Nicotine & Tobacco Research, 2021, 1468–1474

doi:10.1093/ntr/ntab026

Original Investigation

Received August 6, 2020; Editorial Decision February 5, 2021; Accepted February 10, 2021



Original Investigation

Parental Anti-Smoking Encouragement as a Longitudinal Predictor of Young Adult Cigarette and E-cigarette Use in a US National Study

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Abstract

Introduction: Young adulthood is a critical period for the adoption of risk behaviors like tobacco use. Protective factors in adolescence may promote a tobacco-free transition to young adulthood. We examine associations between the frequency of parental anti-smoking encouragement in adolescence and cigarette and e-cigarette use in young adulthood.

Aims and Methods: We analyzed data from Waves 1 (2009–2010, 10th grade, mean age = 16.2 years) and 5 (2013–2014 mean age = 20.3 years) of the US nationally representative NEXT Generation Health Study (n = 1718). At Wave 1, participants reported how often their parents or guardians encourage them to not smoke cigarettes (1 = Rarely or Never, 7 = Frequently). We used separate weighted multiple logistic regression models to model Wave 5 past 30-day cigarette and e-cigarette use as functions of the frequency of parental anti-smoking encouragement at Wave 1, adjusting for sociodemographic and parenting factors, initial substance use, and peer tobacco use. **Results**: The average frequency of parental encouragement to not smoke cigarettes was fairly high (mean = 5.35). At Wave 5, 24.7% and 14.2% of respondents reported cigarette and e-cigarette use in the past 30 days, respectively. Greater frequency of parental anti-smoking encouragement was associated with lower odds of subsequent cigarette smoking (adjusted odds ratio 0.91, 95% confidence interval 0.83, 0.99) but its association with e-cigarette use was not significant (adjusted odds ratio 0.93, 95% confidence interval 0.84, 1.04).

Conclusions: The longitudinal negative association between anti-smoking encouragement and cigarette use suggests that parental anti-tobacco communication could be a long-term protective factor against young adult tobacco use. Our findings may also suggest the importance of product-specific messages in the evolving tobacco use landscape.

Implications: This study builds upon prior investigations of parenting in adolescence as a protective factor against young adult risk behavior. We isolate the frequency of anti-smoking encouragement during adolescence as an actionable factor distinct from other parenting variables. Our findings also suggest that message specificity may be an important factor in parental anti-tobacco communication as youth and young adult tobacco use becomes increasingly dominated by e-cigarettes.

Introduction

The transition from adolescence to young adulthood represents a vulnerable period for the adoption of health risk behaviors like to-bacco use. This period is characterized by environmental changes and increased autonomy, presenting emerging adults with opportunities to adopt or avoid such risk behaviors. 1-2 Tobacco use is prevalent among young adults, which is often linked to long-term use along with significant health consequences. 3-6 One way to prevent young adult tobacco use is to leverage protective factors during adolescence that could promote a healthy and tobacco-free transition into young adulthood.

There is theoretical and empirical precedent supporting parental influence during adolescence on young-adult behaviors. Adolescent individuation theory emphasizes the role of interpersonal relationships, especially familial ones, during the process of identity formation over the course of adolescence.7 In this framework, the constantly evolving relationship between parent and adolescent shapes the development of a more independent self in late adolescence and young adulthood. A supportive and democratic parentteen relationship is thought to promote better adjustment into young adulthood.8 Empirically, longitudinal associations between parenting in adolescence and health behaviors in young adulthood are documented across a variety of outcomes, including smoking9 and drug use.8 Parental communication is a frequently studied factor with demonstrated associations with adolescent tobacco use behavior. 10 Various aspects of anti-tobacco parenting may operate through adolescent cognitions, with attributes like parental monitoring and parental norms and reactions to adolescent smoking linked to negative perceptions of smoking and higher self-efficacy among adolescents. 11,12 However, elements of parenting have also frequently been studied concurrently, making it difficult to disentangle the potential influences of specific practices. For example, Cleveland et al. demonstrated a longitudinal negative association between an aggregate scale of effective parenting and subsequent use of tobacco, alcohol, and marijuana in a sample of African American adolescents. 13

Among studies that linked parental influences in adolescence to smoking in young adulthood, Beach et al. suggest an indirect link between early adolescent supportive parenting and lower young adult smoking through epigenetic stress pathways. Interestingly, Otten et al. demonstrated that adolescent noncompliance with parental expectations at age 18 was a small but significant predictor of smoking progression between ages 18 and 28.14 While these studies demonstrate significant longitudinal associations between parenting during adolescence and smoking in young adulthood, neither examined parent strategies intended to specifically address smoking among their children. Longitudinal analyses of specific elements of tobaccorelated parental communication are needed to investigate tobacco use associations into young adulthood.

It is also critical to consider the role of tobacco-related parental communication in the context of the current adolescent and young adult tobacco use behaviors. Recent data show a rapid rise in e-cigarette use among young adults in the United States, including ever-use rates of 40% among 18–20-year-olds and 46% among 21–24-year-olds.⁵ While the relative long-term safety of e-cigarettes remains unclear, several health risks have been identified, including lung¹⁵ and oral¹⁶ injury as well as nicotine damage to the developing brain.¹⁷ Further, e-cigarette use is associated with increased odds of smoking onset and other tobacco product use in young people.^{3,4,18,19} There is substantial evidence that adolescents and young adults perceive e-cigarettes differently from combustible cigarettes, frequently

characterizing them as a less harmful alternative to cigarettes.^{4,18} These different perceptions lead us to consider whether parental anti-smoking communication would influence e-cigarette use as well.

In the present study, we apply a specific focus on the prospective relationship between parental anti-smoking communication frequency during adolescence and young adulthood smoking and e-cigarette use. Specifically, we hypothesize that more frequent parental anti-smoking communication is associated with lower likelihood of cigarette smoking and of e-cigarette use during young adulthood.

Methods

Study Population

We analyzed data from Waves 1 (2010) and 5 (2014) of the NEXT Generation Health Study. The NEXT study assessed health status, health behaviors, and their risk factors in a nationally representative sample of US adolescents, beginning in 10th grade at Wave 1. African American adolescents were intentionally oversampled in the study to provide a sufficient sample for race and ethnicity-specific analyses. The sample included students from public, private, and religious schools, with school districts or clusters thereof serving as the primary sampling units. Tenth grade classes were randomly selected at participating schools. Initial surveys were completed in school, and subsequent surveys were completed online.

Of the 3796 students sampled, assent and parental consent was obtained for 2619 students prior to Wave 1. Additional adolescents were recruited in subsequent waves. Final sample sizes were 2526 at Wave 1 and 2202 at Wave 5 (retention rate = 76.6%). Among this sample, we analyzed data from 1718 individuals who completed all relevant measures at Waves 1 (mean age = 16.2 years, standard error = 0.03) and 5 (mean age = 20.3 years, standard error = 0.02). Compared with those who included in this analysis, respondents dropped out between Waves 1 and 5 were more likely to be Wave 1 30-day cigarette smokers (chi-square test p < .01). Prevalence of Wave 1 30-day cigarette smoking did not differ between those who included in this analysis and those completed Wave 5 survey with missing data (chi-square test p = .93). Wave 1 parental anti-smoking encourage did not differ across these three groups (F-test p = .77). The NEXT study protocol and materials were approved by the Institutional Review Board of the Eunice Kennedy Shriver National Institute of Child Health and Human Development.

Measures

The exposure variable was a single Wave 1 item asking, "How often do your parents or guardians encourage you to not smoke cigarettes?" with responses on a 7-point Likert-type scale, ranging from 1 (Rarely or Never) to 4 (Occasionally) to 7 (Frequently). Outcomes were binary variables for current use of cigarettes and e-cigarettes at Wave 5. Participants responded to a series of items which followed the question, "On how many occasions (if any) have you done the following things in the LAST 30 DAYS?," offering the options "Never," "Once or twice," "3–5 times," "6–9 times," "10–19 times," "20–39 times," and "40 times or more" for each action or substance. Responses for "Smoked cigarettes" and "Smoked electronic cigarettes," were recoded to create binary variables, never versus once or more, to indicate current cigarette and e-cigarette use, respectively.

Covariates included demographic and socioeconomic factors, variables pertaining to family and peer influences, and baseline substance use measures. Sociodemographic factors were sex (male or female), race and ethnicity (Hispanic or Latino, White, Black, and Other), family affluence, parental education, and urbanicity, all assessed at Wave 1. Family affluence was based on a previously validated adolescent-report measure²⁰ and contained three categories: low, moderate, and high affluence. Parental education was a parent-report measure consisting of three categories-high school or less, some college, and bachelor's degree or more—and measured the higher-educated of both parents. Urbanicity was measured by a three-category variable21 based on the location of the school district: urban, suburban, and rural. Maternal and paternal monitoring were each constructed as scale variables (range: 1-4) by averaging five Wave 1 adolescent-report items for each parent, asking "How much does your mother (or female guardian) or father (or male guardian) really know about...? A. Who your friends are. B. How you spend your money. C. Where you are after school. D. Where you go at night. E. What you do with your free time." Options for each item were 1 (Don't have or see parent or guardian), 2 (Doesn't know anything), 3 (Knows a little), and 4 (Knows a lot). Three self-report variables for Wave 1 substance use were assessed (yes or no): past 30-day cigarette use, past 30-day alcohol use, and past 12-month marijuana use. Covariates also included a measure of current living situation at Wave 5, coded into three categories: with parent(s) or guardian(s), at college, or other. At Wave 5, respondents were asked to report how often their five closest friends (1) smoking cigarettes and (2) use electronic cigarettes (response options: never, almost never, sometimes, often, almost always.) Two binary variables were derived from these responses to represent peer cigarettes and e-cigarettes use at Wave 5 (never vs. ever, which included almost never, sometimes, often, almost always).

Statistical Analysis

Data were weighted to represent the US national population of 10th graders in 2009-2010, accounting for nonresponse and intentional oversampling. Weighted multiple logistic regression models were used to estimate the associations between Wave 1 parental antismoking encouragement and Wave 5 cigarette smoking, adjusting for aforementioned covariates (except peer e-cigarette use). A separate weighted multiple logistic regression models were used to estimate the associations between Wave 1 parental anti-smoking encouragement and Wave 5 e-cigarette use, adjusting for aforementioned covariates (except peer cigarette smoking). We did not include peer cigarette smoking and peer e-cigarette use in the sample model because of their moderately high correlation (r = 0.52). These models yielded adjusted odds ratios for each Wave 5 tobacco use outcome corresponding to unit changes on the 7-point scale for Wave 1 parental anti-smoking encouragement. Further, we tested the interaction between race and ethnicity and Wave 1 parental antismoking encouragement on the two outcomes, excluding the "other" racial and ethnic group due to small sample size. These analyses were conducted in SAS Enterprise version 9.3 (SAS Institute, Cary, NC). Finally, to better represent the associations between the full range of parental anti-smoking encouragement, cigarette smoking, and e-cigarette use, we estimated the marginal probability of Wave 5 cigarette smoking and Wave 5 e-cigarette use by frequency of parent anti-smoking encouragement based on these regression models and plot the results in graphs. Marginal probability models were run in SUDAAN version 11.0.1 (RTI International, Research Triangle Park,

NC) and graphs were generated in SAS Enterprise version 9.4 (SAS Institute, Cary, NC).

Results

Overall, the average frequency of Wave 1 parental encouragement not to smoke cigarettes was 5.35 (standard error = 0.08) on a scale from 1 to 7, representing slightly more than "occasionally." At Wave 1, one in six participants (16.9%) reported using cigarettes in the past 30 days, more than one-third (34.2%) reported consuming alcohol in the past 30 days, and more than one in five (22.4%) reported using marijuana in the past 12 months. As of Wave 5, nearly half (47.3%) of the sample lived with parent(s) or guardian(s). Regarding frequency of substance use among their five closest friends at Wave 5, over one-fourth (26.8%) of respondents reported any cigarette use, and over one-fifth (22.2%) reported any e-cigarette use. At Wave 5, one in four respondents (24.7%) reported using cigarettes in the past 30 days, while one in seven (14.2%) reported using e-cigarettes in the past 30 days. Distributions of independent variable, dependent variables, and covariates are presented in Table 1.

Results from the multivariable logistic regression models indicated that a higher frequency of parental encouragement not to smoke cigarettes, as measured in adolescence at Wave 1, was associated with lower odds of 30-day cigarette smoking in young adulthood, measured 4 years later at Wave 5 (Table 2). As shown in Figure 1, frequency of Wave 1 parental anti-smoking encouragement frequency is negatively associated with marginal probability of Wave 5 30-day cigarette smoking, after accounting for covariates. In contrast, the frequency of parental anti-smoking encouragement at Wave 1 was not significantly associated with 30-day e-cigarette use at Wave 5 (Table 2). We did not find significant interaction between race and ethnicity and Wave 1 parental anti-smoking encouragement on Wave 5 30-day cigarette smoking (p = .35) and 30-day e-cigarette use (p = .31).

Among the covariates, 30-day cigarette use at Wave 1 was associated with more than fivefold greater odds of 30-day cigarette use at Wave 5 (Table 2). Additionally, 30-day alcohol use and 12-month marijuana use at Wave 1 were each associated with approximately doubled odds of 30-day cigarette use at Wave 5 (Table 2). Any use of cigarettes among respondents' five closest friends at Wave 5 was also associated with 10-fold higher odds of Wave 5 30-day cigarette use (Table 2). Results were similar for Wave 5 e-cigarette use, with the exception of Wave 1 alcohol use as a nonsignificant covariate. Thirty-day use of cigarettes at Wave 1 was associated with threefold higher odds of 30-day e-cigarette use at Wave 5, and 12-month use of marijuana at Wave 1 was associated with twofold higher odds of 30-day e-cigarette use at Wave 5 (Table 2). In addition, any use of e-cigarettes among respondents' five closest friends at Wave 5 was associated with more than eleven times greater odds of Wave 5 30-day e-cigarette use (Table 2).

Discussion

While parental communication has frequently been studied as a potential factor in adolescent tobacco use, ¹⁰ these associations have rarely been examined beyond adolescence into young adult-hood. Further, it is unclear if parental anti-smoking communication has an impact in the context of contemporary youth and young adult tobacco use behaviors, as e-cigarette use is increasingly prevalent beyond cigarette smoking. ⁴ We aimed to address

Table 1. Distributions of Independent Variable, Dependent Variables, and Covariates, NEXT Generation Study, 2009–2014 (*N* = 1718)

Characteristic	N	Weighted %
Independent variable		
Wave 1 parental anti-smoking	_	5.35 (0.08)
encouragement (range: 1-7)		
Dependent variable		
Wave 5 past 30-day cigarette smoking		
Yes	337	24.7%
No	1381	75.3%
Wave 5 past 30-day e-cigarette use		
Yes	219	14.2%
No	1499	85.8%
Covariates		
Wave 1 sex		
Male	688	38.6%
Female	1030	61.4%
Wave 1 family affluence		
Low	510	19.8%
Moderate	832	51.2%
High	376	29.0%
Wave 1 race and ethnicity		
Hispanic or Latino	529	17.9%
Black	329	10.9%
White	771	65.9%
Other	89	5.3%
Wave 1 parent education		
High school or less	666	31.4%
Some college	641	39.2%
Bachelor's degree or more	411	29.4%
Wave 1 urbanicity		
Urban	623	11.8%
Suburban	567	49.7%
Rural	528	38.5%
Wave 1 maternal monitoring	_	3.59 (0.03)
(range: 1–4)		
Wave 1 paternal monitoring	_	3.00 (0.04)
(range: 1–4)		
Wave 1 30-day cigarette smoking	203	16.9%
Wave 1 30-day alcohol use	507	34.2%
Wave 1 12-month marijuana use	361	22.4%
Wave 5 residential arrangement		
With parents or guardians	1029	47.3%
On college campus	205	14.9%
Other	484	37.8%
Wave 5 any five closest friends	394	26.8%
smoking cigarettes		
Wave 5 any five closest friends	368	22.2%
using e-cigarettes		

^aMeans and standard errors are presented for continuous variables.

each of these concerns in the present study by examining the frequency of encouragement not to smoke during adolescence and its longitudinal relationship with both cigarette and e-cigarette use in young adulthood. We found that a higher frequency of parental anti-smoking encouragement in adolescence was associated with lower odds of current cigarette use in young adulthood, 4 years later. In contrast, the frequency of parental anti-smoking encouragement in adolescence was not significantly associated with odds of current e-cigarette use in young adulthood, a potential testament to the role of message specificity in contemporary tobacco

prevention. By controlling for parental monitoring, prior substance use, and current peer use, we were able to better isolate the frequency of anti-smoking communication as a factor distinct from several common predictors of young adult substance use.^{22–24}

Interestingly, multiple studies have reached conclusions to the contrary, showing positive associations between the frequency of tobacco-related parental communication and tobacco use risks during adolescence.²⁵⁻²⁷ As noted in a 2017 review, ¹⁰ each of these studies uses the same dataset, the "Family and Health project," from the Netherlands. The communication frequency measure in these studies contained eight items assessing the frequency of parental communication about tobacco-related issues, 28,29 so differing results could be due to measurement differences as well as cultural ones. Several other studies found no association between tobacco-related communication frequency and adolescent smoking using other data sources.^{28,30-32} However, these studies similarly employed a variety of measures for communication frequency, 28,30-32 assessed different smoking groups or endpoints, 30,32 or addressed samples outside the United States. 31,32 Nonetheless, the disparate results in past studies and the present study indicate that the frequency of parental antismoking communication during adolescence remains worthy of further investigation.

The follow-up period of the present findings also varies from previous work, offering another potential explanation for their differences. While past studies have assessed tobacco use outcomes within adolescence, we examine an endpoint in young adulthood, a period marked by increased autonomy, new environments, and shifting influences. Prior work provides perspectives on the potential mechanisms of parental influence in adolescence on tobacco use in young adulthood. For example, parental anti-smoking messaging may operate through negative perceptions of smoking and higher self-efficacy among adolescents. Parental influences may also counteract pro-tobacco peer influences, a pattern which has been observed in adolescence. 33,34

We did not find a statistically significant association between parental anti-smoking encouragement in adolescence and current e-cigarette use in young adulthood. In interpreting this finding, we need to consider the timing of Waves 1 and 5 of the NEXT study with respect to the popularity of e-cigarettes in the United States. Wave 1 data were collected in 2009-2010, before the rapid expansion of e-cigarette use among young people in the United States.4 Thus, it is highly unlikely that parental anti-smoking directives would have discussed e-cigarette use at this time. Therefore, our finding may imply that parental anti-tobacco communication that solely addresses cigarette smoking may not be as impactful on young adult e-cigarette use as cigarette smoking. It is potentially because young adults generally perceive e-cigarettes to be less harmful than cigarettes.35 Further, young adults who perceive e-cigarettes as less harmful are more likely to report using them.³⁶ Consequently, our finding between parent anti-smoking encouragement during adolescence and e-cigarette use during young adulthood suggests that parental communication that specifically addresses e-cigarettes is worth investigating as a potential avenue for intervention against e-cigarette use among young people.

We also noted several associations between substance use in adolescence and cigarette and e-cigarette smoking in young adulthood. The association between adolescent cigarette smoking and young adult cigarette smoking is consistent with a large and longstanding body of research on smoking trajectories. 6,37 Similarly, our findings are consistent with prior research demonstrating that alcohol and

Table 2. Associations Between Wave 1 Parental Anti-Smoking Encouragement, Covariates, and Wave 5 Current Cigarette and E-cigarette Use^a

Characteristic	Cigarette use	E-cigarette use
	AOR (95% CI)	AOR (95% CI)
Independent variable		
Wave 1 parental anti-smoking encouragement	0.91 (0.83, 0.99)	0.93 (0.84, 1.04)
Covariates		
Wave 1 sex (ref: Female)		
Male	1.10 (0.80, 1.53)	1.50 (0.90, 2.50)
Wave 1 family affluence (ref: High)		
Low	1.41 (0.86, 2.31)	0.74 (0.29, 1.86)
Moderate	1.25 (0.86, 1.81)	1.10 (0.63, 1.92)
Wave 1 race and ethnicity (ref: White)		
Hispanic or Latino	0.68 (0.31, 1.50)	0.35 (0.12, 1.01)
Black	0.69 (0.30, 1.60)	0.62 (0.25, 1.51)
Other	1.07 (0.39, 2.91)	0.62 (0.20, 1.94)
Wave 1 parent education (ref: Bachelor's degree or more)		
High school or less	1.57 (0.77, 3.21)	1.88 (0.74, 4.75)
Some college	1.24 (0.72, 2.14)	0.98 (0.41, 2.36)
Wave 1 urbanicity (ref: Urban)		
Suburban	1.71 (0.91, 3.19)	0.77 (0.45, 1.30)
Rural	1.91 (0.81, 4.51)	0.79 (0.35, 1.81)
Wave 1 maternal monitoring	0.99 (0.59, 1.65)	1.08 (0.66, 1.74)
Wave 1 paternal monitoring	0.94 (0.68, 1.30)	0.92 (0.58, 1.45)
Wave 1 30-day cigarette smoking (ref: No)		
Yes	5.44 (3.01, 9.82)	3.06 (1.42, 6.56)
Wave 1 30-day alcohol use (ref: No)		
Yes	1.78 (1.14, 2.76)	0.98 (0.54, 1.80)
Wave 1 12-month marijuana use (ref: No)		
Yes	2.11 (1.12, 3.99)	2.09 (1.02, 4.27)
Wave 5 residential arrangement (ref: with parents or guardians)		
On college campus	0.71 (0.34, 1.46)	0.97 (0.30, 3.07)
Other	1.03 (0.63, 1.69)	0.86 (0.50, 1.49)
Wave 5 any five closest friends using cigarettes (ref: No)		
Yes	10.01 (6.35, 15.79)	_
Wave 5 any five closest friends using e-cigarettes (ref: No)	•	
Yes	_	11.35 (5.94, 21.71)

 $^{^{}a}$ Adjusted odds ratios and 95% confidence intervals are presented. Significant results (p < .05) in bold.

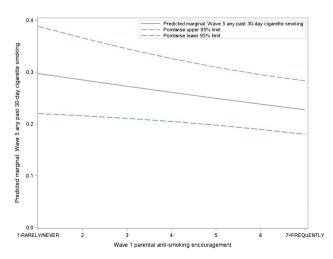


Figure 1. Predicted marginal probability of past 30-day cigarette smoking at Wave 5 by frequency of parental anti-smoking encouragement at Wave 1.

tobacco use trajectories are substantially intertwined^{38,39} and that co-use of tobacco and marijuana is common, though the directionality of the relationship remains unclear as different studies posit

use of each substance as a predictor for the other. 40-42 Our finding of a positive association between adolescent cigarette use and young adult e-cigarette use similarly aligns with past cross-sectional and longitudinal studies emphasizing the prevalence of co-use^{43,44} and is consistent with the belief of e-cigarettes as a less harmful cigarette alternative. 4,45 Similarly, the association between adolescent marijuana use and young adult e-cigarette use is consistent with cross-sectional studies demonstrating increased rates of concurrent use,46 though the status of adolescent marijuana use as a potential longitudinal predictor of e-cigarette use is largely unexplored and worth investigating. Prior reviews have suggested that nicotine and cannabinoids similarly affect neural mechanisms in the developing brain that could lead to increased risk of later substance use and addiction. 46,47 We also found increased odds of cigarette and e-cigarette use among young adults who reported use of the respective substance among their close friends, consistent with well-documented patterns of peer influence on tobacco use among young people. 45,48,49 In the context of the existing literature, our results suggest that intervention efforts focused on reducing multiple forms of substance use among adolescents may be efficacious in reducing young adult cigarette and e-cigarette use.

Some limitations to our study are worth considering. First, the measure of parental anti-smoking encouragement consisted of a

single survey item. While this allowed us to assess the frequency of encouragement as a single aspect of parental tobacco-related communication, it may exclude other forms of tobacco-specific parenting, such as the parent-adolescent discussions of peer influences or tobacco-related harms included in more comprehensive scales.^{28,29} It is also critical to consider the timing of the NEXT study relative to the rapid growth of e-cigarette use among young people in the United States. While our data demonstrate a sufficiently high proportion of e-cigarette use at Wave 5 for meaningful analysis, rates of e-cigarette use among youth and young adults have risen sharply since that data collection in 2014.^{4,50} Specifically, the rapid rise in popularity of JUUL brand e-cigarettes from 2015 to 2017 and beyond represents a major force in rising e-cigarette use among young people.^{51,52} Therefore, future studies are needed to examine the applicability of cigarette-specific parental directives to e-cigarettes now that knowledge and use of e-cigarettes are far more widespread.

In conclusion, our study demonstrates a negative association between the frequency of anti-smoking encouragement toward adolescents and the odds of current cigarette smoking among young adults. This longitudinal association suggests promise for the long-term effectiveness of parent anti-smoking communication on cigarette smoking and could provide an actionable behavior for parents as an intervention for young adult smoking. The weaker, nonsignificant association between parent anti-smoking encouragement and e-cigarette use may indicate the importance of specificity in parental anti-tobacco messaging amid the evolving landscape of adolescent and young adult tobacco use.

Supplementary Material

A Contributorship Form detailing each author's specific involvement with this content, as well as any supplementary data, are available online at https://academic.oup.com/ntr.

Acknowledgments

The authors would like to thank Timothy S. McNeel at Information Management Services, Inc, for his assistance in generating the figures included in this article. Comments and opinions expressed in this article belong to the authors and do not necessarily reflect those of the U.S. Government, Department of Health and Human Services, National Institutes of Health, National Institute of Child Health and Human Development, and National Institute on Minority Health and Health Disparities.

Funding

This work was supported by the Intramural Research Program of the Eunice Kennedy Shriver National Institute of Child Health and Human Development (contract #HHSN275201200001I), the National Heart, Lung and Blood Institute (NHLBI), the National Institute on Alcohol Abuse and Alcoholism (NIAAA), Maternal and Child Health Bureau (MCHB) of the Health Resources and Services Administration (HRSA), and the National Institute on Drug Abuse (NIDA). Dr Choi and Mr Broun's efforts were supported by the Division of Intramural Research, National Institute on Minority Health and Health Disparities.

Declaration of Interests

The authors declare there are no conflicts of interest. The authors have had full access to all of the data in the study and take responsibility for the integrity of the data and accuracy of the data analysis.

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