Electronic Cigarettes Are Another Route to Nicotine Addiction for Youth

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In this issue of JAMA Pediatrics, Primack and colleagues1 show that adolescents and young adults who smoke electronic cigarettes (e-cigarettes) are much more likely than those who had not smoked e-cigarettes to progress to traditional combustible cigarette use. Among 694 youth who were not susceptible to cigarette use, after 1 year, 68.8% of e-cigarette users and only 18.9% of those who had not smoked e-cigarettes had smoked a traditional combustible cigarette.

E-cigarettes, also called electronic nicotine delivery systems, personal vaporizers, vape pens, e-cigars, e-hookahs, or vaping devices, produce an aerosol mix of flavored liquids and nicotine that is inhaled by the user. Electronic nicotine delivery systems can resemble traditional cigarettes, cigars, pipes, or common gadgets such as flashlights, flash drives, or pens. E-cigarette use has increased rapidly in the past decade in both adolescents and adults. The Centers for Disease Control and Prevention’s recent report on cigarette use has increased rapidly in the past decade in both adolescents and adults. The Centers for Disease Control and Prevention’s recent report on cigarette use rates from the National Youth Tobacco Survey increased from 4.5% in 2011 to 13.4% in 2014, affecting more than 2.2 million students.2

The 2009 Family Smoking Prevention and Tobacco Control Act gave the US Food and Drug Administration (FDA) authority over cigarettes, smokeless tobacco products, and loose tobacco products and authorized the Secretary of Health and Human Services to deem other tobacco products subject to the FDA’s jurisdiction. Until these products are under the FDA’s jurisdiction, there will be no federal oversight of e-cigarettes, cigars, or other tobacco products. Most states do not have restrictions in place to protect the public’s health, or the health of children, against these products. Until e-cigarettes, cigars, and other tobacco products are deemed to be under the FDA’s jurisdiction, the FDA has no authority to address the use of candy and fruit flavors in these products or to require liquid nicotine be packaged in childproof containers. The unnecessary delay in regulating these products has put children at risk.3

Health claims from e-cigarettes are implied, including that they can aid in smoking cessation and reduce harm from smoking. However, the truth differs from these claims. While lower levels of toxins are produced by e-cigarettes compared with traditional combustible cigarettes, both the individuals who smoke e-cigarettes and nonsmokers exposed to e-cigarette vapor are exposed to carcinogens4 as well as to particulate toxins, formaldehyde, acetaldehydes, and heavy metals drawn into the lungs.5,6 Animal models show fetal and newborn exposure to e-cigarette vapor results in decreased lung growth and impaired lung function7 and endothelial cell disruption.8 In addition, nicotine is not a benign drug. It is highly addictive, affects the nervous system and the cardiovascular system, and its use leads to significant withdrawal symptoms.9

Many e-cigarette devices mimic conventional cigarettes, use of e-cigarette products in public helps normalize smoking behaviors, and a lack of restrictions on advertising e-cigarettes means that a new generation of smokers is being exposed to smoking imagery on television and other media, leading to greater use by and addiction of nonsmokers.10,11 Many public health experts are concerned that e-cigarette use will renormalize smoking, delay or prevent cessation, promote youth use, and cause former smokers to become addicted again.9 Despite passionate advocacy by some for the potential benefit to smokers from switching to e-cigarette products, the evidence suggests that e-cigarette users are less likely to quit smoking traditional cigarettes than are those who do not use e-cigarettes.12 Similarly, despite the increasing body of evidence detailing the harms from e-cigarettes, the FDA has not acted to assert authority over these alternative tobacco products.

The article by Primack et al is one more piece of evidence that the effect of e-cigarettes on youth is happening now in real time and that these products harm nonsmokers and result in a net harm to society and public health. At a time when many claim to be uncertain about the harms and benefits of e-cigarettes and argue for more studies, these data provide strong longitudinal evidence that e-cigarette use leads to smoking, most likely owing to nicotine addiction. We do not need more research on this question; we have the evidence base, and we have strategies that work to protect nonsmokers from e-cigarettes and other forms of tobacco. What we still need is the political will to act on the evidence and protect our youth.


Progression to Traditional Cigarette Smoking After Electronic Cigarette Use Among US Adolescents and Young Adults

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**IMPORTANCE** Electronic cigarettes (e-cigarettes) may help smokers reduce the use of traditional combustible cigarettes. However, adolescents and young adults who have never smoked traditional cigarettes are now using e-cigarettes, and these individuals may be at risk for subsequent progression to traditional cigarette smoking.

**OBJECTIVE** To determine whether baseline use of e-cigarettes among nonsmoking and nonsusceptible adolescents and young adults is associated with subsequent progression along an established trajectory to traditional cigarette smoking.

**DESIGN, SETTING, AND PARTICIPANTS** In this longitudinal cohort study, a national US sample of 694 participants aged 16 to 26 years who were never cigarette smokers and were attitudinally nonsusceptible to smoking cigarettes completed baseline surveys from October 1, 2012, to May 1, 2014, regarding smoking in 2012-2013. They were reassessed 1 year later. Analysis was conducted from July 1, 2014, to March 1, 2015. Multinomial logistic regression was used to assess the independent association between baseline e-cigarette use and cigarette smoking, controlling for sex, age, race/ethnicity, maternal educational level, sensation-seeking tendency, parental cigarette smoking, and cigarette smoking among friends. Sensitivity analyses were performed, with varying approaches to missing data and recanting.

**EXPOSURES** Use of e-cigarettes at baseline.

**MAIN OUTCOMES AND MEASURES** Progression to cigarette smoking, defined using 3 specific states along a trajectory: nonsusceptible nonsmokers, susceptible nonsmokers, and smokers. Individuals who could not rule out smoking in the future were defined as susceptible.

**RESULTS** Among the 694 respondents, 374 (53.9%) were female and 531 (76.5%) were non-Hispanic white. At baseline, 16 participants (2.3%) used e-cigarettes. Over the 1-year follow-up, 11 of 16 e-cigarette users and 128 of 678 of those who had not used e-cigarettes (18.9%) progressed toward cigarette smoking. In the primary fully adjusted models, baseline e-cigarette use was independently associated with progression to smoking (adjusted odds ratio [AOR], 8.3; 95% CI, 1.2-58.6) and to susceptibility among nonsmokers (AOR, 8.5; 95% CI, 1.3-57.2). Sensitivity analyses showed consistent results in the level of significance and slightly larger magnitude of AORs.

**CONCLUSIONS AND RELEVANCE** In this national sample of US adolescents and young adults, use of e-cigarettes at baseline was associated with progression to traditional cigarette smoking. These findings support regulations to limit sales and decrease the appeal of e-cigarettes to adolescents and young adults.
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n electronic cigarette (e-cigarette) contains a heating element that atomizes a liquid consisting of propylene glycol, glycerin, nicotine, and flavorings into an inhalable aerosol. Compared with traditional combustible cigarettes (hereafter, cigarettes), e-cigarettes emit lower levels of many toxicants. Therefore, many experts view these devices as potentially valuable tools to reduce the harm of tobacco smoking. In support of this goal, some studies suggest that e-cigarettes may help smokers reduce the use of traditional tobacco products.  

However, there are also concerns related to e-cigarettes. First, there is concern that e-cigarette use may inhibit quitting among established cigarette smokers; for example, use of e-cigarettes may make it easier for smokers to cope with indoor smoking restrictions. In support of this concern, observational studies demonstrate that adult smokers who begin to use e-cigarettes seldom completely quit combustible products, especially among those who use e-cigarettes only intermittently.  

There is also concern that e-cigarette marketing could position the product to recruit nonsmoking individuals. In support of this concern, the use of e-cigarettes has increased substantially among both adolescents and young adults. According to data collected in 2014, 13.4% of US high school students have used e-cigarettes in the past 30 days, compared with only 9.2% who smoked cigarettes. One reason this use is particularly problematic is that nicotine is known to have adverse effects on the developing brain. In addition, studies suggest that many adolescents and young adults who are new users of e-cigarettes otherwise may have been less susceptible to tobacco or nicotine use. Therefore, a key public health question is whether e-cigarette users who initially did not smoke cigarettes are at risk for progression to dual use of e-cigarettes and cigarettes or exclusive use of e-cigarettes. There have been few studies that have addressed this question, and to our knowledge none has been longitudinal. In these cross-sectional surveys of US adolescents, use of e-cigarettes has been associated with progression from experimental smoking to established smoking, defined as having smoked 100 cigarettes in one’s lifetime. Use of e-cigarettes has been associated with attitudinal susceptibility to future cigarette smoking, a well-documented milestone along the trajectory to established cigarette smoking. Finally, these studies have shown that use of e-cigarettes has been associated with being open to future cigarette smoking among US young adults aged 18 to 29 years.

However, these cross-sectional studies could not determine whether e-cigarette use preceded cigarette use. Therefore, we conducted a longitudinal study to address whether baseline e-cigarette use was associated with progression along a trajectory to cigarette smoking 1 year later. Based on prior work noted above, we hypothesized that baseline e-cigarette use would predict higher risk of progression to cigarette smoking.

Methods

Participants and Setting

Our data come from the second and third waves of the United States–based Dartmouth Media, Advertising, and Health Study, a national study of adolescents and young adults (aged 16–26 years) recruited via random digit dialing using landline (66.7%) and cellular telephone numbers (33.3%).

The study, which was conducted from October 1, 2012, to May 1, 2014, began to ascertain e-cigarette use at wave 2. Thus, wave 2 (2012-2013) serves as the baseline and wave 3 (2013-2014) serves as follow-up for the current study. Analysis was conducted from July 1, 2014, to March 1, 2015. To be included in the study, participants had to be never smokers and nonsusceptible to smoking at baseline. Susceptibility to future smoking was assessed with 2 items: “If one of your friends offered you a cigarette, would you try it?” and “Do you think you will smoke a cigarette sometime in the next year?” Responses included “definitely yes,” “probably yes,” “probably no,” and “definitely no.” Those who responded “definitely no” to both measures are considered nonsusceptible nonsmokers (NSNS), whereas those who cannot rule out smoking are defined as susceptible. Multiple longitudinal studies show that, compared with NSNS, individuals defined as susceptible nonsmokers (SNS) according to this measure are substantially more likely to try smoking in the near future.

A total of 728 participants met the criteria of being NSNS. At follow-up 1 year later, 507 (69.6%) of these participants were successfully reassessed. Therefore, for analyses that included only complete observed data (sensitivity analysis 1), there was a sample size of 507. For sensitivity analysis 2, we imputed missing data, which added 4 baseline participants, bringing the total sample size to 732. Finally, for primary analyses, we imputed missing data and fixed recanting, which eliminated 38 participants and resulted in a sample size of 694. Adult participants provided verbal informed consent and minor participants provided parental verbal informed consent. Participants received $25 for completion of the Internet-based visual survey at each wave. The Dartmouth Committee for the Protection of Human Subjects approved the study.

Data Collection

Independent and Dependent Variables

Our independent variable was whether participants had ever used an e-cigarette at baseline. The dependent variable was
Substantial proportions of adolescents in prospective surveys of substance use subsequently recant prior reports of substance use.27,28 This recanting occurs, for example, when a participant claims to be a current smoker at baseline but then claims to be a never smoker at follow-up. Our primary models systematically addressed recanting.29 For this logical fix, we assumed reports were accurate until a participant contradicted himself or herself. The contradictory response was then made logically consistent with earlier reports.

We also conducted 2 exploratory sensitivity analyses to examine the robustness of our findings. First, we conducted all analyses using only available data (without imputation). Second, we conducted models that did not fix recanting systematically as described above. While only about 5% of participants contradicted earlier reports and required repair in primary models, we wished to ensure that such contradictions did not affect results.

We used the public-domain R statistical software, version 3.1.2, for statistical analyses. We defined significance with a 2-tailed α of 0.05.

**Results**

Our imputed sample for primary analyses consisted of 694 individuals: 374 female (53.9%), 531 non-Hispanic white (76.5%), 47 non-Hispanic black (6.8%), 53 Hispanic (7.6%), and 63 of other race (9.1%) (Table 1). Only 16 of the 694 participants (2.3%) were e-cigarette users at baseline. Five of 16 individuals who used e-cigarettes at baseline (31.3%) progressed to SNS, while only 63 of 678 of those who did not use e-cigarettes at baseline (9.3%) progressed to SNS (Table 2). Similarly, 6 of 16 individuals who used e-cigarettes at baseline (37.5%) progressed to cigarette smoking, but only 65 of 678 of those who did not use e-cigarettes at baseline (9.6%) progressed to smoking.

Bivariable multinomial logistic regression analyses demonstrated that compared with those who did not smoke e-cigarettes at baseline, those who did smoke e-cigarettes at baseline had larger point estimates of progressing from NSNS to SNS (AOR, 10.7; 95% CI, 1.8-63.4). Similarly, those who smoked e-cigarettes at baseline had larger point estimates of progressing from NSNS to cigarette smoking (AOR, 11.9; 95% CI, 2.1-68.7).

Multivariable multinomial logistic regression analyses demonstrated that compared with those who did not smoke e-cigarettes at baseline, those who did smoke e-cigarettes at baseline had larger point estimates of progressing from NSNS to SNS (AOR, 8.5; 95% CI, 1.3-57.2). Of other covariates in this same model, only younger age was also significantly associated with this transition (Table 3). Similarly, individuals who smoked e-cigarettes at baseline had larger point estimates of progressing from NSNS to cigarette smoking (AOR, 8.3; 95% CI, 1.2-58.6). Of other covariates in this model, only sensation-seeking tendency and having friends who smoke were also associated with this progression.

Exploratory sensitivity analyses showed consistent results in the level of significance and slightly larger magnitude of AORs. For the multivariable models that used only individuals with complete data (without imputation), baseline e-
cigarette use was independently associated with greater odds of progressing from NSNS to SNS (AOR, 11.5; 95% CI, 1.7-77.4) and from NSNS to cigarette smoking (AOR, 10.4; 95% CI, 1.6-69.5). Similarly, when we ignored recanting instead of systematically fixing it, e-cigarette use was independently associated with greater odds of progression from NSNS to SNS (AOR, 9.6; 95% CI, 1.5-59.8) and from NSNS to cigarette smoking (AOR, 9.4; 95% CI, 1.7-52.0).

Discussion

In this study, the use of e-cigarettes at baseline was significantly associated with progression along the trajectory to cigarette smoking over 1 year in a multivariable model that included multiple covariates, even among a population that was attitudinally nonsusceptible to smoking at baseline. These results raise concerns that the many adolescents and young adults who initiate nicotine use through e-cigarettes are at substantially increased risk for later use of cigarettes, even if they do not intend to smoke cigarettes in the future. Thus, while e-cigarettes may potentially represent a product that can reduce harm for established cigarette smokers, they may simultaneously contribute to the development of a new population of cigarette smokers. These results are consistent with previous cross-sectional studies on the association of e-cigarette use and attitudes toward cigarettes and use of cigarettes.15,20,21 These results are also consistent with the fact that many youth are dual users of cigarettes and e-cigarettes.30,31

It is notable that the estimated AOR for baseline e-cigarette use was higher than that for multiple established predictors of smoking. Our results were largely consistent with those of prior studies using similar covariates in that sensation-seeking tendency and friends who smoke were the covariates most strongly associated with initiation of cigarette smoking.32,33

Even though there was substantial risk associated with being an e-cigarette user at baseline, there was only a small number of e-cigarette smokers at baseline (approximately 2.3%). Therefore, it could be interpreted that this small number may not translate into substantial public health risk. However, data published in 2015 suggest that large numbers of youth are initiating e-cigarette use and that as many as half of these individuals do not smoke traditional combustible cigarettes.15,19 Therefore, it will be important to continue surveillance among youth of both e-cigarette use and overlap with use of other tobacco products.

Initial e-cigarette use may lead to subsequent traditional cigarette smoking simply by providing nicotine. Other studies have found that initial exposure to nicotine in other forms, such as smokeless tobacco, can lead to later traditional cigarette smoking.34 Because e-cigarettes deliver nicotine more slowly than traditional cigarettes,35 they may serve as a “nico-
the accessibility of e-cigarettes to youth.40 For example, (Reprinted) JAMA Pediatrics

Abbreviations: NSNS, nonsusceptible nonsmoker; SNS, susceptible nonsmoker.

Tobacco Control Act (http://www.fda.gov/TobaccoProducts

Limited for cigarettes by the 2009 Family Smoking Prevention and

youth-oriented flavorings, even while such flavorings have been

public health efforts that shifted public norms around smoking.

It is also notable that e-cigarettes are available in multiple youth-oriented flavorings, even while such flavorings have been limited for cigarettes by the 2009 Family Smoking Prevention and Tobacco Control Act (http://www.fda.gov/TobaccoProducts/GuidanceComplianceRegulatoryInformation/ucm246129

Evidence that, while our dependent variable spanned the trajectory, it did not include more distal states such as frequent or established smoking. Therefore, our confidence intervals were wide, and more precise estimates will require larger samples of NSNS participants who smoke e-cigarettes. However, it is notable that, despite this low power, we found consistently significant results. It is also a limitation that, while our dependent variable spanned the trajectory from nonsmoking to susceptibility to initiation of smoking, it did not include more distal states such as frequent or established smoking. However, susceptibility and initiation of smoking are known to be important steps on the pathway to established smoking.17 Therefore, our confidence intervals were wide, and more precise estimates will require larger samples of NSNS participants who smoke e-cigarettes. However, it is notable that, despite this low power, we found consistently significant results. It is also a limitation that, while our dependent variable spanned the trajectory from nonsmoking to susceptibility to initiation of smoking, it did not include more distal states such as frequent or established smoking. However, susceptibility and initiation of smoking are known to be important steps on the pathway to established smoking.17

In addition, while the purpose of this analysis was to focus on future trajectories among NSNS participants, it might be valuable for future analyses to examine trajectories among other groups, such as individuals who are SNS or cigarette experimenters at baseline. Another direction for future research would be to examine more fine-grained assessments of e-cigarette use, such as current use or frequency of use, when larger samples with more e-cigarette users are available.

Finally, while our sample was national, it was not nationally representative. However, it is encouraging that rates of tobacco use in our sample were similar to national estimates from that time.41

Table 3. Multivariable Associations Between e-Cigarette Use at Baseline and Progression Along the Cigarette Smoking Trajectory by Follow-up

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Adjusted Odds Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>NSNS to SNS</td>
</tr>
<tr>
<td>e-Cigarette use at baseline (yes vs no)</td>
<td>8.5 (1.3-57.2)</td>
</tr>
<tr>
<td>Age, yb</td>
<td>0.8 (0.7-0.96)</td>
</tr>
<tr>
<td>Sex (male vs female)</td>
<td>1.0 (0.6-1.9)</td>
</tr>
<tr>
<td>Race/ethnicity</td>
<td></td>
</tr>
<tr>
<td>Non-Hispanic black (vs non-Hispanic white)</td>
<td>0.4 (0.1-2.9)</td>
</tr>
<tr>
<td>Hispanic (vs non-Hispanic white)</td>
<td>0.7 (0.2-3.0)</td>
</tr>
<tr>
<td>Other (vs non-Hispanic white)</td>
<td>1.1 (0.4-2.8)</td>
</tr>
<tr>
<td>Maternal educational levela</td>
<td>1.0 (0.8-1.1)</td>
</tr>
<tr>
<td>Sensation-seeking tendencyb</td>
<td>1.9 (0.96-3.6)</td>
</tr>
<tr>
<td>Smoking</td>
<td></td>
</tr>
<tr>
<td>Parentc</td>
<td>0.9 (0.6-1.4)</td>
</tr>
<tr>
<td>Friendsd</td>
<td>0.9 (0.6-1.4)</td>
</tr>
</tbody>
</table>

Abbreviations: NSNS, nonsusceptible nonsmoker; SNS, susceptible nonsmoker.

a Adjusted for all variables in the table.

b Adjusted odds ratios represent increases in odds for each additional year.

c Scores ranged from 1 to 10, with higher scores representing more advanced education.

d Scores ranged from 1 to 4, with higher scores representing greater sensation-seeking tendency.

e Scores ranged from 0 to 3, with 0 representing never a smoker, 1 representing a former smoker, 2 representing a nondaily smoker, and 3 representing a daily smoker.

Scores ranged from 0 to 3, with higher numbers representing a greater proportion of friends who smoke.

tine starter, allowing a new user to advance to cigarette smoking as he or she becomes tolerant of the initial adverse effects. Cigarette users begin to report craving for nicotine within weeks of their first cigarette.36 The same process may drive initial e-cigarette users to seek out cigarettes as a more efficient nicotine delivery device.

Unlike forms of nicotine such as smokeless tobacco, e-cigarettes are designed to mimic the behavioral and sensory act of cigarette smoking. Therefore, even aside from the nicotine content, e-cigarettes may behaviorally accustom individuals to powerful cigarette smoking cues such as inhalation, exhalation, and holding the cigarette.

E-cigarettes are not subject to the many regulations designed to limit cigarette smoking, such as age limits on sales, restriction of flavorings, restrictions on marketing, clean air laws, taxation, and labeling requirements.37-39 These policy gaps may increase the accessibility of e-cigarettes to youth.40 For example, e-cigarettes are marketed on television, representing the first time in more than 40 years that a smoking-related device is advertised on this medium. This marketing may have the unintended consequence of renormalizing cigarette smoking after decades of public health efforts that shifted public norms around smoking.

Our study identified a longitudinal association between baseline e-cigarette use and progression to traditional cigarette smoking among adolescents and young adults. Especially considering the rapid increase in e-cigarette use among youth,17 these findings support regulations to limit sales and decrease the appeal of e-cigarettes to adolescents and young adults.
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