



Published in final edited form as:

*Drug Alcohol Depend.* 2021 March 01; 220: 108496. doi:10.1016/j.drugalcdep.2020.108496.

## Bidirectional associations between e-cigarette use and alcohol use across adolescence

Alyssa Lozano<sup>a</sup>, Feifei Liu<sup>b</sup>, Tae Kyoung Lee<sup>a</sup>, Guillermo Prado<sup>c</sup>, Seth J. Schwartz<sup>a,d</sup>, Adam M. Leventhal<sup>b</sup>, Annemarie R. Kelleghan<sup>b,e</sup>, Jennifer B. Unger<sup>b</sup>, Jessica L. Barrington-Trimis<sup>b,\*</sup>

<sup>a</sup>Department of Public Health Sciences, University of Miami Miller School of Medicine, 1120 NW 14th Street, Miami, FL, 33136, USA

<sup>b</sup>Department of Preventive Medicine, Keck School of Medicine, University of Southern California, 2001 N. Soto Street, Los Angeles, CA, 90089, USA

<sup>c</sup>School of Nursing and Health Studies, University of Miami, Coral Gables, FL, 33143, USA

<sup>d</sup>Departments of Kinesiology, Health Education, and Counseling Psychology, College of Education, University of Texas at Austin, 1912 Speedway, Stop D5000, Austin, TX, 78712, USA

<sup>e</sup>Department of Psychology, University of Southern California, 3620 S. McClintock Ave. SGM 501, Los Angeles, CA, 90089, USA

### Abstract

**Introduction:** Evidence on prospective bidirectional associations between e-cigarette and alcohol use among adolescents can inform prevention and policy but is largely absent from the literature.

**Methods:** Data were drawn from a prospective cohort of students attending 10 Los Angeles high schools ( $N = 3396$ ; baseline mean age = 14.1,  $SD = 0.4$ ). Students completed surveys every 6-months from 2013 to 2017; 8 total waves. Analyses were restricted to (a) individuals who were never users of alcohol ( $N = 2394$ ) or (b) individuals who were never users of e-cigarettes ( $N = 2704$ ) at baseline. Repeated-measures, generalized linear mixed models were used to estimate the adjusted odds of past 6-month alcohol and e-cigarette initiation, in separate models.

**Results:** Among alcohol never-users at baseline, 15.7 % ( $N = 375$ ) initiated alcohol use over the study period. Compared to never-users of e-cigarettes, those who reported use of e-cigarettes had 3.5 times the odds of subsequently initiating alcohol use in the following wave ( $OR = 3.54$ ; 95 %

\*Corresponding author at: Department of Preventive Medicine, Keck School of Medicine, University of Southern California, 2001 N. Soto Street, 312G, Los Angeles, CA, 90089, USA. jtrimis@usc.edu (J.L. Barrington-Trimis).

#### Contributors

Ms. Lozano formulated the research question, interpreted the results, wrote and edited the manuscript, and approved the manuscript as submitted. Ms. Liu conducted the analyses, contributed to interpretation of the results, critically reviewed the manuscript, and approved the manuscript as submitted. Drs. Lee, Prado, and Schwartz contributed to formulating the research question, interpretation of results, editing the manuscript, and approved the manuscript as submitted. Dr. Leventhal designed the study, collected data, critically reviewed the manuscript, and approved the manuscript as submitted. Ms. Kelleghan contributed to interpretation of the results, wrote and edited the manuscript, critically reviewed the manuscript, and approved the manuscript as submitted. Dr. Unger contributed to formulating the research question and interpretation of the results, wrote, edited, and critically reviewed the manuscript, and approved the manuscript as submitted. Dr. Barrington-Trimis contributed to formulating the research question and interpretation of the results, provided oversight and mentorship to the first-author regarding the scope and design of the manuscript, critically reviewed the manuscript, and approved the manuscript as submitted.

CI: 2.81, 4.47). Stronger associations were observed for males (OR = 4.94; 95 % CI: 3.78, 6.45) than for females (OR = 3.21; 95 % CI: 2.33, 4.41;  $p_{\text{interaction}} = 0.04$ ). Among e-cigarette never-users at baseline, 26.3 % (N = 709) initiated e-cigarette use over the study period. Compared to never-users of alcohol, those who reported use of alcohol had 3.2 times the odds of subsequently initiating e-cigarette use in the following wave (OR = 3.23; 95 % CI: 2.68, 3.89). This association did not differ by gender.

**Conclusions:** E-cigarette and alcohol use can be markers to identify youth at risk for future alcohol and e-cigarette use, respectively. Research examining mechanisms underlying these associations is needed to infer causality.

## Keywords

e-Cigarettes; Alcohol; Adolescence; Longitudinal analysis; Tobacco

## 1. Introduction

E-cigarettes have been the most commonly used tobacco product in the United States among adolescents since 2014 (Gentzke et al., 2019; Wang et al., 2018). Most e-cigarettes contain nicotine (Morean et al., 2016), which is addictive and adversely affects the developing adolescent brain (England et al., 2015; Yuan et al., 2015). Adolescent e-cigarette users with no history of combustible cigarette use are at elevated risk of subsequently initiating use of combustible cigarettes (Soneji et al., 2017) and may progress to more frequent and heavier cigarette use (i.e., increased number of days smoked and amount of cigarettes smoked) compared to those who have not used e-cigarettes (Barrington-Trimis et al., 2018; Leventhal et al., 2016). Several studies also have found that e-cigarette use is associated with subsequent initiation of alcohol use (Cho et al., 2018; Curran et al., 2018; Kristjansson et al., 2015; Unger et al., 2016).

Alcohol is the most commonly used *substance* among youth (Johnston et al., 2019) and has historically been the first substance that adolescents consume (Barry et al., 2016). As with nicotine, alcohol exerts potentially damaging effects on adolescent brain development (Squeglia and Gray, 2016). Use of alcohol in adolescence can lead to problematic drinking behaviors in adulthood (Temmen and Crockett, 2018; Tubman et al., 2019). However, the association of alcohol use with subsequent e-cigarette initiation has not been established.

Most research examining co-occurring patterns of e-cigarette and alcohol use is cross-sectional and focused on young adults (Hefner et al., 2019; Roys et al., 2019; Saddleson et al., 2015; Thrul et al., 2019). However, both of these products are commonly experimented within adolescence (Hoffman et al., 2001) and are mutually reinforcing (Hershberger and Cyders, 2017). Specifically, using nicotine increases alcohol cravings, decreases the subjective effects of alcohol, and increases alcohol consumption (Verplaetse and McKee, 2017). Similarly, alcohol consumption increases the craving to smoke, predicts earlier smoking initiation, and is associated with greater frequency of smoking (Verplaetse and McKee, 2017). Given the risks associated with use of e-cigarettes and alcohol individually and simultaneously, it is imperative to examine the potential bidirectionality of initiation of these two substances.

This study investigated the association of e-cigarette use with subsequent alcohol use initiation, and of alcohol use with subsequent e-cigarette use initiation, using 8 waves of data collected every 6 months (Fall 2013-Spring 2017) from a prospective cohort of high school-aged adolescents in Southern California. Given differences in rates of substance use by gender and ethnicity, we also explored whether any observed bidirectional associations differed as a function of gender or ethnicity.

## 2. Methods

### 2.1. Participants and procedures

Data were collected as part of the Happiness & Health Study, a prospective cohort study of substance use and mental health among high school students in the Los Angeles, CA, metropolitan area. Data collection involved 8 assessment waves occurring each semester (every 6-months) from Fall 2013 (9th grade) to Spring 2017 (12th grade). At each wave, paper-and-pencil surveys were administered in students' classrooms. Students not in class during data collections completed telephone or internet surveys. All 4100 English-speaking, 9th-grade students not enrolled in special education classes were eligible to participate. Of the 3874 assenting students (94.5 %), 3396 parents (87.7 %) provided consent. Data were collected from 3383 participants at baseline, 3292 (97.0 %) at the 6-month follow-up, 3281 (96.6 %) at the 12-month follow-up, 3251 (96 %) at the 18-month follow-up, 3232 (96 %) at the 24-month follow-up, 3078 (91 %) at the 30-month follow-up, 3168 (94 %) at the 36-month follow-up, and 3140 (94 %) at the 42-month follow-up.

### 2.2. Ethics statement

The University of Southern California Institutional Review Board approved the study. Written or verbal parental consent and student assent were obtained prior to data collection.

### 2.3. Measures

**2.3.1. e-Cigarette and alcohol use**—At baseline, participants were asked whether they had ever used e-cigarettes or alcohol (not including drinking a few sips of wine for religious purposes) (yes/no). Responses to these two items were used to establish the two analytic samples: (1) baseline alcohol never users to examine associations with alcohol initiation and (2) e-cigarette never users at baseline to examine associations with subsequent e-cigarette initiation. At each subsequent wave, participants reported past 6-month use (yes/no) of e-cigarettes and alcohol, which were used to determine initiation of each product among those who had not previously used that product. Because surveys were administered every 6 months, assessment of past 6-month use is sufficient to determine any initiation of a product between waves.

#### 2.3.2. Covariates

**2.3.2.1. Sociodemographic characteristics:** Sociodemographic characteristics, including age, gender (male/female), race/ethnicity (recoded to Hispanic, Non-Hispanic White, or other because of small numbers of African Americans and Asian Americans), and highest parental education level (some high school or less, high school graduate, some college,

college graduate, advanced degree, don't know or missing), were assessed using self-report responses.

**2.3.2.2. Other tobacco product use.:** At baseline, participants reported lifetime (yes/no) use of any other tobacco products (e.g. cigarettes, smokeless tobacco, big cigars, little cigars or cigarillos, hookah water pipe, blunts, or other forms of tobacco). These questions were used to create a composite variable for any prior tobacco product use (yes/no).

**2.3.2.3. Other covariates.:** We considered the following potential baseline and time-varying covariates that have been strongly associated with e-cigarette and alcohol use in prior literature (General, 2016; Smit et al., 2018):

**2.3.2.3.1. Baseline covariates.:** Family living situation (“Who do you live with most of the time?” both biological parents vs other); depressive symptoms, using the 20-item Center for Epidemiologic Studies Depression Scale (Radloff, 1991); impulsivity, using the 5-item Temperament and Character Inventory impulsivity subscale (Cloninger et al., 1994); delinquent behavior, measured using a sum of frequency ratings for 11 different behaviors (e.g. lying to parents, stealing) (Thompson et al., 2007).

**2.3.2.3.2. Time-varying covariates.:** In models evaluating the association of e-cigarette use with subsequent alcohol initiation, we considered the following time-varying covariates as potential confounders of the association: benefits of alcohol use (“I think I might enjoy, experience pleasure, or feel good using alcohol” [4-option Likert-type scale, strongly disagree-strongly agree]), risk perceived with alcohol use (“I think I might feel bad, sick or embarrassed using alcohol” [4-option Likert-type scale, strongly disagree-strongly agree]), number of friends using alcohol (0–5 friends), susceptibility to alcohol use (3 items: use if friends were to offer [definitely not — definitely yes], intention to use in the next 6 months [definitely not — definitely yes], curiosity about use [definitely not — definitely yes]). In models evaluating the association of alcohol use with subsequent e-cigarette initiation, we similarly considered the following time-varying covariates as potential confounders of the association: benefits of e-cigarette use, risks associated with e-cigarette use, number of friends using e-cigarettes, and susceptibility to e-cigarette use.

## 2.4. Data analysis

Generalized linear mixed models relating a time-varying binary outcome  $Y_{ij}$  for person  $i$  at wave  $j$  ( $j = 1, \dots, 8$ ) were estimated:

$$\text{logodds}(Y_{ij} = 1) = \beta_0 + \beta_1 x_{i,j-1} + \dots + U_i$$

to a time-varying  $x_{i,j-1}$  (lagged to the previous wave) with a normally distributed participant-level random intercept ( $U_i$ ) to account for the within-participant correlation inherent in repeated measures analyses. In Model 1,  $Y_{ij}$  was alcohol initiation and  $x_{i,j-1}$  was e-cigarette use. Thus,  $\beta_1$  is an average time lagged effect of e-cigarette use across 8 waves. In Model 2,  $Y_{ij}$  was e-cigarette use and  $x_{i,j-1}$  was alcohol initiation. All models were initially adjusted for wave (as a categorical variable), gender, race/ethnicity, parental education, school, and

lifetime tobacco product use at wave 1. Additional variables (see “other covariates” above) were evaluated to determine whether any other factors confounded the main associations, as noted by a change in the effect estimate of more than 15 % (Kleinbaum et al., 2013); no other variables confounded either association, and thus were not included in final models. For categorical covariates with missing values for some observations, these observations were retained by including a missing category. We included an interaction term to evaluate whether effect estimates differed by gender (e.g., baseline e-cigarette use x gender), or ethnicity (Hispanic, Non-Hispanic White, and other). We also examined whether estimates differed over time (by wave); no differences in estimates by wave were observed. Statistical analyses were conducted using “proc glimmix” in SAS version 9.4 (SAS Institute Inc).

### 3. Results

#### 3.1. Descriptive analyses

The majority of the sample was female (51.9 %), and 14 years of age at baseline (81.9 %). The sample was 42.4 % Hispanic, 40.8 % Non-Hispanic White, and 16.8 % Other. Among alcohol never-users, 51.1 % (N = 1224) initiated alcohol use over the subsequent 3.5 years, and among e-cigarette never-users, 32.7 % (N = 884) initiated e-cigarette use over the subsequent 3.5 years. Table 1 displays participants’ sociodemographic characteristics.

#### 3.2. Associations between baseline e-cigarette use and alcohol use at follow-up assessments

Among those with no history of alcohol use at baseline, past 6-month e-cigarette use (vs. no e-cigarette use) was associated with greater odds of alcohol use initiation in the subsequent 6 months, after adjusting for covariates (OR, 3.95 [95 %CI, 3.22–4.83]) (Table 2).

#### 3.3. Associations between baseline alcohol use and e-cigarette use at follow-up assessments

Among those with no history of e-cigarette use at baseline, past 6-month alcohol use (vs. no alcohol use) was associated with greater odds of e-cigarette use initiation in the subsequent 6 months, after adjusting for covariates (OR, 3.23 [95 %CI, 2.68–3.89]) (Table 2).

#### 3.4. Interaction by gender and race/ethnicity

The association of e-cigarette use with subsequent alcohol initiation was stronger for males (OR, 4.94; [95 % CI, 3.78–6.45]) than for females (OR, 3.21; [95 % CI, 2.33–4.41]; p-interaction = 0.04; Table 3). No difference was observed by gender for the association of alcohol use with subsequent e-cigarette initiation (males: OR, 3.87; [95 % CI, 3.03–4.96]; females: OR, 3.94; [95 % CI, 3.23–4.82]; p-interaction = 0.91). Estimates of the association of e-cigarette use with subsequent alcohol initiation or alcohol use with subsequent e-cigarette initiation did not differ by race/ethnicity.

### 4. Discussion

E-cigarette use was associated with a greater likelihood of subsequent alcohol use initiation, and alcohol use was associated with greater odds of subsequent e-cigarette use initiation.

Stronger associations of e-cigarette use with subsequent alcohol use were observed for males (vs. females). Findings were robust to adjustment for a number of potential confounders.

There are likely multiple mechanisms underlying these associations. First, it is possible that these associations are due (in part) to peer influences. Adolescence is a time when there is a substantive emphasis on relationships with peers. Adolescents often seek approval from other peers (Leung et al., 2014), which in turn makes them subject to peer influence (Gray and Squeglia, 2018). The popularity and acceptance of e-cigarettes among peers (Barrington-Trimis et al., 2015; Kong et al., 2014; Park et al., 2019) is a primary reason for adolescent e-cigarette use. Further, peer use of e-cigarettes is identified as a stronger risk factor for subsequent e-cigarette initiation compared to use by family members or those living in the adolescent's home (Urman et al., 2018). Adolescents also typically perceive that more peers are using e-cigarettes than are actually doing so (Gorukanti et al., 2017).

Similar findings have been reported for alcohol use; a recent study reported that adolescents were more likely to report alcohol use themselves if they believed that their best friend used alcohol (Colder et al., 2017; Jacobs et al., 2016; Leung et al., 2014; Schuler et al., 2019; Trucco, 2020). Adolescents' perceptions of their peers' alcohol use has also been associated with increases in positive alcohol expectancies and with decreases in negative alcohol expectancies (Colder et al., 2017; Trucco et al., 2011). The bidirectional associations of e-cigarette use with subsequent alcohol use, and alcohol use with subsequent e-cigarette use, could thus result from peer influences. Adolescents may perceive that use of e-cigarettes and alcohol may facilitate peer approval and acceptance (Camenga et al., 2018a; Sellers et al., 2018). For example, adolescents previously only using e-cigarettes may use alcohol to obtain additional peer approval or acceptance; similarly, those using alcohol only may seek additional peer approval via use of e-cigarettes. Peer influences may override the decision making process among youth, who often favor immediate rewards (i.e., peer acceptance or approval) over concerns about future consequences (e.g., consequences of substance use, including addiction, adverse health effects, etc.) (Somerville et al., 2010). Given that nicotine and alcohol both affect brain regions associated with the rewarding properties of drugs of abuse (Verplaetse and McKee, 2017), combined exposure to both alcohol and nicotine may promote incentivized learning processes by which adolescents may develop substance use disorders in adulthood (Spoelder et al., 2015). If e-cigarettes and alcohol are both used at social events, adolescents using one of these substances may be exposed to, have increased access to, and experience potentially increased peer pressure to use, the other substance.

The association of e-cigarette use with subsequent alcohol initiation and of alcohol use with subsequent e-cigarette initiation could also be due to the overall normalization of substance use and of co-use of multiple substances. Over time, e-cigarette and alcohol use have become less stigmatized and more accepted as normative behavior (Sznitman and Taubman, 2016). Norms have been further supported via exposure to normalization of use on social media. Several studies have reported that never-users of e-cigarettes who were exposed to advertising on social media were more likely to subsequently initiate e-cigarette use (Camenga et al., 2018b; Pokhrel et al., 2018a, b), and adolescents who are more frequently exposed to alcohol-related media content were more likely to believe that a greater number



of their friends consume alcohol and that such use is socially acceptable (Beullens and Vandebosch, 2016; Moreno and Whitehill, 2014; Unger et al., 2003). Youth using one substance may be exposed to social media portraying use of the other substance, or co-use of both e-cigarettes and alcohol (which are commonly used together), thus increasing the likelihood that users of one product may initiate use of the other.

Given that e-cigarette use and alcohol use appear to be mutually reinforcing, and polysubstance use emerges during adolescence and early adulthood (Choi et al., 2018; Delk et al., 2019), prevention programs targeting peer group norms of alcohol and nicotine use at early developmental stages might be especially beneficial for adolescents (i.e., prior to onset of polysubstance use) (Zheng et al., 2019). Perceived peer norms are related to adolescents' interpretations of the images that they see in the media (Elmore et al., 2017); it is thus imperative to address the multiple factors that may contribute to youths' initiation of e-cigarette and/or alcohol use. Media literacy – defined as an individual's ability to evaluate and access marketing messages and make interpretations based on those messages (Aufderheide, 1993; Jackson et al., 2018) – may serve as a key target for interventions to reduce media influences on adolescent substance use. Such interventions could be tailored to counter specific types of advertisements and influences (e.g. social media, portrayals in entertainment), and to multiple substances, providing analytical thinking skills and techniques to help youth understand these messages and ways to offset them.

The present study was characterized by several strengths, including the use of repeated measures in 8 waves of data collected over 4 years in a demographically diverse sample, with a high retention rate of the cohort. Further, we considered confounding by a number of different variables, including impulsivity, depressive symptoms, delinquent behavior, perceptions of risk and benefit associated with use, and susceptibility to use. Despite these strengths, several limitations remain. Characteristics of e-cigarettes (e.g., nicotine strength, type of nicotine [salted vs. freebase] and flavor) were not assessed, so we were unable to determine whether frequency of use or type of e-cigarette used was differentially associated with initiation of alcohol use. We also did not have specific data on characteristics of alcohol products (e.g., type of alcohol [beer or wine vs. hard liquor]) to determine whether such characteristics may be differentially associated with subsequent e-cigarette initiation. The self-report nature of the survey may have introduced social desirability bias. There may also be unmeasured confounders of the associations observed in this sample. Finally, this sample was drawn from a specific region of the United States. As such, results may not be generalizable to other geographic locations with different norms surrounding alcohol and e-cigarette use.

## 5. Conclusion

Adolescent e-cigarette use was associated with subsequent alcohol use initiation, and alcohol use was associated with subsequent e-cigarette use initiation. Although it is unclear what mechanisms may underlie these bidirectional associations, prevention and intervention efforts could be used to simultaneously reduce use of e-cigarettes and alcohol. Future studies should consider an examination of these associations from a developmental perspective to

elucidate mechanisms underlying these associations and to develop targeted prevention and intervention efforts.

## Acknowledgements

Research reported in this publication was supported by grant numbers K01DA042950 and R01DA033296 from the National Institute for Drug Abuse at NIH, grant R01CA229617 from the National Cancer Institute, grant U54CA180905 from the National Cancer Institute and Food and Drug Administration Center for Tobacco Products, and grant 27-IR-0034 from the Tobacco Related Disease Research Program (TRDRP).

### Role of funding source

Research reported in this publication was supported by grant numbers K01DA042950 and R01DA033296 from the National Institute for Drug Abuse at NIH, grant R01CA229617 from the National Cancer Institute, grant U54CA180905 from the National Cancer Institute and Food and Drug Administration Center for Tobacco Products, and grant 27-IR-0034 from the Tobacco Related Disease Research Program (TRDRP). The funder had no role in the design and conduct of the study; collection, management, analysis, or interpretation of the data; preparation, review, or approval of the manuscript; or decision to submit the manuscript for publication.

## Abbreviations:

<b>OR</b>	odds ratio
<b>CI</b>	confidence interval

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**Table 1**

Demographic characteristics of the analytic sample of never e-cigarette users and never alcohol users.

	Never Alcohol Users N (col %)	Never E-Cigarette Users N (col %)
<b>Gender</b>		
Female	1242 (51.9)	1488 (55.0)
Male	1152 (48.1)	1216 (45.0)
<b>Age</b>		
12–13	131 (5.5)	139 (5.1)
14	1960 (81.9)	2222 (82.2)
15–16	282 (11.8)	317 (11.7)
Don't know	21 (0.9)	26 (1.0)
<b>Race/Ethnicity</b>		
Hispanic	1016 (42.4)	1245 (46.0)
Other	976 (40.8)	1009 (37.3)
White	402 (16.8)	450 (16.6)
<b>Highest Parental Education Level</b>		
Don't know	339 (14.2)	368 (13.6)
8th or less	66 (2.8)	91 (3.4)
Some high school	154 (6.4)	190 (7.0)
High school graduate	303 (12.7)	373 (13.8)
Some college	388 (16.2)	446 (16.5)
College graduate	707 (29.5)	761 (28.1)
Advanced degree	437 (18.3)	475 (17.6)
<b>Wave 1 Tobacco Use</b>		
No	2129 (88.9)	2300 (85.1)
Yes	240 (10.0)	375 (13.9)
<b>Any Alcohol Initiation Across Follow-up</b>		
No	1170 (48.9)	-
Yes	1224 (51.1)	-
<b>Any E-cigarette Initiation Across Follow-up</b>		
No	-	1820 (67.3)
Yes	-	884 (32.7)

**Table 2**

Association of E-cigarette Use (or Alcohol use) with Initiation of Alcohol (or E-cigarette Use) at Subsequent 6-Month Follow-up.

	<b>Initiation of Other Product at Subsequent 6 Month Follow-up</b>		<b>Odds Ratio (95 % CI)<sup>b</sup></b>	<b>P-value</b>
	<b>No N<sup>a</sup> (%)</b>	<b>Yes N (%)</b>		
Past 6-month use of E-Cigarettes				
No	9724 (90.1)	1069 (9.9)	Ref	
Yes	349 (69.2)	155 (30.8)	3.54 (2.81, 4.47)*	<.0001
Past 6-month use of Alcohol				
No	11,342 (95.1)	581 (4.9)	Ref	
Yes	1771 (85.4)	303 (14.6)	3.23 (2.68, 3.89)*	<.0001

<sup>a</sup>Frequency is noted for observations.

<sup>b</sup>Model adjusted for age, gender, race/ethnicity, highest parental education, school, wave, and history of any tobacco product use.

**Table 3**

Differential Association of E-cigarette Use (or Alcohol use) with Initiation of Alcohol (or E-cigarette Use) at Subsequent 6-Month Follow-up by Gender.

		Males			Females				
		Initiation of Other Product at Subsequent 6 Month Follow-up			Initiation of Other Product at Subsequent 6 Month Follow-up				
		No N (%)	Yes N (%)	Odds Ratio (95 % CI) <sup>a</sup>	No N (%)	Yes N (%)	Odds Ratio (95 % CI) <sup>a</sup>	P-value	Interaction
Ever use of E-Cigarettes									
No	4795 (91.5)	447 (8.5)		Ref	4929 (88.8)	622 (11.2)	Ref		0.04
Yes	206 (68.4)	95 (31.6)		4.94 (3.78, 6.45)	143 (70.4)	60 (29.6)	3.21 (2.33, 4.41)		
Ever use of Alcohol									
No	5177 (94.4)	305 (5.6)		Ref	6165 (95.7)	276 (4.3)	Ref		0.91
Yes	546 (83.5)	108 (16.5)		3.87 (3.03, 4.96)	1225 (86.3)	195 (13.7)	3.94 (3.23, 4.82)		

<sup>a</sup>Model adjusted for age, gender, race/ethnicity, highest parental education, school, wave and history of any tobacco product use.