Adolescent E-Cigarette, Hookah, and Conventional Cigarette Use and Subsequent Marijuana Use

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abstract

OBJECTIVES: Noncigarette tobacco products may confer a risk of marijuana use similar to combustible cigarettes. We examined whether adolescent electronic cigarette (e-cigarette), hookah, or combustible cigarette use is associated with initiating and currently using marijuana as well as using both tobacco and marijuana concurrently.

METHODS: Adolescents from 10 public schools in Los Angeles, California, completed in-classroom surveys at baseline (fall 2013, ninth grade) and at a 24-month follow-up (fall 2015, 11th grade). Among adolescents who never used marijuana at baseline (N = 2668), associations of baseline e-cigarette, hookah, or combustible cigarette use with ever marijuana use (initiation), current marijuana use (past 30 days), and current dual use of marijuana and these tobacco products at the 24-month follow-up were examined.

RESULTS: Baseline ever versus never e-cigarette use was associated with initiation (odds ratio [OR] 3.63; 95% confidence interval [CI] 2.69–4.90) and current (OR 3.67; 95% CI 2.51–5.36) marijuana use 24 months later. Ever versus never hookah use was associated with initiation (OR 3.55; 95% CI 2.49–5.08) and current (OR 4.10; 95% CI 2.69–6.25) marijuana use 24 months later. Similar associations were observed for combustible cigarette smoking and initiation (OR 4.30; 95% CI 2.79–6.63) and current use of marijuana (OR 1.97; 95% CI 1.05–3.68). Current use of any of these tobacco products at baseline was associated with current use of both tobacco and marijuana (OR 2.28; 95% CI 1.47–3.55) 24 months later.

CONCLUSIONS: The association between tobacco use and subsequent marijuana use across adolescence extends to multiple tobacco products.

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WHAT'S KNOWN ON THIS SUBJECT: Combustible cigarette smoking is associated with the initiation of marijuana use, earlier onset of marijuana use, more rapid escalation in use, and the development of nicotine and cannabis dependence.

WHAT THIS STUDY ADDS: We offer new evidence for a prospective relationship between adolescent electronic cigarette and hookah use and the risk of initiating and currently using marijuana.

Combustible cigarette smoking is associated with the initiation of marijuana use, earlier onset of marijuana use, more rapid escalation in use, and the development of nicotine and cannabis dependence.[1–4] The adverse health consequences of cigarette smoking and marijuana use have been documented,[5,6] with more severe and persistent negative outcomes seen when use is initiated during adolescence and when both substances are used.[1,7,8]

Although adolescent cigarette smoking has declined significantly over the past decade,[9] approximately one-third of US adolescents report currently using at least 1 tobacco product, an increase of 35% since 2011.[9] This increase is attributable to the use of alternative nicotine-delivery products, such as electronic cigarettes (e-cigarettes) and hookah.[10,11] More than 11% of high school students currently use e-cigarettes,[12] and an estimated 5% to 11% currently smoke hookah.[12–15] Whether the well-established comorbidity between combustible cigarette smoking and subsequent marijuana use in adolescence translates to e-cigarette and hookah use is unknown.

Data revealing that the use of e-cigarettes and hookah are associated with risk of adolescent marijuana use and co-use would be important evidence for guiding marijuana and tobacco policies to protect adolescent health.[10,16] The diversity of marijuana products, such as vaporized and edible forms, offers more opportunities for co-use. In addition, if use of e-cigarettes and hookah increases the likelihood of marijuana use, the health risks of increased youth marijuana use should be included in models of the net population effects of alternative tobacco products.[17] We examined whether adolescent use of e-cigarettes and hookah is associated with the risk of initiating and regularly using marijuana as well

as using both substances among high school students from ages 14 to 16 years.

METHODS

Participants and Procedure

Data were collected as part of a longitudinal survey of substance use and mental health among high school students in Los Angeles, California. 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. To enroll in the study, students and their parents were required to provide active written or verbal assent and consent, respectively. Data collection involved 5 assessment waves that took place ~6 months apart: baseline (fall 2013, ninth grade), 6-month follow-up (spring 2014, ninth grade), 12-month follow-up (fall 2014, 10th grade), 18-month follow-up (spring 2015, 10th grade), and 24-month follow-up (fall 2015, 11th Grade). Waves 1 and 5 are the focus of this investigation because current use of all forms of marijuana was assessed at wave 5. At each wave, paper-and-pencil surveys were administered in students' classrooms. Students who were absent completed an interviewer-administered phone survey or a Web-based survey. The University of Southern California Institutional Review Board approved the study.

Measures

Each measure described below has been shown to have adequate psychometric properties in adolescent samples.[9,18–20]

Tobacco Product Use and Marijuana Use

At baseline and the 24-month follow-up, items based on the Youth Risk Behavior Surveillance Survey[9,18]

were used to assess ever use and current use (past 30-day use; yes or no) of e-cigarettes, combustible cigarettes, and a hookah water pipe; use of any type of marijuana product at baseline; and use of 3 different marijuana products (combustible, vaped, and edible) at follow-up. Responses to the baseline questions of ever tobacco use (combustible cigarette, e-cigarette, and hookah) served as the primary exposure variable. Outcomes were ever use (yes or no) and current use (past 30-day use; yes or no) of (1) combustible marijuana, (2) vaped marijuana, and (3) edible marijuana. The terms "ever-marijuana users" and "never-marijuana user" are used to refer to adolescents who ever and never used any of the 3 forms of marijuana, respectively. The relationship between other tobacco products (eg, smokeless tobacco and cigars) and marijuana were not examined because of a low prevalence of use and because we were interested in evaluating novel associations between newer tobacco products and marijuana.

Covariates

Variables that potentially overlapped with the risk for tobacco use and the risk of marijuana use were selected a priori as covariates on the basis of previous studies.[20–26] Covariates included sociodemographic, environmental, and interpersonal variables.

Sociodemographics

Sociodemographic characteristics, including age, sex, ethnicity, race, and highest parental education, were assessed by using self-report items.

Environmental Factors

Indicators of the proximal environment included family living situation, which was measured with the item, "Who do you live with most of the time?" (both biological parents versus other).[22] Family history of smoking was measured by using

the question, "Does anyone in your immediate family (brothers, sisters, parents, and/or grandparents) have a history of smoking cigarettes?" (yes or no). Peer smoking was assessed with responses to the item, "In the last 30 days, how many of your 5 closest friends have smoked cigarettes?" (range: 0–5).[9] Similar questions were used to measure family history of substance and peer marijuana use.

Intrapersonal Factors

Affective and self-regulatory psychological processes linked with tobacco use, marijuana use, and other risky behaviors were assessed. Depressive symptoms were measured by using the 20-item Center for Epidemiologic Studies Depression Scale (CESD)[19] composite sum past-week frequency rating (eg, 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 Inventory (TCI) Impulsivity subscale sum score, which is used to assess tendency toward acting on instinct without conscious deliberation (eg, "I often do things based on how I feel at the moment"; range: 0–5).[20]

Statistical Analysis

Multinomial polytomous regression models were used to test the association between baseline tobacco product use and marijuana product use 24 months later across 3 outcome categories: (0) never use, (1) past use (ie, initiated or ever use but no use in the past 30 days), and (2) current use (ie, use in the past 30 days). Adolescents who reported no marijuana use at baseline formed the sample for analyses. Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated to estimate the risk of past or current use of each marijuana product in relation to never use. Separate unadjusted models were used for each predictor (combustible cigarettes, e-cigarettes,

TABLE 1 Sample Characteristics of Ninth-Grade Never-Marijuana Users (N = 2688) by Baseline Ever-Tobacco Use Status

Baseline Characteristics[a]	Total (N = 2668)	Baseline Tobacco Product Use		P
		Never (n = 2188)	Ever (n = 480)	
Sex, n (%)				
Female	1450 (54.3)	1205 (55.1)	245 (51.0)	.11[b]
Male	1218 (45.7)	983 (44.9)	235 (49.0)	
Age, mean (SD)	14.56 (0.40)	14.55 (0.39)	14.61 (0.43)	.10[c]
Race and/or ethnicity, n (%)				
Hispanic	1194 (45.3)	968 (44.7)	226 (48.1)	.12[b]
Asian American	627 (23.8)	534 (24.7)	93 (19.8)	
White	448 (17.0)	372 (17.2)	76 (16.2)	
African American	130 (4.9)	106 (4.9)	24 (5.1)	
Other	237 (9.0)	186 (8.6)	51 (10.9)	
Parental college education, n (%)	1247 (53.6)	1060 (55.5)	187 (44.7)	<.001[b]
Environmental factors, n (%)				
Lives with both biological parents	1786 (67.2)	1501 (68.9)	285 (59.6)	<.001[b]
Family history of smoking	1580 (61.7)	1251 (59.5)	329 (71.5)	<.001[b]
Family history of drug use	399 (15.6)	300 (14.3)	99 (21.6)	<.001[b]
Peer combustible cigarette use	332 (12.7)	221 (10.3)	111 (23.7)	<.001[b]
Peer marijuana use	698 (26.7)	468 (21.8)	230 (49.0)	<.001[b]
Interpersonal factors, mean (SD)				
TCI Impulsivity subscale	2.43 (1.47)	2.34 (1.49)	2.80 (1.37)	.004[c]
CESD	14.04 (11.44)	13.31 (10.99)	16.88 (12.45)	<.001[c]

[a] Totals vary because of missing values.
[b] Calculated by using the χ^2 test.
[c] Calculated by using the independent samples t test.

hookah, and any of these products). School-level clustering was recoded to the district level and entered as a fixed effect because of the low prevalence of current marijuana vaping at 1 of the participating schools. Variables listed in Table 1, including sociodemographic, environmental, and interpersonal factors that are linked to adolescent tobacco and marijuana use, were added in subsequent separate adjusted models as potential confounders.

To assess the unique effects of each individual tobacco product, a set of combined polytomous regression models were run, in which lifetime use of e-cigarettes, hookah, and combustible cigarettes were included as simultaneous predictors to elucidate the incremental effect of each product after controlling for their covariance with one another. Missing data on covariates were handled by using multiple imputation with the Markov Chain Monte Carlo method of data augmentation.[27–29]

Continuous variables were rescaled (mean = 0; SD = 1) for regression models to facilitate interpretation. Analyses were conducted by using IBM SPSS Statistics for Windows version 24.0 (IBM SPSS Statistics, IBM Corporation, Armonk, NY). Significance was set to .05, and all tests were 2 tailed.

RESULTS

Study Sample

All ninth-grade English-speaking students who were not in special education (eg, because of severe learning disabilities) were eligible to participate (N = 4100). Of the assenting students (N = 3874; 94.5%), 3396 (87.7%) provided parental consent, from whom data were collected for 3383 (99.6%) at baseline and 3232 (95.2%) 24 months later. The sample was limited to those adolescents who provided data on lifetime tobacco product use, lifetime marijuana use, marijuana product use at follow-up, and those

TABLE 2 Prevalence of Baseline Tobacco Product Use Status and Follow-up Marijuana Product Use

Baseline Regressors	Marijuana Product Use at 24-Mo Follow-up											
	Combustible Marijuana			Vaping Marijuana			Marijuana Edibles			Any Marijuana Product		
	Never (N = 2033), n (%)	Past (N = 413), n (%)	Current (N = 213), n (%)	Never (N = 2407), n (%)	Past (N = 187), n (%)	Current (N = 68), n (%)	Never (N = 2237), n (%)	Past (N = 312), n (%)	Current (N = 116), n (%)	Never (N = 1947), n (%)	Past (N = 490), n (%)	Current (N = 231), n (%)
Combustible cigarettes												
Never use	1983 (78.0)	361 (14.2)	197 (7.8)	2319 (91.2)	162 (6.4)	62 (2.4)	2163 (85.0)	274 (10.8)	108 (4.2)	1903 (74.7)	431 (16.9)	215 (8.4)
Ever use	50 (42.7)	52 (44.4)	15 (12.8)	87 (73.7)	25 (21.2)	6 (5.1)	74 (62.2)	38 (31.9)	7 (5.9)	44 (37.0)	59 (49.6)	16 (13.4)
E-cigarettes												
Never use	1888 (80.1)	309 (13.1)	160 (6.8)	2168 (91.9)	139 (5.9)	51 (2.2)	2047 (86.7)	231 (9.8)	84 (3.6)	1819 (76.9)	372 (15.7)	173 (7.3)
Ever use	138 (47.4)	102 (35.1)	51 (17.5)	229 (78.4)	47 (16.1)	16 (5.5)	182 (62.3)	80 (27.4)	30 (10.3)	120 (41.0)	116 (39.6)	57 (19.5)
Hookah												
Never use	1934 (79.3)	340 (13.9)	164 (6.7)	2247 (92.1)	147 (6.0)	47 (1.9)	2110 (86.4)	249 (10.2)	84 (3.4)	1859 (76.0)	408 (16.7)	180 (7.4)
Ever use	88 (43.1)	70 (34.3)	46 (22.5)	146 (71.6)	39 (19.1)	19 (9.3)	115 (56.1)	61 (29.8)	29 (14.1)	77 (37.6)	79 (38.5)	49 (23.9)
Any tobacco product												
Never use	1804 (82.7)	252 (11.5)	126 (5.8)	2040 (93.4)	104 (4.8)	39 (1.8)	1937 (88.6)	184 (8.4)	64 (2.9)	1746 (79.8)	305 (13.9)	137 (6.3)
Ever use	229 (48.1)	161 (33.8)	86 (18.1)	366 (76.6)	83 (17.4)	29 (6.1)	300 (62.6)	128 (26.7)	51 (10.6)	201 (41.9)	185 (38.5)	94 (19.6)
No. tobacco products[a]												
0	1804 (82.7)	252 (11.5)	126 (5.8)	2040 (93.4)	104 (4.8)	39 (1.8)	1937 (88.6)	184 (8.4)	64 (2.9)	1746 (79.8)	305 (13.9)	137 (6.3)
1	187 (52.2)	110 (30.7)	61 (17.0)	283 (78.6)	60 (16.7)	17 (4.7)	239 (66.4)	85 (23.6)	36 (10.0)	165 (45.7)	129 (35.7)	67 (18.6)
≥2	42 (35.6)	51 (43.2)	25 (21.2)	83 (70.3)	23 (19.5)	12 (10.2)	61 (51.3)	43 (36.1)	15 (12.6)	36 (30.3)	56 (47.1)	27 (22.7)

Past use includes any noncurrent use of the respective product during the past 24 months; current use includes any use of the respective product during the past 30 days.
a Includes combustible cigarettes, e-cigarettes, and hookah.

who had never used marijuana at baseline (N = 2668). The sample characteristics are summarized in Table 1. There were positive associations between ever use of the tobacco products at baseline and all environmental and interpersonal characteristics (Table 1).

Descriptive Analyses

Baseline never-marijuana users with (N = 2668) versus without (N = 149) follow-up data did not differ in ever use of tobacco (e-cigarettes, hookah, and combustible cigarettes) at baseline or sociodemographic, environmental, or interpersonal characteristics except for being composed of more boys than girls (P = .02) and living without versus with both biological parents (P = .03).

Associations Between Baseline Tobacco Ever Use and Marijuana Use at Follow-up in Baseline Never-Marijuana Users

Among never-marijuana users at baseline, 231 (8.7%) reported current use of at least 1 marijuana product at the 24-month follow-up, whereas 490 (18.4%) reported having used at least 1 product in the past 24 months leading up to the follow-up (Table 2).

Table 3 shows the results of models that were unadjusted and adjusted for covariates. Here, we summarize the results of the adjusted models. Among baseline never-marijuana users, baseline ever (versus never) use of e-cigarettes was associated with the initiation of marijuana use (39.6% vs 15.7%; OR 3.63; 95% CI 2.69–4.90) and current marijuana use (19.5% vs 7.3%; OR 3.67; 95% CI 2.51–5.36) at the 24-month follow-up. Baseline ever (versus never) use of hookah was associated with the initiation of marijuana use (38.5% vs 16.7%; OR 3.55; 95% CI 2.49–5.08) and current use of any marijuana (23.9% vs 7.4%; OR 4.10; 95% CI 2.69–6.25) at the 24-month follow-up. Baseline ever

TABLE 3 Association of Baseline Multiple Tobacco Product Use and Covariates With Multiple Marijuana Product Outcomes at 24-Month Follow-up

Baseline Regressors, Ever Use	Outcome at 24-Mo Follow-up							
	Combustible Marijuana		Vaping Marijuana		Marijuana Edibles		Any Marijuana Product	
	Current Versus Never, OR (95% CI)	Past Versus Never, OR (95% CI)	Current Versus Never, OR (95% CI)	Past Versus Never, OR (95% CI)	Current Versus Never, OR (95% CI)	Past Versus Never, OR (95% CI)	Current Versus Never, OR (95% CI)	Past Versus Never, OR (95% CI)
Unadjusted models[a]								
Combustible cigarettes	2.92 (1.61–5.32)***	5.73 (3.82–8.59)***	2.48 (1.04–5.92)*	4.11 (2.56–6.62)***	1.82 (0.82–4.06)	4.07 (2.69–6.16)***	3.10 (1.71–5.60)***	5.98 (3.99–8.98)***
E-cigarettes	4.72 (3.27–6.79)***	4.56 (3.43–6.06)***	3.27 (1.83–5.87)***	3.21 (2.24–4.60)***	4.34 (2.77–6.80)***	3.93 (2.92–5.29)***	5.45 (3.81–7.80)***	4.74 (3.58–6.27)***
Hookah	5.54 (3.73–8.22)***	4.61 (3.29–6.47)***	5.36 (3.04–9.47)***	4.19 (2.81–6.24)***	5.69 (3.56–9.11)***	4.68 (3.31–6.60)***	5.89 (3.97–8.74)***	4.89 (3.49–6.86)***
Any product	5.37 (3.94–7.31)***	5.02 (3.95–6.40)***	4.14 (2.52–6.79)***	4.42 (3.24–6.03)***	5.10 (3.45–7.53)***	4.50 (3.48–5.82)***	5.96 (4.40–8.07)***	5.26 (4.16–6.65)***
No. products	3.13 (2.53–3.88)***	3.30 (2.76–3.94)***	2.43 (1.81–3.27)***	2.52 (2.06–3.07)***	2.74 (2.13–3.51)***	2.84 (2.38–3.39)***	3.43 (2.76–4.26)***	3.50 (2.93–4.19)***
Adjusted models[b]								
Combustible cigarettes	1.90 (1.01–3.57)*	4.16 (2.70–6.41)***	1.54 (0.62–3.87)	2.90 (1.75–4.79)***	1.06 (0.46–2.45)	2.77 (1.77–4.32)***	1.97 (1.05–3.68)*	4.30 (2.79–6.63)***
E-cigarettes	3.15 (2.14–4.64)***	3.42 (2.53–4.63)***	2.08 (1.12–3.86)*	2.38 (1.63–3.47)***	2.99 (1.86–4.79)***	2.85 (2.08–3.91)***	3.67 (2.51–5.36)***	3.63 (2.69–4.90)***
Hookah	3.91 (2.56–5.97)***	3.40 (2.37–4.86)***	3.79 (2.05–7.01)***	2.95 (1.94–4.50)***	3.94 (2.39–6.48)***	3.20 (2.22–4.61)***	4.10 (2.69–6.25)***	3.55 (2.49–5.08)***
Any product	3.79 (2.73–5.27)***	3.81 (2.95–4.92)***	2.90 (1.70–4.93)***	3.33 (2.40–4.62)***	3.59 (2.38–5.43)***	3.26 (2.48–4.28)***	4.21 (3.05–5.81)***	4.00 (3.12–5.14)***
No. products	2.55 (2.01–3.24)***	2.80 (2.30–3.40)***	1.94 (1.38–2.71)***	2.11 (1.70–2.63)***	2.19 (1.66–2.89)***	2.31 (1.90–2.80)***	2.77 (2.18–3.51)***	2.95 (2.42–3.59)***
Combined adjusted models[b]								
Combustible cigarettes	1.39 (0.72–2.68)	3.16 (2.01–4.96)***	1.13 (0.44–2.96)	2.22 (1.31–3.76)**	0.73 (0.31–1.74)	2.06 (1.29–3.28)**	1.43 (0.75–2.74)	3.27 (2.08–5.14)***
E-cigarettes	2.41 (1.60–3.65)***	2.66 (1.93–3.68)***	1.30 (0.65–2.58)	1.81 (1.21–2.72)**	2.22 (1.33–3.71)**	2.20 (1.57–3.08)***	2.87 (1.91–4.30)***	2.86 (2.09–3.94)***
Hookah	3.04 (1.94–4.76)***	2.38 (1.62–3.49)***	3.47 (1.79–6.75)***	2.25 (1.44–3.53)***	3.19 (1.88–5.41)***	2.37 (1.61–3.50)***	3.07 (1.97–4.80)***	2.49 (1.70–3.65)***

a Unadjusted models include only the respective baseline tobacco product variable as the sole regressor.
b Adjusted models include the respective baseline tobacco product variable, age, sex, race and/or ethnicity, parental education, family history of combustible cigarette and drug use, peer combustible cigarette use and marijuana use, TCI Impulsivity subscale, and CESD as simultaneous regressors. Combined adjusted models include all baseline tobacco products as simultaneous predictors and all covariate regressors.
* $P < .05$; ** $P < .01$; *** $P < .001$.

(versus never) combustible cigarette smoking was associated with the initiation of marijuana use (49.6% vs 16.9%; OR 4.30; 95% CI 2.79–6.63) and current marijuana use (13.4% vs 8.4%; OR 1.97; 95% CI 1.05–3.68) at the 24-month follow-up.

We evaluated the associations between use of 1 of the 3 tobacco products at baseline (e-cigarettes, hookah, and combustible cigarettes) and use of the 3 different forms of marijuana (combustible marijuana, vaping marijuana, and marijuana edibles) 24 months later. Baseline ever (versus never) e-cigarette use or hookah use was associated with initiating and currently using all 3 forms of marijuana (all $P < .05$). These same relationships were observed for baseline combustible cigarette use with the exception of current (but not ever) marijuana vaping and marijuana edible consumption outcomes at follow-up. Moreover, ever use of any of these 3 tobacco products at baseline was prospectively associated with the initiation of marijuana use (38.5% vs 13.9%; OR 4.00; 95% CI 3.12–5.14) and current marijuana use at the 24-month follow-up (19.6% vs 6.3%; OR 4.21; 95% CI 3.05–5.81). For each additional tobacco product used at baseline, adolescents had 3.5 times–greater odds of initiating marijuana use in the last 24 months (95% CI 2.93–4.19) and 3.4 times–greater odds of currently using marijuana (95% CI 2.76–4.26).

The associations between tobacco and marijuana remained significant in both the unadjusted and adjusted models across all individual tobacco and marijuana products (Table 3). In combined polytomous regression models that we used to test the effect of ever use of combustible cigarettes, e-cigarettes, and hookah as simultaneous predictors, each individual tobacco product use retained significant effects on past (versus never) marijuana product use even after covariate adjustment. In

the same models, significant effects were observed for e-cigarettes and hookah on current (versus never) marijuana product use, whereas combustible cigarettes did not.

Associations Between Baseline Ever- Tobacco Use and Dual Use of Tobacco and Marijuana at Follow-up

In the sample of never-marijuana users, adolescents who currently (versus never) used 1 of the 3 tobacco products (either e-cigarettes, hookah, or combustible cigarettes) at baseline were more likely to report current use of 1 of these tobacco products 24 months later (9.0% vs 3.6%; OR 2.38; 95% CI 1.58–3.58), current use of a marijuana product 24 months later (11.7% vs 3.3%; OR 3.23; 95% CI 2.18–4.79), and current dual use of 1 of these tobacco products and marijuana (7.9% vs 3.0%; OR 2.28; 95% CI 1.47–3.55; Table 4).

DISCUSSION

In the current study, we offer new evidence for a prospective relationship between adolescent e-cigarette and hookah use and the risk of initiating and currently using marijuana. E-cigarette and hookah use at age 14 years was associated with a 3.6- to fourfold increase in the odds of initiating and currently using marijuana 2 later. Similar to combustible cigarette smoking, the use of e-cigarettes or hookah in early adolescence more than doubled the odds of currently using both tobacco and marijuana by midadolescence.

These findings suggest that newer forms of tobacco likely increase adolescent vulnerability to marijuana use and dual use of marijuana and tobacco even in the context of other factors that are also correlated with marijuana use. Associations between the use of these tobacco products with subsequent marijuana use could reflect shared genetic liability to use both tobacco and marijuana

TABLE 4 Association of Baseline Tobacco Product Use and Dual Product Use at 24-Month Follow-up

Baseline Regressor, Ever Any Tobacco Product Use	Current Product Use at 24-Mo Follow-up		
	Tobacco Product[a] Versus None, OR (95% CI)	Marijuana Product[b] Versus None, OR (95% CI)	Dual Product[c] Versus None, OR (95% CI)
Unadjusted model	3.22 (2.18–4.75)***	4.48 (3.10–6.48)***	3.41 (2.24–5.17)***
Adjusted model	2.38 (1.58–3.59)***	3.24 (2.19–4.81)***	2.33 (1.49–3.64)***

Current use includes any use of the respective product during the past 30 days.
[a] Current use of any combustible cigarettes, e-cigarettes, or hookah.
[b] Current use of any combustible marijuana, vaping marijuana or marijuana edibles.
[c] Current use of any combustible cigarettes, e-cigarettes, or hookah and any combustible marijuana, vaping marijuana or marijuana edibles.
*** P < .001.

as well as environmental features that make co-use more likely.[1] An environment characterized by peer use, easier access, and shared perceptions of reduced risk increase the likelihood that e-cigarettes, hookah, and (ultimately) marijuana will be used.[30–32] Even after adjusting for many of these shared risk factors for tobacco and marijuana use, the models remained robust, which increases our confidence that the observed associations were not attributable to another variable.

Indeed, the use of e-cigarettes and hookah may foster adolescent marijuana use. Nicotine primes the brain's reward system by enhancing the level of pleasure experienced from subsequent drug exposures, such as to marijuana.[33] Adolescents who initiate marijuana with (versus without) previous nicotine exposure may experience more pleasure from their initial marijuana use experience and progress more rapidly to regular marijuana use.[4,33] Research reveals that a bout of hookah smoking can yield 1.7 times more nicotine than that of a combustible cigarette.[34] As such, it is not surprising that the association between hookah smoking and subsequent use of all forms of marijuana use are the strongest. We did not measure whether adolescents had used electronic liquid (e-liquid) without nicotine or tobacco-free (herbal) forms of hookah at baseline, and therefore, we cannot confirm the role of nicotine in the current results. Yet, 63% of current adolescent

e-cigarette users at follow-up reported using e-liquid with nicotine, and teenagers who report using e-liquids without nicotine may also be inadvertently exposed because nicotine has been detected in >90% of e-liquids sampled, including those that are labeled as nicotine free.[35,36]

Additionally, airway adaptations that occur as part of hookah smoking and e-cigarette vaping may facilitate marijuana smoking and vaping by reducing sensitivity to the irritation caused by the inhalation of marijuana products. Repeated inhalation of hot hookah smoke and habituation to the "throat hit" associated with propylene glycol in e-liquid may render the transition to smoking or vaping marijuana more pleasant and thus likely to be repeated. It is important to point out that hookah is the only tobacco product of the 3 studied that is characterized by flavor and combustion. Perhaps these combined features, in addition to a shared form of administration (eg, water pipe), foster the use of both hookah and marijuana.

The associations between e-cigarette and hookah use and subsequent marijuana use are stronger than those for combustible cigarettes. E-cigarette and hookah use is more prevalent than combustible cigarette smoking among adolescents, yet e-cigarettes and hookah are far less regulated.[10,37] Federal regulations do not currently restrict youth-targeted advertising and promotion or sales of youth-friendly flavors of

e-cigarette and hookah products.[10,38] Likewise, access does not currently appear to be a significant barrier to use. For example, of the adolescents who reported smoking hookah, 27% smoked it at a friend's house, 8% smoked at a hookah bar or café, 8% smoked at home, 6% smoked somewhere else, 8% smoked at multiple locations, and 43% chose not to indicate where they smoke hookah. Recent trends in marijuana policy across numerous states in the United States are moving toward increasing legalization; such trends have been associated with a higher prevalence of use of both marijuana and tobacco.[31,39] With the data from the current study, we raise questions regarding the impact of less restrictive policies on the use and co-use of newer tobacco products and marijuana in the adolescent population. These data are used to support strict policies to prevent tobacco product and marijuana product sales to minors. Hookah smoking has many of the same health risks as combustible cigarette smoking.[40] Although some e-cigarette advocates may not be alarmed by youth trying e-cigarettes, concerns should be heightened by the finding that e-cigarette use is associated with marijuana use as well as dual use.

Dual use of tobacco and marijuana is particularly troubling because it increases the likelihood of an adolescent becoming dependent on both nicotine and cannabis.[1,41] Adolescents are likely to continue to use both because of greater withdrawal symptoms and declines in cognitive functioning during abstinence than adolescents who only use tobacco.[42] As such, interventions and regulations to prevent adolescent e-cigarette, hookah, and marijuana use are critical.

The study has several strengths, including having a demographically diverse sample that was measured during a developmentally vulnerable period for substance use, using repeated measures of tobacco and marijuana initiation and current use, excluding adolescents who had ever used marijuana at baseline to clarify temporal precedence, and having high participation and retention rates.

A limitation of this study is that the frequency of marijuana use was not measured, only use in the past 30 days. As such, we are not able to determine whether e-cigarette or hookah use is associated with a specific level of marijuana use beyond current use. Likewise, specific characteristics of e-cigarettes and hookah (eg, flavoring) were not assessed; thus, the role of these characteristics in marijuana uptake cannot be determined.

The sample was drawn from a specific location, which may lessen generalizability. However, given that California has decriminalized marijuana for recreational use, the present sample may offer a snapshot of the likely associations between novel tobacco products and marijuana use in a state where tobacco regulations are more restrictive and marijuana use is more normalized. It is important to note that the prevalence of e-cigarette and hookah use in the current study are comparable to those rates identified in national studies.[43] Lastly, this is an observational study and the first to examine these associations. Inferences regarding whether the identified associations are causal cannot be made but should be the subject of future research. It will also be valuable to identify mechanisms that drive marijuana use among adolescents who have used e-cigarettes and hookah.

CONCLUSIONS

Adolescents who used e-cigarettes or hookah at baseline compared with those who did not were more likely to report initiation and current use of marijuana as well as dual use of tobacco and marijuana. The association between tobacco use and subsequent marijuana use across adolescence extends to multiple tobacco products.

ABBREVIATIONS

CESD: Center for Epidemiologic Studies Depression Scale
CI: confidence interval
e-cigarette: electronic cigarette
e-liquid: electronic liquid
OR: odds ratio
TCI: Temperament and Character Inventory

REFERENCES

1. Agrawal A, Budney AJ, Lynskey MT. The co-occurring use and misuse of cannabis and tobacco: a review. *Addiction.* 2012;107(7):1221–1233

2. Peters EN, Budney AJ, Carroll KM. Clinical correlates of co-occurring cannabis and tobacco use: a systematic review. *Addiction.* 2012;107(8):1404–1417

3. Agrawal A, Scherrer JF, Lynskey MT, et al. Patterns of use, sequence of onsets and correlates of tobacco and cannabis. *Addict Behav.* 2011;36(12):1141–1147

4. Agrawal A, Madden PAF, Martin NG, Lynskey MT. Do early experiences with cannabis vary in cigarette smokers? *Drug Alcohol Depend*. 2013;128(3):255–259

5. US Department of Health and Human Services. *The Health Consequences of Smoking—50 Years of Progress: A Report of the Surgeon General*. Atlanta, GA: US Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health; 2014. Available at: https://www.surgeongeneral.gov/library/reports/50-years-of-progress/full-report.pdf

6. Volkow ND, Baler RD, Compton WM, Weiss SRB. Adverse health effects of marijuana use. *N Engl J Med*. 2014;370(23):2219–2227

7. Lubman DI, Cheetham A, Yücel M. Cannabis and adolescent brain development. *Pharmacol Ther*. 2015;148:1–16

8. Rooke SE, Norberg MM, Copeland J, Swift W. Health outcomes associated with long-term regular cannabis and tobacco smoking. *Addict Behav*. 2013;38(6):2207–2213

9. Kann L, McManus T, Harris WA, et al. Youth risk behavior surveillance - United States, 2015. *MMWR Surveill Summ*. 2016;65(6):1–174

10. Soneji S, Sargent J, Tanski S. Multiple tobacco product use among US adolescents and young adults. *Tob Control*. 2016;25(2):174–180

11. Kasza KA, Ambrose BK, Conway KP, et al. Tobacco-product use by adults and youths in the United States in 2013 and 2014. *N Engl J Med*. 2017;376(4):342–353

12. Jamal A, Gentzke A, Hu SS, et al. Tobacco use among middle and high school students - United States, 2011-2016. *MMWR Morb Mortal Wkly Rep*. 2017;66(23):597–603

13. Gilreath TD, Leventhal A, Barrington-Trimis JL, et al. Patterns of alternative tobacco product use: emergence of hookah and e-cigarettes as preferred products amongst youth. *J Adolesc Health*. 2016;58(2):181–185

14. Barnett TE, Livingston MD. Hookah use among adolescents: differential cognitions about hookah and cigarettes. *Addict Behav*. 2017;75:75–78

15. Huang LL, Sutfin EL, Kowitt S, Patel T, Ranney L, Goldstein AO. Trends and correlates of hookah use among high school students in North Carolina. *N C Med J*. 2017;78(3):149–155

16. Kilmer B. Recreational cannabis - minimizing the health risks from legalization. *N Engl J Med*. 2017;376(8):705–707

17. Kalkhoran S, Glantz SA. E-cigarettes and smoking cessation in real-world and clinical settings: a systematic review and meta-analysis. *Lancet Respir Med*. 2016;4(2):116–128

18. Johnston LD, O'Malley PM, Miech RA, Bachman JG, Schulenberg J. *Monitoring the Future National Survey Results on Drug Use, 1975-2016: Overview, Key Findings on Adolescent Drug Use*. Ann Arbor, MI: University of Michigan; 2017

19. Radloff LS. The use of the Center for Epidemiologic Studies Depression Scale in adolescents and young adults. *J Youth Adolesc*. 1991;20(2):149–166

20. Cloninger CR, Przybeck TR, Svrakic DM, Wetzel RD. *The Temperament and Character Inventory (TCI): A Guide to its Development and Use*. St Louis, MO: Center for Psychobiology of Personality; 1994

21. Camenga DR, Kong G, Cavallo DA, et al. Alternate tobacco product and drug use among adolescents who use electronic cigarettes, cigarettes only, and never smokers. *J Adolesc Health*. 2014;55(4):588–591

22. Covey LS, Tam D. Depressive mood, the single-parent home, and adolescent cigarette smoking. *Am J Public Health*. 1990;80(11):1330–1333

23. Tyas SL, Pederson LL. Psychosocial factors related to adolescent smoking: a critical review of the literature. *Tob Control*. 1998;7(4):409–420

24. Wills TA, Knight R, Williams RJ, Pagano I, Sargent JD. Risk factors for exclusive e-cigarette use and dual e-cigarette use and tobacco use in adolescents. *Pediatrics*. 2015;135(1). Available at: www.pediatrics.org/cgi/content/full/135/1/e43

25. Cohn A, Villanti A, Richardson A, et al. The association between alcohol, marijuana use, and new and emerging tobacco products in a young adult population. *Addict Behav*. 2015;48:79–88

26. Brook JS, Zhang C, Leukefeld CG, Brook DW. Marijuana use from adolescence to adulthood: developmental trajectories and their outcomes. *Soc Psychiatry Psychiatr Epidemiol*. 2016;51(10):1405–1415

27. Rubin DB. *Multiple Imputation for Nonresponse in Surveys*. Chichester, NY: John Wiley & Sons; 1989

28. Donneau AF, Mauer M, Lambert P, Molenberghs G, Albert A. Simulation-based study comparing multiple imputation methods for non-monotone missing ordinal data in longitudinal settings. *J Biopharm Stat*. 2015;25(3):570–601

29. Schafer JL, Olsen MK. Multiple imputation for multivariate missing-data problems: a data analyst's perspective. *Multivariate Behav Res*. 1998;33(4):545–571

30. Roditis ML, Halpern-Felsher B. Adolescents' perceptions of risks and benefits of conventional cigarettes, e-cigarettes, and marijuana: a qualitative analysis. *J Adolesc Health*. 2015;57(2):179–185

31. Cerdá M, Wall M, Feng T, et al. Association of state recreational marijuana laws with adolescent marijuana use. *JAMA Pediatr*. 2017;171(2):142–149

32. Roditis M, Delucchi K, Cash D, Halpern-Felsher B. Adolescents' perceptions of health risks, social risks, and benefits differ across tobacco products. *J Adolesc Health*. 2016;58(5):558–566

33. Levine A, Huang Y, Drisaldi B, et al. Molecular mechanism for a gateway drug: epigenetic changes initiated by nicotine prime gene expression by cocaine. *Sci Transl Med*. 2011;3(107):107ra109

34. Cobb C, Ward KD, Maziak W, Shihadeh AL, Eissenberg T. Waterpipe tobacco smoking: an emerging health crisis in the United States. *Am J Health Behav*. 2010;34(3):275–285

35. Davis B, Dang M, Kim J, Talbot P. Nicotine concentrations in electronic cigarette refill and do-it-yourself fluids. *Nicotine Tob Res*. 2015;17(2):134–141

36. Raymond BH, Collette-Merrill K, Harrison RG, Jarvis S, Rasmussen RJ. The nicotine content of a sample of e-cigarette liquid manufactured in the United States. *J Addict Med*. 2018;12(2):127–131

37. Huang J, Tauras J, Chaloupka FJ. The impact of price and tobacco control policies on the demand for electronic nicotine delivery systems. *Tob Control*. 2014;23(suppl 3):iii41–iii47

38. Mitchell Hamline School of Law. Tobacco control. 2017. Available at: www.publichealthlawcenter.org/topics/tobacco-control. Accessed July 25, 2017

39. Wang JB, Ramo DE, Lisha NE, Cataldo JK. Medical marijuana legalization and cigarette and marijuana co-use in adolescents and adults. *Drug Alcohol Depend*. 2016;166:32–38

40. Akl EA, Gaddam S, Gunukula SK, Honeine R, Jaoude PA, Irani J. The effects of waterpipe tobacco smoking on health outcomes: a systematic review. *Int J Epidemiol*. 2010;39(3):834–857

41. Rubinstein ML, Rait MA, Prochaska JJ. Frequent marijuana use is associated with greater nicotine addiction in adolescent smokers. *Drug Alcohol Depend*. 2014;141:159–162

42. Jacobsen LK, Pugh KR, Constable RT, Westerveld M, Mencl WE. Functional correlates of verbal memory deficits emerging during nicotine withdrawal in abstinent adolescent cannabis users. *Biol Psychiatry*. 2007;61(1):31–40

43. Ambrose BK, Day HR, Rostron B, et al. Flavored tobacco product use among us youth aged 12-17 years, 2013-2014. *JAMA*. 2015;314(17):1871–1873