

Original Investigation

Progression to Traditional Cigarette Smoking After Electronic Cigarette Use Among US Adolescents and Young Adults

Brian A. Primack, MD, PhD; Samir Soneji, PhD; Michael Stoolmiller, PhD; Michael J. Fine, MD, MSc; James D. Sargent, MD

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IMPORTANCE Electronic cigarettes (e-cigarettes) may help smokers reduce the use of traditional combustible cigarettes. However, adolescents and young adults who have never smoked traditional cigarettes are now using e-cigarettes, and these individuals may be at risk for subsequent progression to traditional cigarette smoking.

OBJECTIVE To determine whether baseline use of e-cigarettes among nonsmoking and nonsusceptible adolescents and young adults is associated with subsequent progression along an established trajectory to traditional cigarette smoking.

DESIGN, SETTING, AND PARTICIPANTS In this longitudinal cohort study, a national US sample of 694 participants aged 16 to 26 years who were never cigarette smokers and were attitudinally nonsusceptible to smoking cigarettes completed baseline surveys from October 1, 2012, to May 1, 2014, regarding smoking in 2012-2013. They were reassessed 1 year later. Analysis was conducted from July 1, 2014, to March 1, 2015. Multinomial logistic regression was used to assess the independent association between baseline e-cigarette use and cigarette smoking, controlling for sex, age, race/ethnicity, maternal educational level, sensation-seeking tendency, parental cigarette smoking, and cigarette smoking among friends. Sensitivity analyses were performed, with varying approaches to missing data and recanting.

EXPOSURES Use of e-cigarettes at baseline.

MAIN OUTCOMES AND MEASURES Progression to cigarette smoking, defined using 3 specific states along a trajectory: nonsusceptible nonsmokers, susceptible nonsmokers, and smokers. Individuals who could not rule out smoking in the future were defined as susceptible.

RESULTS Among the 694 respondents, 374 (53.9%) were female and 531 (76.5%) were non-Hispanic white. At baseline, 16 participants (2.3%) used e-cigarettes. Over the 1-year follow-up, 11 of 16 e-cigarette users and 128 of 678 of those who had not used e-cigarettes (18.9%) progressed toward cigarette smoking. In the primary fully adjusted models, baseline e-cigarette use was independently associated with progression to smoking (adjusted odds ratio [AOR], 8.3; 95% CI, 1.2-58.6) and to susceptibility among nonsmokers (AOR, 8.5; 95% CI, 1.3-57.2). Sensitivity analyses showed consistent results in the level of significance and slightly larger magnitude of AORs.

CONCLUSIONS AND RELEVANCE In this national sample of US adolescents and young adults, use of e-cigarettes at baseline was associated with progression to traditional cigarette smoking. These findings support regulations to limit sales and decrease the appeal of e-cigarettes to adolescents and young adults.

Author Affiliations: Author affiliations are listed at the end of this article.

Corresponding Author: Brian A. Primack, MD, PhD, Division of General Internal Medicine, Department of Medicine, University of Pittsburgh School of Medicine, 230 McKee Pl, Ste 600, Pittsburgh, PA 15213.

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An electronic cigarette (e-cigarette) contains a heating element that atomizes a liquid consisting of propylene glycol, glycerin, nicotine, and flavorings into an inhalable aerosol.¹ Compared with traditional combustible cigarettes (hereafter, cigarettes), e-cigarettes emit lower levels of many toxicants.²⁻⁴ Therefore, many experts view these devices as potentially valuable tools to reduce the harm of tobacco smoking. In support of this goal, some studies suggest that e-cigarettes may help smokers reduce the use of traditional tobacco products.⁵⁻⁸

However, there are also concerns related to e-cigarettes. First, there is concern that e-cigarette use may inhibit quitting among established cigarette smokers; for example, use of e-cigarettes may make it easier for smokers to cope with indoor smoking restrictions.⁹ In support of this concern, observational studies demonstrate that adult smokers who begin to use e-cigarettes seldom completely quit combustible products,⁹⁻¹¹ especially among those who use e-cigarettes only intermittently.¹²⁻¹⁴

There is also concern that e-cigarette marketing could position the product to recruit nonsmoking individuals. In support of this concern, the use of e-cigarettes has increased substantially among both adolescents¹⁵ and young adults.¹⁶ According to data collected in 2014, 13.4% of US high school students have used e-cigarettes in the past 30 days, compared with only 9.2% who smoked cigarettes.¹⁷ One reason this use is particularly problematic is that nicotine is known to have adverse effects on the developing brain.¹⁸

In addition, studies suggest that many adolescents and young adults who are new users of e-cigarettes otherwise may have been less susceptible to tobacco or nicotine use.^{17,19} Therefore, a key public health question is whether e-cigarette users who initially did not smoke cigarettes are at risk for progression to dual use of e-cigarettes and cigarettes or exclusive use of cigarettes. There have been few studies that have addressed this question,^{15,20,21} and to our knowledge none has been longitudinal. In these cross-sectional surveys of US adolescents, use of e-cigarettes has been associated with progression from experimental smoking to established smoking, defined as having smoked 100 cigarettes in one's lifetime.²¹ Use of e-cigarettes has been associated with attitudinal susceptibility to future cigarette smoking,¹⁵ a well-documented milestone along the trajectory to established cigarette smoking.²²⁻²⁴ Finally, these studies have shown that use of e-cigarettes has been associated with being open to future cigarette smoking among US young adults aged 18 to 29 years.²⁰

However, these cross-sectional studies could not determine whether e-cigarette use preceded cigarette use. Therefore, we conducted a longitudinal study to address whether baseline e-cigarette use was associated with progression along a trajectory to cigarette smoking 1 year later. Based on prior work noted above, we hypothesized that baseline e-cigarette use would predict higher risk of progression to cigarette smoking.

Methods

Participants and Setting

Our data come from the second and third waves of the United States-based Dartmouth Media, Advertising, and Health Study, a national study of adolescents and young adults (aged 16-26

At a Glance

- We aimed to determine whether baseline use of e-cigarettes among nonsmoking and nonsusceptible adolescents and young adults was associated with progression to cigarette smoking.
- Among 694 participants who were nonsusceptible nonsmokers at baseline, after 1 year 11 of 16 e-cigarette users (68.8%) and 128 of 678 of those who had not used e-cigarettes (18.9%) progressed toward cigarette smoking.
- In analyses that controlled for all covariates, baseline e-cigarette use was independently associated with progression to smoking (adjusted odds ratio [AOR], 8.3; 95% CI, 1.2-58.6) and progression to susceptibility (AOR, 8.5; 95% CI, 1.3-57.2) among initially nonsusceptible nonsmokers.
- Sensitivity analyses showed consistent results in the level of significance and slightly larger magnitude of adjusted odds ratios.
- These findings support regulations that decrease the accessibility and appeal of e-cigarettes to nonsmoking adolescents and young adults.

years) recruited via random digit dialing using landline (66.7%) and cellular telephone numbers (33.3%).

The study, which was conducted from October 1, 2012, to May 1, 2014, began to ascertain e-cigarette use at wave 2. Thus, wave 2 (2012-2013) serves as the baseline and wave 3 (2013-2014) serves as follow-up for the current study. Analysis was conducted from July 1, 2014, to March 1, 2015. To be included in the study, participants had to be never smokers and nonsusceptible to smoking at baseline. Susceptibility to future smoking was assessed with 2 items: "If one of your friends offered you a cigarette, would you try it?" and "Do you think you will smoke a cigarette sometime in the next year?" Responses included "definitely yes," "probably yes," "probably no," and "definitely no." Those who responded "definitely no" to both measures are considered nonsusceptible nonsmokers (NSNS), whereas those who cannot rule out smoking are defined as susceptible.²³ Multiple longitudinal studies show that, compared with NSNS, individuals defined as susceptible nonsmokers (SNS) according to this measure are substantially more likely to try smoking in the near future.^{25,26}

A total of 728 participants met the criteria of being NSNS. At follow-up 1 year later, 507 (69.6%) of these participants were successfully reassessed. Therefore, for analyses that included only complete observed data (sensitivity analysis 1), there was a sample size of 507. For sensitivity analysis 2, we imputed missing data, which added 4 baseline participants, bringing the total sample size to 732. Finally, for primary analyses, we imputed missing data and fixed recanting, which eliminated 38 participants and resulted in a sample size of 694. Adult participants provided verbal informed consent and minor participants provided parental verbal informed consent. Participants received \$25 for completion of the Internet-based visual survey at each wave. The Dartmouth Committee for the Protection of Human Subjects approved the study.

Data Collection

Independent and Dependent Variables

Our independent variable was whether participants had ever used an e-cigarette at baseline. The dependent variable was progression along the trajectory to cigarette smoking. To opera-

Table 1. Description of the Sample by Use of e-Cigarettes at Baseline

Characteristic	e-Cigarette Use at Baseline		P Value ^a
	Yes (n = 16)	No (n = 678)	
Age, mean (SD), y	19.5 (2.0)	20.0 (2.4)	.40
Female sex, No. (%)	5 (31.3)	369 (54.4)	.08
Race/ethnicity, No. (%) ^b			
Non-Hispanic white	12 (75.0)	519 (76.5)	
Non-Hispanic black	1 (6.3)	46 (6.8)	.97
Hispanic	1 (6.3)	52 (7.7)	
Other	2 (12.5)	61 (9.0)	
Maternal educational level, mean (SD) ^c	7.5 (1.8)	6.9 (2.5)	.42
Sensation-seeking tendency, mean (SD) ^d	2.6 (0.5)	2.1 (0.5)	<.001
Smoking, mean (SD)			
Parent ^e	0.44 (0.81)	0.44 (0.74)	.99
Friend ^f	0.94 (0.85)	0.74 (0.66)	.23

^a P values were computed using Pearson χ^2 tests for categorical variables and t tests for continuous variables.

^b Race/ethnicity was self-reported.

^c Scores ranged from 1 to 10, with higher scores representing more advanced education.

^d Scores ranged from 1 to 4, with higher scores representing greater sensation-seeking tendency.

^e Scores ranged from 0 to 3, with 0 representing never a smoker, 1 representing a former smoker, 2 representing a nondaily smoker, and 3 representing a daily smoker.

^f Scores ranged from 0 to 3, with higher numbers representing a greater proportion of friends who smoke.

tionalize this construct, we categorized each individual as being in 1 of 3 states along the trajectory: (1) a nonsmoker who was also not susceptible to future smoking (NSNS), (2) a nonsmoker who is susceptible to smoking (SNS), or (3) a cigarette smoking initiator, defined as someone who has smoked at least 1 puff of a cigarette in her or his lifetime. By inclusion criteria, all participants began the study as an NSNS. By follow-up, some participants remained NSNS and others progressed to either SNS or cigarette smoking initiation.

Covariates

We also assessed respondent characteristics that have been previously associated with cigarette smoking¹⁷⁻¹⁹ and could also be associated with e-cigarette use, including sex, age, race/ethnicity, and maternal educational level, which ranged from 0 (did not complete eighth grade) to 10 (completed a graduate or professional degree). We used a composite measure of sensation-seeking tendency previously found to be related to cigarette smoking and other high-risk health behaviors based on 6 items, such as "I like to do dangerous things" (Cronbach α , 0.72).²⁰ Parental smoking was assessed as never (0), former (1), occasional (2), and daily (3), and scores for mothers and fathers were averaged. Finally, we asked how many of the respondents' close friends smoked cigarettes, with response choices of none (0), few (1), more than a few (2), or most (3).

Statistical Analysis

First, we assessed the proportion of baseline respondents who remained as NSNS or transitioned to SNS or a cigarette smok-

ing initiator by whether they had used e-cigarettes at baseline. Second, we fit a multinomial logistic regression model to assess the independent association between e-cigarette use at baseline and progression along the trajectory of cigarette smoking from NSNS to SNS and NSNS to cigarette smoking initiator.

As is the case with most longitudinal telephone studies, attrition from baseline to follow-up was substantial enough to potentially create bias. In a logistic regression including all the predictors under consideration, increased loss to follow-up was associated with being male (adjusted odds ratio [AOR], 2.0; 95% CI, 1.4-2.8), older age (AOR, 1.1; 95% CI, 1.05-1.2), and parental smoking (AOR, 1.5; 95% CI, 1.2-1.8). To address attrition bias, therefore, our primary models imputed data. We created 32 imputed data sets using a chained equation approach and then combined the estimates from each of the 32 multinomial logistic regression analyses, accounting for sampling and imputation uncertainty. The imputation model included auxiliary variables from both wave 1 (prior to baseline in this study) and wave 2 (baseline in this study) in an attempt to improve prediction of missing values. These auxiliary variables were work status, home ownership, and household income. The imputation model was carried out to 25 iterations, and diagnostic plots for chain means and variances did not suggest convergence problems. We did not use sampling weights because by wave 2 attrition had already substantially altered the sample size and composition compared with wave 1. Because the baseline sample was not nationally representative, we sought to minimize bias associated with loss to follow-up by imputing missing data rather than using survey weights.

Substantial proportions of adolescents in prospective surveys of substance use subsequently recant prior reports of substance use.^{27,28} This recanting occurs, for example, when a participant claims to be a current smoker at baseline but then claims to be a never smoker at follow-up. Our primary models systematically addressed recanting.²⁹ For this logical fix, we assumed reports were accurate until a participant contradicted himself or herself. The contradictory response was then made logically consistent with earlier reports.

We also conducted 2 exploratory sensitivity analyses to examine the robustness of our findings. First, we conducted all analyses using only available data (without imputation). Second, we conducted models that did not fix recanting systematically as described above. While only about 5% of participants contradicted earlier reports and required repair in primary models, we wished to ensure that such contradictions did not affect results.

We used the public-domain R statistical software, version 3.1.2, for statistical analyses. We defined significance with a 2-tailed α of 0.05.

Results

Our imputed sample for primary analyses consisted of 694 individuals: 374 female (53.9%), 531 non-Hispanic white (76.5%), 47 non-Hispanic black (6.8%), 53 Hispanic (7.6%), and 63 of other race (9.1%) (Table 1). Only 16 of the 694 participants (2.3%) were

Table 2. Transitions From Baseline to Follow-up According to Baseline Use of e-Cigarettes

Trajectory From NSNS	No. (%)		
	All Participants (N = 694)	e-Cigarette Use at Baseline	
		Yes (n = 16)	No (n = 678)
Remain NSNS	555 (80.0)	5 (31.3)	550 (81.1)
Progress to SNS	68 (9.8)	5 (31.3)	63 (9.3)
Progress to smoker	71 (10.2)	6 (37.5)	65 (9.6)

Abbreviations: NSNS, nonsusceptible nonsmoker; SNS, susceptible nonsmoker.

e-cigarette users at baseline. Five of 16 individuals who used e-cigarettes at baseline (31.3%) progressed to SNS, while only 63 of 678 of those who did not use e-cigarettes at baseline (9.3%) progressed to SNS (Table 2). Similarly, 6 of 16 individuals who used e-cigarettes at baseline (37.5%) progressed to cigarette smoking, but only 65 of 678 of those who did not use e-cigarettes at baseline (9.6%) progressed to smoking.

Bivariable multinomial logistic regression analyses demonstrated that compared with those who did not smoke e-cigarettes at baseline, those who did smoke e-cigarettes at baseline had larger point estimates of progressing from NSNS to SNS (AOR, 10.7; 95% CI, 1.8-63.4). Similarly, those who smoked e-cigarettes at baseline had larger point estimates of progressing from NSNS to cigarette smoking (AOR, 11.9; 95% CI, 2.1-68.7).

Multivariable multinomial logistic regression analyses demonstrated that compared with those who did not smoke e-cigarettes at baseline, those who did smoke e-cigarettes at baseline had larger point estimates of progressing from NSNS to SNS (AOR, 8.5; 95% CI, 1.3-57.2). Of other covariates in this same model, only younger age was also significantly associated with this transition (Table 3). Similarly, individuals who smoked e-cigarettes at baseline had larger point estimates of progressing from NSNS to cigarette smoking (AOR, 8.3; 95% CI, 1.2-58.6). Of other covariates in this model, only sensation-seeking tendency and having friends who smoke were also associated with this progression.

Exploratory sensitivity analyses showed consistent results in the level of significance and slightly larger magnitude of AORs. For the multivariable models that used only individuals with complete data (without imputation), baseline e-cigarette use was independently associated with greater odds of progressing from NSNS to SNS (AOR, 11.5; 95% CI, 1.7-77.4) and from NSNS to cigarette smoking (AOR, 10.4; 95% CI, 1.6-69.5). Similarly, when we ignored recanting instead of systematically fixing it, e-cigarette use was independently associated with greater odds of progression from NSNS to SNS (AOR, 9.6; 95% CI, 1.5-59.8) and from NSNS to cigarette smoking (AOR, 9.4; 95% CI, 1.7-52.0).

Discussion

In this study, the use of e-cigarettes at baseline was significantly associated with progression along the trajectory to cigarette smoking over 1 year in a multivariable model that included multiple covariates, even among a population that was

Table 3. Multivariable Associations Between e-Cigarette Use at Baseline and Progression Along the Cigarette Smoking Trajectory by Follow-up

Characteristic	Adjusted Odds Ratio (95% CI) ^a	
	NSNS to SNS	NSNS to Cigarette Smoking Initiator
e-Cigarette use at baseline (yes vs no)	8.5 (1.3-57.2)	8.3 (1.2-58.6)
Age, y ^b	0.8 (0.7-0.96)	0.9 (0.8-1.04)
Sex (male vs female)	1.0 (0.6-1.9)	0.8 (0.4-1.5)
Race/ethnicity		
Non-Hispanic black (vs non-Hispanic white)	0.4 (0.1-2.9)	2.2 (0.7-7.0)
Hispanic (vs non-Hispanic white)	0.7 (0.2-3.0)	1.4 (0.5-4.3)
Other (vs non-Hispanic white)	1.1 (0.4-2.8)	0.5 (0.1-1.9)
Maternal educational level ^c	1.0 (0.8-1.1)	1.0 (0.8-1.1)
Sensation-seeking tendency ^d	1.9 (0.96-3.6)	2.6 (1.3-5.2)
Smoking		
Parent ^e	0.9 (0.6-1.4)	1.0 (0.6-1.6)
Friend ^f	0.9 (0.6-1.4)	1.8 (1.2-2.9)

Abbreviations: NSNS, nonsusceptible nonsmoker; SNS, susceptible nonsmoker.

^a Adjusted for all variables in the table.

^b Adjusted odds ratios represent increases in odds for each additional year.

^c Scores ranged from 1 to 10, with higher scores representing more advanced education.

^d Scores ranged from 1 to 4, with higher scores representing greater sensation-seeking tendency.

^e Scores ranged from 0 to 3, with 0 representing never a smoker, 1 representing a former smoker, 2 representing a nondaily smoker, and 3 representing a daily smoker.

^f Scores ranged from 0 to 3, with higher numbers representing a greater proportion of friends who smoke.

attitudinally nonsusceptible to smoking at baseline. These results raise concerns that the many adolescents and young adults who initiate nicotine use through e-cigarettes^{17,19} are at substantially increased risk for later use of cigarettes, even if they do not intend to smoke cigarettes in the future. Thus, while e-cigarettes may potentially represent a product that can reduce harm for established cigarette smokers, they may simultaneously contribute to the development of a new population of cigarette smokers. These results are consistent with previous cross-sectional studies on the association of e-cigarette use and attitudes toward cigarettes and use of cigarettes.^{15,20} These results are also consistent with the fact that many youth are dual users of cigarettes and e-cigarettes.^{30,31}

It is notable that the estimated AOR for baseline e-cigarette use was higher than that for multiple established predictors of smoking. Our results were largely consistent with those of prior studies using similar covariates in that sensation-seeking tendency and friends who smoke were the covariates most strongly associated with initiation of cigarette smoking.^{32,33}

Even though there was substantial risk associated with being an e-cigarette user at baseline, there was only a small number of e-cigarette smokers at baseline (approximately 2.3%). Therefore, it could be interpreted that this small number may not translate into substantial public health risk. However, data published in 2015 suggest that large numbers of youth are initiating e-cigarette use and that as many as half of these individuals do not smoke traditional combustible

cigarettes.^{15,19} Therefore, it will be important to continue surveillance among youth of both e-cigarette use and overlap with use of other tobacco products.

Initial e-cigarette use may lead to subsequent traditional cigarette smoking simply by providing nicotine. Other studies have found that initial exposure to nicotine in other forms, such as smokeless tobacco, can lead to later traditional cigarette smoking.³⁴ Because e-cigarettes deliver nicotine more slowly than traditional cigarettes,³⁵ they may serve as a “nicotine starter,” allowing a new user to advance to cigarette smoking as he or she becomes tolerant of the initial adverse effects. Cigarette users begin to report craving for nicotine within weeks of their first cigarette.³⁶ The same process may drive initial e-cigarette users to seek out cigarettes as a more efficient nicotine delivery device.

Unlike forms of nicotine such as smokeless tobacco, e-cigarettes are designed to mimic the behavioral and sensory act of cigarette smoking. Therefore, even aside from the nicotine content, e-cigarettes may behaviorally accustom individuals to powerful cigarette smoking cues such as inhalation, exhalation, and holding the cigarette.

E-cigarettes are not subject to the many regulations designed to limit cigarette smoking, such as age limits on sales, restriction of flavorings, restrictions on marketing, clean air laws, taxation, and labeling requirements.³⁷⁻³⁹ These policy gaps may increase the accessibility of e-cigarettes to youth.⁴⁰ For example, e-cigarettes are marketed on television, representing the first time in more than 40 years that a smoking-related device is advertised on this medium. This marketing may have the unintended consequence of renormalizing cigarette smoking after decades of public health efforts that shifted public norms around smoking.

It is also notable that e-cigarettes are available in multiple youth-oriented flavorings, even while such flavorings have been limited for cigarettes by the 2009 Family Smoking Prevention and Tobacco Control Act (<http://www.fda.gov/TobaccoProducts/GuidanceComplianceRegulatoryInformation/ucm246129.htm>). If indeed e-cigarettes are primarily meant to serve as a possible harm reduction tool for addicted smokers, youth-oriented flavorings such as apple bubble gum, banana cream pie, and chocolate candy cane may be counterproductive. It may therefore be prudent to limit e-cigarette characteristics that may be particularly attractive to young people.

Therefore, the results from our study may be important for the US Food and Drug Administration to consider as it debates a proposed rule determining how to exercise their authority over e-cigarettes.^{28,29} For example, currently Internet sales, marketing, flavors, and labeling are not regulated, all of which likely

facilitate access by youth, and the proposed rule does not address many of these issues.^{28,29} However, if future studies demonstrate that e-cigarettes are valuable for smoking cessation among cigarette smokers who wish to quit,⁵ the US Food and Drug Administration and other regulatory authorities will have a challenging regulatory balance to maintain. This task will be even more complex given the additional concerns noted previously that raise questions about the efficacy of e-cigarette use in promoting quitting and concerns around the detrimental effect of nicotine on the adolescent brain.

The most important limitation of this study was that the relatively small number of individuals who used e-cigarettes at baseline limited our statistical power. Baseline data were collected in 2012, and in even only the past couple of years e-cigarette use has increased substantially.¹⁷ Therefore, our confidence intervals were wide, and more precise estimates will require larger samples of NSNS participants who smoke e-cigarettes. However, it is notable that, despite this low power, we found consistently significant results. It is also a limitation that, while our dependent variable spanned the trajectory from nonsmoking to susceptibility to initiation of smoking, it did not include more distal states such as frequent or established smoking. However, susceptibility and initiation of smoking are known to be important steps on the pathway to established cigarette smoking.²³

In addition, while the purpose of this analysis was to focus on future trajectories among NSNS participants, it might be valuable for future analyses to examine trajectories among other groups, such as individuals who are SNS or cigarette experimenters at baseline. Another direction for future research would be to examine more fine-grained assessments of e-cigarette use, such as current use or frequency of use, when larger samples with more e-cigarette users are available.

Finally, while our sample was national, it was not nationally representative. However, it is encouraging that rates of tobacco use in our sample were similar to national estimates from that time.⁴¹

Conclusions

Our study identified a longitudinal association between baseline e-cigarette use and progression to traditional cigarette smoking among adolescents and young adults. Especially considering the rapid increase in e-cigarette use among youth,¹⁷ these findings support regulations to limit sales and decrease the appeal of e-cigarettes to adolescents and young adults.

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Author Affiliations: Division of General Internal Medicine, Department of Medicine, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania (Primack, Fine); Center for Research on Media, Technology, and Health, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania (Primack); Division of Adolescent

Medicine, Department of Pediatrics, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania (Primack); Norris Cotton Cancer Center, Geisel School of Medicine, Dartmouth University, Hanover, New Hampshire (Soneji, Sargent); Dartmouth Institute for Health Policy and Clinical Practice, Geisel School of Medicine, Dartmouth University, Hanover, New Hampshire (Soneji, Sargent); Oregon Social Learning Center, College of Education, University of Oregon, Eugene (Stoolmiller); Center for Health Equity and Research Promotion, VA Pittsburgh Healthcare System,

Pittsburgh, Pennsylvania (Fine); Department of Pediatrics, Geisel School of Medicine, Dartmouth University, Hanover, New Hampshire (Sargent).

Author Contributions: Drs Stoolmiller and Sargent had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Soneji, Sargent.
Acquisition, analysis, or interpretation of data: All authors.

Drafting of the manuscript: Primack, Soneji, Stoolmiller.

Critical revision of the manuscript for important intellectual content: All authors.

Statistical analysis: Primack, Soneji, Stoolmiller.

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