

Electronic Cigarettes and Future Marijuana Use: A Longitudinal Study

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abstract

BACKGROUND: Cigarettes have been strongly associated with subsequent marijuana use among adolescents, but electronic cigarettes (e-cigarettes) are now rapidly replacing traditional cigarettes among youth. This study examines associations between youth e-cigarette use and subsequent marijuana use in a national sample.

METHODS: Youth (aged 12–17 years) never marijuana users at wave 1 ($n = 10\,364$; 2013–2014) from the Population Assessment of Tobacco and Health study were followed-up in 1 year (wave 2, 2014–2015). Multivariable logistic regressions were performed to evaluate associations between e-cigarette use at wave 1 and ever/heavy marijuana use in the past 12 months (P12M) and at wave 2.

RESULTS: Among never marijuana users, e-cigarette ever use (versus never use) at wave 1 was associated with increased likelihood of marijuana P12M use (adjusted odds ratio [aOR] = 1.9; 95% confidence interval [CI]: 1.4–2.5) at wave 2. There was a significant interaction between e-cigarette use and age ($P < .05$) with aOR = 2.7 (95% CI: 1.7–4.3) for adolescents aged 12 to 14 and aOR = 1.6 (95% CI: 1.2–2.3) for adolescents aged 15 to 17. The association with heavy marijuana use was significant among younger adolescents (aOR = 2.5; 95% CI: 1.2–5.3) but was not among older adolescents. Heavier e-cigarette use at wave 1 yielded higher odds of P12M and heavy marijuana use at wave 2 for younger adolescents.

CONCLUSIONS: E-cigarette use predicts subsequent marijuana use among youth, with a stronger associations among young adolescents. Reducing youth access to e-cigarettes may decrease downstream marijuana use.



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WHAT'S KNOWN ON THIS SUBJECT: Cigarettes have been strongly associated with subsequent marijuana use among adolescents, but electronic cigarettes (e-cigarettes) are now rapidly replacing traditional cigarettes among youth. A growing body of literature shows that e-cigarettes could increase the subsequent risk of cigarette smoking among youth.

WHAT THIS STUDY ADDS: Youth e-cigarette use was associated with subsequent marijuana use, especially among young adolescents aged 12 to 14 years. Policies influencing the exposure of youth to e-cigarettes may have downstream effects on uptake of marijuana.

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Although the prevalence of current cigarette smoking among youth declined from 28% in 1996 to 8% in 2016,^{1,2} electronic cigarette (e-cigarette) use is gaining popularity.³ Among teenagers, the use of e-cigarettes has outpaced the use of traditional cigarettes, especially among young adolescents.^{1,4} It is also indicated in studies that marijuana remains the substance with the highest prevalence of use among youth; current use among high school seniors is nearly double that of current cigarette use.⁴ Moreover, teenagers' attitudes are moving toward greater acceptance of marijuana. For instance, the percentage of high school seniors who perceived the occasional use of marijuana as harmful dropped from 27.4% in 2009 to 17.1% in 2016.⁴

In a growing body of longitudinal studies, it has been shown that youth who use e-cigarettes have higher odds of smoking cigarettes later,^{5–9} suggesting that e-cigarettes might increase the risk of future cigarette use among adolescents. Researchers have also systematically evaluated cigarette smoking and marijuana use among adolescents. Authors of most longitudinal studies that examined cigarette smoking before marijuana use generally supported the association between baseline cigarette use and progression to use of other addictive substances (eg, marijuana).^{10–12} Although e-cigarettes are marketed as less harmful alternatives to smoking,¹³ most youth are not using e-cigarettes to quit smoking. Instead, youth are attracted by the novelty of e-cigarettes and a wide variety of flavors specifically designed to appeal to the youth market.¹⁴ If youth e-cigarette use follows the same pattern as cigarette smoking, widespread use could expose youth to social environments that encourage substance use, thereby accelerating youths' transitions to

the use of other substances with more adverse health effects.^{15,16}

Researchers in a few cross-sectional studies also examined the drug use patterns among adolescents, including poly use of e-cigarettes, marijuana, and other substances.^{17,18} These studies revealed complex drug use patterns, and researchers identified higher risks of poly-drug use among e-cigarette users (versus nonusers).^{17,18} Authors of cross-sectional studies have identified a high prevalence of marijuana vaping in both youth and adult populations.^{19–21} Researchers in a longitudinal study of Hispanic young adults further reported that e-cigarette use increased the likelihood of transitioning from nonusers to users of cigarettes or marijuana over a 1-year period.¹⁵ However, studies are needed to evaluate the longitudinal associations of e-cigarette use and future marijuana use among adolescents in population-based samples.

Youth undergo multiple stages of development, and thus the role of e-cigarette use in an individual's drug use patterns may differ by age.¹⁷ The age of e-cigarette initiation is similar to that of alcohol and marijuana, with a rapid increase after age 14 years and peaking around age 17 to 18 years.²² Because younger e-cigarette users were more likely to be nonusers of traditional drugs,¹⁷ and adolescents who initiate substance use at an earlier age have higher risks for addiction and adverse health outcomes,^{23,24} we hypothesize that there might be an interaction between e-cigarette use and age in association with subsequent marijuana use. The risk difference in association between e-cigarette use and subsequent marijuana transition by age group has not been assessed in published studies.

To address these gaps, we analyzed the Population Assessment of Tobacco and Health (PATH) survey to examine the associations of

e-cigarette use (ever or number of e-cigarettes and/or cartridges used) at baseline (wave 1) and subsequent marijuana use (past 12 months [P12M] or heavy use) 1 year later (wave 2). We further stratified the analyses by age groups (12–14 and 15–17 years old) to enhance our understanding of this potential relationship.

METHODS

Data

Data on e-cigarette and marijuana use were obtained from wave 1 and wave 2 of the PATH study, a longitudinal cohort study of tobacco use behaviors, attitudes, and beliefs among a nationally representative sample of US civilian, noninstitutionalized individuals aged 12 years and older.²⁵ A 4-stage, stratified probability sample design was used in the PATH study, and further details regarding the data collection, study design, and methods can be found elsewhere.^{25,26} In this study, we used the public-use files of young participants aged 12 to 17 years at wave 1, continuing young participants (those still aged <18 years), and those who had become adults (age ≥18 years; "aged-up adults") at wave 2.

Wave 1 of the PATH study was collected from September 2013 to December 2014 with 13 651 youth and 32 320 adults. Wave 2 of PATH was collected from October 2014 to October 2015 with 12 172 youth and 28 362 adults. The weighted response rate for the wave 1 household screener was 54.0%. Among screened households, the overall weighted response rate for the wave 1 youth interview was 78.4%. The weighted retention rate for continuing youth at wave 2 was 88.4%, and the weighted recruitment rate for aged-up adults was 85.7%.^{25,26} Because the PATH research team provides publicly available deidentified data, this study was determined to be nonhuman

subjects research by the Children’s Mercy Institutional Review Board.

Measures

E-cigarette Use at Wave 1

All participants were shown a brief description and pictures of e-cigarettes followed by a question, “Have you seen or heard of e-cigarettes before this study?” Those who responded positively were asked, “Have you ever used an e-cigarette, even 1 or 2 times?” Those who responded “Yes” were categorized as e-cigarette ever users at wave 1. For the dose-response analysis, the number of e-cigarettes and/or cartridges used in an entire life was measured by an ordinal variable ranging from 0 (no use) to 7 (100 or more).²⁷ See Fig 1.

Marijuana Use at Wave 1 and Wave 2

Ever use of marijuana at wave 1 was defined by 2 items from the PATH study: “Have you ever used marijuana, hash, THC, grass, pot, or weed?” and “Have you ever smoked part of all of a cigar, cigarillo, or filter cigar with marijuana in it?” Those who responded “No” to both of these questions were categorized as marijuana never users at wave 1. Those who responded “Yes” to either of these questions were categorized as marijuana ever users at wave 1.

At wave 2, marijuana never users at wave 1 who reported using marijuana in the P12M were categorized as marijuana P12M users. On the basis of an additional item, “Which substances did you use weekly or more often?” we further categorized those who responded “marijuana, hash, THC, grass, pot, or weed” as marijuana heavy users at wave 2.

Other Substance Use at Wave 1

Cigarette ever users were defined by the following item: “Have you ever tried cigarette smoking, even 1 or 2 puffs?” Those who responded “Yes” were categorized as cigarette

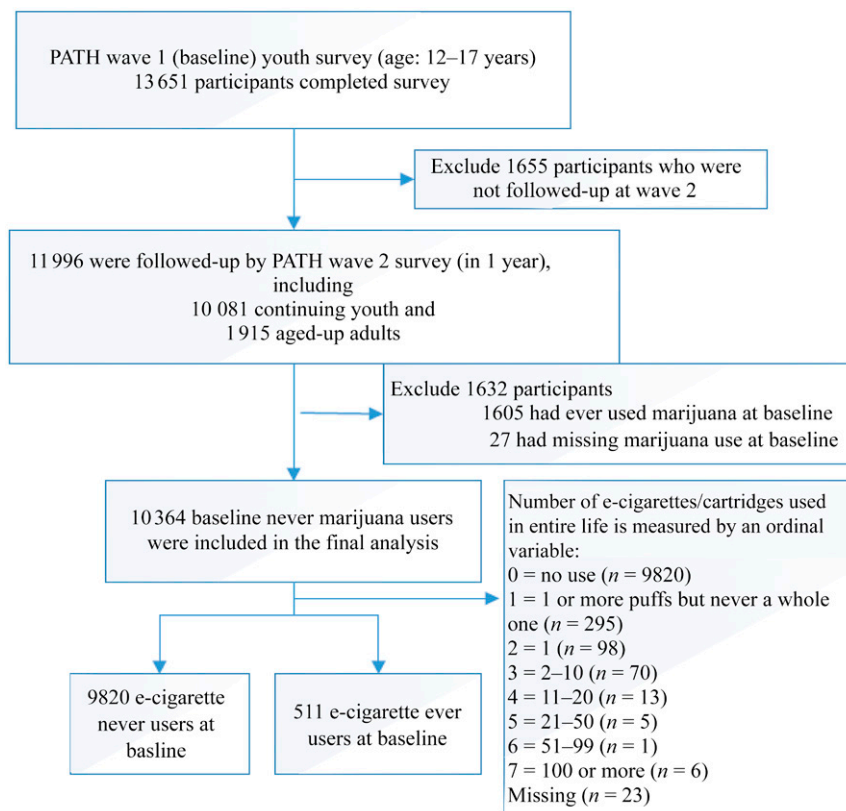


FIGURE 1
Flowchart for participants selected in the final study.

ever users. Alcohol ever users were participants who responded “Yes” to the following item: “Have you ever used alcohol at all, including sips of someone’s drink or your own drink?” Those who reported ever misuse of prescription drugs (ie, Ritalin, Adderall, painkillers, sedatives, or tranquilizers) were categorized as nonmedical ever users of prescription drugs. Those who reported ever using cocaine or crack, stimulants like methamphetamine or speed, heroin, inhalants, solvents, or hallucinogens were categorized as other illicit drug ever users.

Sensation Seeking

Sensation seeking was assessed by 3 items modified from the Brief Sensation Seeking Scale.²⁸ Participants were asked to indicate the extent of agreement on the 5-point scale to the following: “I like new and exciting experiences, even if I have to break the rules”;

“I like to do frightening things”; and “I prefer friends who are exciting and unpredictable.” Sensation seeking was calculated as the average response to these 3 items (Cronbach’s $\alpha = 0.76$).²⁸

Covariates

Several covariates were included to control for potential confounding effects: age (12–14 or 15–17 years old), sex (male or female), race and/or ethnicity (non-Hispanic [NH] white, NH African American, Hispanic, or NH other), grade performance (“mostly A’s” was classified as “A,” “A’s and B’s or mostly B’s” was classified as “B,” and “B’s and C’s or mostly C’s or below” was classified as “C or below”), parental education (less than high school, high school graduate, some college, or bachelor’s degree or greater), and region (Northeast, South, Midwest, West).

Statistical Methods

Weighted estimates of demographic characteristics and substance use at wave 1 were calculated for the overall sample and stratified by e-cigarette ever use status. Balanced repeated replication method with Fay's adjustment = 0.3 was used to increase stability in variance estimation.^{29,30} Confidence intervals (CIs) at the 95% level were calculated by using Wilson's method. For continuing youth, wave 2 sampling weights in youth data were used; for aged-up adults, wave 2 sampling weights in adult data were used.²⁷ Separate multivariable logistic regressions were used to examine the associations of e-cigarette use (ever, number of e-cigarettes/cartridges used) at wave 1 on subsequent marijuana use (P12M or heavy use) at wave 2 among marijuana never users at wave 1. Stratified analyses were conducted by age group (12–14 and 15–17 years old at wave 1). Adjusted odds ratios (aORs) were calculated in the multivariable analysis, in which all risk factors and covariates were included. Statistical analyses were performed by using SAS 9.4 (SAS Institute, Inc, Cary, NC), and *P* values <.05 were considered statistically significant.

RESULTS

Study Sample

A total of 11 996 young participants aged 12 to 17 years completed both the wave 1 and wave 2 surveys. Ever users of marijuana (*n* = 1605; 13.4%) and subjects with missing marijuana ever use status (*n* = 27) at wave 1 were excluded. The final analysis included 10 364 never marijuana users at wave 1 (Fig 1). As compared with ever marijuana users, never marijuana users tend to be younger and less likely to report using cigarettes, e-cigarettes, and other substances (Supplemental Table 5).

Sample Characteristics and Prevalence of Substance Use at Wave 1

Overall, 44.4% of never marijuana users were aged 15 to 17 years, and 48.8% were female. NH white users accounted for 55.1% of respondents, followed by Hispanic users (21.7%), NH African American users (13.9%), and NH other users (9.4%) (Table 1). In terms of substance use, 5.1% of adolescents reported ever use of e-cigarettes, 6.0% reported ever smoking cigarettes, 31.0% reported ever drinking alcohol, 7.3% reported ever nonmedical use of prescription drugs, and 0.2% reported ever use of other illicit drugs.

Significant differences between e-cigarette never and ever users were observed. E-cigarette ever users were more likely than e-cigarette never users to be older, male, white, and have poorer grade performance. They were also more likely to report sensation seeking, smoking cigarettes, drinking, and ever nonmedical use of prescription drugs and using other illicit drugs.

Temporal Association With Marijuana P12M and Heavy Use at Wave 2

Overall, 8.7% of never marijuana users at wave 1 reported use of marijuana at wave 2. More than 1 in 4 (26.6%) adolescents who ever used e-cigarettes at wave 1 reported subsequent marijuana use at wave 2, as compared with 7.7% of adolescents who never used e-cigarettes at wave 1 (*P* < .05) (Table 2). After adjusting for demographic factors and other substance use, e-cigarette ever users at wave 1 were more likely to report subsequent P12M marijuana use at wave 2 (aOR = 1.9; CI: 1.4–2.5). Older age, being female, being African American, and having lower grade performance all had significantly elevated adjusted odds for wave 2 marijuana P12M use. In addition, wave 1 sensation seeking and cigarette and alcohol ever use

had significantly elevated odds for wave 2 marijuana use.

Overall, 2.8% of marijuana never users at wave 1 reported heavy use of marijuana at wave 2. Female participants (versus male participants) and adolescents with a grade performance of “C or below” (versus those with “A”) were more likely to report heavy use of marijuana at wave 2. Sensation seeking, cigarette ever use, and alcohol ever use at wave 1 were associated with higher odds of reporting heavy use of marijuana at wave 2.

Age-Stratified Analysis of the Temporal Association Between E-cigarette Use and Subsequent Marijuana Use

There were significant interactions between age group (12–14 years and 15–17 years) and marijuana P12M (*P* < .05) and heavy (*P* < .05) use (Table 3, Supplemental Fig 2). The association between baseline e-cigarette use and P12M marijuana use at wave 2 was significant among both younger adolescents aged 12 to 14 years (29.2% vs 5.5%; aOR = 2.7; CI: 1.7–4.3) and older adolescents aged 15 to 17 years (25.3% vs 10.6%; aOR = 1.6; CI: 1.2–2.3). Moreover, the association between baseline e-cigarette use and subsequent heavy marijuana use was significant among young adolescents (12.0% vs 1.9%; aOR = 2.5; CI: 1.2–5.3) but was not significant among older adolescents.

We tested a dose-response relationship between the amount of e-cigarettes used and subsequent marijuana use in Table 4. Reporting a larger number of e-cigarettes/cartridges used in a lifetime at wave 1 was associated with higher odds of P12M (aOR = 1.7; CI: 1.3–2.0) and heavy (aOR = 1.6; CI: 1.2–2.2) marijuana use for younger adolescents.

TABLE 1 Sample Characteristics and Substance Use Prevalence, Overall and Stratified by E-cigarette Use Status Among Never Marijuana Users at Wave 1, PATH Study 2013–2015

Marijuana Never Users at Wave 1	Total		Wave 1 E-cigarette Ever Use				P ^a
	n	Weighted % (95% CI) ^b	n	Weighted % (95% CI) ^b	n	Weighted % (95% CI) ^b	
Age, y							<.0001
12–14	5901	55.6 (54.7–56.6)	5703	56.9 (55.9–57.9)	177	31.7 (27.8–35.8)	
15–17	4463	44.4 (43.4–45.3)	4117	43.1 (42.1–44.1)	334	68.3 (64.2–72.2)	
Sex							<.0001
Male	5298	51.2 (50.2–52.1)	4971	50.6 (49.7–51.6)	307	60.2 (55.9–64.4)	
Female	5066	48.8 (47.9–49.8)	4849	49.4 (48.4–50.3)	204	39.8 (35.6–44.1)	
Race and/or ethnicity							.0205
NH white	5079	55.1 (54.1–56.0)	4783	54.7 (53.7–55.7)	284	61.5 (57.3–65.7)	
NH African American	1418	13.9 (13.2–14.5)	1361	14.0 (13.3–14.7)	50	11.4 (8.8–14.5)	
Hispanic	2932	21.7 (20.9–22.5)	2790	21.8 (21.0–22.6)	129	19.5 (16.3–23.1)	
NH others	935	9.4 (8.8–9.9)	886	9.5 (8.9–10.1)	48	7.6 (5.6–10.3)	
Grade performance							<.0001
A	2807	29.2 (28.1–30.4)	2739	30.0 (28.9–31.2)	65	14.7 (11.7–18.3)	
B	4528	43.4 (42.2–44.5)	4306	43.5 (42.4–44.6)	213	42.3 (37.7–46.9)	
C or below	2986	27.4 (26.3–28.6)	2733	26.5 (25.4–27.6)	232	43.1 (38.7–47.6)	
Parental education							.0110
Less than high school	2097	17.5 (16.3–18.8)	1985	17.4 (16.2–18.7)	100	17.5 (14.1–21.6)	
High school graduate	1874	17.4 (16.3–18.6)	1752	17.2 (16.0–18.4)	115	21.5 (17.6–26.0)	
Some college	3256	31.5 (30.0–33.0)	3064	31.3 (29.7–32.8)	183	36.1 (31.8–40.6)	
Bachelor's degree or greater	3068	33.6 (31.4–35.9)	2953	34.1 (31.8–36.5)	110	24.9 (20.2–30.3)	
Region							.0110
Northeast	1482	16.5 (15.8–17.2)	1422	16.7 (16.0–17.5)	59	13.4 (10.7–16.8)	
South	2314	21.8 (21.1–22.7)	2193	21.9 (21.0–22.7)	114	21.1 (17.7–25.0)	
Midwest	3932	38.1 (37.2–39.0)	3699	37.7 (36.8–38.7)	218	44.8 (40.1–49.5)	
West	2636	23.6 (22.8–24.4)	2506	23.7 (22.9–24.6)	120	20.6 (17.4–24.4)	
E-cigarette ever use							—
No	9820	94.9 (94.5–95.4)	9820	100.0	—	—	
Yes	511	5.1 (4.6–5.5)	—	—	511	100.0	
Cigarette ever use							<.0001
No	9732	94.0 (93.3–94.6)	9416	96 (95.6–96.5)	285	55.7 (51.1–60.3)	
Yes	619	6.0 (5.4–6.7)	393	4.0 (3.5–4.4)	225	44.3 (39.7–48.9)	
Alcohol ever use							<.0001
No	7226	69.0 (67.6–70.4)	7013	70.7 (69.3–72.1)	185	36.1 (31.5–40.9)	
Yes	3088	31.0 (29.6–32.4)	2759	29.3 (27.9–30.7)	325	63.9 (59.1–68.5)	
Nonmedical use of prescription drugs ^c							.0011
No	9467	92.7 (92.1–93.3)	8992	92.9 (92.3–93.5)	446	89.2 (86.2–91.6)	
Yes	743	7.3 (6.7–7.9)	684	7.1 (6.5–7.7)	57	10.8 (8.4–13.8)	
Other illicit drug ever use ^d							<.0001
No	10255	99.8 (99.7–99.8)	9725	99.8 (99.7–99.9)	500	99.0 (97.8–99.6)	
Yes	29	0.2 (0.2–0.3)	22	0.2 (0.1–0.3)	7	1.0 (0.4–2.2)	
Sensation seeking (mean and SE) ^e	10164	2.54 ± 0.01	9633	2.51 ± 0.01	502	3.08 ± 0.05	<.0001

—, not applicable.

^a Rao-Scott χ^2 test was performed to compare the distribution of sample characteristics and substance use by e-cigarette use status at wave 1.

^b Researchers of the PATH study oversampled adult tobacco users, young adults aged 18–24 y, and African Americans, so weighted estimates were calculated to reflect the prevalence in population.

^c Prescription drugs include Ritalin, Adderall, painkillers, sedatives, or tranquilizers.

^d Other illicit drugs include cocaine or crack, stimulants like methamphetamine or speed, heroin, inhalants, solvents, or hallucinogens.

^e Sensation seeking was based on 5-point scales, labeled “strongly disagree,” “disagree,” “neither agree nor disagree,” “agree,” and “strongly agree.”

DISCUSSION

It is suggested in the results from this longitudinal study that baseline e-cigarette use independently predicts subsequent marijuana use among youth after controlling for social-demographic factors, sensation

seeking, and other substance use. The overall prevalence of ever e-cigarette use among adolescents was 10.6% in the PATH 2013–2014 study (Supplemental Table 5), which is aligned with the prevalence reported by the National Youth

Tobacco Survey (8.1% in 2013).³ At wave 1, never marijuana users had a significantly lower prevalence of e-cigarette ever use as compared with marijuana users (5.1% vs 46.4%). To avoid confounding effects, baseline marijuana users were

TABLE 2 Temporal Association of E-cigarette Use and Covariates at Wave 1 With Marijuana Use at Wave 2 Among Baseline Marijuana Never Users, PATH Study, 2013–2015

Marijuana Never Users at Wave 1	Marijuana P12M Use at Wave 2				Marijuana Heavy Use at Wave 2		
	<i>n</i>	<i>n</i>	Weighted % (95% CI)	aOR ^a	<i>n</i>	Weighted % (95% CI)	aOR ^a
Total	10364	897	8.7 (8.1–9.3)	—	286	2.8 (2.4–3.2)	—
E-cigarette ever use							
No	9820	759	7.7 (7.1–8.4)	Reference	245	2.5 (2.2–3.0)	Reference
Yes	511	137	26.6 (22.6–31.0)	1.9 (1.4–2.5)***	41	7.9 (5.6–10.9)	1.3 (0.8–2.1) ^b
Age, y							
12–14	5901	373	6.2 (5.6–6.9)	Reference	128	2.2 (1.8–2.7)	Reference
15–17	4463	524	11.8 (10.7–13.0)	1.4 (1.2–1.7)***	158	3.6 (3–4.4)	1.1 (0.8–1.6)
Male	5298	431	8.2 (7.5–9.1)	Reference	118	2.2 (1.8–2.8)	Reference
Female	5066	466	9.1 (8.3–10.1)	1.2 (1–1.4)*	168	3.4 (2.9–4.0)	1.6 (1.2–2.2)**
Race and/or ethnicity							
NH white	5079	418	8.5 (7.6–9.4)	Reference	147	2.9 (2.5–3.5)	Reference
NH African American	1418	156	11.2 (9.4–13.4)	1.8 (1.3–2.4)***	39	2.9 (2.0–4.2)	1.2 (0.8–2.0)
Hispanic	2932	240	8.3 (7.3–9.3)	1.0 (0.8–1.2)	79	2.8 (2.2–3.6)	1.0 (0.7–1.5)
NH others	935	83	7.1 (5.5–9.1)	0.9 (0.7–1.3)	21	1.9 (1.1–3.3)	0.7 (0.4–1.2)
Grade performance							
A	2807	161	5.6 (4.7–6.6)	Reference	47	1.7 (1.2–2.3)	Reference
B	4528	384	8.8 (8.0–9.6)	1.4 (1.1–1.7)**	113	2.7 (2.2–3.3)	1.4 (0.9–2.3)
C or below	2986	349	11.9 (10.5–13.4)	1.8 (1.4–2.3)***	125	4.2 (3.5–5.1)	2.2 (1.4–3.6)**
Parental education							
Less than high school	2097	190	9.3 (8.2–10.6)	Reference	61	2.9 (2.2–3.7)	Reference
High school graduate	1874	174	9.2 (8.0–10.6)	0.9 (0.7–1.1)	60	3.3 (2.6–4.3)	1.1 (0.8–1.6)
Some college	3256	302	9.3 (8.2–10.4)	0.9 (0.7–1.1)	97	3 (2.4–3.7)	0.9 (0.6–1.3)
Bachelor’s degree or greater	3068	221	7.4 (6.4–8.5)	0.9 (0.7–1.1)	64	2.3 (1.7–3.0)	0.9 (0.6–1.3)
Region							
Northeast	1482	141	9.9 (8.2–11.8)	Reference	50	3.5 (2.5–5.0)	Reference
South	2314	213	9.1 (8.0–10.4)	0.8 (0.7–1.1)	65	2.8 (2.2–3.6)	0.7 (0.5–1.2)
Midwest	3932	318	8.0 (7.0–9.1)	0.7 (0.5–0.9)*	100	2.5 (2.0–3.1)	0.6 (0.4–1.0)
West	2636	225	8.5 (7.2–10.0)	0.9 (0.7–1.2)	71	2.8 (2.0–4.0)	0.8 (0.5–1.4)
Cigarette ever use							
No	9732	732	7.5 (6.9–8.2)	Reference	227	2.4 (2.1–2.8)	Reference
Yes	619	163	26.5 (22.6–30.9)	2.0 (1.5–2.7)***	59	9.4 (7.1–12.3)	2.1 (1.4–3.2)***
Alcohol ever use							
No	7226	392	5.3 (4.8–5.9)	Reference	108	1.6 (1.2–1.9)	Reference
Yes	3088	499	16.2 (14.8–17.8)	2.3 (1.9–2.8)***	177	5.6 (4.8–6.6)	2.4 (1.8–3.3)***
Nonmedical use of prescription drugs							
No	9467	784	8.3 (7.7–9.0)	Reference	247	2.6 (2.3–3.0)	Reference
Yes	743	101	13.1 (10.4–16.4)	1.2 (0.9–1.5)	37	5.0 (3.4–7.3)	1.2 (0.8–1.8)
Other illicit drug ever use							
No	10255	883	8.7 (8.0–9.3)	Reference	282	2.8 (2.4–3.2)	Reference
Yes	29	5	17.4 (7.5–35.1)	1.0 (0.3–3.4)	3	12.0 (4.3–29)	2.4 (0.7–8.7)
Sensation seeking ^c	—	—	—	1.6 (1.5–1.7)***	—	—	1.7 (1.5–2)***

—, not applicable.

^a aOR was calculated in the multivariable logistic regression, in which the explanatory variables included all listed variables (demographics, substance ever use, and sensation seeking) at wave 1.

^b There were significant interactions between age and e-cigarette use. See Table 3.

^c aOR corresponds to 1 U increase in the risk of sensation seeking (5-point scale).

* $P < .05$;

** $P < .01$;

*** $P < .001$.

excluded from analysis, which led to a low prevalence of e-cigarette use at baseline in this study. For associations between e-cigarette and subsequent marijuana use, the aORs were lower than the crude ratios. As shown in Supplemental Table 6,

the reduction was most affected by ever use of cigarettes, followed by drinking alcohol and sensation seeking, and slightly affected by age and grade performance. There are several possible reasons why e-cigarette use might be associated

with subsequent marijuana initiation. On the one hand, e-cigarettes may simply be a marker of risk-taking behavior; e-cigarette users are more likely to smoke cigarettes and drink alcohol, which are also associated with marijuana use.^{31,32}

TABLE 3 Age-Stratified Analysis of the Temporal Association Between E-cigarette Ever Use at Wave 1 and Marijuana Use at Wave 2 Among Baseline Marijuana Never Users, PATH Study, 2013–2015

Marijuana Never Users at Wave 1	E-cigarette Ever Use at Wave 1	Marijuana P12M Use at Wave 2			Marijuana Heavy Use at Wave 2		
		<i>n</i>	Weighted % (95% CI)	aOR ^a	<i>n</i>	Weighted % (95% CI)	aOR ^a
Aged 12–14 (<i>n</i> = 5901) ^b	No (<i>n</i> = 5703)	321	5.5 (4.9–6.2)	REF	107	1.9 (1.5–2.3)	REF
	Yes (<i>n</i> = 177)	52	29.2 (23.0–36.2)	2.7 (1.7–4.3) ^{***}	21	12.0 (7.6–18.5)	2.5 (1.2–5.3) [*]
Aged 15–17 (<i>n</i> = 4463) ^b	No (<i>n</i> = 4117)	438	10.6 (9.5–11.9)	REF	138	3.4 (2.8–4.2)	REF
	Yes (<i>n</i> = 334)	85	25.3 (21.0–30.3)	1.6 (1.2–2.3) ^{**}	20	5.9 (3.8–9.1)	0.9 (0.5–1.5)
Interaction between age group and e-cigarette ever use ^c	—	—	—	2.1 (1.3–3.3) ^{**}	—	—	3.1 (1.5–6.4) ^{**}

—, not applicable.

^a For all models, aOR was adjusted by sensation seeking, ever use of cigarettes, drinking, nonmedical use of prescription drugs and other illicit drugs, and demographics (sex, race and/or ethnicity, grade performance, parental education, and region) at wave 1.

^b Separate multivariable logistic regression models were performed for youth aged 12–14 years and youth aged 15–17 years, respectively.

^c A joint model was constructed to evaluate the main effects of age and e-cigarette use, along with an interaction between age and e-cigarette use. Interaction aOR indicates that e-cigarette use (versus no use) at baseline was associated with higher risks of marijuana use at wave 2 among younger adolescents than among older adolescents.

^{*} *P* < .05;

^{**} *P* < .01;

^{***} *P* < .001.

TABLE 4 Age-Stratified Analysis of the Temporal Association Between the Number of E-cigarettes and/or Cartridges Used at Wave 1 and Marijuana Use at Wave 2 Among Baseline Marijuana Never Users, PATH Study, 2013–2015

Marijuana Never Users at Wave 1	Marijuana P12M Use at Wave 2		Marijuana Heavy Use at Wave 2		
	No. E-cigarettes and/or Cartridges Used at Wave 1 ^a	<i>n</i>	aOR ^b	<i>n</i>	aOR ^b
All adolescents, <i>n</i> = 10 364	897	1.3 (1.1–1.5) ^{***}	286	1.2 (1.0–1.5)	
Aged 12–14 y (<i>n</i> = 5901)	373	1.7 (1.3–2.0) ^{***}	128	1.6 (1.2–2.2) ^{**}	
Aged 15–17 y (<i>n</i> = 4463)	524	1.2 (1.0–1.4)	158	0.9 (0.7–1.3)	
Interaction between e-cigarette use and age group ^c	—	1.5 (1.2–1.9) ^{**}	—	1.8 (1.2–2.6) ^{**}	

—, not applicable.

^a A dose-response analysis was conducted by treating the number of e-cigarette cartridges used as an ordinal variable, and aOR corresponds to 1 U increase in the scale.

^b For all models, aOR was adjusted by sensation seeking, ever use of cigarettes, drinking, nonmedical use of prescription drugs and other illicit drugs, and demographics (sex, race and/or ethnicity, grade performance, parental education, and region) at wave 1.

^c Significant interaction indicates that that number of e-cigarettes used at baseline was associated with higher risks of marijuana use at wave 2 among younger adolescents than among older adolescents.

^{**} *P* < .01;

^{***} *P* < .001.

Alternatively, because the brain is still developing during the teenage years, nicotine exposure might lead to changes in the central nervous system that predispose teenagers to dependence on other drugs of abuse.³³ Experimenting with e-cigarettes might also increase a youth's curiosity about marijuana, reduce perceived harm of marijuana use, and increase the social access to marijuana from peers and friends. As a result of marketing and social media promotion,^{34,35} vaping

cannabis is gaining popularity.^{19,20} Youth who experiment with e-cigarettes may use the same device or switch to newer generation devices for vaping marijuana,^{20,36} which could lead to use of substance with stronger addictive effects.³⁷

With these findings, we highlight the importance of policy and education to reduce risks for youth. Currently, e-cigarette and marijuana are the 2 most commonly used substances by teenagers. The FDA has extended its

authority to regulate e-cigarettes, and the first round of these new regulations, including mandatory age and photo identification checks to prevent illegal sales of newly regulated tobacco products to minors, went into effect on August 8, 2016³⁸ (after data collected for this study). Data from this study may have implications for state authorities that presently vary greatly in their enforcement of e-cigarette sales and legal access to marijuana.^{39–41} It is important for health providers and educators to advise youth about the risks of e-cigarette use, including the propensity of progression to marijuana use after e-cigarette use. Policies to prevent youth use of e-cigarettes and reduce youth access to e-cigarettes, such as expanding smoke-free policies and Tobacco 21 policies, should be considered as well.

In research on the developmental trajectory of substance use and addiction, the critical role of nicotine initiation at an early age has been highlighted. For instance, smoking at a young age increases the likelihood of becoming an addicted daily smoker.^{2,24,42,43} Our study revealed heterogeneity in the associations

of e-cigarette use on subsequent marijuana use by age group. The temporal association between baseline e-cigarette use and initiation of marijuana use was larger among younger adolescents aged 12 to 14 years than among older adolescents aged 15 to 17 years. This finding is consistent with previous cross-sectional studies in which it was indicated that younger high school students were more likely to use e-cigarettes to vape cannabis, and that e-cigarettes may have made inroads among younger users who have low risks of using traditional substances.^{17,20} As youth start to initiate e-cigarettes as early as 7 years old,⁴⁴ the interaction between age and subsequent marijuana use underscores the importance of starting prevention efforts on e-cigarette and other substance use at an earlier age because these youth have the most to gain. In addition, we found that youth who reported a larger number of e-cigarettes and/or cartridges used in a lifetime at baseline were more likely to be subsequent marijuana heavy users. Because the regular use of marijuana

during adolescence is of particular concern for adverse health effects,⁴⁵ we add to the existing literature by identifying the quantity of e-cigarette use as a risk factor for marijuana heavy use.

This study is subject to several limitations. First, both e-cigarette and marijuana use were self-reported. Thus, reporting and recall biases might have occurred, especially for younger respondents.⁴⁶ Second, not all youth included in wave 1 of the PATH study responded to the wave 2 survey. However, attrition was not associated with a previous history of substance use (Supplemental Table 5). Finally, the investigators of the PATH study did not ask respondents about what substances youth vaped in their e-cigarettes, which could include flavoring only, nicotine, or marijuana derivatives.⁴⁷ Therefore, we were not able to ascertain which specific vaped substances had effects on subsequent marijuana use.

Future studies are needed to investigate the underlying mechanism of substance transition and evaluate long-term impacts of

e-cigarette use. Our study revealed that e-cigarette use was associated with an increased risk of subsequent marijuana use among youth, with a stronger temporal association among younger adolescents. With these findings, we suggest that the widespread use of e-cigarettes among youth may have implications for the uptake of other drugs of abuse beyond nicotine and tobacco products.

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ABBREVIATIONS

aOR: adjusted odds ratio
 CI: confidence interval
 e-cigarette: electronic cigarette
 NH: non-Hispanic
 PATH: Population Assessment of Tobacco and Health
 P12M: past 12 months

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