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Authors

Vogel, Erin A
Prochaska, Judith J
Ramo, Danielle E
et al.

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Original article

Adolescents' E-Cigarette Use: Increases in Frequency, Dependence, and Nicotine Exposure Over 12 Months

 Erin A. Vogel, Ph.D.^a, Judith J. Prochaska, Ph.D., M.P.H.^b, Danielle E. Ramo, Ph.D.^a,
 Jerome Andres^c, and Mark L. Rubinstein, M.D.^{d,*}
^a Department of Psychiatry and Weill Institute for Neurosciences, University of California, San Francisco, San Francisco, California^b Stanford Prevention Research Center, Department of Medicine, Stanford University, Stanford, California^c University of California, Berkeley, Berkeley, California^d Division of Adolescent & Young Adult Medicine, University of California, San Francisco, San Francisco, California

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 A B S T R A C T

Purpose: This study examined changes in e-cigarette and dual-use frequency, levels of nicotine exposure and e-cigarette dependence, and device and e-liquid preferences over 12 months.

Methods: Adolescents (N = 173, aged 13–18 years) who reported past-month e-cigarette use and at least 10 lifetime uses were recruited from the San Francisco Bay Area. The sample was 75.1% male, 54.9% non-Hispanic White, mean age 16.6 years (standard deviation = 1.2); 26.6% reported past-month cigarette smoking at baseline (i.e., dual use). At baseline, 6-month, and 12-month follow-up, participants provided saliva samples for cotinine testing and self-reported e-cigarette use frequency, dependence, past-month smoking, product preference, and flavor preference.

Results: Most (80.3%) were still using e-cigarettes at 12 months, and daily use increased from 14.5% to 29.8%. Model testing indicated an overall increase from baseline to 12 months in frequency of e-cigarette use ($F(2, 166) = 5.69, p = .004$), dependence ($F(2, 164) = 5.49, p = .005$), and cotinine levels ($F(2, 103) = 4.40, p = .038$). Among those reporting only e-cigarette use at baseline, 28.8% reported combustible cigarette use during follow-up. Among those reporting dual use at baseline, 57.1% were still dual using at 12 months, 31.4% reported e-cigarette use only, and none abstained from both products. Higher nicotine delivering e-cigarette devices (i.e., Juul, mods) became more popular over time, whereas flavor preferences (i.e., fruit, mint/menthol, and candy) remained stable.

Conclusions: Adolescents' e-cigarette use persisted over a 12-month period with significant increases in frequency of use, nicotine exposure, and e-cigarette dependence. Transitions from single to dual and dual to single nicotine product use were observed in approximately one in three users over the study period.

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 IMPLICATIONS AND
 CONTRIBUTION

Findings indicate persistence in adolescents' e-cigarette use over 12 months, with increased frequency of use, nicotine exposure, and dependence and little evidence of a smoking cessation benefit among dual users. Flavor preferences remained stable. Efforts to reduce adolescent e-cigarette use should include regulatory action addressing kid-friendly flavors and youth access.

Conflicts of interest: J.J.P. has provided consultation to pharmaceutical and technology companies that make medications and other treatments for quitting smoking and has served as an expert witness in lawsuits against the tobacco companies. D.E.R. has consulted for Carrot, Inc., which makes a tobacco cessation device. M.L.R. has consulted for Pfizer on research involving smoking cessation medication and for Carrot, Inc. E.A.V. and J.A. have no financial relationships relevant to this article to disclose. The first draft of the article was written by E.A.V. No honoraria, grants, or other forms of payment were given to anyone to produce the article.

* Address correspondence to: Mark L. Rubinstein, M.D., Division of Adolescent & Young Adult Medicine, University of California, San Francisco, 3333 California Street, Suite 245, San Francisco, CA 94118.

E-mail address: mark.rubinstein@ucsf.edu (M.L. Rubinstein).

E-cigarette use, or vaping, among adolescents has become a public health concern, with 26.7% of high school seniors reporting past-month vaping in 2018 [1], and 900,000 middle and high school students reporting daily or near-daily use [2]. Adolescents' use of e-cigarettes is associated with an increased risk of subsequent cigarette initiation [3] and frequent use [4], an increased risk of nicotine dependence [5], and exposure to potentially toxic chemicals [6–14]. Despite harm reduction claims by e-cigarette companies, in cross-sectional studies, e-cigarette use among adolescent and young adult dual users (i.e., cigarette smokers who also vape) is associated with smoking a greater number of cigarettes per day [15], more frequent smoking [16], and fewer attempts to quit smoking [17].

Notably little is known about the stability of adolescents' use of e-cigarettes over time, such as whether nondaily use progresses into daily use and whether daily use is sustained. The potential for harm from exposure to nicotine and toxicants is likely to be greater with sustained and frequent use over time. Study of longitudinal patterns of adolescent e-cigarette use is needed to model the potential for harm from these products. Furthermore, research is needed to articulate adolescent patterns of dual product use over time and the resulting levels of nicotine and toxicant exposure. It remains unclear, for example, whether dual users succeed in reducing and stopping their cigarette use or whether they continue to dual use over time.

The stability in adolescents' e-cigarette preferred type or brand also has not been examined. E-cigarette brands that are popular today among adolescents (e.g., Juul) can deliver nicotine from a single compact pod that equals that of a pack of cigarettes, in attractive flavors, and with easy concealment for use in settings where cigarettes may be forbidden (e.g., school, home). These characteristics may facilitate the progression from intermittent to frequent use and nicotine dependence. Alternatively, low nicotine content and/or low device appeal may result in adolescents losing interest in e-cigarettes over time, with diminishing frequency and dependence risk.

Among adults, research indicates that evolving from a simpler e-cigarette device (e.g., closed system) to a more complex modifiable device (i.e., "mod") is a common pattern and is associated with greater dependence on e-cigarettes [18]. Despite rapid growth in the e-cigarette market in recent years, research has not yet examined whether or how adolescents' preferred devices change over time, particularly with regard to nicotine delivery and exposure.

Finally, minimal research has examined changes in adolescents' reasons for initiating, continuing, and/or quitting e-cigarette use over time. In cross-sectional survey studies, adolescents' top reasons for experimenting with e-cigarettes include curiosity, appealing flavors, friends' use, and perceived benefits compared with cigarettes [19–22]. However, reasons may shift over time, as adolescents move from experimentation to sustained use. The literature on youth initiation and transition to regular use of combustible cigarettes shows that media/marketing and social influences motivate initiation, whereas the drive for nicotine due to addiction motivates regular use [3]. These nicotine product use patterns observed with combustible cigarettes warrant investigation with e-cigarettes. With e-cigarettes, adolescents who begin experimenting because of curiosity or appealing flavors may subsequently use to alleviate withdrawal symptoms.

The present study followed a cohort of adolescent e-cigarette users over 12 months' time to examine patterns of e-cigarette use frequency, nicotine exposure, and dependence, product use and flavor preference, and motivators to use and cease use. The primary objectives were to determine persistence in e-cigarette and dual use and the stability in frequency and dependence measures of e-cigarette use. We also examined changes in device and e-liquid preferences and reasons for using e-cigarettes. This longitudinal study adds to the literature by providing an understanding of shifts in tobacco and nicotine product use over time among adolescents based on self-report and biomarkers of exposure.

Methods

Participants and procedures

Adolescents (aged 13–18 years) from the San Francisco Bay Area who reported having used an e-cigarette at least once in the past 30 days and at least 10 times in their lives were recruited for a longitudinal study on teen vaping between May 2015 and April 2017. Advertisements were posted on social media and in the community around the Bay Area. Interested individuals were directed to the study Web site, where they could submit their information to be contacted by study staff to complete eligibility screening. Eligible participants who provided informed consent were scheduled for a baseline session where they completed self-report measures and provided a saliva sample for cotinine testing. Participants returned for follow-up measures and cotinine testing 6 and 12 months after baseline. Study incentives were \$30 for the baseline, \$35 for the 6-month, and \$40 for the 12-month follow-up visits. Parental consent was waived under California law 6929(b). Cessation information and local treatment options were provided. The research design and study procedures were approved by the University of California, San Francisco Institutional Review Board.

Measures

Demographic characteristics of age, sex, race/ethnicity, and mother's level of education were reported by participants. E-cigarette use frequency in a typical month was self-reported ranging from 0 to 30 days. E-cigarette dependence was measured using the 10-item Penn State Electronic Cigarette Dependence Index (scored as 0–3 = not dependent; 4–8 low dependence; 9–12 medium dependence; 13+ = high dependence) [23], which was strongly correlated with cotinine levels in this sample [24]. Salivary cotinine was measured at baseline, 6, and 12 months. Saliva samples were analyzed at the Clinical Pharmacology Laboratory at the University of California, San Francisco. Levels of salivary cotinine were measured using liquid chromatography-tandem mass spectrometry [25], reported in nanogram per milliliter, and log-transformed to normalize the distribution. Past-month traditional cigarette smoking was assessed with the item: "Have you smoked a cigarette in the past 30 days?" (yes/no). Product preference was assessed by asking participants: "What kind of e-cigarette device do you use most often?" (Juul, other brand name [i.e., Blu, Njoy], hookah pen/e-hookah, vape pen, I build/make my own, e-pipe, e-cigar, other, unknown). Given the popularity of Juul among adolescents at the time the study was conducted, Juul was added as its own option

separate from other brand name e-cigarettes. Participants who selected “other” were asked to specify their device. Responses were recoded into mod (i.e., modified/homemade device), Juul, vape pen, or other (e.g., Sourin)/unknown based on prior work [26]. E-cigarette flavors were assessed with the item: “What flavor e-cigarette do you usually use?” Choices included fruit, candy, menthol, tobacco, and others. Those who selected “other” were asked to specify their flavor of choice. Reasons for e-cigarette initiation were assessed at baseline by asking participants to report up to three reasons for starting to use e-cigarettes (open-ended). Reasons for e-cigarette continued use were assessed at 6 and 12 months by having participants select up to three reasons for continuing to use e-cigarettes from the following options: my friends are using them, my family members are using them, they look cool, I am addicted (I can’t stop), I want to quit smoking regular cigarettes, I think they are safer than regular cigarettes, I like the taste, they are fun, they are easy to hide from adults, or other. Those who selected “other” were asked to specify their reason. Reasons for quitting e-cigarettes were assessed with an open-ended item at 12 months among those who reported quitting using e-cigarettes.

Data coding and analyses

For the open-ended responses, two independent coders (E.A.V. and J.A.) read participants’ reasons for initiating and quitting e-cigarette use and created initial codes for each. E.A.V. reviewed both sets of codes, drafted a coding scheme, coded all data, and refined the coding scheme. All data were coded again by both E.A.V. and J.A. (reasons for initiating: 92.6% agreement; reasons for quitting: 90.0% agreement). Coders discussed discrepancies until consensus was reached. Each response was coded into one best-fitting category. Reasons for continuing use were closed-ended and did not require coding.

Descriptive statistics were run on baseline and follow-up data to examine the frequency of e-cigarette and cigarette use; preferred devices; preferred flavors; and reasons for initiating, continuing, and quitting e-cigarette use. Among e-cigarette only users and those reporting recent dual use of combustibles at baseline, we examined transitions in nicotine product use categories. Repeated-measures analyses of variance were used to assess differences in e-cigarette use frequency, dependence symptoms, self-perceived dependence, and cotinine levels from baseline to 6- and 12-month follow-up. A lower-bound correction was used when Mauchly’s test indicated a violation of the assumption of sphericity. When the omnibus test was significant, we ran simple contrasts to identify where the changes over time were significant. Cochran’s Q tests were used to assess differences in device preference and reasons for initiating and continuing use over time.

Results

Sample description

Three hundred eighty-six adolescents were screened, 229 were found to be eligible, and 180 agreed to participate. Of the 180 who completed a baseline survey, 173 adolescents met criteria for using an e-cigarette at least once in the prior 30 days and at least 10 lifetime uses. The sample was 75.1% male (N = 130), mean age = 16.6 years (standard deviation = 1.2), 54.9% White, 13.3% multiple races/ethnicities, 10.4% Asian, 1.2%

African American, 1.2% Pacific Islander, and 5.2% other race/ethnicity. Mother’s education was 54.3% college degree or higher, 39.9% some college or less, and 5.8% unknown. Participant characteristics are largely consistent with demographics of adolescent e-cigarette users (i.e., majority male, non-Hispanic White, higher socioeconomic status, and older adolescents [27]).

Study retention

Follow-up rates were 69.4% (N = 120) at 6 months, and 73.4% (N = 127) at 12 months. Likelihood of attrition at 12 months did not differ by age, race, sex, mother’s education, or baseline e-cigarette frequency, dependence, or cotinine level ($p > .13$).

Changes in e-cigarette frequency, dependence, and cotinine

At the 12-month follow-up, 80.3% of the sample continued to use e-cigarettes, and daily use increased from 14.5% of the sample at baseline to 18.1% at 6-month follow-up, and 29.8% at 12-month follow-up. Table 1 summarizes frequency of use, e-cigarette dependence, and cotinine levels for the sample at each time point. Model testing indicated an overall increase from baseline to 12 months in the frequency of e-cigarette use, $F(2, 164) = 5.49, p = .005$. Simple contrasts showed the significant increase occurred from baseline to 12 months ($F(1, 82) = 5.82, p = .018$), and not baseline to 6 months. E-cigarette dependence, measured with the Electronic Cigarette Dependence Index, also significantly increased over time, $F(2, 166) = 5.64, p = .004$. Again, the significant increase occurred from baseline to 12 months ($F(1, 83) = 10.57, p = .002$), and not baseline to 6 months. Cotinine levels significantly increased over time, $F(2, 103) = 4.40, p = .038$, both from baseline to 6 months ($F(1, 103) = 5.69, p = .019$) and from baseline to 12 months ($F(1, 103) = 6.43, p = .013$).

Transitions in e-cigarette and cigarette use over time

Figure 1 illustrates transitions from baseline to 12-month follow-up in e-cigarette and cigarette use among e-cigarette only users and recent dual users (defined as participants who both vaped and smoked in the past 30 days). Among baseline e-cigarette only users, the most common pattern was continued e-cigarette only use; however, over the 12-month follow-up, 28.8% (n = 30) also reported combustible cigarette use by 12 months (n = 17, 19.1% at 6 months; n = 19, 20.7% at 12 months). Among those reporting dual use at baseline, 57.1% (n = 20) were still dual using at 12 months, 31.4% (n = 11) reported e-cigarette use only, and none abstained from both

Table 1
Frequency, dependence, and cotinine levels at each time point

	Baseline, N = 173	6 mo, N = 120	12 mo, N = 127
Frequency in days/month, M (SD)	15.4 (9.8)	15.0 (11.3)	19.6 (9.7)
Daily use, n (%)	25 (14.5)	21 (18.1)	31 (29.8)
ECDI dependence score, M (SD)	3.4 (3.9)	4.5 (4.4)	5.1 (4.6)
No dependence, n (%)	108 (62.4)	61 (52.6)	47 (45.6)
Low dependence, n (%)	42 (24.3)	34 (29.3)	32 (31.1)
Medium dependence, n (%)	17 (9.8)	12 (10.3)	15 (14.6)
High dependence, n (%)	6 (3.5)	9 (7.8)	9 (8.7)
Cotinine in ng/ml, median (IQR)	2.1 (35.2)	9.1 (85.4)	10.8 (79.6)

ECDI = Electronic Cigarette Dependence Index; IQR = interquartile range; SD = standard deviation.

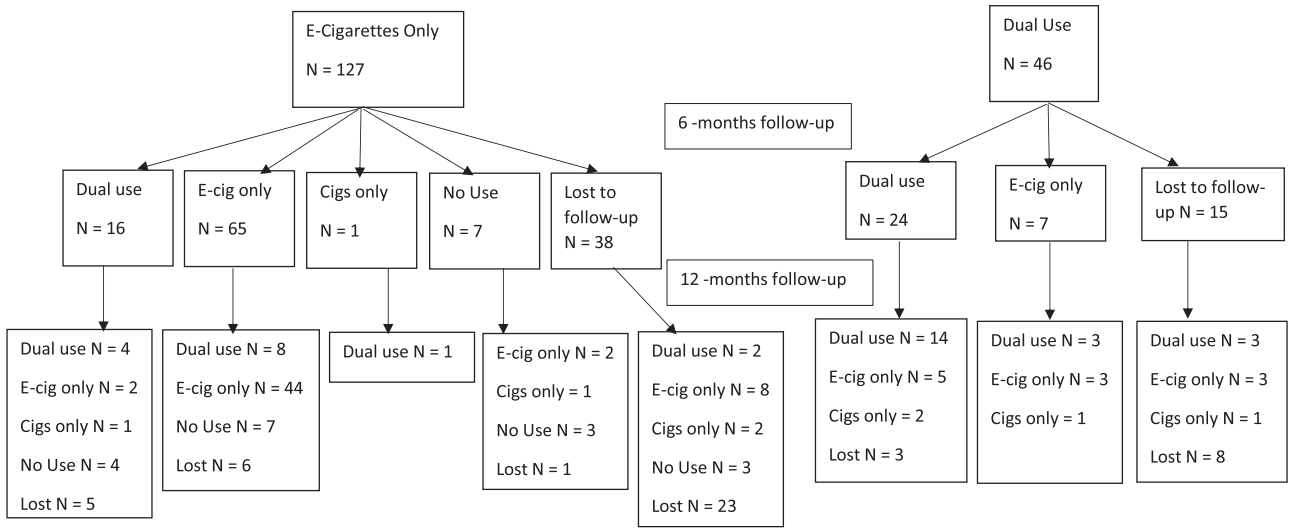


Figure 1. Use of e-cigarettes and cigarettes reported at each time point.

products. In the full sample, smoking prevalence increased slightly over time, from 26.6% (n = 46) at baseline to 33.9% (n = 43) at 12-month follow-up.

Changes in e-Cigarette device and e-liquid preferences over time

At baseline, vape pens were the most commonly used device (n = 59, 34.1%), followed by mods (n = 56, 32.4%), Juul (n = 38, 22.0%), and other/unknown devices (n = 20, 11.6%). At 6 months, mods had become the most popular device (n = 45, 37.5%), followed by Juul (n = 36, 30.0%), vape pens (n = 30, 25.0%), and other/unknown devices (n = 9, 7.5%). By 12 months, Juul had become the most popular device (n = 52, 48.1%), followed by mods (n = 34, 31.5%), with vape pens (n = 11, 10.2%) and other/unknown devices (n = 11, 10.2%) becoming less popular. The proportion of participants reporting Juul as their most commonly used device significantly increased over time ($\chi^2(2) = 31.27$,

$p < .001$). Figure 2 illustrates changes in device type preferences over time.

At baseline, 6 months, and 12 months, the most popular flavors were fruit (baseline: n = 110, 63.6%; 6 months: n = 71, 59.2%; 12 months: n = 43, 40.6%), menthol/mint (baseline: n = 30, 17.3%; 6 months: n = 34, 28.3%; 12 months: n = 39, 36.8%), and candy (baseline: n = 25, 14.5%; 6 months: n = 18, 15.0%; 12 months: n = 11, 10.4%).

Reasons for initiating or continuing e-cigarette use

The proportion of participants reporting using e-cigarettes for enjoyment increased significantly from baseline (n = 60, 35.7%) to 6- and 12-month follow-up (6 months: n = 77, 64.2%; 12 months: n = 69, 63.3%; $\chi^2(2) = 16.32$, $p < .001$), as did the proportion reporting using e-cigarettes for flavors (baseline: n = 47, 28.0%; 6 months: n = 66, 55.0%; 12 months: n = 48, 44.4%;

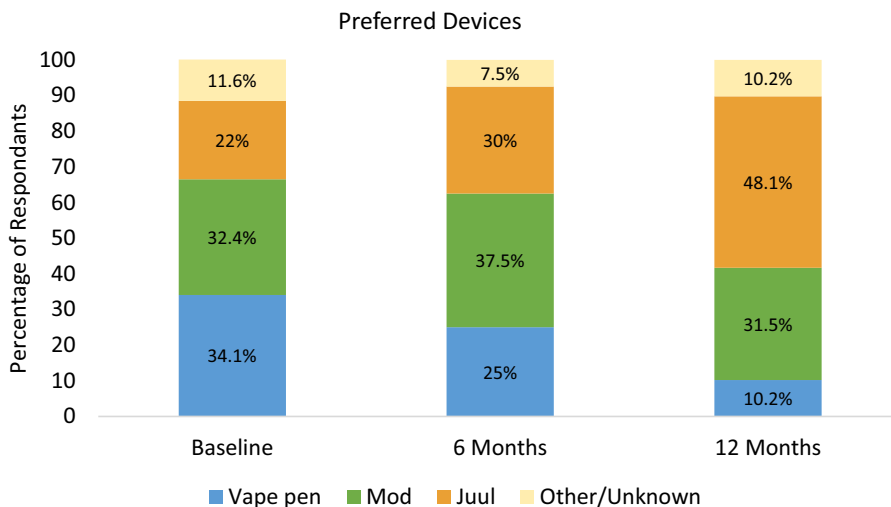


Figure 2. Preferred devices at each time point. Note: Includes data from all responding at each follow-up.

$\chi^2(2) = 21.14, p < .001$). The proportion reporting e-cigarette use for social reasons did not change significantly over time (baseline: $n = 71$; 42.3%; 6 months: $n = 56$, 46.7%; 12 months: $n = 53$, 49.1%; $\chi^2(2) = 2.00, p = .368$). At baseline, 40 participants (23.8%) reported using e-cigarettes as a substitute for cigarettes and/or cannabis. Among those who reported having quit e-cigarettes at the 12-month follow-up and provided reasons ($n = 19$), the most common reasons for quitting were a desire for self-improvement ($n = 14$, 73.7%), difficulty maintaining an e-cigarette device (e.g., broken device, inability to afford refills; $n = 9$, 47.4%), and getting in trouble for vaping at school or home ($n = 7$, 36.8%).

Discussion

In this longitudinal study of adolescent e-cigarette use with self-reported and biomarker data, 80.3% of the sample continued to use e-cigarettes at 12 months, with significantly greater e-cigarette use frequency, dependence, and nicotine exposure. The percentage of daily e-cigarette users doubled from 14.5% at baseline to 29.8% at 12-month follow-up. The patterns of e-cigarette use observed over time indicate substantial persistence and the use of greater amounts of nicotine over time (i.e., tolerance). These findings lend support to concerns regarding the addictiveness of e-cigarettes for adolescents [28]. In the United States, prevalence of past-month e-cigarette use increased dramatically among adolescents in 2018, whereas cigarette use declined and cannabis use remained constant [1]. Results of this study suggest that increased prevalence of recent e-cigarette use may lead to frequent use, dependence, and greater nicotine exposure.

Dependence scores at baseline were low on average, with most participants meeting a classification of “not dependent,” and 13.3% meeting a classification of moderate to heavy dependence. By 12 months, the percentage classified with moderate to heavy dependence increased to 23.3%. These findings would suggest that factors other than dependence are driving early use of e-cigarettes, and that over the course of just 1 year, more teens become daily users and more heavily dependent.

Along with the self-reported increase in frequency of e-cigarette use and dependence, cotinine levels increased over time, reflecting increased exposure to nicotine. The increase in cotinine levels may be both the result of increased dependence and a catalyst for the development of dependence. Adolescents who become increasingly dependent on e-cigarettes may increase their nicotine use, thereby worsening dependence. Notably, devices with higher nicotine yield (e.g., Juul, mods) became increasingly popular over the course of the 12-month trial, consistent with the reports of greater nicotine dependence and higher cotinine levels. Transitions from single to dual and dual to single nicotine product use were observed in approximately one in three users over the study period. None of the baseline dual users abstained from both products at either follow-up, which may be partially due to their higher dependence on e-cigarettes at baseline [26], as well as the normalization of smoking behavior [29] and associations between smoking cues [30] that can perpetuate use of both products.

Consistent with prior research [19–22], adolescent participants offered a wide range of reasons for e-cigarette use. The top three reasons for initiating and continuing use were socializing, enjoyment, and flavors. The top three reasons for quitting were a desire for self-improvement, difficulty maintaining an e-cigarette device, and getting in trouble for vaping at home or school.

The top flavors were fruit, menthol/mint, and candy. Taken together with experimental research demonstrating the influence of flavors on adolescents' product choices [31–33], these findings suggest that efforts to reduce adolescent e-cigarette use ought to include regulatory action that addresses kid-friendly flavors. Little research has examined adolescents' reasons for quitting e-cigarette use, and our findings preliminarily suggest that adolescents perceive parental controls and appropriate disciplinary consequences to be impactful.

Limitations and future directions

All participants were recruited from the San Francisco Bay Area, and a majority were male and White, which may limit generalizability. The sample size was relatively small, although adequate to detect significant differences over time in this repeated-measures study design. The combination of self-report and biomarker data was a study strength.

Over the course of a year, the vast majority of adolescents continued to use e-cigarettes, daily use increased from 14.5% to 29.8%, and product type evolved to higher nicotine delivery devices, with Juul being the most preferred brand at 12 months. Flavor preferences stayed fairly constant (i.e., fruit/mint/candy focused), and dependence and cotinine levels increased. Transitions from single to dual and dual to single nicotine product use were observed in approximately one in three users over the study period in about equal proportions. None of the baseline dual users abstained from both products at either follow-up. The findings indicate persistence in adolescents' e-cigarette use, with significant increases in frequency of use and nicotine exposure over time and with associated increases in dependence.

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References

- [1] National adolescent drug trends in 2018 [press release]. Ann Arbor, MI: Monitoring the Future; 2018.
- [2] Cullen KA, Ambrose BK, Gentzke AS, et al. Use of electronic cigarettes and any tobacco product among middle and high school students — United States, 2011–2018. Atlanta, GA. 2018.
- [3] Department of Health & Human Services (US). Preventing tobacco use among youth and young adults: A report of the surgeon general. Atlanta, GA: Centers for Disease Control and Prevention; 2012.
- [4] Barrington-Trimis JL, Kong G, Leventhal AM, et al. E-cigarette use and subsequent smoking frequency among adolescents. *Pediatrics* 2018;142:e20180486.
- [5] Lanza ST, Vasilenko SA. New methods shed light on age of onset as a risk factor for nicotine dependence. *Addict Behav* 2015;50:161–4.
- [6] Bitzer ZT, Goel R, Reilly SM, et al. Effect of flavoring chemicals on free radical formation in electronic cigarette aerosols. *Free Radic Biol Med* 2018;120:72–9.
- [7] Lisko JG, Tran H, Stanfill SB, et al. Chemical composition and evaluation of nicotine, tobacco alkaloids, pH and selected flavors in e-cigarette cartridges and refill solutions. *Nicotine Tob Res* 2015;17:1270–8.

- [8] Behar RZ, Luo W, Lin SC, et al. Distribution, quantification and toxicity of cinnamaldehyde in electronic cigarette refill fluids and aerosols. *Tob Control* 2016;25(Suppl 2):ii94–102.
- [9] Khlystov A, Samburova V. Flavoring compounds dominate toxic aldehyde production during e-cigarette vaping. *Environ Sci Technol* 2016;50:13080–5.
- [10] Kosmider L, Sobczak A, Prokopowicz A, et al. Cherry-flavoured electronic cigarettes expose users to the inhalation irritant, benzaldehyde. *Thorax* 2016;71:376–7.
- [11] LeBouf RF, Burns DA, Ranpara A, et al. Headspace analysis for screening of volatile organic compound profiles of electronic juice bulk material. *Anal Bioanal Chem* 2018;410:5951–60.
- [12] Lim HH, Shin HS. Determination of volatile organic compounds including alcohols in refill fluids and cartridges of electronic cigarettes by headspace solid-phase micro extraction and gas chromatography-mass spectrometry. *Anal Bioanal Chem* 2017;409:1247–56.
- [13] Qu Y, Kim K-H, Szulejko JE. The effect of flavor content in e-liquids on e-cigarette emissions of carbonyl compounds. *Environ Res* 2018;166:324–33.
- [14] Rubinstein ML, Delucchi K, Benowitz NL, Ramo DE. Adolescent exposure to toxic volatile organic chemicals from E-cigarettes. *Pediatrics* 2018;14:e20173557.
- [15] Park S, Lee H, Min S. Factors associated with electronic cigarette use among current cigarette-smoking adolescents in the Republic of Korea. *Addict Behav* 2017;69:22–6.
- [16] Brikmans K, Petersen A, Doran N. E-cigarette use, perceptions, and cigarette smoking intentions in a community sample of young adult non-daily cigarette smokers. *Psychol Addict Behav* 2017;31:336–42.
- [17] Huang L-L, Kowitz SD, Sutfin EL, et al. Electronic cigarette use among high school students and its association with cigarette use and smoking cessation. *North Carolina Youth Tobacco Surveys, 2011 and 2013. Prev Chronic Dis* 2016;13:150564.
- [18] Yingst J, Veldheer S, Hrabovsky S, et al. Factors associated with electronic cigarette users' device preferences and transition from first generation to advanced generation devices. *Nicotine Tob Res* 2015;17:1242–6.
- [19] Bold KW, Kong G, Cavallo DA, et al. Reasons for trying e-cigarettes and risk of continued use. *Pediatrics* 2016;138:e20160895.
- [20] Kong G, Morean ME, Cavallo DA, et al. Reasons for electronic cigarette experimentation and discontinuation among adolescents and young adults. *Nicotine Tob Res* 2015;17:847–54.
- [21] Patrick ME, Miech RA, Carlier C, et al. Self-reported reasons for vaping among 8th, 10th, and 12th graders in the US: Nationally-representative results. *Drug Alcohol Depend* 2016;165:275–8.
- [22] Tsai J, Walton K, Coleman BN, et al. Reasons for electronic cigarette use among middle and high school students— National Youth Tobacco Survey, United States, 2016. *MMWR Morb Mortal Wkly Rep* 2018;67:196–200.
- [23] Foulds J, Veldheer S, Yingst J, et al. Development of a questionnaire for assessing dependence on electronic cigarettes among a large sample of ex-smoking e-cigarette users. *Nicotine Tob Res* 2015;17:186–92.
- [24] Vogel EA, Prochaska JJ, Rubinstein ML. Measuring e-cigarette addiction among adolescents. *Tob Control*, in press.
- [25] Jacob P 3rd, Yu L, Duan M, et al. Determination of the nicotine metabolites cotinine and trans-3'-hydroxycotinine in biologic fluids of smokers and non-smokers using liquid chromatography - tandem mass spectrometry: Biomarkers for tobacco smoke exposure and for phenotyping cytochrome P450 2A6 activity. *J Chromatogr B Analyt Technol Biomed Life Sci* 2011;879:267–76.
- [26] Vogel EA, Ramo DE, Rubinstein ML. Prevalence and correlates of adolescents' e-cigarette use frequency and dependence. *Drug Alcohol Depend* 2018;188:109–12.
- [27] Hartwell G, Thomas S, Egan M, et al. E-cigarettes and equity: A systematic review of differences in awareness and use between sociodemographic groups. *Tob Control* 2017;26:e85–91.
- [28] Durmowicz EL. The impact of electronic cigarettes on the paediatric population. *Tob Control* 2014;23:ii41–6.
- [29] Schneider S, Diehl K. Vaping as a catalyst for smoking? An initial model on the initiation of electronic cigarette use and the transition to tobacco smoking among adolescents. *Nicotine Tob Res* 2016;18:647–53.
- [30] Conklin CA. Environments as cues to smoke: Implications for human extinction-based research and treatment. *Exp Clin Psychopharmacol* 2006;14:12–9.
- [31] Pepper J, Ribisl K, Brewer N. Adolescents' interest in trying flavoured e-cigarettes. *Tob Control* 2016;25:ii62–6.
- [32] Shang C, Huang J, Chaloupka F, Emery S. The impact of flavour, device type, and warning messages on youth preferences for electronic nicotine delivery systems: Evidence from an online discrete choice experiment. *Tob Control* 2017;0:1–9.
- [33] Vasiljevic M, Petrescu DC, Marteau TM. Impact of advertisements promoting candy-like flavoured e-cigarettes on appeal of tobacco smoking among children: An experimental study. *Tob Control* 2016;25:e107–12.