



BUSINESS DAY

Selling a Poison by the Barrel: Liquid Nicotine for E-Cigarettes

By **MATT RICHTEL** MARCH 23, 2014

A dangerous new form of a powerful stimulant is hitting markets nationwide, for sale by the vial, the gallon and even the barrel.

The drug is nicotine, in its potent, liquid form — extracted from tobacco and tinctured with a cocktail of flavorings, colorings and assorted chemicals to feed the fast-growing electronic cigarette industry.

These “e-liquids,” the key ingredients in e-cigarettes, are powerful neurotoxins. Tiny amounts, whether ingested or absorbed through the skin, can cause vomiting and seizures and even be lethal. A teaspoon of even highly diluted e-liquid can kill a small child.

But, like e-cigarettes, e-liquids are not regulated by federal authorities. They are mixed on factory floors and in the back rooms of shops, and sold legally in stores and online in small bottles that are kept casually around the house for regular refilling of e-cigarettes.

Evidence of the potential dangers is already emerging. Toxicologists warn that e-liquids pose a significant risk to public health, particularly to children, who may be drawn to their bright colors and fragrant flavorings like cherry, chocolate and bubble gum.

“It’s not a matter of if a child will be seriously poisoned or killed,” said Lee Cantrell, director of the San Diego division of the California Poison Control System and a professor of pharmacy at the University of California, San Francisco. “It’s a matter of when.”

Reports of accidental poisonings, notably among children, are soaring. Since 2011, there appears to have been one death in the United States, a suicide by an adult who injected nicotine. But less serious cases have led to a surge in calls to poison control centers. Nationwide, the number of cases linked to e-liquids jumped to 1,351 in 2013, a 300 percent increase from 2012, and the number is on pace to double this year, according to information from the National Poison Data System. Of the cases in 2013, 365 were referred to hospitals, triple the previous year's number.

Examples come from across the country. Last month, a 2-year-old girl in Oklahoma City drank a small bottle of a parent's nicotine liquid, started vomiting and was rushed to an emergency room.

That case and age group is considered typical. Of the 74 e-cigarette and nicotine poisoning cases called into Minnesota poison control in 2013, 29 involved children age 2 and under. In Oklahoma, all but two of the 25 cases in the first two months of this year involved children age 4 and under.

In terms of the immediate poison risk, e-liquids are far more dangerous than tobacco, because the liquid is absorbed more quickly, even in diluted concentrations.

"This is one of the most potent naturally occurring toxins we have," Mr. Cantrell said of nicotine. But e-liquids are now available almost everywhere. "It is sold all over the place. It is ubiquitous in society."

The surge in poisonings reflects not only the growth of e-cigarettes but also a shift in technology. Initially, many e-cigarettes were disposable devices that looked like conventional cigarettes. Increasingly, however, they are larger, reusable gadgets that can be refilled with liquid, generally a combination of nicotine, flavorings and solvents. In Kentucky, where about 40 percent of cases involved adults, one woman was admitted to the hospital with cardiac problems after her e-cigarette broke in her bed, spilling the e-liquid, which was then absorbed through her skin.

The problems with adults, like those with children, owe to carelessness and lack of understanding of the risks. In the cases of exposure in children, "a lot of parents didn't realize it was toxic until the kid started vomiting," said Ashley Webb, director of the Kentucky Regional Poison Control Center at

Kosair Children's Hospital.

The increased use of liquid nicotine has, in effect, created a new kind of recreational drug category, and a controversial one. For advocates of e-cigarettes, liquid nicotine represents the fuel of a technology that might prompt people to quit smoking, and there is anecdotal evidence that is happening. But there are no long-term studies about whether e-cigarettes will be better than nicotine gum or patches at helping people quit. Nor are there studies about the long-term effects of inhaling vaporized nicotine.

Unlike nicotine gums and patches, e-cigarettes and their ingredients are not regulated. The Food and Drug Administration has said it plans to regulate e-cigarettes but has not disclosed how it will approach the issue. Many e-cigarette companies hope there will be limited regulation.

"It's the wild, wild west right now," said Chip Paul, chief executive officer of Palm Beach Vapors, a company based in Tulsa, Okla., that operates 13 e-cigarette franchises nationwide and plans to open 50 more this year. "Everybody fears F.D.A. regulation, but honestly, we kind of welcome some kind of rules and regulations around this liquid."

Mr. Paul estimated that this year in the United States there will be sales of one million to two million liters of liquid used to refill e-cigarettes, and it is widely available on the Internet. Liquid Nicotine Wholesalers, based in Peoria, Ariz., charges \$110 for a liter with 10 percent nicotine concentration. The company says on its website that it also offers a 55 gallon size. Vaporworld.biz sells a gallon at 10 percent concentrations for \$195.

Mr. Paul said he was worried that some manufacturers outside the United States — China is a major center of e-cigarette production — were not always delivering the concentrations and purity of nicotine they promise. Some retailers, Mr. Paul said, "are selling liquid and they don't have a clue what is in it."

Cynthia Cabrera, executive director of Smoke Free Alternatives Trade Association, said she would also favor regulations, including those that would include childproof bottles and warning labels, and also manufacturing standards. But she said many companies already were doing that voluntarily, and that parents also needed to take some responsibility.

“You wouldn’t leave a bottle of Ajax out,” she said. Advocates of e-cigarettes sometimes draw comparisons between nicotine and caffeine, characterizing both as recreational stimulants that carry few risks. But that argument is not established by science, and many health advocates take issue with the comparison.

“There’s no risk to a barista no matter how much caffeine they spill on themselves,” said Dr. Neal L. Benowitz, a professor at the University of California, San Francisco, who specializes in nicotine research. “Nicotine is different.”

Without proper precautions, like wearing gloves while mixing e-liquids, these products “represents a serious workplace hazard,” he said.

The nicotine levels in e-liquids varies. Most range between 1.8 percent and 2.4 percent, concentrations that can cause sickness, but rarely death, in children. But higher concentrations, like 10 percent or even 7.2 percent, are widely available on the Internet. A lethal dose at such levels would take “less than a tablespoon,” according to Dr. Cantrell, from the poison control system in California. “Not just a kid. One tablespoon could kill an adult,” he said.

A version of this article appears in print on March 24, 2014, on page A1 of the New York edition with the headline: Selling a Poison by the Barrel: Liquid Nicotine for E-Cigarettes.

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Cessation and E-Cigarettes

Cessation: What is Proven to Work

- The US Food and Drug Administration has approved seven Nicotine Replacement Therapies (NRT) for smoking cessation, five of which contain nicotine - patch, gum, lozenge, nasal spray and inhaler – and two oral medications which are prescribed and nicotine-free – varenicline (Chantix) and bupropion (Zyban).
(<http://www.fda.gov/forconsumers/consumerupdates/ucm198176.htm#nicotine>)
- There are two Cochrane Reviews (2012 and 2013) which assess the efficacy of the FDA approved NRT therapies (<http://www.biblioteca.cochrane.com/pdf/CD000146.pdf>) and compare their quit outcomes (<http://www.cochrane.org/features/pharmacological-interventions-smoking-cessation-overview-and-network-meta-analysis>). E-cigarettes are not included.

International and National Organization Policy Statements

- The World Health Organization, Legacy Foundation, American Lung Association, and the American Cancer Society, among others, have released policy statements against or expressing concern about the safety of using e-cigarettes and the lack of efficacy in using as a cessation device. There is insufficient data on health risks.
- **The WHO's public statement on e-cigarettes: "Strongly advised not to use them."**

Research on E-Cigarettes and Exposure

- One of the first laboratory studies on the effects of e-cigarette vapor found that human cells exposed to e-cigarette vapor exhibited similar mutations to those exposed to tobacco smoke.
(http://clincancerres.aacrjournals.org/content/20/2_Supplement/B16.abstract)

Peer-Reviewed Research on E-Cigarettes: Evidence is Weak as a Cessation Device, May Promote Dual Use

Studies among adults show decreased tobacco cessation and increased dual use

- Awareness and use of e-cigarettes is increasing rapidly. Results from a large national survey published in *Nicotine and Tobacco Research* showed that *awareness of e-cigarettes among U.S. adults increased by nearly 50% from 2010-2011, and ever use of e-cigarettes doubled.* Awareness and ever-use of e-cigarettes was significantly higher among current smokers than former and never smokers, with one in five current smokers reporting having used e-cigarettes.
(<http://ntr.oxfordjournals.org/content/early/2013/02/20/ntr.ntt013.abstract>)
- These findings are corroborated by a study using a large national sample of smokers in Great Britain. The authors found that e-cigarette users are heavier smokers and are more likely to report having tried to quit in the past year. This study also showed near-universal awareness of e-cigarettes among smokers and recent ex-smokers.
(<http://www.sciencedirect.com/science/article/pii/S0306460314000744>)

- A study of callers to six states' Quitlines (Alere) found that one in three respondents reported ever using or trying e-cigarettes. Fifty-one percent used e-cigarettes to help quit other tobacco products and 15% to replace other tobacco use. *However, respondents reporting e-cigarette use were significantly less likely to be tobacco abstinent at the time of the 7 month follow-up survey than those who had never tried e-cigarettes.*
(<http://ntr.oxfordjournals.org/content/early/2013/05/07/ntr.ntt061.abstract.html?papetoc>)
- Research suggests that e-cigarettes do not break the cycle of nicotine addiction among smokers using them to quit. A longitudinal study of daily e-cigarette users found that 89% of daily e-cigarette users were still users one year after baseline. Furthermore, individuals using both conventional and e-cigarettes at follow up had not significantly decreased their conventional cigarette consumption from baseline.
(<http://www.sciencedirect.com/science/article/pii/S0306460313003304>)
- A study published in the American Journal of Public Health found that smokers who had tried e-cigarettes were significantly more likely to be unsuccessful quitters than smokers who had never tried to quit.
(http://ajph.aphapublications.org/doi/abs/10.2105/AJPH.2012.301070?url_ver=Z39.88-2003&rfr_id=ori:rid:crossref.org&rfr_dat=cr_pub%3dpubmed)

Studies among youth show increased prevalence & suggest gateway to tobacco use

- The Centers for Disease Control and Prevention report that *e-cigarette use among U.S. youth has doubled in the past two years*, and 80% of current high school e-cigarette users are also users of conventional cigarettes.
(<http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6235a6.htm>)
- The Centers for Disease Control and Prevention recently issued a warning that the number of calls to poison control centers involving e-cigarette liquids have skyrocketed, from 1 per month in September 2010 to 215 per month in February 2014. E-cigarette liquid containers are not required to be childproof, yet they may appeal to children since they are brightly colored and come in fruit and candy flavors. (<http://www.cdc.gov/media/releases/2014/p0403-e-cigarette-poison.html>)
- Data from the National Youth Tobacco Survey (NYTS) corroborated that rates of e-cigarette use are increasing rapidly among U.S. youth. In addition, the authors found that U.S. middle and high school e-cigarette users are more likely to be current, established smokers. Among youth experimenting with conventional cigarettes, those who had used e-cigarettes were more likely to have used conventional cigarettes in the last month or year, reflecting high rates of dual use. *The authors concluded that "use of e-cigarettes does not discourage, and may encourage, conventional cigarette use among U.S. adolescents."*
(<http://archpedi.jamanetwork.com/article.aspx?articleid=1840772>)
- An editorial from the NYTS study above stresses that with the use of e-cigarettes rising among youth and their potential as a gateway to conventional cigarettes, *it is imperative that "policy makers act quickly"* to reduce the health risks and potential harms of this product.
(<http://archpedi.jamanetwork.com/article.aspx?articleid=1840771>)

- A 2013 study of over 75,000 Korean youth using the Korea Youth Risk Behavior survey showed that *e-cigarette use is strongly associated with current and heavier cigarette smoking*. The study's authors, which include a leading tobacco researcher from the University of California, San Francisco, found that youth interested in quitting reported the most e-cigarette use and may be regarding the product as a cessation method. ([http://www.jahonline.org/article/S1054-139X\(13\)00748-9/abstract](http://www.jahonline.org/article/S1054-139X(13)00748-9/abstract))

Study showing results pointing toward potential harm reduction

- An editorial in the Journal of the American Medical Association noted that e-cigarette profits have doubled every year since 2008. With a lack of developed research, industry regulations, and informed policies, it remains unknown whether they should be seen as a threat to tobacco cessation or a potential source of harm reduction. (<http://jama.jamanetwork.com/article.aspx?articleid=1812971>)
- "E-cigarettes, with or without nicotine, were modestly effective at helping smokers to quit, with similar achievement of abstinence as with patches, and few adverse effects." ([http://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(13\)61842-5/abstract](http://www.thelancet.com/journals/lancet/article/PIIS0140-6736(13)61842-5/abstract)).

Title: *Gateway to Addiction? A Survey of Popular Electronic Cigarette Manufacturers and Marketing to Youth*

Date: April 14, 2014

Authors: Senator Richard J. Durbin (D-IL), Representative Henry A. Waxman (D-CA), Senators Tom Harkin (D-IA), John D. Rockefeller IV (D-WV), Richard Blumenthal (D-CT), Edward J. Markey (D-MA), Sherrod Brown (D-OH), Jack Reed (D-RI), Barbara Boxer (D-CA), Jeff Merkley (D-OR), and Representative Frank Pallone Jr. (D-NJ)

- This report was made to answer questions surrounding e-cigarette brands and their marketing strategies. It investigated 9 major e-cigarette companies: Altria, R.J. Reynolds Vapor Co, NJOY, Eonsmoke, LOGIC, VMR, Lorillard, Green Smoke, and Lead by Sales. The companies provided written responses to questions from this investigation. If they did not provide complete responses the information was gathered from the company websites and other information that is publically available.
- E-cigarettes are not subject to the same marketing/advertising restrictions as conventional!
- The report provided 8 major findings from the investigation.
 1. **“Many surveyed e-cigarette companies are promoting their products through sponsorship of youth-oriented events, and some companies are offering free samples of e-cigarettes.”**
 - Companies with sponsored events: R.J. Reynolds Co, NJOY, LOGIC, VMR, Lorillard, and Green Smoke
 - Companies distributing free samples: Altria, R.J Reynolds, NJOY, LOGIC, VMR, Lorillard, Green Smoke, and Lead by Sales.
 2. **“Surveyed e-cigarette companies market e-cigarettes in flavors that appear to be designed to appeal to youth.”**
 - 6 Companies: R.J Reynolds Co, VMR, Lorillard, Eonsmoke, Green Smoke, and Lead by Sales.
 3. **“E-cigarettes are available for purchase in stores and online by children and teenagers”**
 - Some of the companies surveyed require retailers to not sell their products to people under the age of 18 and to only display their products where they are accessible through only direct contact with a store employee. However, “they only apply to venders that participate in promotional programs or with which one company has a ‘direct relationship’”
 - 3 companies (not named) do not have any restrictions on product placement.
 - 7/9 companies sell their product online and 3 (NJOY, Lorillard, and Eonsmoke) do not require any sort of age verification to enter their site.
 4. **“Surveyed e-cigarette manufacturers have significantly increased marketing expenditures”**
 - 5 of the 9 companies provided expenditure information and revealed that between 2012 and 2013 spending was increased by 164%.

5. **“Many surveyed e-cigarette companies air television and radio advertisements, often with celebrity spokespeople, including during events and programs with youth viewership.”**
 - E-cigs are *not* federally banned from television and radio advertising like conventional cigarettes. 7/9 companies run these advertisements.
 - 4/9 surveyed companies (Lorillard, Green Smoke, NJOY, and Lead by Sales) have used celebrity spokespeople.
6. **“Surveyed e-cigarette companies extensively utilize social media and product websites to promote their products.”**
 - 3/8 companies who have social media accounts (Eonsmoke, VMR, and Lead by Sales) do not have social media age restrictions, “even where age restriction functionality is available.”
7. **“E-cigarette product warning labels lack uniformity and may confuse or mislead consumers.”**
 - All surveyed companies except Lead by Sales have health warning or disclaimer on their packages but they are variable.
8. **“Most surveyed e-cigarette companies support some form of regulation.”**
 - 6/9 companies support some form of regulation.

Original Investigation

Electronic Cigarettes and Conventional Cigarette Use Among US Adolescents

A Cross-sectional Study

Lauren M. Dutra, ScD; Stanton A. Glantz, PhD

IMPORTANCE Electronic cigarette (e-cigarette) use is increasing rapidly among adolescents, and e-cigarettes are currently unregulated.

OBJECTIVE To examine e-cigarette use and conventional cigarette smoking.

DESIGN, SETTING, AND PARTICIPANTS Cross-sectional analyses of survey data from a representative sample of US middle and high school students in 2011 (n = 17 353) and 2012 (n = 22 529) who completed the 2011 and 2012 National Youth Tobacco Survey.

EXPOSURES Ever and current e-cigarette use.

MAIN OUTCOMES AND MEASURES Experimentation with, ever, and current smoking, and smoking abstinence.

RESULTS Among cigarette experimenters (≥ 1 puff), ever e-cigarette use was associated with higher odds of ever smoking cigarettes (≥ 100 cigarettes; odds ratio [OR] = 6.31; 95% CI, 5.39-7.39) and current cigarette smoking (OR = 5.96; 95% CI, 5.67-6.27). Current e-cigarette use was positively associated with ever smoking cigarettes (OR = 7.42; 95% CI, 5.63-9.79) and current cigarette smoking (OR = 7.88; 95% CI, 6.01-10.32). In 2011, current cigarette smokers who had ever used e-cigarettes were more likely to intend to quit smoking within the next year (OR = 1.53; 95% CI, 1.03-2.28). Among experimenters with conventional cigarettes, ever use of e-cigarettes was associated with lower 30-day (OR = 0.24; 95% CI, 0.21-0.28), 6-month (OR = 0.24; 95% CI, 0.21-0.28), and 1-year (OR = 0.25; 95% CI, 0.21-0.30) abstinence from cigarettes. Current e-cigarette use was also associated with lower 30-day (OR = 0.11; 95% CI, 0.08-0.15), 6-month (OR = 0.11; 95% CI, 0.08-0.15), and 1-year (OR = 0.12; 95% CI, 0.07-0.18) abstinence. Among ever smokers of cigarettes (≥ 100 cigarettes), ever e-cigarette use was negatively associated with 30-day (OR = 0.61; 95% CI, 0.42-0.89), 6-month (OR = 0.53; 95% CI, 0.33-0.83), and 1-year (OR = 0.32; 95% CI, 0.18-0.56) abstinence from conventional cigarettes. Current e-cigarette use was also negatively associated with 30-day (OR = 0.35; 95% CI, 0.18-0.69), 6-month (OR = 0.30; 95% CI, 0.13-0.68), and 1-year (OR = 0.34; 95% CI, 0.13-0.87) abstinence.

CONCLUSIONS AND RELEVANCE Use of e-cigarettes was associated with higher odds of ever or current cigarette smoking, higher odds of established smoking, higher odds of planning to quit smoking among current smokers, and, among experimenters, lower odds of abstinence from conventional cigarettes. Use of e-cigarettes does not discourage, and may encourage, conventional cigarette use among US adolescents.

 Editorial

 Supplemental content at jamapediatrics.com

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Electronic cigarettes (e-cigarettes) are devices that deliver a heated aerosol of nicotine in a fashion that mimics conventional cigarettes while delivering lower levels of toxins than a conventional combusted cigarette.¹⁻⁴ They are being aggressively marketed using the same messages and media channels (plus the Internet) that cigarette companies used to market conventional cigarettes in the 1950s and 1960s,⁵ including on television and radio where cigarette advertising has been prohibited for more than 40 years.

In addition to these traditional media, e-cigarettes have established a strong advertising presence on the Internet, and e-cigarette companies heavily advertise their products through electronic communication. Studies have demonstrated for decades that youth exposure to cigarette advertising causes youth smoking.⁶ Electronic cigarettes are also sold using characterizing flavors (eg, strawberry, licorice, chocolate) that are banned in cigarettes in the United States because they appeal to youths. The 2011 and 2012 National Youth Tobacco Survey (NYTS) revealed that e-cigarette use among youths in grades 6 through 12 doubled between 2011 and 2012, from 3.3% to 6.8%.⁷ As with adults,⁷⁻¹⁰ concurrent use of e-cigarettes and conventional cigarettes was also high, with 76.3% of current e-cigarette users reporting concurrent use of conventional cigarettes in 2012.⁷ Likewise, e-cigarettes were introduced to Korea in 2007 using marketing techniques similar to those used in the United States, and use among adolescents rapidly increased: in 2011, 4.7% of Korean adolescents were using e-cigarettes, 76.7% of whom were dual users.³

The prevalence of e-cigarette use is also rising among adults in the United States. In a web-based survey,¹¹ 3.3% of adults in 2010 and 6.2% in 2011 had ever used an e-cigarette. In addition, awareness of these products among adults increased from 40.9% in 2010 to 57.9% in 2011. Current cigarette smokers had significantly higher levels of ever e-cigarette use than former and never cigarette smokers in both years.

Electronic cigarettes are marketed as smoking cessation aids^{5,12-14} and many adult e-cigarette users cite the desire to stop smoking conventional cigarettes as their reason for using them.^{8,15-17} However, the value of e-cigarettes as a cigarette substitute has been questioned because of high levels of dual use with conventional cigarettes.^{3,8,9,11,18-20} In addition, 2 longitudinal population studies of adult smokers contradict claims that e-cigarettes are effective cessation aids: one (in the United States, United Kingdom, Canada, and Australia) found that e-cigarette use is not associated with quitting conventional cigarettes²¹ and the other (in the United States) found significantly less quitting.¹⁷ (A randomized clinical trial²² found that e-cigarettes were not superior to nicotine patches for smoking cessation, but both interventions showed low quit rates and there was no control group of spontaneous quitters.) A cross-sectional US study²³ also found that unsuccessful cigarette quitters were significantly more likely to have ever tried e-cigarettes in comparison with individuals who had never tried to quit. Likewise, a cross-sectional study of Korean adolescents³ found that they were using e-cigarettes as smoking cessation aids (odds ratio [OR] = 1.58; 95% CI, 1.39-1.79 for e-cigarette use among students who had made a quit attempt compared with

those who had not) but were less likely to have quit smoking (OR = 0.10; 95% CI, 0.09-0.12).

To further understand the relationship between e-cigarette use with conventional cigarette use and quitting, this study used data from the 2011 and 2012 NYTS to examine the relationship between e-cigarette use and both conventional cigarette smoking and smoking cessation among US adolescents.

Methods

Data Source

The NYTS is a nationally representative cross-sectional sample of students from US middle and high schools (grades 6-12) located in all 50 states and the District of Columbia that was developed to inform national and state tobacco prevention and control programs.²⁴ The 2011 sample included 18 866 students (88.0% response rate) from 178 schools (83.2% response rate), and the 2012 sample included 24 658 students (91.7% response rate) from 228 schools (80.3% response rate). The NYTS is an anonymous, self-administered, 81-item, pencil-and-paper questionnaire that includes indicators of tobacco use (including cigarettes, cigars; smokeless tobacco, kreteks, pipes, and emerging tobacco products), tobacco-related beliefs, attitudes about tobacco products, smoking cessation, exposure to secondhand smoke, ability to purchase tobacco products, and exposure to protobacco and antitobacco influences.²⁵ It uses a 3-stage clustered probability sampling design without replacement to select primary sampling units (county, several small counties, portion of large county), schools within each primary sampling unit, and students within each school. Non-Hispanic black and Hispanic students are oversampled. Written permission to participate is obtained from parents or legal guardians.²⁴ Institutional review board approval was waived because we used data from a deidentified public-use data set.

Variables

Conventional cigarette experimenters were defined as adolescents who responded yes to the question "Have you ever tried cigarette smoking, even 1 or 2 puffs?" Ever smokers of conventional cigarettes were defined as those who replied "100 or more cigarettes (5 or more packs)" to the question "About how many cigarettes have you smoked in your entire life?" Current smokers of conventional cigarettes were those who had smoked at least 100 cigarettes and smoked in the past 30 days.

In 2011, intention to quit smoking within the next year was measured among current cigarette smokers using the question "I plan to stop smoking cigarettes for good within the next..." Respondents who chose any time within the next year (7 days, 30 days, 6 months, or 1 year) were classified as intending to quit; those who responded "I do not plan to stop smoking cigarettes within the next year" were classified as not intending to quit. This question was not asked in 2012. We measured quit attempts with the question "During the past 12 months, how many times did you stop smoking for 1 day or longer because you were trying to quit smoking cigarettes for good?" Those who responded 1 or more times were consid-

Table 1. Sociodemographic Characteristics of Respondents in the 2011 and 2012 National Youth Tobacco Survey by Ever and Current Use of Electronic Cigarettes in 2011 and 2012*

Characteristic	2011 (n = 17 353)			2012 (n = 22 529)		
	All ^b	E-cigarette Use ^c		All ^b	E-cigarette Use ^c	
		Ever	Current		Ever	Current
Respondents, No. (%)		511 (3.1)	174 (1.1)		1450 (6.5)	462 (2.0)
Age, mean (SD), y	14.7 (0.1)	15.8 (0.1) ^d	15.3 (0.2) ^d	14.6 (0.1)	15.9 (0.1) ^d	15.7 (0.1) ^d
Gender, No. (%)						
Male	8544 (50.6)	296 (3.9) ^d	114 (1.6) ^d	11 093 (50.1)	863 (7.7) ^d	305 (2.7) ^d
Female	8809 (49.4)	215 (2.4)	60 (0.6)	11 436 (49.9)	587 (5.3)	157 (1.4)
Race, No. (%)						
Non-Hispanic white	6731 (56.6)	274 (3.8) ^d	81 (1.2) ^e	11 311 (54.7)	878 (7.8) ^d	257 (2.2) ^d
Non-Hispanic black	3102 (13.9)	28 (1.2)	12 (0.6)	2886 (13.5)	79 (2.8)	28 (1.1)
Other	7520 (29.5)	209 (2.8)	80 (1.0)	8332 (31.8)	493 (5.7)	177 (2.1)
Ever cigarette smoking, No. (%) ^f						
Ever	860 (5.6)	234 (30.8) ^d	80 (10.3) ^d	972 (4.5)	562 (57.1) ^d	237 (23.5) ^d
Never	16 493 (94.4)	277 (1.5)	94 (0.5)	21 557 (95.5)	888 (4.1)	225 (1.0)
Dual ever use ^g	232 (1.7)			562 (2.6)		
Current cigarette smoking, No. (%) ^h						
Smoker	778 (5.0)	219 (31.9) ^d	76 (10.6) ^d	869 (4.0)	505 (57.2) ^d	230 (25.7) ^d
Nonsmoker	16 575 (95.0)	292 (1.6)	98 (0.6)	21 660 (96.0)	945 (4.4)	232 (1.1)
Dual current use ⁱ	75 (0.5)			230 (1.0)		

Abbreviation: e-cigarette, electronic cigarette.

^a Respondents with missing values for e-cigarette use, cigarette smoking, and covariates are excluded.^b Percentages are by column.^c Percentages are by row. Ever e-cigarette use indicates having ever tried an e-cigarette, and current e-cigarette use indicates having used an e-cigarette in the past 30 days.^d $P < .01$.^e $P < .05$.^f Smoked at least 100 cigarettes in lifetime.^g Percentages are of the entire sample who have ever used e-cigarettes and ever smoked conventional cigarettes.^h Smoked at least 100 cigarettes in lifetime and at least a puff of a cigarette in the past 30 days.ⁱ Percentages are of the entire sample who are currently using e-cigarettes and conventional cigarettes.

ered having made an attempt; those who responded "I did not try to quit during the past 12 months" were considered not having made a quit attempt.

Abstinence from conventional cigarettes for 30 days, 6 months, and 1 year was based on responses to the question "When was the last time you smoked a cigarette, even 1 or 2 puffs?" "Not in the past 30 days but in the past 6 months" was coded as 30-day abstinence, "not in the past 6 months but in the past year" as 6-month abstinence, and "1 to 4 years ago" or "5 or more years ago" as 1-year abstinence.

Ever e-cigarette users were defined as adolescents who responded "electronic cigarettes or e-cigarettes, such as Ruyan or NJOY," to the question "Which of the following tobacco products have you ever tried, even just 1 time?" Current e-cigarette users were those who responded "e-cigarettes" to the question "During the past 30 days, which of the following tobacco products did you use on at least 1 day?"

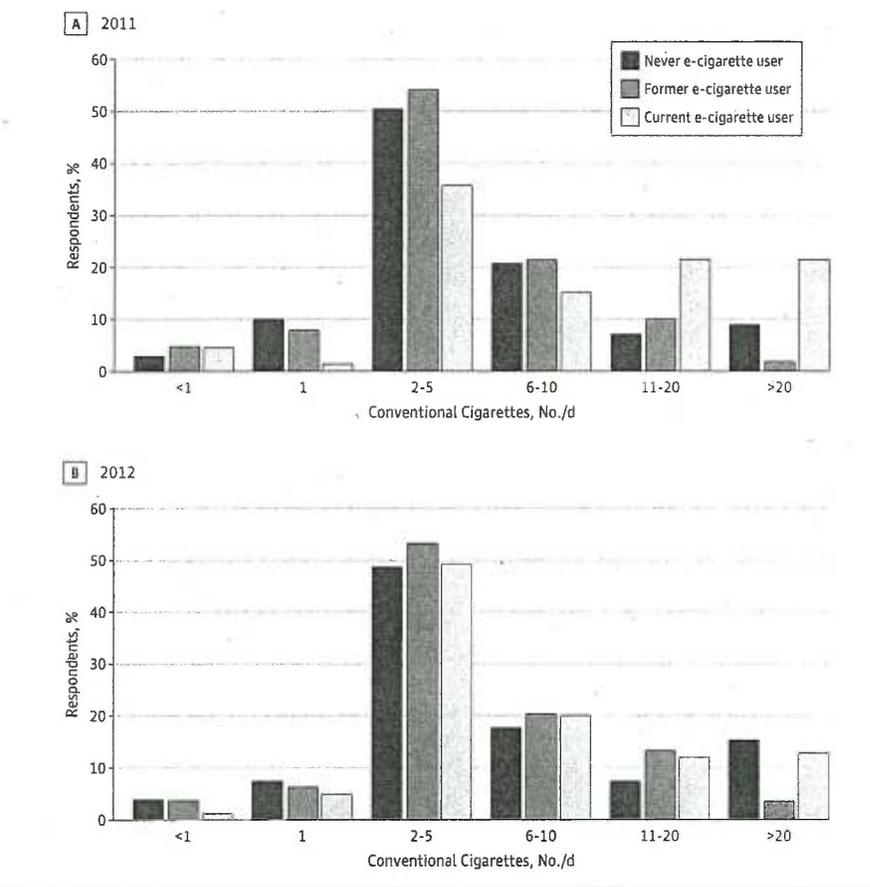
Covariates included race, gender, and age (in years, continuous). Race and ethnicity were coded based on answers to the questions "Are you Hispanic or Latino?" and "What race or races do you consider yourself to be?" (white, black, Asian, American Indian/Alaskan Native, or Native Hawaiian/Pacific Islander). Responses were collapsed into non-Hispanic white, non-Hispanic black, and other to obtain at least 20 ever e-cigarette users in each category.

Statistical Analysis

The 92.0% of respondents (17 353 of 18 866) in 2011 and 91.4% of respondents (22 529 of 24 658) in 2012 with complete data on conventional cigarette use, e-cigarette use, and covariates were included in this analysis using SAS-callable SUDAAN (SAS version 9.3, SAS Institute, Inc; SUDAAN version 11.0.0, RTI International), which accounted for the stratified clustered sampling design of the NYTS, and Stata version 12.1 (StataCorp LP), which was used to pool the data from both years. Sampling weights were used in all analyses to adjust for nonresponse and the probability of selection and to match the sample's sociodemographic characteristics with those of US middle and high school students in 2011.^{24,25}

The PROC CROSSTAB procedure was used for χ^2 analyses of categorical demographic variables by e-cigarette use. The PROC DESCRIPT and PROC REGRESS (generalized linear model) procedures provided means and P values for bivariate analyses of continuous and ordinal variables. All descriptive statistics and ORs were adjusted for stratification variables and weights. The PROC LOGIST procedure was used to obtain ORs and 95% confidence intervals from multivariable logistic regression models of e-cigarette use and cigarette smoking, intention to quit, quit attempts, and abstinence from cigarettes, adjusting for demographic covariates. Because the NYTS study designs in 2011 and 2012 were essentially identical, we pooled

Figure. Electronic Cigarette Use and Conventional Cigarette Smoking in 2011 and 2012



Current e-cigarette use in 2011 (A) and 2012 (B) was associated ($P = .003$ in 2011; $P = .001$ in 2012) with heavier smoking among conventional smokers (≥ 100 cigarettes in lifetime, having smoked in past 30 days). Participants were a representative sample of US middle and high school students who responded to the National Youth Tobacco Survey. Current e-cigarette users had used e-cigarettes in the past 30 days. Former e-cigarette users had tried e-cigarettes but had not used e-cigarettes in the past 30 days. Never e-cigarette users had never tried an e-cigarette. The numbers of conventional cigarettes smoked per day are on the days cigarettes were smoked during the past 30 days.

adjusted ORs for e-cigarette use in 2011 and 2012 using a fixed-effects meta-analysis with the Stata metan command. As expected, there was no evidence of heterogeneity between the 2 years (median P value for heterogeneity = .32; range, .09-.98).

Results

In 2011, 3.1% of the study sample had ever tried e-cigarettes (1.7% dual ever use, 1.5% only e-cigarettes) and 1.1% were current e-cigarette users (0.5% dual use, 0.6% only e-cigarettes). In 2012, 6.5% of the sample had tried e-cigarettes (2.6% dual use, 4.1% only e-cigarettes) and 2.0% were current e-cigarette users (1.0% dual use, 1.1% only e-cigarettes). Ever and current e-cigarette use varied significantly by sociodemographic characteristics (Table 1). Ever e-cigarette users were significantly more likely to be male ($P < .01$), white ($P < .01$), and older ($P < .01$). Ever conventional cigarette smokers (≥ 100 cigarettes in lifetime) were significantly more likely than never smokers to have tried e-cigarettes ($P < .01$) and to be current e-cigarette users ($P < .01$). Compared with nonsmokers (never and former smokers), current cigarette smokers were significantly more likely to have used e-cigarettes ($P < .01$) and to be current e-cigarette users ($P < .01$). In 2011, 45.4% of ever e-cigarette users had never been estab-

lished smokers of conventional cigarettes and 49.7% of current e-cigarette users were current smokers of conventional cigarettes. In 2012, 61.2% of ever e-cigarette users had never been established smokers and 49.8% of current e-cigarette users were current cigarette smokers.

Reflecting high levels of dual use, ever and current e-cigarette use was associated with very high odds of experimentation with cigarettes, ever cigarette smoking, and current cigarette smoking (eTable 1 and eTable 2 in Supplement).

Among current smokers, current e-cigarette use was associated with higher levels of cigarette smoking ($P = .003$ for 2011; $P = .001$ for 2012) (Figure).

In pooled analyses, among experimenters (ever smoked a puff), ever e-cigarette use was positively associated with being an established smoker (≥ 100 cigarettes; OR = 6.31; 95% CI, 5.39-7.39) and current cigarette smoking (≥ 100 cigarettes and smoked in past 30 days; OR = 5.96; 95% CI, 5.67-6.27). Current e-cigarette use was also associated with ever cigarette smoking (OR = 7.42; 95% CI, 5.63-9.79) and current cigarette smoking (OR = 7.88; 95% CI, 6.01-10.32) (Table 2). Table 3 shows separate analyses by year.

Use of e-cigarettes was also associated with lower odds of abstinence. Among experimenters, ever e-cigarette use associated with lower odds of 30-day (OR = 0.24; 95% CI, 0.21-

Table 2. Pooled Analysis of Ever and Current Electronic Cigarette Use and Cigarette Smoking in the 2011 and 2012 National Youth Tobacco Survey^a

Dependent Variable	OR (95% CI)				
	Cigarette Smoking Status ^b		Abstinence From Cigarettes ^c		
	Ever	Current	30 d ^d	6 mo ^e	1 y ^f
Cigarette experimenters (n = 10 850) ^g					
Ever e-cigarette use ^h	6.31 (5.39-7.39)	5.96 (5.67-6.27)	0.24 (0.21-0.28)	0.24 (0.21-0.28)	0.25 (0.21-0.30)
Current e-cigarette use ⁱ	7.42 (5.63-9.79)	7.88 (6.01-10.32)	0.11 (0.08-0.15)	0.11 (0.08-0.15)	0.12 (0.07-0.18)
Ever cigarette smokers (n = 1832) ^b					
Ever e-cigarette use ^h	0.61 (0.42-0.89)	0.53 (0.33-0.83)	0.32 (0.18-0.56)
Current e-cigarette use ⁱ	0.35 (0.18-0.69)	0.30 (0.13-0.68)	0.34 (0.13-0.87)

Abbreviations: e-cigarette, electronic cigarette; OR, odds ratio; ellipses, not applicable.

^a Excludes respondents with missing values for e-cigarette use, cigarette smoking, and covariates.

^b Ever cigarette smoking indicates having smoked at least 100 cigarettes in lifetime, and current cigarette smoking indicates having smoked at least 100 cigarettes in lifetime and at least a puff of a cigarette in the past 30 days.

^c Based on answers to "When was the last time you smoked a cigarette, even 1 or 2 puffs?"

^d Responded "not in the past 30 days but in the past 6 months" to the

abstinence question.

^e Responded "not in the past 6 months but in the past year" to the abstinence question.

^f Responded "1 to 4 years ago" or "5 or more years ago" to the abstinence question.

^g Smoked at least 1 puff of a cigarette.

^h Ever tried an e-cigarette.

ⁱ Used an e-cigarette in the past 30 days.

Table 3. Association of Electronic Cigarette Use With Ever and Current Smoking Among Adolescents Reporting Experimentation With Conventional Cigarettes in the 2011 and 2012 National Youth Tobacco Survey^a

Dependent Variable	Smoking, OR (95% CI)			
	2011 (n = 5169)		2012 (n = 5681)	
	Ever ^b	Current ^c	Ever ^b	Current ^c
Ever e-cigarette use ^d				
Adjusted	7.66 (5.44-10.79)	7.43 (5.39-10.22)	5.99 (5.02-7.16)	5.61 (4.66-6.76)
Age, y	1.33 (1.23-1.44)	1.30 (1.20-1.41)	1.24 (1.17-1.33)	1.25 (1.16-1.35)
Race				
Non-Hispanic white	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]
Non-Hispanic black	0.37 (0.23-0.57)	0.43 (0.28-0.67)	0.44 (0.29-0.69)	0.47 (0.31-0.72)
Non-Hispanic other	0.72 (0.54-0.97)	0.76 (0.57-1.01)	0.73 (0.58-0.92)	0.77 (0.60-0.99)
Male	1.39 (1.13-1.70)	1.44 (1.16-1.78)	1.53 (1.26-1.86)	1.44 (1.18-1.74)
Unadjusted	8.52 (6.06-11.98)	8.31 (6.02-11.46)	6.97 (5.76-8.44)	6.52 (5.37-7.93)
Current e-cigarette use ^e				
Adjusted	7.46 (4.12-13.49)	6.84 (3.95-11.84)	7.41 (5.41-10.14)	8.24 (6.04-11.23)
Age, y	1.35 (1.25-1.46)	1.32 (1.23-1.43)	1.29 (1.22-1.37)	1.30 (1.22-1.39)
Race				
Non-Hispanic white	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]
Non-Hispanic black	0.31 (0.20-0.47)	0.36 (0.24-0.55)	0.32 (0.21-0.50)	0.35 (0.23-0.53)
Non-Hispanic other	0.67 (0.50-0.89)	0.69 (0.52-0.92)	0.61 (0.48-0.77)	0.64 (0.49-0.84)
Male	1.38 (1.13-1.70)	1.44 (1.16-1.77)	1.55 (1.27-1.90)	1.45 (1.19-1.77)
Unadjusted	6.84 (4.01-11.67)	6.49 (3.92-10.76)	7.52 (5.69-9.93)	8.31 (6.28-11.00)

Abbreviations: e-cigarette, electronic cigarette; OR, odds ratio.

^a Excludes respondents with missing values for e-cigarette use, cigarette smoking, and covariates. Experimentation indicates ever tried smoking cigarettes, even 1 or 2 puffs.

^b Smoked at least 100 cigarettes in lifetime.

^c Smoked at least 100 cigarettes in lifetime and at least a puff of a cigarette in the past 30 days.

^d Ever tried an e-cigarette (in 2011, n = 468 [9.1% of experimenters]; in 2012, n = 1313 [23.1% of experimenters]).

^e Used an e-cigarette in the past 30 days (in 2011, n = 154 [3.0% of experimenters]; in 2012, n = 423 [7.4% of experimenters]).

0.28), 6-month (OR = 0.24; 95% CI, 0.21-0.28), and 1-year (OR = 0.25; 95% CI, 0.21-0.30) abstinence from conventional cigarettes. Current e-cigarette use was also associated with lower odds of 30-day (OR = 0.11; 95% CI, 0.08-0.15), 6-month (OR = 0.11; 95% CI, 0.08-0.15), and 1-year (OR = 0.12; 95% CI, 0.07-0.18) abstinence from conventional cigarettes. Table 4 shows analyses by year.

Among ever cigarette smokers (≥100 cigarettes), ever e-cigarette use was negatively associated with 30-day (OR = 0.61; 95% CI, 0.42-0.89), 6-month (OR = 0.53; 95% CI, 0.33-0.83), and

1-year (OR = 0.32; 95% CI, 0.18-0.56) abstinence from conventional cigarettes. Current e-cigarette use was also negatively associated with 30-day (OR = 0.35; 95% CI, 0.18-0.69), 6-month (OR = 0.30; 95% CI, 0.13-0.68), and 1-year (OR = 0.34; 95% CI, 0.13-0.87) abstinence from conventional cigarettes. Table 5 shows analyses by year.

In adjusted analyses for 2011, among current smokers, ever e-cigarette use was associated with planning to stop smoking within the next year (OR = 1.53; 95% CI, 1.03-2.28), but current e-cigarette use was not (OR = 1.34; 95% CI, 0.62-2.90). In

Table 4. Ever and Current Electronic Cigarette Use by Abstinence From Smoking Conventional Cigarettes Among Adolescents Reporting Experimentation With Conventional Cigarettes in the 2011 and 2012 National Youth Tobacco Survey^a

Dependent Variable	Abstinence, OR (95% CI) ^b					
	2011 (n = 5169)			2012 (n = 5681)		
	30 d ^c	6 mo ^d	1 y ^e	30 d ^c	6 mo ^d	1 y ^e
Ever e-cigarette use^f						
Adjusted	0.22 (0.16-0.29)	0.21 (0.16-0.28)	0.21 (0.15-0.31)	0.25 (0.21-0.29)	0.25 (0.21-0.30)	0.27 (0.22-0.33)
Age, y	0.91 (0.86-0.95)	0.94 (0.90-0.98)	0.98 (0.94-1.02)	0.91 (0.87-0.96)	0.94 (0.89-0.99)	0.95 (0.91-1.00)
Race						
Non-Hispanic white	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]
Non-Hispanic black	1.43 (1.04-1.96)	1.91 (1.51-2.41)	2.18 (1.72-2.75)	1.33 (1.06-1.68)	1.98 (1.54-2.54)	2.07 (1.65-2.60)
Non-Hispanic other	1.20 (0.99-1.46)	1.40 (1.21-1.61)	1.53 (1.33-1.77)	1.09 (0.94-1.26)	1.25 (1.06-1.48)	1.36 (1.13-1.65)
Male	0.91 (0.78-1.07)	0.90 (0.76-1.06)	0.82 (0.67-1.00)	0.83 (0.73-0.93)	0.87 (0.76-1.00)	0.90 (0.77-1.05)
Unadjusted	0.20 (0.15-0.27)	0.19 (0.15-0.25)	0.19 (0.13-0.28)	0.23 (0.20-0.26)	0.22 (0.19-0.27)	0.24 (0.19-0.29)
Current e-cigarette use^g						
Adjusted	0.15 (0.08-0.27)	0.15 (0.07-0.32)	0.17 (0.07-0.38)	0.10 (0.07-0.14)	0.10 (0.06-0.16)	0.10 (0.06-0.17)
Age, y	0.89 (0.85-0.93)	0.93 (0.89-0.97)	0.97 (0.93-1.01)	0.88 (0.84-0.93)	0.92 (0.87-0.96)	0.93 (0.89-0.98)
Race						
Non-Hispanic white	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]
Non-Hispanic black	1.57 (1.16-2.12)	2.05 (1.63-2.57)	2.32 (1.84-2.92)	1.62 (1.27-2.06)	2.33 (1.79-3.03)	2.39 (1.88-3.03)
Non-Hispanic other	1.26 (1.04-1.51)	1.45 (1.27-1.66)	1.58 (1.38-1.82)	1.23 (1.05-1.44)	1.38 (1.17-1.64)	1.49 (1.22-1.81)
Male	0.91 (0.78-1.06)	0.89 (0.76-1.06)	0.81 (0.67-0.99)	0.83 (0.74-0.93)	0.87 (0.76-0.99)	0.90 (0.78-1.03)
Unadjusted	0.15 (0.08-0.27)	0.14 (0.06-0.32)	0.15 (0.07-0.35)	0.09 (0.06-0.14)	0.09 (0.06-0.15)	0.10 (0.06-0.16)

Abbreviations: e-cigarette, electronic cigarette; OR, odds ratio.

^a Excludes respondents with missing values for e-cigarette use, cigarette smoking, and covariates. Experimentation indicates ever tried smoking cigarettes, even 1 or 2 puffs.

^b Based on answers to "When was the last time you smoked a cigarette, even 1 or 2 puffs?"

^c Responded "not in the past 30 days but in the past 6 months" to the abstinence question.

^d Responded "not in the past 6 months but in the past year" to the abstinence question.

^e Responded "1 to 4 years ago" or "5 or more years ago" to the abstinence question.

^f Ever tried an e-cigarette (in 2011, n = 468 [9.1% of experimenters]; in 2012, n = 1313 [23.1% of experimenters]).

^g Used an e-cigarette in the past 30 days (in 2011, n = 154 [3.0% of experimenters]; in 2012, n = 423 [7.4% of experimenters]).

contrast, in pooled analyses, neither ever e-cigarette use (OR = 1.01; 95% CI, 0.77-1.34) nor current e-cigarette use (OR = 0.89; 95% CI, 0.61-1.30) was significantly associated with having made a quit attempt in the past 12 months after adjusting for covariates.

We also ran all analyses unadjusted by demographic variables, with little impact on the effects of e-cigarette use, indicating that the results were not due to confounding by demographic variables (Tables 3, 4, and 5).

Discussion

As with adults,⁸⁻¹⁰ dual use of e-cigarettes and conventional cigarettes is high among adolescents and increasing rapidly. Adolescents who had ever experimented with cigarettes (smoked at least a puff) and used e-cigarettes were more likely to report having smoked at least 100 cigarettes and to be current smokers than adolescents who never used e-cigarettes. Thus, in combination with the observations that e-cigarette users are heavier smokers and less likely to

have stopped smoking cigarettes, these results suggest that e-cigarette use is aggravating rather than ameliorating the tobacco epidemic among youths. These results call into question claims^{15,26,27} that e-cigarettes are effective as smoking cessation aids.

Our US results are consistent with those for Korean youths,³ with high levels of dual use in both populations. Current e-cigarette users (past 30 days) were much less likely to have abstained from smoking cigarettes in the past 30 days in both populations (≥ 1 puff but not in past 30 days: OR = 0.10; 95% CI, 0.09-0.12 in Korean youths vs OR = 0.15; 95% CI, 0.08-0.28 for experimenters with cigarettes in US youths). Among current cigarette-smoking youths in Korea, there was a significant association between current e-cigarette use and attempting to quit smoking in the past 12 months (OR = 1.67; 95% CI, 1.48-1.90), but there was not a significant association for US youths (OR = 1.20; 95% CI, 0.65-2.23). This difference may reflect behavioral differences between the 2 countries but may also reflect the lower power in our study. The Korean sample was much larger than ours (75 643 vs 17 320 individuals, respectively) with higher prevalence of current (12.1% vs 5.0%)

Table 5. Ever and Current Electronic Cigarette Use by Abstinence From Smoking Conventional Cigarettes Among Ever Smokers in the 2011 and 2012 National Youth Tobacco Survey^a

Dependent Variable	Abstinence, OR (95% CI) ^b					
	2011 (n = 860)			2012 (n = 972)		
	30 d ^c	6 mo ^d	1 y ^e	30 d ^c	6 mo ^d	1 y ^e
Ever e-cigarette use^f						
Adjusted	0.57 (0.31-1.04)	0.48 (0.18-1.23)	0.40 (0.10-1.53)	0.64 (0.40-1.03)	0.54 (0.32-0.90)	0.30 (0.16-0.56)
Age, y	1.09 (0.98-1.22)	1.08 (0.93-1.26)	0.99 (0.85-1.15)	0.94 (0.80-1.10)	0.94 (0.80-1.10)	0.93 (0.77-1.12)
Race						
Non-Hispanic white	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]
Non-Hispanic black	0.81 (0.22-3.01)	1.65 (0.38-7.07)	2.55 (0.44-14.80)	0.40 (0.16-0.99)	0.52 (0.14-1.87)	0.48 (0.10-2.23)
Non-Hispanic other	1.12 (0.72-1.74)	1.30 (0.66-2.55)	1.59 (0.60-4.19)	1.08 (0.65-1.79)	1.23 (0.62-2.45)	1.22 (0.61-2.41)
Male	0.87 (0.53-1.42)	1.49 (0.67-3.34)	1.97 (0.72-5.40)	1.53 (0.98-2.38)	1.55 (0.85-2.80)	1.74 (0.82-3.69)
Unadjusted	0.56 (0.31-1.02)	0.47 (0.19-1.18)	0.38 (0.10-1.48)	0.69 (0.44-1.09)	0.57 (0.35-0.92)	0.31 (0.17-0.58)
Current e-cigarette use^g						
Adjusted	0.61 (0.23-1.64)	0.73 (0.20-2.71)	0.79 (0.14-4.42)	0.22 (0.09-0.56)	0.17 (0.06-0.49)	0.24 (0.08-0.75)
Age, y	1.08 (0.97-1.21)	1.07 (0.92-1.25)	0.99 (0.85-1.15)	0.92 (0.78-1.07)	0.91 (0.78-1.08)	0.90 (0.74-1.09)
Race						
Non-Hispanic white	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]
Non-Hispanic black	0.91 (0.25-3.38)	1.89 (0.46-7.84)	2.96 (0.52-16.73)	0.40 (0.17-0.94)	0.56 (0.17-1.81)	0.65 (0.16-2.58)
Non-Hispanic other	1.19 (0.77-1.85)	1.40 (0.72-2.73)	1.74 (0.65-4.65)	1.16 (0.69-1.98)	1.35 (0.67-2.73)	1.38 (0.68-2.78)
Male	0.85 (0.52-1.39)	1.44 (0.65-3.15)	1.86 (0.68-5.09)	1.61 (1.04-2.49)	1.60 (0.90-2.84)	1.71 (0.82-3.57)
Unadjusted	0.56 (0.22-1.47)	0.75 (0.20-2.83)	0.89 (0.16-4.95)	0.25 (0.10-0.61)	0.20 (0.07-0.53)	0.27 (0.09-0.81)

Abbreviations: e-cigarette, electronic cigarette; OR, odds ratio.

^a Excludes respondents with missing values for e-cigarette use, cigarette smoking, and covariates. Ever smokers are those who have smoked at least 100 cigarettes in lifetime.^b Based on answers to "When was the last time you smoked a cigarette, even 1 or 2 puffs?"^c Responded "not in the past 30 days but in the past 6 months" to the abstinence question.^d Responded "not in the past 6 months but in the past year" to the abstinence question.^e Responded "1 to 4 years ago" or "5 or more years ago" to the abstinence question.^f Ever tried an e-cigarette (in 2011, n = 234 [27.2% of ever cigarette smokers]; in 2012, n = 562 [57.8% of ever smokers]).^g Used an e-cigarette in the past 30 days (in 2011, n = 80 [9.3% of ever cigarette smokers]; in 2012, 237 [24.4% of ever smokers]).

and ever (26.3% vs 5.6%) cigarette smoking and current (4.7% vs 1.1%) and ever (9.4% vs 3.1%) e-cigarette use.

Although e-cigarettes deliver many fewer toxins and at much lower levels than conventional cigarettes,²⁸⁻³⁰ they contain nicotine, a highly addictive substance,³¹ in doses designed to mimic cigarettes. Animal models suggest that, through its effect on cholinergic pathways, nicotine may have permanent effects on the brain and behavior^{32,33} such as dysregulation of the limbic system, which can lead to long-term difficulties with behavioral regulation, attention, memory, and motivation, among other functions.^{33,34} The adolescent human brain may be particularly vulnerable to the effects of nicotine because it is still developing.³⁵⁻³⁷

This is a cross-sectional study, which only allows us to identify associations, not causal relationships. Our results are also limited by the lack of information about motivation for using e-cigarettes (eg, popularity, trendy, smoking cessation) and the fact that they only apply to middle and high school students, not all US youths.

In comparison with the 8.0% and 8.6% of respondents who had missing data in 2011 and 2012, respectively, and were

dropped, our analytical sample had slightly more girls (2011: 42.9% vs 49.4%, $P = .007$; 2012: 38.3% vs 49.9%, $P < .001$) and more white respondents (2011: 39.5% vs 56.6%, $P < .001$; 2012: 39.8% vs 54.7%, $P < .001$) (eTable 3 in Supplement). In 2012 only, our sample compared with students with missing data also had a lower prevalence of e-cigarette use (6.5% vs 10.2%; $P = .002$) and was slightly younger (mean age, 14.6 vs 14.2 years; $P < .001$). There were no significant differences by any of the other demographic, e-cigarette use, or cigarette smoking variables.

Conclusions

While the cross-sectional nature of our study does not allow us to identify whether most youths are initiating smoking with conventional cigarettes and then moving on to (usually dual use of) e-cigarettes or vice versa, our results suggest that e-cigarettes are not discouraging use of conventional cigarettes. Among experimenters with conventional cigarettes, e-cigarette use is associated with established cigarette smoking and lower rates of abstinence from conventional cigarettes. The debate over

e-cigarettes^{2,28,31,38-40} has centered on whether e-cigarettes could be useful as a harm-reduction strategy in established adult cigarette smokers. The results of our study together with those from the study in Korea³ suggest that e-cigarettes may contribute to nicotine addiction and are unlikely to discourage conventional cigarette smoking among youths.

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