicates clinical practice from assessment to treatment outcome monitoring. Estimating the amount of nicotine ingested daily via e-cigarettes (to determine an appropriate starting dose for NRT, for example) can be challenging. Factors that contribute to the amount of nicotine ingested – including nicotine concentration, voltage of the device, and temperature achieved by the heat source – vary significantly across devices. The labels for nicotine concentration are also often ambiguous (e.g., low/medium) or inaccurate. Unlike combustible tobacco products, ecigarettes can be used almost undetectably, instantly, anywhere and anytime, potentially resulting in frequent, intermittent use throughout the day. Although some self-report measures have been developed to assess vaping intensity, 12 clinical experience calls into question how reliably adolescents recall and report their use. Similarly, e-cigarette devices also can reduce detectability of THC use, as they decrease the smell often accompanied by combustion of cannabis. 4 Again, easier access and lowered detectability may lead to more frequent use of cannabis and potentially more serious addiction.

Reliable monitoring of vaping is especially critical in certain treatment models, such as contingency management (CM), where patients can earn rewards for achieving and maintaining abstinence. Although there are urine cotinine tests to index ongoing nicotine use as well as other biological markers to assess ongoing combustible tobacco (e.g., breath CO), there are no tests that specifically detect and differentiate e-cigarette use from other sources of nicotine, including NRT. This is problematic, because patients on NRT would screen positive for nicotine whether or not they were also vaping. In such cases, clinicians are reliant exclusively on youths' self-reported use and collateral reports of observed use without an objective biomarker of use. Thus, although contingency management is one of the most effective psychosocial treatments for substance use disorders generally, this drug testing problem dramatically limits the applicability of contingency management to vaping specifically.

Recommendations and Future Directions

Overcoming the aforementioned challenges will require substantial progress toward closing major gaps in the research literature around prevention and treatment interventions for adolescent e-cigarette cessation, strategies for measuring and monitoring e-cigarette use, and approaches to curtailing use of other substances via e-cigarettes.

First and foremost, we need more empirical data derived from robustly designed RCTs to assess the effectiveness of existing interventions on NUDs among adolescents. For example, because it is unclear which youth characteristics predicted higher risk of adverse events when using pharmacological treatments, future research should identify patient-level genetic and epigenetic factors that affect success of the pharmacological treatments to inform patient-tailored clinical decisions. Additional data are needed on how to both bolster

effectiveness and optimize implementation of behavioral and web-/text-based interventions – with or without concurrent pharmacological interventions – to achieve positive, durable outcomes. Questions about how best to involve parents and other supportive adults in youths' treatment should be examined since caregivers are often involved in monitoring youth behavior, managing contingencies, reinforcing progress, and implementing other contextual interventions for other substance use disorders in youth. Moreover, given youths' perceptions of e-cigarette use as safe, research is needed on what messaging strategies are most effective in conveying the potential harms of vaping, as well as to motivate youth to quit.

To address challenges with monitoring use of e-cigarettes, more research should be conducted to develop consistent, validated units of nicotine intake via vaping devices including via biospecimens. Researchers should closely monitor adolescent e-cigarette use patterns to find if they show different use patterns compared to combustible tobacco products. In particular, observations with shorter intervals (e.g., ecological momentary assessment) could help capture use profiles. Clinicians should collect detailed information pertaining to adolescent nicotine intake (e.g., cartridge nicotine concentration, average number of puffs per use, frequency of use, device brands) to index the amount of nicotine intake and inform treatment decisions. Urine screens may also be useful but potential for other sources of nicotine (NRT) should be considered when interpreting positive screens until e-cigarette specific biomarkers can be detected in clinical practice. Similarly, clinicians should routinely assess and monitor other substance consumed via e-cigarette devices (e.g., types and sources of the substances) beyond nicotine solutions and screen for symptoms of EVALI. The scope of the problems involving vaping of cannabis and other illicit substances should be characterized and monitored in representative samples, as well as in trials evaluating vaping treatments.

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