

## Original Investigation

# Association of Electronic Cigarette Use With Initiation of Combustible Tobacco Product Smoking in Early Adolescence

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**IMPORTANCE** Exposure to nicotine in electronic cigarettes (e-cigarettes) is becoming increasingly common among adolescents who report never having smoked combustible tobacco.

**OBJECTIVE** To evaluate whether e-cigarette use among 14-year-old adolescents who have never tried combustible tobacco is associated with risk of initiating use of 3 combustible tobacco products (ie, cigarettes, cigars, and hookah).

**DESIGN, SETTING, AND PARTICIPANTS** Longitudinal repeated assessment of a school-based cohort at baseline (fall 2013, 9th grade, mean age = 14.1 years) and at a 6-month follow-up (spring 2014, 9th grade) and a 12-month follow-up (fall 2014, 10th grade). Ten public high schools in Los Angeles, California, were recruited through convenience sampling. Participants were students who reported never using combustible tobacco at baseline and completed follow-up assessments at 6 or 12 months (N = 2530). At each time point, students completed self-report surveys during in-classroom data collections.

**EXPOSURE** Student self-report of whether he or she ever used e-cigarettes (yes or no) at baseline.

**MAIN OUTCOMES AND MEASURES** Six- and 12-month follow-up reports on use of any of the following tobacco products within the prior 6 months: (1) any combustible tobacco product (yes or no); (2) combustible cigarettes (yes or no); (3) cigars (yes or no); (4) hookah (yes or no); and (5) number of combustible tobacco products (range: 0-3).

**RESULTS** Past 6-month use of any combustible tobacco product was more frequent in baseline e-cigarette ever users (n = 222) than never users (n = 2308) at the 6-month follow-up (30.7% vs 8.1%, respectively; difference between groups in prevalence rates, 22.7% [95% CI, 16.4%-28.9%]) and at the 12-month follow-up (25.2% vs 9.3%, respectively; difference between groups, 15.9% [95% CI, 10.0%-21.8%]). Baseline e-cigarette use was associated with greater likelihood of use of any combustible tobacco product averaged across the 2 follow-up periods in the unadjusted analyses (odds ratio [OR], 4.27 [95% CI, 3.19-5.71]) and in the analyses adjusted for sociodemographic, environmental, and intrapersonal risk factors for smoking (OR, 2.73 [95% CI, 2.00-3.73]). Product-specific analyses showed that baseline e-cigarette use was positively associated with combustible cigarette (OR, 2.65 [95% CI, 1.73-4.05]), cigar (OR, 4.85 [95% CI, 3.38-6.96]), and hookah (OR, 3.25 [95% CI, 2.29-4.62]) use and with the number of different combustible products used (OR, 4.26 [95% CI, 3.16-5.74]) averaged across the 2 follow-up periods.

**CONCLUSIONS AND RELEVANCE** Among high school students in Los Angeles, those who had ever used e-cigarettes at baseline compared with nonusers were more likely to report initiation of combustible tobacco use over the next year. Further research is needed to understand whether this association may be causal.

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Nicotine is addictive when delivered in tobacco smoke, which provides a significant dose that travels quickly to the brain after inhalation.<sup>1</sup> Combustible tobacco, which has well-known health consequences, has long been the dominant nicotine-delivering product used in the population. Electronic cigarettes (e-cigarettes), which are devices that deliver inhaled aerosol generally containing nicotine, are becoming increasingly popular, particularly among adolescents, including teens who have never used combustible tobacco.<sup>2,3</sup> According to 2014 US estimates, 16% of 10th graders reported use of e-cigarettes within the past 30 days, of whom 43% reported never having tried combustible cigarettes.<sup>3</sup>

Whether use of e-cigarettes is associated with risk of initiating combustible tobacco use is unknown. Enjoyment of the sensations and the pharmacological effects of inhaling nicotine via e-cigarettes could increase the propensity to try other products that similarly deliver inhaled nicotine, including combustible tobacco products.

If e-cigarette use is a risk factor for initiation of combustible tobacco use, the high prevalence of e-cigarette use in the adolescent population could ultimately perpetuate and potentially enlarge the epidemic of tobacco-related illness. Because the first year of high school is a vulnerable period for initiating risky behaviors,<sup>4</sup> this study investigated whether adolescents entering the 9th grade in Los Angeles, California, who reported ever using e-cigarettes were more likely to initiate the use of combustible tobacco during the subsequent year.

## Methods

### Participants and Procedures

Data were collected as part of a longitudinal survey of substance use and mental health among high school students. Approximately 40 public high schools in the Los Angeles metropolitan area were approached about participating in this study. These schools were chosen because of their diverse demographic characteristics and proximity. Ten schools agreed to participate in the study (school characteristics appear in eTable 1 in the [Supplement](#)).

To enroll in the study, students were required to provide active written or verbal assent and their parents were required to provide active written or verbal consent. Data collection involved 3 assessment waves that took place approximately 6 months apart: baseline (fall 2013 during 9th grade), 6-month follow-up (spring 2014 also during 9th grade), and 12-month follow-up (fall 2014 during 10th grade).

At each wave, paper-and-pencil surveys were administered in students' classrooms onsite. Students not in class during data collections completed telephone or Internet surveys. The University of Southern California institutional review board approved the study.

### Measures

Each study measure has shown adequate psychometric properties in previous youth samples.<sup>5-9</sup>

### e-Cigarette and Combustible Tobacco Product Use

At each wave, items based on the Youth Behavior Risk Surveillance<sup>5</sup> and Monitoring the Future<sup>6</sup> surveys assessed lifetime and past 6-month use (yes or no) of e-cigarettes, combustible cigarettes (described as even a few puffs), full-size cigars, little cigars or cigarillos, hookah water pipe, and blunts (marijuana rolled in a tobacco leaf or cigar casing). Response to the lifetime e-cigarette use question at baseline was the primary exposure variable.

Outcomes were any use during the prior 6 months of (1) any combustible tobacco product (yes or no); (2) combustible cigarettes (yes or no); (3) cigars (full-size cigars, little cigars, or blunts; yes or no); (4) hookah (yes or no); and (5) the total number of combustible tobacco products used among the cigarette, cigar, and hookah categories (range, 0-3). A composite cigar variable was used because of the infrequent use of individual cigar products. Blunt use was included given the high prevalence in this sample, association with adolescent e-cigarette use in past work,<sup>10</sup> and evidence that there are significant tobacco smoke toxicants in blunt smoke.<sup>11</sup>

A sensitivity analysis was conducted that compared the rates of nonblunt cigar use at the 6- and 12-month follow-up assessments by baseline e-cigarette use. The terms *ever smokers* and *never smokers* are used to refer to adolescents who ever and never, respectively, used at least 1 of the combustible tobacco products.

### Covariates

Variables peripheral to a putative pathway by which e-cigarette use may be directly associated with risk of combustible tobacco use initiation, yet potentially overlapping with both e-cigarette and combustible tobacco use, were selected a priori as covariates based on previous literature.<sup>10,12-16</sup> Covariates were selected from the following 3 domains.

**Sociodemographics** | Sociodemographic characteristics, including age, sex, race/ethnicity, and highest parental education level, were assessed using self-report responses to investigator-defined forced-choice items ([Table 1](#)).

**Environmental Factors** | Indicators of the proximal environment included family living situation, measured with the question, "Who do you live with most of the time?" (both biological parents vs other).<sup>12</sup> Family history of smoking was measured using the question, "Does anyone in your immediate family (brothers, sisters, parents, or grandparents) have a history of smoking cigarettes?" (yes or no). Peer smoking was assessed by responses to the question, "In the last 30 days, how many of your 5 closest friends have smoked cigarettes?" (range, 0-5).<sup>17</sup>

**Intrapersonal Factors** | Mental health, personality traits, and psychological processes linked with experimentation, risky behavior, and smoking were assessed. Depressive symptoms were measured using the 20-item Center for Epidemiologic Studies Depression Scale<sup>8</sup> composite sum past week frequency rating (score range for each item: 0 [rarely or none of the time; 0-1 day] to 3 [most or all of the time; 5-7 days]). Impulsivity was measured with the 5-item Temperament and Character In-

Table 1. Sample Characteristics by e-Cigarette Use Status Among Never Smokers at Baseline<sup>a</sup>

	Total (N = 2530) <sup>b</sup>	Never Use of e-Cigarettes (n = 2308)	Ever Use of e-Cigarettes (n = 222)	<i>P</i> Value
<b>Sociodemographics</b>				
Sex (n = 2524) <sup>c</sup>				
Male	1181 (46.8)	1052 (45.7)	129 (58.6)	<.001 <sup>d</sup>
Female	1343 (53.2)	1252 (54.3)	91 (41.4)	
Age, mean (95% CI), y (n = 2519) <sup>c</sup>	14.06 (14.04-14.07)	14.05 (14.04-14.07)	14.10 (14.05-14.15)	.11 <sup>e</sup>
Race/ethnicity (n = 2487) <sup>c</sup>				
American Indian/Alaska Native	21 (0.8)	19 (0.8)	2 (0.9)	.02 <sup>d</sup>
Asian	472 (19.0)	432 (19.0)	40 (18.7)	
Black	119 (4.8)	107 (4.7)	12 (5.6)	
Hispanic	1099 (44.2)	998 (43.9)	101 (47.2)	
Native Hawaiian/Pacific Islander	89 (3.6)	74 (3.3)	15 (7.0)	
White	404 (16.2)	383 (16.9)	21 (9.8)	
Other <sup>f</sup>	142 (5.7)	134 (5.9)	8 (3.7)	
Multietnic or multiracial	141 (5.7)	126 (5.5)	15 (7.0)	
Highest parental education level (n = 2200) <sup>c</sup>				
≤8th grade	72 (3.3)	69 (3.4)	3 (1.6)	.03 <sup>g</sup>
Some high school	171 (7.8)	151 (7.5)	20 (10.4)	
High school graduate	334 (15.2)	298 (14.8)	36 (18.8)	
Some college	428 (19.5)	384 (19.1)	44 (22.9)	
College graduate	741 (33.7)	683 (34.0)	58 (30.2)	
Graduate degree	454 (20.6)	423 (21.1)	31 (16.2)	
<b>Environmental Factors</b>				
Lives with both biological parents (n = 2510) <sup>c</sup>	1688 (67.3)	1563 (68.3)	125 (56.6)	<.001 <sup>d</sup>
Family history of smoking (n = 2430) <sup>c</sup>	1487 (61.2)	1337 (60.3)	150 (70.8)	.003 <sup>d</sup>
Peer smoking, mean (95% CI) (n = 2484) <sup>c</sup>	0.22 (0.19-0.25)	0.20 (0.17-0.23)	0.46 (0.32-0.59)	<.001 <sup>d</sup>
<b>Intrapersonal Factors, Mean (95% CI)</b>				
CESD Scale for depressive symptoms (n = 2490) <sup>c,h</sup>	13.49 (13.06-13.93)	13.37 (12.91-13.82)	14.80 (13.27-16.33)	.07 <sup>e</sup>
TCI subscale for impulsivity (n = 2481) <sup>c,i</sup>	2.39 (2.33-2.45)	2.35 (2.29-2.41)	2.76 (2.58-2.94)	<.001 <sup>e</sup>
Substance use, No. (%)	454 (17.9)	345 (15.0)	109 (49.1)	<.001 <sup>d</sup>
Delinquent behavior (n = 2496) <sup>c</sup>	14.64 (14.50-14.79)	14.43 (14.29-14.57)	16.88 (16.12-17.64)	<.001 <sup>e</sup>
Smoking susceptibility (n = 2506) <sup>c</sup>	1.11 (1.10-1.12)	1.10 (1.09-1.11)	1.22 (1.16-1.27)	<.001 <sup>e</sup>
Smoking expectancies (n = 2502) <sup>c,j</sup>	1.39 (1.37-1.41)	1.38 (1.36-1.40)	1.48 (1.40-1.55)	.02 <sup>e</sup>

Abbreviations: CESD, Center for Epidemiologic Studies Depression; TCI, Temperament and Character Inventory.

<sup>a</sup> Data are expressed as No. (%) unless otherwise indicated. Never smokers at baseline defined as those who have never used any of the 3 combustible tobacco products (ie, combustible cigarettes, cigars, hookah).

<sup>b</sup> Indicates No. of students who completed follow-up assessments at 6 or 12 months.

<sup>c</sup> The denominator is for the data in column 2 and is provided due to missing data for this variable in each column in this row (or rows; the denominators for columns 3 and 4 are not provided).

<sup>d</sup> Calculated using the  $\chi^2$  test.

<sup>e</sup> Calculated using the independent samples t test.

<sup>f</sup> Students selected "other" in response to the forced-choice race/ethnicity question because they did not self-identify with any of the categories provided.

<sup>g</sup> Calculated using the Spearman  $\rho$  test.

<sup>h</sup> Score range: 0 (rarely or none of the time; 0-1 day) to 3 (most or all of the time; 5-7 days) for each symptom  $\times$  20 symptoms.

<sup>i</sup> Score range: 0-5 (example item: "I often do things based on how I feel at the moment"; score based on the sum of true or false responses to 5 items).

<sup>j</sup> Assessed using the average of the 2 responses for "I think I might enjoy ... smoking" and (reversed) "I think I might feel bad ... from smoking." Score range: 1-4; a response of strongly disagree, 1; disagree, 2; agree, 3; and strongly agree, 4.

ventory impulsivity subscale, which assesses tendency toward acting on instinct without conscious deliberation (eg, "I often do things based on how I feel at the moment," true or false items summed to total score with a score range of 0-5).<sup>18</sup>

Use of non-nicotine or tobacco substances was measured using items from the Youth Behavior Risk Surveillance and Monitoring the Future surveys assessing ever use of alcohol and 13 separate illicit and prescription substances of abuse (use of  $\geq 1$  vs 0 substances). Delinquent behavior was measured with a sum of frequency ratings for engaging in 11 different behaviors (eg, stealing, lying to parents; score range: 1 [never] to 6 [ $\geq 10$  times]) within the past 6 months.<sup>19</sup>

Susceptibility to smoking was measured using a 3-item index,<sup>9</sup> averaging responses to the following 3 questions: "Would you try smoking a cigarette if one of your best friends

offered it to you?" "Do you think you would smoke in the next 6 months?" "Are you curious about smoking?" Responses corresponded to the following scores: a response of definitely not received a score of 1; probably not, 2; probably yes, 3; and definitely yes, 4. Smoking outcome expectancies were assessed using the average of the 2 responses<sup>20</sup> for "I think I might enjoy ... smoking" and (reversed) "I think I might feel bad ... from smoking." Responses corresponded to the following scores: a response of strongly disagree received a score of 1; disagree, 2; agree, 3; and strongly agree, 4.

### Data Analysis

The prevalence and association of e-cigarette and combustible tobacco use in the overall baseline sample are reported first. Then, in the sample of baseline never smokers, corre-

lates of study attrition and descriptive statistics are reported. Primary analyses used repeated-measures, generalized-linear mixed models,<sup>21</sup> an extension of logistic regression, in which each participant had 2 time points of follow-up data (at 6 and 12 months). Separate models were constructed for each binary outcome (ie, any combustible tobacco product, cigarettes, cigars, hookah) and the ordinal number of combustible products (cumulative logit) outcome at the 6- and 12-month follow-up periods.

All models included baseline e-cigarette use, school, and time (6-month vs 12-month follow-up) as fixed effects and were fit with and without adjustment for all covariates. The parameter estimate from each regressor or covariate reflected the association with the outcome averaged across the 2 follow-up periods. To explore whether the association between baseline e-cigarette and combustible tobacco use differed across the follow-up periods, the baseline e-cigarette  $\times$  time interaction term was added to each model in a subsequent step. Participants with missing data on baseline e-cigarette use or the respective outcome variable were not included in the models.

Missing data on covariates were accounted for using a multiple-imputation approach,<sup>22</sup> which replaces each missing value with a set of plausible values that represent the uncertainty about the correct value to impute. Using the Markov-chain Monte Carlo method for missing at random assumptions and the available covariate data, 5 multiply-imputed data sets were created. The parameter estimates from the models tested in each imputed data set were pooled and presented as a single estimate. The amount of missing data for each covariate is indicated in Table 1. Continuous variables were rescaled (mean = 0, SD = 1) for the models to facilitate interpretation.

Statistical analyses were conducted using SAS version 9.3 (SAS Institute Inc).<sup>23</sup> Significance was set to .05 and all tests were 2-tailed. A Bonferroni-Holm correction<sup>24</sup> for multiple tests was applied.

## Results

### Study Sample

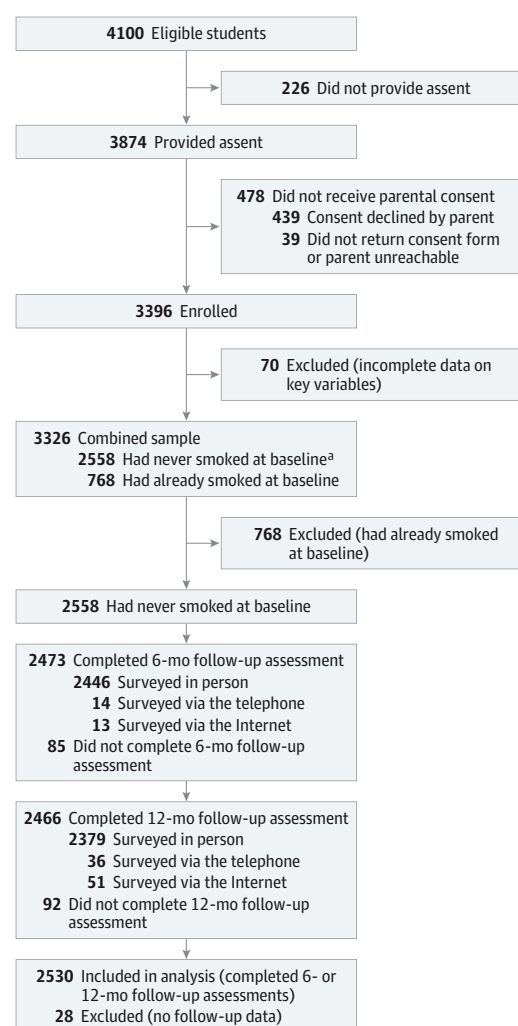
All 9th-grade, English-speaking students not enrolled in special education classes (ie, those with severe learning disabilities) were eligible to participate (N = 4100). Of the 3874 assenting students (94.5%), 3396 parents (87.7%) provided consent. Data were collected for 3383 participants (99.6%) at baseline, 3293 (97.0%) at the 6-month follow-up, and 3282 (96.6%) at the 12-month follow-up. The analytic samples available for the analyses appear in the Figure.

### Descriptive Analyses

In the combined sample of ever smokers (n = 768) and never smokers (n = 2558), baseline e-cigarette ever use was positively associated with baseline ever use of each combustible tobacco product; prevalence ranged from 10.5% to 15.2% for the combustible tobacco products and the prevalence of ever use of e-cigarettes was 18.6% (Table 2).

Baseline never smokers with (N = 2530) vs without (n = 28) follow-up data did not differ by baseline e-cigarette use or any

Figure. Flow of Adolescent Students in Study to Assess e-Cigarette Use at Baseline and Later Use of Combustible Tobacco Products



<sup>a</sup> Includes all 3 combustible tobacco products (ie, combustible cigarettes, cigars, hookah).

sociodemographic characteristic except for age in which participants without data were older ( $P = .006$ ). There were positive associations of e-cigarette use with male sex, Native Hawaiian/Pacific Islander ethnicity, lower parental education level, and most environmental and intrapersonal factors (Table 1).

### Associations Between Baseline e-Cigarette Use and Combustible Tobacco Use at Follow-up Assessments

In the sample of students who were never smokers of combustible tobacco products at baseline, baseline e-cigarette ever users were more likely to report past 6-month use of any combustible tobacco product at the 6-month follow-up (30.7% vs 8.1% in never users; difference between groups in prevalence rates, 22.7% [95% CI, 16.4%-28.9%]) and at the 12-month follow-up (25.2% vs 9.3%, respectively; difference between groups, 15.9% [95% CI, 10.0%-21.8%]) (Table 3).

Table 2. Prevalence and Cross-sectional Association of Baseline e-Cigarette Use and Combustible Tobacco Use<sup>a</sup>

	Combined Sample (n = 3326) <sup>b</sup>	Never Use of e-Cigarettes (n = 2709)	Ever Use of e-Cigarettes (n = 617)	Difference in Prevalence Rates, % (95% CI)
<b>Ever Use</b>				
Any combustible tobacco product	768 (23.1)	376 (13.9)	392 (63.5)	49.7 (45.6-53.7)
Combustible cigarettes (n = 3320) <sup>c</sup>	349 (10.5)	153 (5.7)	196 (32.0)	26.4 (22.6-30.2)
Cigars (n = 3324) <sup>c</sup>	419 (12.6)	168 (6.2)	251 (40.8)	34.6 (30.6-38.6)
Hookah (n = 3304) <sup>c</sup>	501 (15.2)	220 (8.2)	281 (46.5)	38.3 (34.2-42.4)
<b>No. of different combustible tobacco products</b>				
0	2558 (76.9)	2333 (86.1)	225 (36.5)	
1	401 (12.1)	245 (9.0)	156 (25.3)	
2	233 (7.0)	97 (3.6)	136 (22.0)	
3	134 (4.0)	34 (1.3)	100 (16.2)	

<sup>a</sup> Data are expressed as No. (%) unless otherwise indicated. All *P* value comparisons yielded values <.001 and were calculated using the  $\chi^2$  test.

<sup>b</sup> Total is larger than 2530 participants because it includes students who did not have data from follow-up assessments at 6 or 12 months and includes both ever and never smokers at baseline.

<sup>c</sup> The denominator is for the data in column 2 and is provided due to missing data for this variable in each column in this row (the denominators for columns 3 and 4 are not provided).

Table 3. Prevalence of Combustible Tobacco Product Use During Past 6 Months at 2 Follow-up Periods<sup>a</sup>

	Combustible Tobacco Use During Past 6 mo			Difference in Prevalence Rates, % (95% CI)
	Total (N = 2530) <sup>b</sup>	Never Use of e-Cigarettes (n = 2308)	Ever Use of e-Cigarettes (n = 222)	
<b>6-mo Follow-up</b>				
Any combustible tobacco product (n = 2473) <sup>c</sup>	249 (10.1)	182 (8.1)	67 (30.7)	22.7 (16.4-28.9)
Combustible cigarettes (n = 2468) <sup>c</sup>	89 (3.6)	68 (3.0)	21 (9.7)	6.7 (2.7-10.7)
Cigars (n = 2443) <sup>c</sup>	107 (4.4)	70 (3.1)	37 (17.3)	14.2 (9.0-19.3)
Hookah (n = 2434) <sup>c</sup>	160 (6.6)	122 (5.5)	38 (17.8)	12.3 (7.1-17.5)
<b>No. of different combustible tobacco products (n = 2472)<sup>c</sup></b>				
0	2223 (89.9)	2072 (91.9)	151 (69.3)	
1	166 (6.7)	122 (5.4)	44 (20.2)	
2	59 (2.4)	42 (1.9)	17 (7.8)	
3	24 (1.0)	18 (0.8)	6 (2.8)	
<b>12-mo Follow-up</b>				
Any combustible tobacco product (n = 2463) <sup>c</sup>	264 (10.7)	210 (9.3)	54 (25.2)	15.9 (10.0-21.8)
Combustible cigarettes (n = 2462) <sup>c</sup>	91 (3.7)	74 (3.3)	17 (7.9)	4.7 (1.0-8.4)
Cigars (n = 2374) <sup>c</sup>	126 (5.3)	93 (4.3)	33 (16.2)	11.9 (6.8-17.0)
Hookah (n = 2371) <sup>c</sup>	152 (6.4)	127 (5.9)	25 (12.3)	6.4 (1.8-11.0)
<b>No. of different combustible tobacco products (n = 2462)<sup>c</sup></b>				
0	2198 (89.3)	2038 (90.7)	160 (74.8)	
1	181 (7.4)	143 (6.4)	38 (17.8)	
2	61 (2.5)	50 (2.2)	11 (5.1)	
3	22 (0.9)	17 (0.8)	5 (2.3)	

<sup>a</sup> Data are expressed as No. (%) unless otherwise indicated. All *P* value comparisons yielded values <.001 and were calculated using the  $\chi^2$  test.

<sup>b</sup> Indicates No. of students who completed follow-up assessments at 6 or 12 months.

<sup>c</sup> The denominator is for the data in column 2 and is provided due to missing data for this variable in each column in this row (or rows; the denominators for columns 3 and 4 are not provided).

The unadjusted estimate for the association of baseline use of e-cigarettes with use of any combustible tobacco product averaged across the 2 follow-up periods was statistically significant (odds ratio [OR], 4.27 [95% CI, 3.19-5.71]; Table 4). In this model, the estimate for time of data collection was not significant (OR, 1.09 [95% CI, 0.90-1.32]), indicating no change in the prevalence of use of any combustible tobacco product across the 6- and 12-month follow-up periods. The e-cigarette  $\times$  time interaction was not significant (OR, 0.64 [95% CI, 0.39-1.04]), indicating that the strength of association between baseline e-cigarette use and use of any combustible tobacco product did not significantly differ between the 6-month and 12-month follow-up periods.

In the adjusted model, baseline e-cigarette ever use was associated with use of any combustible tobacco product averaged across the 2 follow-up periods over and above the covariates (OR, 2.73 [95% CI, 2.00-3.73]). Parameter estimates for covariates in the adjusted models indicated that lower parental education and baseline peer smoking, impulsivity, ever use of non-nicotine or tobacco substances, delinquent behavior, and smoking expectancies were positively associated with any combustible tobacco use averaged across the 2 follow-up periods (Table 4 and eTable 2 in the Supplement). These particular covariates also were associated with baseline e-cigarette ever use (Table 1).

At both follow-up periods, the prevalence of combustible cigarette smoking, cigar use, and hookah use was higher among



Table 4. Association of Baseline e-Cigarette Ever Use and Covariates With Combustible Tobacco Product Use Outcomes at 6- and 12-Month Follow-up Periods Among Never Smokers at Baseline

	Any Combustible Tobacco Product		Combustible Cigarettes		Cigars		Hookah		No. of Different Combustible Tobacco Products	
	OR (95% CI) <sup>a</sup>	P Value	OR (95% CI) <sup>a</sup>	P Value	OR (95% CI) <sup>a</sup>	P Value	OR (95% CI) <sup>a</sup>	P Value	OR (95% CI) <sup>b</sup>	P Value
<b>Unadjusted Models<sup>c</sup></b>										
Ever e-cigarette use	4.27 (3.19-5.71)	<.001	2.65 (1.73-4.05)	<.001	4.85 (3.38-6.96)	<.001	3.25 (2.29-4.62)	<.001	4.26 (3.16-5.74)	<.001
Time (12- vs 6-mo follow-up)	1.09 (0.90-1.32)	.38	1.03 (0.76-1.39)	.85	1.25 (0.95-1.64)	.11	0.99 (0.78-1.25)	.90	1.08 (0.89-1.30)	.45
Ever e-cigarette use × time <sup>d</sup>	0.64 (0.39-1.04)	.07	0.73 (0.34-1.56)	.41	0.68 (0.36-1.26)	.22	0.60 (0.32-1.12)	.11	0.64 (0.39-1.03)	.07
<b>Adjusted Models<sup>e</sup></b>										
<b>Categorical covariates<sup>f</sup></b>										
Female	0.88 (0.70-1.11)	.28	1.50 (1.05-2.15)	.03	1.48 (1.06-2.06)	.02	0.67 (0.51-0.90)	.007	0.92 (0.73-1.17)	.52
Hispanic ethnicity	1.09 (0.82-1.44)	.55	0.91 (0.59-1.39)	.65	0.97 (0.66-1.43)	.87	1.33 (0.97-1.83)	.08	1.11 (0.83-1.48)	.48
Lives with both biological parents	0.80 (0.64-1.01)	.07	0.96 (0.67-1.37)	.80	0.58 (0.42-0.80)	<.001	0.82 (0.62-1.08)	.15	0.80 (0.63-1.01)	.06
Substance use	2.33 (1.81-2.99)	<.001	1.35 (0.91-2.00)	.14	2.42 (1.72-3.42)	<.001	2.25 (1.67-3.01)	<.001	2.24 (1.73-2.90)	<.001
Family history of smoking	1.11 (0.88-1.41)	.37	1.34 (0.91-1.98)	.14	0.95 (0.68-1.32)	.75	0.99 (0.74-1.32)	.94	1.11 (0.87-1.42)	.39
<b>Continuous covariates<sup>g</sup></b>										
Age	1.07 (0.96-1.20)	.23	1.13 (0.96-1.34)	.15	1.12 (0.95-1.31)	.17	0.97 (0.84-1.11)	.64	1.07 (0.95-1.20)	.27
Parental education	0.83 (0.73-0.94)	.004	0.81 (0.67-0.97)	.03	0.88 (0.72-1.06)	.18	0.86 (0.74-1.01)	.07	0.83 (0.73-0.95)	.007
Peer smoking	1.13 (1.00-1.28)	.05	1.08 (0.90-1.30)	.41	1.18 (1.00-1.38)	.05	1.16 (1.01-1.34)	.03	1.13 (1.00-1.28)	.05
CESD Scale for depressive symptoms	0.95 (0.84-1.08)	.42	1.07 (0.89-1.29)	.45	0.97 (0.81-1.15)	.70	0.99 (0.85-1.14)	.87	0.97 (0.86-1.10)	.66
TCI subscale for impulsivity	1.23 (1.09-1.38)	<.001	1.11 (0.93-1.33)	.25	1.14 (0.97-1.35)	.11	1.28 (1.11-1.46)	<.001	1.22 (1.09-1.38)	<.001
Delinquent behavior	1.38 (1.18-1.61)	<.001	1.35 (1.10-1.66)	.004	1.39 (1.14-1.70)	.001	1.38 (1.14-1.66)	<.001	1.40 (1.20-1.63)	<.001
Smoking susceptibility	1.08 (0.92-1.26)	.37	1.46 (1.18-1.80)	<.001	0.98 (0.79-1.21)	.84	0.94 (0.77-1.14)	.53	1.09 (0.93-1.29)	.28
Smoking expectancies	1.24 (1.10-1.41)	<.001	1.19 (0.98-1.44)	.08	1.43 (1.20-1.69)	<.001	1.26 (1.08-1.46)	.003	1.27 (1.12-1.44)	<.001
<b>Regressors</b>										
Ever e-cigarette use	2.73 (2.00-3.73)	<.001	1.75 (1.10-2.77)	.02	2.96 (2.00-4.38)	<.001	2.26 (1.56-3.29)	<.001	2.73 (1.99-3.75)	<.001
Time (12- vs 6-mo follow-up)	1.09 (0.90-1.33)	.37	1.03 (0.76-1.40)	.85	1.26 (0.95-1.67)	.10	0.98 (0.77-1.24)	.84	1.08 (0.89-1.32)	.42
Ever e-cigarette use × time <sup>d</sup>	0.64 (0.38-1.05)	.08	0.74 (0.34-1.61)	.44	0.68 (0.36-1.29)	.23	0.59 (0.31-1.12)	.11	1.54 (0.94-2.51)	.08

Abbreviations: CESD, Center for Epidemiologic Studies Depression Scale; OR, odds ratio; TCI, Temperament and Character Inventory.

<sup>a</sup> From repeated binary logistic regression model predicting respective outcome from baseline e-cigarette ever use status (yes or no), including school fixed effects.

<sup>b</sup> From repeated ordinal logistic regression model predicting the number of different combustible tobacco products used from baseline e-cigarette ever use status (yes or no), including school fixed effects with the OR reflecting the change in odds of being in a category with use of 1 or more tobacco products (3 vs ≤2; ≥2 vs ≤1; ≥1 vs 0) associated with the covariate or regressor.

<sup>c</sup> For the 2 res log pseudo-likelihood fit indices, the following values are without and with (in parentheses) the interaction term: 24 932.93 (24 946.6) for any tobacco product, 28 391.21 (28 397.11) for combustible cigarettes, 27 019.65 (27 050.36) for cigars, 26 131.31 (26 137.37) for hookah, and 70 339.66 (70 411.89) for No. of tobacco products.

<sup>d</sup> Interaction term added in subsequent model; parameter estimates for other regressors or covariates are from the model excluding the interaction term.

<sup>e</sup> For the range of -2 res log pseudo-likelihood fit indices across the 5 imputed data sets for adjusted models, the following values are without and with (in parentheses) the interaction term: 25 701.9-25 743.77 (25 717.24-25 759.27) for any tobacco product, 29 378.05-29 461.92 (29 382.85-29 467.24) for combustible cigarettes, 28 211.45-28 286.11 (28 238.77-28 312.83) for cigars, 27 193.74-27 282.15 (27 209.93-27 297.96) for hookah, and 73 652.58-73 852.15 (73 730.36-73 930.47) for No. of tobacco products.

<sup>f</sup> The prevalence of combustible tobacco use outcomes at the 2 follow-up periods by covariate category membership appears in eTable 2 in the [Supplement](#).

<sup>g</sup> Rescaled (mean = 0, SD = 1) such that the ORs indicate the change in odds in the outcome associated with an increase in 1 SD unit on the covariate continuous scale.

baseline e-cigarette ever users compared with never users (Table 3). Averaged across the 2 follow-up periods in the unadjusted models, there was an association of baseline e-cigarette ever use with use of combustible cigarettes (OR, 2.65 [95% CI, 1.73-4.05]), cigars (OR, 4.85 [95% CI, 3.38-6.96]), and hookah (OR, 3.25 [95% CI, 2.29-4.62]) (Table 4).

In addition, relative to baseline e-cigarette never users, e-cigarette ever users were more likely to be using at least 1 more combustible tobacco product (ie, 3 vs  $\leq 2$ ;  $\geq 2$  vs  $\leq 1$ ; and  $\geq 1$  vs 0) averaged across the 2 follow-up assessments (OR, 4.26 [95% CI, 3.16-5.74]) (Table 4). Each OR estimate for e-cigarette ever use remained significant in the adjusted models and after applying the Bonferroni-Holm correction for multiple comparisons. The magnitudes of the ORs for e-cigarette ever use were reduced from the unadjusted to adjusted models for each outcome, and a common set of covariates (peer smoking, impulsivity, ever use of non-nicotine or tobacco substances, delinquent behavior, and smoking expectancies) were associated with most outcomes in the adjusted models (Table 4 and eTable 2 in the [Supplement](#)). Time and the e-cigarette  $\times$  time interaction were nonsignificant in all models, suggesting no change in each outcome's prevalence rate or degree of association with baseline e-cigarette use across the 2 follow-up periods. Additional results can be found in the [Supplement](#) (eSensitivity Analyses).

### Supplementary Analyses

Using the same modeling strategy as applied for the primary analysis, the association between baseline combustible tobacco ever use and past 6-month use (initiation) of e-cigarettes at the 2 follow-up periods was analyzed. These analyses included ever smokers at baseline but excluded ever users of e-cigarettes to model initiation of e-cigarette use. Baseline ever use of each combustible tobacco product was positively associated with e-cigarette use averaged across the 2 follow-up periods in the unadjusted and adjusted models, except for cigars in the adjusted model ( $P = .06$ ; eTables 3-5 in the [Supplement](#)).

## Discussion

These data provide new evidence that e-cigarette use is prospectively associated with increased risk of combustible tobacco use initiation during early adolescence. Associations were consistent across unadjusted and adjusted models, multiple tobacco product outcomes, and various sensitivity analyses. Based on these data, it is unlikely that the high prevalence of adolescent dual users of e-cigarettes and combustible tobacco reported in recent national cross-sectional surveys<sup>2,3</sup> is entirely accounted for by adolescent smokers who later initiate e-cigarette use. Supplementary analyses showed that adolescents who ever (vs never) smoked at baseline were more likely to initiate e-cigarette use during the follow-up period. Collectively, these results raise the possibility that the association between e-cigarette and combustible tobacco use initiation may be bidirectional in early adolescence.

During the age period captured in this study (fall 9th grade to fall 10th grade), adolescents adjust to the transition from

middle school to high school, which is often accompanied by movement to a school with a larger, more diverse student body, new social contexts, increased exposure to older adolescents, and new academic demands.<sup>4</sup> Early adolescence is also a period of uneven brain development in which the neural circuits that underlie motivation to seek out novel experiences develop more rapidly than circuits involving impulse control and effective decision making.<sup>25</sup> Consequently, the expression of a propensity to initiate combustible tobacco use may be heightened during this age period.

The observed association between e-cigarette use and combustible tobacco use initiation may be explained by several mechanisms. It is possible that common risk factors for both e-cigarette and combustible tobacco use are responsible for the use of these 2 products and the order of onset of e-cigarette use relative to combustible tobacco use may not be determined by a causal sequence. Some teens may be more likely to use e-cigarettes prior to combustible tobacco because of beliefs that e-cigarettes are not harmful or addictive,<sup>16,26</sup> youth-targeted marketing,<sup>27</sup> availability of e-cigarettes in flavors attractive to youths,<sup>16,27</sup> and ease of accessing e-cigarettes due to either an absence or inconsistent enforcement of restrictions against sales to minors.<sup>28</sup>

We attempted to analytically address the possible influence of shared risk factors by adjusting for sociodemographic, environmental, and intrapersonal characteristics that presumably could affect use of both types of products. Adjusting for these factors reduced the OR estimates associated with e-cigarette use, but the associations remained statistically significant. In the adjusted models, baseline e-cigarette use was associated with a significant increase in odds of smoking initiation that ranged from 1.75 to 2.96, depending on the outcome.

Although it remains possible that factors not accounted for in this study may explain the association between e-cigarette use and initiation of combustible tobacco use, it is also plausible that exposure to e-cigarettes, which have evolved to become effective nicotine delivery devices, may play a role in risk of smoking initiation. Newer-generation e-cigarette devices with higher-voltage batteries and efficient machinery have been shown to heat e-cigarette solutions to high temperatures, which results in nicotine-rich aerosols that effectively and quickly deliver nicotine to the user, generating desirable psychoactive effects that may carry abuse liability.<sup>29,30</sup>

The neurodevelopmental and social backdrop of early adolescence may promote risk-taking behavior,<sup>25</sup> and neural plasticity may sensitize the adolescent brain to the effects of nicotine.<sup>31</sup> Hence, adolescent never smokers exposed to nicotine-rich e-cigarette aerosols and the pleasant sensations associated with vaping could be more liable to experiment with other nicotine-containing products, including combustible tobacco. Because this is an observational study, and one of the first to address this issue, inferences regarding whether this association is or is not causal cannot yet be made.

The study has several strengths, including a demographically diverse sample, repeated measures of tobacco use, exclusion of ever smokers at baseline, a high follow-up rate, comprehensive assessment of multiple combustible tobacco products, and statistical control for important covariates. A

limitation of the study is that e-cigarette use was measured only as any use and product characteristics (eg, nicotine strength and flavor) were not assessed. Thus, whether a specific frequency or type of e-cigarette use is associated with the initiation of combustible tobacco could not be determined.

This study focuses solely on initiation outcomes; however, future research should evaluate whether e-cigarette use is associated with an increased risk of escalating to regular, frequent use of combustible tobacco. The current sample was drawn from a specific location, which may restrict generalizability.

The age period focused on in this study captured an important, but brief window of susceptibility. In this and other samples,<sup>2,3</sup> youths commonly initiated use of combustible to-

bacco prior to 9th grade and e-cigarette use after 9th grade, suggesting that investigating other ages is warranted. Some important covariates (eg, advertising exposure, sensation seeking, and academic performance) were not assessed and should be included in future work.

## Conclusions

Among high school students in Los Angeles, those who had ever used e-cigarettes at baseline compared with nonusers were more likely to report initiation of combustible tobacco use over the next year. Further research is needed to understand whether this association may be causal.

### ARTICLE INFORMATION

**Author Contributions:** Dr Leventhal had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

**Study concept and design:** Leventhal, Strong, Unger, Sussman, Audrain-McGovern.

**Acquisition, analysis, or interpretation of data:** Leventhal, Strong, Kirkpatrick, Unger, Riggs, Stone, Khoddam, Samet, Audrain-McGovern.

**Drafting of the manuscript:** Leventhal, Sussman, Stone, Khoddam, Samet, Audrain-McGovern.

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**Administrative, technical, or material support:** Kirkpatrick, Sussman, Stone, Khoddam, Samet.

**Study supervision:** Leventhal, Kirkpatrick, Unger, Samet, Audrain-McGovern.

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## Supplementary Online Content

Leventhal AM, Strong DR, Kirkpatrick MG, et al. Association of electronic cigarette use with initiation of combustible tobacco product smoking in early adolescence. *JAMA*. doi:10.1001/jama.2015.8950

**eTable 1.** Characteristics of Participating Schools in Reference to Los Angeles County Schools

**eTable 2.** Prevalence of Past 6-Month Combustible Tobacco Use at 6- and 12-Month Follow-Ups by Baseline Covariate Status among Baseline Never-Smokers

**eTable 3.** Prevalence of Past 6-month E-Cigarette Use at 6- and 12-Month Follow-Ups by Baseline Ever Combustible Tobacco Use Among Baseline Never E-Cigarette Users

**eTable 4.** Association of Baseline Combustible Tobacco Use and Covariates to E-Cigarette Use at 6- and 12-Month Follow Ups among Baseline E-cigarette Never-Users

**eTable 5.** Prevalence of Past 6-Month E-Cigarette Use at 6- and 12-Month Follow-Ups by Baseline Covariate Status among Baseline E-Cigarette Never-Users

**eSensitivity Analyses.**

**eReferences.**

This supplementary material has been provided by the authors to give readers additional information about their work.

**eTable 1.** Characteristics of Participating Schools in Reference to Los Angeles County Schools

Baseline Covariates/ Predictors	School										Los Angeles County*
	1	2	3	4	5	6	7	8	9	10 <sup>a</sup>	
Total School Enrollment, <i>N</i>	1,502	2,664	2,176	1,990	2,403	1,734	2,267	2,153	1,026	-	505,582
Total Study Enrollment, <i>N</i>	313	471	413	435	461	246	459	394	154	50	
Gender, <i>n</i> (%)											
Female	735 (48.9%)	1,287 (48.3%)	1,058 (48.6%)	950 (47.7%)	1,161 (48.3%)	839 (48.4%)	1,094 (48.3%)	1,079 (50.1%)	530 (51.7%)	-	246,904 (48.8%)
Male	767 (51.1%)	1,377 (51.7%)	1,118 (51.4%)	1,040 (52.3%)	1,242 (51.7%)	895 (51.6%)	1,173 (51.7%)	1,074 (49.9%)	496 (48.3%)	-	258,678 (51.2%)
Ethnicity, <i>n</i> (%)											
American Indian/Alaska Native	4 (0.3%)	2 (0.1%)	8 (0.4%)	3 (0.2%)	4 (0.2%)	1 (0.1%)	3 (0.1%)	5 (0.2%)	2 (0.2%)	-	1,925 (0.4%)
Asian/Pacific Islander**	198 (13.2%)	307 (11.5%)	1,412 (64.9%)	556 (27.9%)	200 (8.3%)	72 (4.2%)	213 (9.4%)	105 (4.9%)	842 (82.1%)	-	56,916 (11.3%)
Black/African American	166 (11.1%)	59 (2.2%)	141 (6.5%)	324 (16.3%)	38 (1.6%)	34 (2.0%)	53 (2.3%)	88 (4.1%)	23 (2.2%)	-	44,045 (8.7%)
Hispanic/Latino	1,057 (70.4%)	1,253 (47.0%)	386 (17.7%)	904 (45.4%)	838 (34.9%)	1,548 (89.3%)	1,390 (61.3%)	1,837 (85.3%)	94 (9.2%)	-	320,164 (63.3%)
White	65 (4.3%)	962 (36.1%)	169 (7.8%)	164 (8.2%)	1,225 (51.0%)	59 (3.4%)	535 (23.6%)	103 (4.8%)	49 (4.8%)	-	73,256 (14.5%)
Multi-ethnic/Multi-Racial	12 (0.8%)	81 (3.0%)	60 (2.8%)	39 (2.0%)	98 (4.1%)	20 (1.2%)	73 (3.2%)	15 (0.7%)	16 (1.6%)	-	9,276 (1.8%)
Eligible for Free lunch, <i>n</i> (%)	1,028 (68.4%)	640 (24.0%)	380 (17.5%)	855 (43.0%)	332 (13.8%)	1,334 (76.9%)	881 (38.9%)	1,536 (71.3%)	124 (12.1%)	-	260,894 (51.6%)

Note. Data from U.S. Department of Education, National Center for Education Statistics, Common Core of Data (CCD), "Local Education Agency (School District) Universe Survey", 2012-13 v.1a; "Public Elementary/Secondary School Universe Survey", 2012-13 v.1a. <sup>a</sup>CCD Data unavailable for school number 10. \*\*Combined Asian/Native Hawaiian/Pacific Islander category.

**eTable 2.** Prevalence of Past 6-Month Combustible Tobacco Use at 6- and 12-Month Follow-Ups by Baseline Covariate Status among Baseline Never-Smokers

Outcomes	Covariates									
	Gender		Ethnicity		Living Situation		Family History of Smoking		Substance Use	
	Male (N=1,154)	Female (N=1,328)	Hispanic (N=1,080)	Other (N=1,410)	Lives with Both Biological Parents (N=1,664)	Other (N=802)	Yes (N=1,456)	No (N=933)	Ever Use (N=477)	Never Use (N=2,040)
<b>6-Month Follow-Up</b>										
Any Combustible Tobacco Product, <i>n</i> (%)	117 (10.1%)	134 (10.1%)	142 (13.2%)	111 (7.9%)	153 (9.2%)	99 (12.3%)	167 (11.5%)	75 (8.0%)	101 (22.6%)	152 (7.5%)
Combustible Cigarettes, <i>n</i> (%)	57 (5.0%)	33 (2.5%)	47 (4.4%)	43 (3.1%)	60 (3.6%)	29 (3.6%)	58 (4.0%)	26 (2.8%)	25 (5.6%)	65 (3.2%)
Cigars, <i>n</i> (%)	60 (5.3%)	50 (3.8%)	56 (5.3%)	55 (4.0%)	57 (3.5%)	53 (6.7%)	74 (5.1%)	30 (3.3%)	48 (11.0%)	63 (3.1%)
Hookah, <i>n</i> (%)	66 (5.8%)	96 (7.4%)	102 (9.6%)	61 (4.4%)	102 (6.2%)	60 (7.7%)	105 (7.3%)	53 (5.8%)	66 (15.1%)	97 (4.8%)
Number of Different Combustible Tobacco Products, <i>n</i> (%)										
0 products	1,037 (89.9%)	1,191 (89.9%)	935 (86.8%)	1,298 (92.1%)	1,510 (90.8%)	703 (87.7%)	1,288 (88.5%)	858 (92.0%)	346 (77.4%)	1,887 (92.6%)
1 product	64 (5.6%)	101 (7.6%)	94 (8.7%)	73 (5.2%)	102 (6.1%)	65 (8.1%)	111 (7.6%)	50 (5.4%)	69 (15.4%)	98 (4.8%)
2 products	40 (3.5%)	21 (1.6%)	33 (3.1%)	28 (2.0%)	36 (2.2%)	25 (3.1%)	42 (2.9%)	16 (1.7%)	26 (5.8%)	35 (1.7%)
3 products	13 (1.1%)	12 (0.9%)	15 (1.4%)	10 (0.7%)	15 (0.9%)	9 (1.1%)	14 (1.0%)	9 (1.0%)	6 (1.3%)	19 (0.9%)
<b>12-Month Follow-Up</b>										
Any Combustible Tobacco Product, <i>n</i> (%)	116 (10.2%)	151 (11.4%)	140 (13.0%)	127 (9.1%)	153 (9.2%)	114 (14.3%)	168 (11.6%)	86 (9.3%)	108 (24.2%)	159 (7.8%)
Combustible Cigarettes, <i>n</i> (%)	44 (3.9%)	47 (3.5%)	42 (3.9%)	49 (3.5%)	53 (3.2%)	38 (4.8%)	64 (4.4%)	25 (2.7%)	35 (7.9%)	56 (2.8%)
Cigars, <i>n</i> (%)	71 (6.5%)	57 (4.5%)	65 (6.2%)	63 (4.7%)	70 (4.3%)	58 (7.7%)	72 (5.2%)	48 (5.4%)	54 (12.6%)	74 (3.8%)
Hookah, <i>n</i> (%)	54 (4.9%)	100 (7.8%)	86 (8.2%)	68 (5.1%)	88 (5.5%)	66 (8.8%)	101 (7.2%)	49 (5.5%)	61 (14.3%)	93 (4.8%)

Number of Different Combustible Tobacco Products, n (%)										
0 products	1,027	1,176	940	1,270	1,508	682	1,284	838	338	1,872
	(89.9%)	(88.6%)	(87.0%)	(90.9%)	(90.8%)	(85.7%)	(88.4%)	(90.7%)	(75.8%)	(92.2%)
1 product	75	108	97	86	110	73	112	59	74	109
	(6.6%)	(8.1%)	(9.0%)	(6.2%)	(6.6%)	(9.2%)	(7.7%)	(6.4%)	(16.6%)	(5.4%)
2 products	29	33	33	29	28	34	43	18	26	36
	(2.5%)	(2.5%)	(3.1%)	(2.1%)	(1.7%)	(4.3%)	(3.0%)	(2.0%)	(5.8%)	(1.8%)
3 products	12	10	10	12	15	7	13	9	8	14
	(1.1%)	(0.8%)	(0.9%)	(0.9%)	(0.9%)	(0.9%)	(0.9%)	(1.0%)	(1.8%)	(0.7%)

Note. Sample Ns and respective denominator category Ns range due to missing data on covariates and outcomes. Covariate data not imputed.



**eTable 3.** Prevalence of Past 6-month E-Cigarette Use at 6- and 12-Month Follow-Ups by Baseline Ever Combustible Tobacco Use Among Baseline Never E-Cigarette Users

Baseline Ever Combustible Tobacco Use		Past 6-Month E-Cigarette Use	
Category	Overall Prevalence of Respective Combustible Tobacco Use Category	6-Month Follow-Up	12-Month Follow-Up
Any Combustible Tobacco Product			
Never Use, <i>n</i> (%)	2,305 (86.2%)	192 (8.6%)	148 (6.6%)
Ever Use, <i>n</i> (%)	368 (13.8%)	128 (37.7%)	102 (29.1%)
Difference in prevalence rates, % (95%CI)	-	29.1 (23.8, 34.4)*	22.5 (17.6, 27.3)*
Combustible Cigarettes			
Never Use, <i>n</i> (%)	2,523 (94.4%)	264 (10.8%)	207 (8.5%)
Ever Use, <i>n</i> (%)	149 (5.6%)	56 (40.9%)	43 (29.9%)
Difference in prevalence rates, % (95%CI)	-	30.1 (21.7, 38.4)*	21.4 (13.9, 29.0)*
Cigars			
Never Use, <i>n</i> (%)	2,511 (93.9%)	261 (10.7%)	206 (8.4%)
Ever Use, <i>n</i> (%)	162 (6.1%)	59 (39.3%)	44 (28.6%)
Difference in prevalence rates, % (95%CI)	-	28.6 (20.7, 36.5)*	20.1 (12.9, 27.4)*
Hookah			
Never Use, <i>n</i> (%)	2,450 (92.0%)	239 (10.1%)	185 (7.8%)
Ever Use, <i>n</i> (%)	214 (8.0%)	79 (40.5%)	65 (32.0%)
Difference in prevalence rates, % (95%CI)	-	30.5 (23.5, 37.5)*	24.3 (17.8, 30.8)*
Number of Different Combustible Tobacco Products			
0 products, <i>n</i> (%)	2,305 (86.2%)	192 (8.6%)	148 (6.6%)
1 product, <i>n</i> (%)	242 (9.1%)	74 (32.7%)	64 (27.8%)
2 products, <i>n</i> (%)	95 (3.6%)	42 (48.8%)	26 (28.3%)
3 products, <i>n</i> (%)	31 (1.2%)	12 (42.9%)	12 (41.4%)

Note. Sample includes participants with follow-up data on e-cigarette use. \*Chi-square test,  $p < .001$ .

**eTable 4.** Association of Baseline Combustible Tobacco Use and Covariates to E-Cigarette Use at 6- and 12-Month Follow Ups among Baseline E-cigarette Never-Users

Baseline Regressors and Covariates	Baseline Combustible Tobacco Use Regressor Variable									
	Any Tobacco Product Ever (vs. Never) Use <sup>a</sup>		Cigarettes Ever (vs. Never) use <sup>b</sup>		Cigars Ever (vs. Never) Use <sup>c</sup>		Hookah Ever (vs. Never) Use <sup>d</sup>		Number of Tobacco Products (0 – 3) <sup>e</sup>	
	OR (95%CI) <sup>f</sup>	P	OR(95%CI) <sup>f</sup>	P	OR (95%CI) <sup>f</sup>	P	OR (95%CI) <sup>f</sup>	P	OR (95%CI) <sup>f</sup>	P
<b>Unadjusted Models</b>										
Baseline combustible tobacco use variable	5.82 (4.62, 7.35)	<.001	5.00 (3.60, 6.92)	<.001	4.67 (3.38, 6.43)	<.001	5.51 (4.16, 7.30)	<.001	2.75 (2.39, 3.18) <sup>f</sup>	<.001
Time (12- vs. 6-month follow-up)	0.72 (0.60, 0.87)	<.001	0.73 (0.61, 0.88)	<.001	0.74 (0.61, 0.88)	.001	0.73 (0.61, 0.88)	.001	0.72 (0.60, 0.87)	<.001
Baseline ever combustible tobacco use variable x Time <sup>g</sup>	0.89 (0.59, 1.32)	.55	0.78 (0.45, 1.35)	.37	0.77 (0.45, 1.32)	.35	0.91 (0.56, 1.46)	.69	0.87 (0.68, 1.11)	.27
<b>Adjusted Models</b>										
Categorical covariates										
Female (vs. male)	1.24 (0.99, 1.55)	.06	1.22 (0.97, 1.52)	.08	1.21 (0.97, 1.52)	.09	1.28 (1.03, 1.61)	.03	1.25 (1.00, 1.56)	.05
Hispanic (vs. other) ethnicity	1.07 (0.83, 1.38)	.60	1.05 (0.81, 1.34)	.73	1.04 (0.81, 1.33)	.78	1.01 (0.79, 1.30)	.93	1.04 (0.81, 1.34)	.76
Lives with both biological parents (vs. other living situation)	0.84 (0.68, 1.05)	.13	0.84 (0.68, 1.05)	.12	0.82 (0.66, 1.03)	.09	0.81 (0.65, 1.01)	.06	0.84 (0.68, 1.05)	.13
Substance ever (vs. never) use	1.89 (1.46, 2.44)	<.001	2.50 (1.96, 3.18)	<.001	2.49 (1.93, 3.20)	<.001	2.28 (1.78, 2.91)	<.001	2.03 (1.57, 2.62)	<.001
Family history of smoking	1.10 (0.87, 1.39)	.42	1.12 (0.89, 1.41)	.34	1.13 (0.89, 1.42)	.31	1.09 (0.87, 1.38)	.45	1.10 (0.87, 1.39)	.41

(yes vs. no)										
Continuous covariates <sup>h</sup>										
Age	0.99 (0.89, 1.10)	.82	1.00 (0.90, 1.12)	.93	1.01 (0.91, 1.12)	.84	1.00 (0.90, 1.12)	.94	1.00 (0.90, 1.11)	.97
Parental education	0.95 (0.83, 1.07)	.39	0.94 (0.83, 1.06)	.32	0.94 (0.83, 1.06)	.31	0.93 (0.82, 1.06)	.29	0.94 (0.83, 1.06)	.30
Peer smoking	1.04 (0.93, 1.17)	.48	1.05 (0.94, 1.18)	.37	1.06 (0.94, 1.18)	.35	1.05 (0.94, 1.18)	.38	1.03 (0.92, 1.16)	.56
CESD-Depressive Symptoms	0.99 (0.88, 1.11)	.81	0.97 (0.86, 1.09)	.59	0.97 (0.87, 1.09)	.63	0.98 (0.87, 1.10)	.72	0.99 (0.88, 1.11)	.84
TCI-Impulsivity	1.21 (1.09, 1.35)	<.001	1.22 (1.09, 1.36)	<.001	1.21 (1.09, 1.35)	<.001	1.21 (1.08, 1.35)	<.001	1.22 (1.10, 1.36)	<.001
Delinquent Behavior	1.22 (1.07, 1.40)	.003	1.31 (1.15, 1.49)	<.001	1.30 (1.14, 1.48)	<.001	1.24 (1.09, 1.42)	.001	1.22 (1.07, 1.39)	.004
Smoking susceptibility	1.09 (0.95, 1.24)	.21	1.09 (0.95, 1.25)	.20	1.16 (1.02, 1.32)	.03	1.14 (1.00, 1.30)	.06	1.07 (0.93, 1.22)	.33
Smoking expectancies	1.13 (1.00, 1.27)	.05	1.14 (1.01, 1.28)	.04	1.14 (1.01, 1.29)	.03	1.14 (1.01, 1.29)	.03	1.14 (1.01, 1.28)	.04
Regressors										
Baseline ever combustible tobacco use variable	3.05 (2.31, 4.03)	<.001	1.88 (1.28, 2.76)	.001	1.43 (0.98, 2.09)	.06	2.94 (2.16, 3.99)	<.001	1.75 (1.46, 2.09) <sup>i</sup>	<.001
Time (12- vs. 6-month follow-up)	0.71 (0.59, 0.86)	<.001	0.72 (0.60, 0.87)	<.001	0.72 (0.60, 0.87)	<.001	0.72 (0.60, 0.87)	<.001	0.72 (0.59, 0.87)	<.001
Baseline combustible tobacco use variable x Time <sup>g</sup>	0.89 (0.59, 1.33)	.56	0.78 (0.44, 1.38)	.39	0.78 (0.45, 1.35)	.37	0.92 (0.56, 1.50)	.73	0.88 (0.69, 1.13)	.32

Note. All analyses include only never users of combustible tobacco products at baseline. -2 Res Log Pseudo-Likelihood fit index for unadjusted models without the interaction term: <sup>a</sup>26,375.48, <sup>b</sup>25,946.03, <sup>c</sup>25,937.55, <sup>d</sup>25,986.36, <sup>e</sup>26,211.32. -2 Res Log Pseudo-Likelihood fit index for unadjusted models with the interaction term: <sup>a</sup>26,364.92, <sup>b</sup>25,938.1, <sup>c</sup>25,928.98, <sup>d</sup>25,982.23, <sup>e</sup>26,199.99. Range of -2 Res Log Pseudo-Likelihood fit indices for adjusted models without the interaction term across the five imputed data sets: <sup>a</sup>26,817.48 – 26,838.87, <sup>b</sup>26,664.97 – 26,689.90, <sup>c</sup>26,663.48 – 26,691.34, <sup>d</sup>26,660.61 – 26,691.55, <sup>e</sup>26,695.88 – 26,722.52. Range of -2 Res Log Pseudo-Likelihood fit indices for adjusted models with the interaction term across the five imputed data sets: <sup>a</sup>26,806.89 – 26,827.96, <sup>b</sup>26,656.18 – 26,680.96, <sup>c</sup>26,653.08 – 26,680.67, <sup>d</sup>26,656.94 – 26,687.71, <sup>e</sup>26,683.8 – 26,709.99. <sup>i</sup>OR from binary repeated logistic regression model predicting e-cigarette use at follow-ups from baseline ever use of the respective combustible tobacco product variable including school fixed effects. <sup>g</sup>Interaction term added in subsequent model; parameter estimates for other regressors/covariates are from model excluding the interaction term. <sup>h</sup>Continuous covariates rescaled ( $M=0$ ,  $SD=1$ ), such that the ORs indicate the change in odds in the outcome associated with an increase in one standard deviation unit on the covariate continuous scale. <sup>i</sup>OR indicates the change in odds of e-cigarette use averaged across the two follow-ups associated with an increase in one tobacco product used at baseline. CESD = Center for Epidemiologic Studies Depression Scale. TCI = Temperament and Character Inventory.

**eTable 5.** Prevalence of Past 6-Month E-Cigarette Use at 6- and 12-Month Follow-Ups by Baseline Covariate Status among Baseline E-Cigarette Never-Users

	Covariates									
	Gender		Ethnicity		Living Situation		Family History of Smoking		Substance Use	
E-Cigarette Use in the Prior 6 Months	Male (N=1,160)	Female (N=1,429)	Hispanic (N=1,170)	Other (N=1,429)	Lives with Both Biological Parents (N=1,719)	Other (N=853)	Yes (N=1,534)	No (N=955)	Ever Use (N=584)	Never Use (N=2,010)
6-Month Follow-Up, n (%)	141 (12.2%)	179 (12.6%)	182 (15.8%)	138 (9.7%)	188 (11.0%)	131 (15.4%)	214 (14.0%)	96 (10.1%)	156 (27.0%)	164 (8.2%)
12-Month Follow-Up, n (%)	126 (10.9%)	123 (8.6%)	119 (10.2%)	131 (9.2%)	143 (8.3%)	105 (12.3%)	165 (10.8%)	73 (7.6%)	124 (21.2%)	126 (6.3%)

Note. Total sample Ns and respective denominator category Ns range due to missing data on covariates and outcomes. Covariate data not imputed.



## eSensitivity Analyses

We categorized the sample of baseline never-smokers into ‘non-users’ (reported no past 6-month use of any tobacco product at both follow-ups;  $n=2,007$  [83.4%]), ‘experimenters’ (past 6-month use of any combustible product at 6-month but not 12-month follow-up;  $n=139$  [5.8%]), ‘later initiators’ (reported past 6-month use of any combustible product at 12-month but not 6-month follow-up;  $n=161$  [6.7%]), and ‘sustained users’ (reported past 6-month use of any combustible product at both follow-ups;  $n=99$  [4.1%]). A polytomous generalized linear mixed model (GLMM) using a generalized logit function including school and baseline ever e-cigarette use as fixed effects with ‘non-users’ as the reference category showed that baseline ever (vs. never) e-cigarette users were more likely to be ‘experimenters’ ( $OR[95\% CI]=7.92[5.18, 12.11]$ ;  $n=43[20.5\%]$  vs.  $n=96[4.4\%]$ , % difference [95% CI]=16.1[8.2, 25.0]), ‘later initiators’ ( $OR[95\% CI]=4.74[3.04, 7.40]$ ;  $n=33[15.7\%]$  vs.  $n=128[5.8\%]$ , % difference [95% CI]=9.9[2.75, 17.1]), or ‘sustained users’ ( $OR[95\% CI]=4.33[2.53, 7.41]$ ;  $n=21[10.0\%]$  vs.  $n=78[3.6\%]$ , % difference [95% CI]= 6.4[0.5, 12.3]) of combustible tobacco.

To clarify the role of blunt use in the findings, post-hoc analyses excluding blunts from the cigar use classifications were performed. Past 6-month non-blunt cigar use was more prevalent in baseline ever (vs. never) e-cigarette users at the 6-month ( $n=13[5.4\%]$  vs.  $n=26[1.1\%]$ , % difference [95% CI], 4.3[1.4, 7.2]) and 12-month ( $n=19[8.4\%]$  vs.  $n=57[2.6\%]$ , % difference [95% CI], 5.8[2.1, 9.5]) follow-ups.

To examine the impact of attrition, the unadjusted and adjusted GLMMs for the any combustible tobacco product outcome using the same strategy as the primary analysis were refit under the assumption that participants with missing data had used combustible tobacco at that follow-up, and then assuming that participants with missing data had not used at the respective follow-up. Under both conditions, baseline e-cigarette ever use was associated with any combustible tobacco use at follow-ups in all models.

Following from prior work,<sup>1</sup> participants were characterized as possible mischievous responders based on extreme responses on index variables. Adolescents were categorized into those who were 2.5 SD above or below the mean for height, weight, and delinquent behaviors versus those who were not. From there, an ‘extreme responder’ score was created based on the number of extreme responses across these three variables (zero vs. one vs. two vs. three). Among baseline e-cigarette ever-users, the proportions in each extreme responder score category were: zero ( $n=201$ , 89.3%), one ( $n=20$ , 8.9%), two ( $n=3$ , 1.3%), and three ( $n=1$ , 0.4%). The corresponding proportions of extreme responder score categories among baseline e-cigarette never-users were: zero ( $n=2145$ , 91.9%), one ( $n=155$ , 6.6%), two ( $n=30$ , 1.3%), and three ( $n=3$ , 0.1%). The extreme responder score proportions did not significantly differ between baseline e-cigarette ever (vs. never) users ( $p=0.40$ ), suggesting that mischievous responses did not account for the associations involving e-cigarette use found in the primary analysis.

### **eReferences**

1. Robinson-Cimpian JP. Inaccurate estimation of disparities due to mischievous responders: Several suggestions to assess conclusions. *Educational Researcher*. 2014;43(4):171-185.