HHS Public Access

Author manuscript

JAMA Pediatr. Author manuscript; available in PMC 2017 October 25.

Published in final edited form as:

JAMA Pediatr. 2017 August 01; 171(8): 788–797. doi:10.1001/jamapediatrics.2017.1488.

Association Between Initial Use of e-Cigarettes and Subsequent Cigarette Smoking Among Adolescents and Young Adults:

A Systematic Review and Meta-analysis

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Obtained funding: Soneji, Barrington-Trimis, Wills, Unger, Gibson, Primack, Andrews, Spindle, Eissenberg, Hornik.
Administrative, technical, or material support: Soneji, Sargent.
Study supervision: Soneji, Wills, Sargent.

Conflict of Interest Disclosures: Dr Eissenberg reported being a paid consultant in litigation against the tobacco industry and reported being named on a patent application for a device that measures the puffing behavior of e-cigarette users. No other disclosures were reported.

Disclaimer: The content is solely the responsibility of the authors and does not necessarily represent the views of the National Institutes of Health or the US Food and Drug Administration.

Additional Contributions: Sharon Black, MSLIS (University of Pennsylvania), Heather Blunt, MSLIS (Dartmouth College), and Heather Johnson, MLIS (Dartmouth College) assisted in conducting the literature search. None received compensation.

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Abstract

IMPORTANCE—The public health implications of e-cigarettes depend, in part, on whether e-cigarette use affects the risk of cigarette smoking.

OBJECTIVE—To perform a systematic review and meta-analysis of longitudinal studies that assessed initial use of e-cigarettes and subsequent cigarette smoking.

DATA SOURCES—PubMed, EMBASE, Cochrane Library, Web of Science, the 2016 Society for Research on Nicotine and Tobacco 22nd Annual Meeting abstracts, the 2016 Society of Behavioral Medicine 37th Annual Meeting & Scientific Sessions abstracts, and the 2016 National Institutes of Health Tobacco Regulatory Science Program Conference were searched between February 7 and February 17, 2017. The search included indexed terms and text words to capture concepts associated with e-cigarettes and traditional cigarettes in articles published from database inception to the date of the search.

STUDY SELECTION—Longitudinal studies reporting odds ratios for cigarette smoking initiation associated with ever use of e-cigarettes or past 30-day cigarette smoking associated with past 30-day e-cigarette use. Searches yielded 6959 unique studies, of which 9 met inclusion criteria (comprising 17 389 adolescents and young adults).

DATA EXTRACTION AND SYNTHESIS—Study quality and risk of bias were assessed using the Newcastle-Ottawa Scale and the Risk of Bias in Non-randomized Studies of Interventions tool, respectively. Data and estimates were pooled using random-effects meta-analysis.

MAIN OUTCOMES AND MEASURES—Among baseline never cigarette smokers, cigarette smoking initiation between baseline and follow-up. Among baseline non-past 30-day cigarette smokers who were past 30-day e-cigarette users, past 30-day cigarette smoking at follow-up.

RESULTS—Among 17 389 adolescents and young adults, the ages ranged between 14 and 30 years at baseline, and 56.0% were female. The pooled probabilities of cigarette smoking initiation were 30.4% for baseline ever e-cigarette users and 7.9% for baseline never e-cigarette users. The pooled probabilities of past 30-day cigarette smoking at follow-up were 21.5% for baseline past 30-day e-cigarette users and 4.6% for baseline non-past 30-day e-cigarette users. Adjusting for known demographic, psychosocial, and behavioral risk factors for cigarette smoking, the pooled odds ratio for subsequent cigarette smoking initiation was 3.62 (95% CI, 2.42–5.41) for ever vs never e-cigarette users, and the pooled odds ratio for past 30-day cigarette smoking at follow-up was 4.28 (95% CI, 2.52–727) for past 30-day e-cigarette vs non-past 30-day e-cigarette users at baseline. A moderate level of heterogeneity was observed among studies (I^2 = 60.1%).

CONCLUSIONS AND RELEVANCE—e-Cigarette use was associated with greater risk for subsequent cigarette smoking initiation and past 30-day cigarette smoking. Strong e-cigarette regulation could potentially curb use among youth and possibly limit the future population-level burden of cigarette smoking.

The prevalence of e-cigarette use has risen rapidly since introduction of this product to the United States in 2007. Among US high school students, the prevalence of past 30-day use of e-cigarettes increased 10-fold from 1.5% in 2011 to 16.0% in 2015, when the prevalence of past 30-day e-cigarette use in this population exceeded its prevalence of past 30-day cigarette smoking (9.3%).[1] e-Cigarette use occurs at an appreciable prevalence among both cigarette-smoking and never cigarette-smoking youth.[2–4] Furthermore, longitudinal studies[5–10] have reported that e-cigarette use is associated with an increased risk of cigarette smoking initiation among never cigarette-smoking adolescents and young adults even after adjusting for known demographic, psychosocial, and behavioral risk factors. Recently, the US Surgeon General noted this increased risk as an important public health concern.[11]

Although some studies suggest that the use of e-cigarettes may help adults quit smoking,[12] e-cigarettes may confer a public health harm if their use leads to a substantially (1) greater number of youth who initiate cigarette smoking compared with the number of youth who would have initiated cigarette smoking in the absence of e-cigarettes or (2) greater number of youth who currently smoke compared with the number of youth who would have currently smoked in the absence of e-cigarettes.[13,14] It is important to obtain generalizable estimates of these 2 risks to establish the potential public health influence of e-cigarette use among adolescents and young adults.[11] Therefore, we conducted the first systematic review

and meta-analysis to date of longitudinal studies to obtain generalizable estimates of risk for cigarette smoking associated with e-cigarette use across a wide range of populations, study settings, and confounding demographic, psychosocial, and behavioral influences. We followed the Meta-analysis of Observational Studies in Epidemiology (MOOSE) guidelines for our systematic review.

Methods

Data Sources and Searches

We completed a comprehensive literature search of MEDLINE's PubMed (1946 to present), EMBASE (1974 to present), Wiley's Cochrane Library (2016 issue 7), and Web of Science (1900 to present) between February 7 and February 17, 2017. The search included indexed terms and text words to capture concepts associated with e-cigarettes and traditional cigarettes in articles published from database inception to the date of the search (see eTables 1–4, eFigure 1, and eFigure 2 in the Supplement for full search strategies). There were no language or study design restrictions. The search strategy was adjusted for the syntax appropriate for each database. We also completed a comprehensive search of the 2016 Society for Research on Nicotine and Tobacco 22nd Annual Meeting abstracts, the 2016 Society of Behavioral Medicine 37th Annual Meeting & Scientific Sessions abstracts, and the 2016 National Institutes of Health Tobacco Regulatory Science Program Conference. We searched abstracts from these annual meetings and the conference separately because they are not included in any of the electronic databases.

The included studies were approved by the following institutional review boards: University of Southern California, Dartmouth College, University of Hawaii, Hawaii State Department of Education, University of Pittsburgh, University of Pennsylvania, Virginia Commonwealth University, and University of Michigan. For all included studies, participants 18 years or older provided written informed consent, and participants 17 years or younger provided written assent and parental informed consent.

Study Selection

We included studies that evaluated the association between e-cigarette use among never cigarette smokers at baseline and cigarette smoking initiation between baseline and follow-up (Figure 1). We also included studies that evaluated the association between past 30-day e-cigarette use at baseline and past 30-day cigarette smoking at follow-up. We included longitudinal studies and excluded cross-sectional studies given the temporal ordering of the research question. Three investigators (S.S., J.Y., and R.D.) independently reviewed the title, abstract, and text of the studies. The interrater agreement among the 3 reviewers, measured by Fleiss K, was 86.1%. When the investigators disagreed on study inclusion, they discussed to reach consensus based on inclusion and exclusion criteria.

Data Extraction

Data extracted from each study included the following: study location, comparison group (eg, never e-cigarette users), time between baseline and follow-up, and a list of demographic, psychosocial, and behavioral characteristics included in each study's

multivariable statistical analysis. Demographic characteristics included age, sex, race/ethnicity, and parental educational level. Psychosocial and behavioral characteristics included levels of self-esteem, sensation seeking, rebelliousness, delinquent behavior, depressive symptoms, impulsivity, smoking susceptibility, peer smoking, parental smoking, and use of other substances (alcohol, illicit drugs, and other tobacco products). eTable 5 in the Supplement lists details of the psychosocial and behavioral characteristics. We evaluated the quality of the included studies using the Newcastle-Ottawa Scale (NOS), which assesses the quality of nonrandomized studies in meta-analyses and considers selection of the study groups, comparability across groups, and ascertainment of the outcome of interest.[15] We assessed the risk of bias using the Risk of Bias in Non-randomized Studies of Interventions (ROBINS-I) tool, which considers biases from confounding, selection of participants into the studies, missing data, and measurement of outcomes.[16] Two investigators (S.S. and J.L.B.T.) evaluated each study against rubrics provided by the NOS and the ROBINS-I tool. If investigators' scores differed on a specific domain of either the NOS or the ROBINS-I tool, they discussed to reach consensus based on the rubrics.

Statistical Analysis

We calculated the observed probability of cigarette smoking initiation among baseline never cigarette smokers by their baseline e-cigarette use. We then calculated the corresponding unadjusted odds ratio using data across all included studies. Next, we estimated the pooled odds ratio for cigarette smoking initiation among baseline ever e-cigarette users compared with never e-cigarette users by fitting a random-effects meta-analysis model. The meta-analysis model included as data the multivariable regression results of each study that adjusted for known demographic, psychosocial, and behavioral risk factors for cigarette smoking.

Similarly, we calculated the observed probability of past 30-day ("current") cigarette smoking at follow-up among baseline noncurrent cigarette smokers by their baseline use of e-cigarettes in the past 30 days. We then fit a random-effects meta-analysis model to estimate the pooled odds ratio for current cigarette smoking at follow-up among baseline noncurrent cigarette smokers who used e-cigarettes in the past 30 days compared with baseline noncurrent cigarette smokers who did not use e-cigarettes in the past 30 days. The meta-analysis model also included as data the multivariable regression results of each study that adjusted for known risk factors for cigarette smoking.

For both analyses, we assessed statistical heterogeneity using the I^2 statistic, which measures the percentage of total variation due to heterogeneity among studies rather than by chance.[17] For the cigarette smoking initiation analysis, we then assessed the source of heterogeneity between studies by conducting subgroup analysis. We consider the following subgroups: adolescent vs young adult studies (based on the mean age of respondents at baseline), baseline year of study (before 2014 vs 2014 or later), and regional vs national sample. We selected 2014 as the cut point for the subgroup because youths' past 30-day e-cigarette use after 2013 grew substantially.[1]

We conducted a sensitivity analysis to assess the influence of selection bias (eg, publication bias) on the pooled adjusted odds ratio estimated by fitting a Copas selection model.[18–21]

Briefly, the Copas selection model simultaneously models the outcome and selection in which the chance of observation (or publication) of a study is inversely proportional to the standard error of its outcome. We used a computer program (R, version 3.2.3; The Comprehensive R Archive Network) for all statistical analyses.

Results

Of 6959 unique studies identified, 9 studies[5–10,22–24] met all inclusion criteria (comprising 16 621 adolescents and young adults) and were included in the systematic review and meta-analysis (Figure 1). Seven studies[5–10,22] examined cigarette smoking initiation between baseline and follow-up and included a total of 8168 participants who were never cigarette smokers at baseline (of whom 1174 were ever e-cigarette users at baseline). Two studies[23,24] examined past 30-day cigarette smoking and included a total of 2084 participants who were not past 30-day cigarette smokers at baseline (of whom 119 were past 30-day e-cigarette users at baseline). Baseline and follow-up data were collected between 2012 and 2016 for these studies (Table 1). The age of participants across studies ranged between 14 and 30 years old at baseline, and 56.0% were female. The setting of 5 studies[5,7–9,23] was regional (3 in the Los Angeles, California, area; 1 in Oahu, Hawaii; and 1 in Richmond, Virginia), while the remaining 4 studies[6,10,22,24] were US national-based samples recruited through random-digit dial (2 studies), nationally representative online panels (1 study), and national representative school-based samples (1 study). All studies adjusted for demographic, psychosocial, and behavioral risk factors that could be correlated with e-cigarette use and cigarette smoking. Three studies[5,9,23] received a score of 6 of 9 on the NOS, and the remaining 6 studies[6–8,10,22,24] received a score of 5 of 9 on the NOS (score range, 0–9; eTable 6 in the Supplement). In addition, the overall risk of bias was moderate for all studies based on the ROBINS-I tool (eTable 7 in the Supplement).

Among baseline never cigarette smokers, the unadjusted odds ratio for cigarette smoking initiation ranged between 3.50 and 7.78 across studies for those who had ever tried e-cigarettes compared with those who had never tried e-cigarettes (Figure 2). Pooling across the 7 studies[5–10,22] that examined initiation, the probabilities of cigarette smoking initiation were 30.4% for baseline ever e-cigarette users and 7.9% for baseline never e-cigarette users, for an unadjusted odds ratio of 5.12 (95% CI, 4.41–5.95). Combining the data and multivariable regression results from the 7 studies in a random-effects meta-analysis, the pooled adjusted odds ratio for subsequent cigarette smoking initiation was 3.62 (95% CI, 2.42–5.41) for baseline ever e-cigarette users compared with baseline never e-cigarette users.

Among baseline noncurrent cigarette smokers, the unadjusted odds ratio for current cigarette smoking at follow-up ranged between 4.71 and 11.18 across studies for those who had used e-cigarettes in the past 30 days at baseline compared with those who had not used e-cigarettes in the past 30 days at baseline (Figure 3). Pooling across both studies[23,24] that examined current cigarette smoking, the probabilities of current cigarette smoking at follow-up were 21.5% for baseline past 30-day e-cigarette users and 4.6% for baseline non–past 30-day e-cigarette users, for an unadjusted odds ratio of 5.68 (95% CI, 3.49–9.24). Combining the data and multivariable regression results from the 2 studies in a random-effects meta-analysis, the pooled adjusted odds ratio for past 30-day cigarette smoking at follow-up was

4.28 (95% CI, 2.52–7.27) for baseline past 30-day e-cigarette users compared with baseline non–past 30-day e-cigarette users.

We observed evidence of moderate heterogeneity (Cochran *Q*) in the 7 studies[5–10,22] of cigarette smoking initiation (Q_6 = 15.04, P = .02, I^2 = 60%). Adolescent-based studies[5,7,8] (ie, the mean age of respondents at baseline <18 years) exhibited greater heterogeneity than young adult–based studies[6,9,10,22] (ie, the mean age of respondents at baseline ≥18 years) (Table 2). After excluding the 3 adolescent-based studies, the pooled adjusted odds ratio for cigarette smoking initiation was 4.27 (95% CI, 2.74–6.63), and this exclusion diminished the heterogeneity among the studies, which was no longer statistically significant (*P* = .50). Similarly, after excluding the 4 studies[5–7,22] conducted before 2014, the pooled adjusted odds ratio of cigarette smoking initiation was 4.48 (95% CI, 3.06–6.57),and this exclusion diminished the heterogeneity among the studies, which was no longer statistically significant (*P* = .37). Finally, after excluding the 4 regional-based studies,[5,7–9] the pooled adjusted odds ratio of cigarette smoking initiation was 6.11 (95% CI, 3.03–12.33), and this exclusion diminished the heterogeneity among the studies, which was no longer statistically significant (*P* = .72).

We conducted a sensitivity analysis to assess the influence of selection bias on the pooled adjusted odds ratio for cigarette smoking initiation by fitting a Copas selection model (eAppendix, eFigure 3, eTable 8, and eTable 9 in the Supplement). Adjusting for selection bias, the Copas selection model estimated that the pooled adjusted odds ratio for cigarette smoking initiation was 3.01 (95% CI, 2.02–4.47) compared with the random-effects model estimate of 3.62 (95% CI, 2.42–5.41).

Discussion

In this systematic review and meta-analysis, results from 9 longitudinal studies were consistent in finding that e-cigarette use is associated with an increased risk of future cigarette smoking initiation and current cigarette smoking even after adjusting for potentially confounding demographic, psychosocial, and behavioral risk factors. Our results suggest that e-cigarette use is a strong risk factor for cigarette smoking among adolescents and young adults because the magnitude of the pooled odds ratios approximately equaled or exceeded that of other known risk factors, including parental, sibling, and peer cigarette smoking and high levels of sensation seeking and risk taking.[25,26] Our results indicate that e-cigarette use is an independent risk factor for cigarette smoking because we included studies that adjusted for numerous known risk factors for cigarette smoking in our analysis.

e-Cigarette use may represent a risk factor for cigarette smoking initiation and current cigarette smoking for several behavioral and physiological reasons. First, e-cigarette use mimics the behavioral scripts of cigarette smoking. The use of e-cigarettes involves hand-to-mouth movements, puffing (which brings the e-cigarette aerosol into the mouth), inhalation of the mixture into the lungs, and exhalation.[6] For example, the same exhalation techniques used to produce smoke rings with traditional cigarettes can be used to make rings of aerosol with e-cigarettes.[27] Therefore, adolescents and young adults, even those who primarily use e-cigarettes without nicotine, may acquire and learn cigarette smoking–related behavioral

scripts through the use of e-cigarettes that ultimately make the transition to cigarette smoking more natural.

Second, adolescents and young adults who use nicotine-containing e-cigarettes may become addicted to nicotine because e-cigarette aerosol contains highly oxidizing free-base nicotine —the most addictive form of nicotine—that is easily absorbed by the body.[28] As a result, e-cigarette users may be more inclined to experiment with and transition to combustible cigarettes and other forms of inhalable nicotine to more effectively satiate their nicotine cravings. Even youth who report using nicotine-free (ie, flavor only) e-cigarettes may still inhale aerosolized nicotine; laboratory-based studies[29–31] using gas chromatography and mass spectrometry revealed substantial discrepancies between reported and actual nicotine content. In addition, inhaling pleasurable flavors may provide a positive sensory experience similar to smokers' reports about inhaling cigarette smoke.

Third, e-cigarette use may activate cognitive or behavioral processes that increase the risk of smoking. For example, e-cigarette users show increases in positive expectancies about cigarette smoking and increases in affiliation with peers who smoke cigarettes.[32] These cognitive and behavioral effects may operate independent of other processes to increase the risk of smoking among adolescents who try e-cigarettes.

Whether e-cigarettes represent a public health harm or benefit depends, in part, on the number of adolescents and young adults who initiate cigarette smoking after the use of e-cigarettes and if these individuals would likely have begun cigarette smoking in the absence of e-cigarettes. Although some models suggest that e-cigarette use is merely a marker for high-risk adolescents who would have smoked cigarettes any way,[14] empirical evidence indicates that e-cigarette use differentially occurs among youth who are not at high risk for cigarette smoking based on established risk factors.[4,5,33] For example, Wills et al[34] found that the effect of e-cigarette use on cigarette smoking initiation was stronger among study participants who were at lower risk at baseline on 3 indexes for smoking compared with those who were at higher risk. Barrington-Trimis et al[8] similarly found that the effect of e-cigarette use on cigarette smoking initiation was stronger for youth who were not susceptible to cigarette smoking compared with youth who were susceptible to cigarette smoking. Therefore, e-cigarette use does not appear to be just a marker for high-risk youth; rather, e-cigarette use is a true risk factor for cigarette smoking initiation.[34] If, indeed, e-cigarette use increases the likelihood of subsequent cigarette smoking initiation among otherwise low-risk adolescents, then the use of e-cigarettes could slow or reverse the decline in adolescent cigarette smoking that has occurred since 1996.[35]

Strengths and Limitations

We note several strengths of this research for addressing the possibility that e-cigarette use is a risk factor for cigarette smoking. First, all of the included studies were longitudinal; hence, e-cigarette use temporally preceded cigarette smoking initiation and past 30-day cigarette smoking. Second, pooling across studies, all of which adjusted for numerous covariates, we found substantial effect sizes of e-cigarette use on cigarette smoking initiation and current cigarette smoking. Third, the studies occurred over a short period (2012–2016); therefore, the level of external risk factors (eg, price of cigarettes) remained constant. Fourth, we found

consistent evidence across multiple studies that e-cigarette use increased the risk of cigarette smoking initiation. Perhaps more concerning from a public health perspective, we also found evidence that e-cigarette use increased the risk of subsequent past 30-day cigarette smoking, which includes regular daily cigarette smoking. Therefore, several aspects of the association between e-cigarette use and cigarette smoking suggest a causal correlation, namely, its association, consistency, specificity, temporality, and biological and behavioral plausibility.

We also note several limitations. First, the overall risk of bias was moderate for all studies because, in part, the risk of bias due to confounding was moderate. All studies accounted for varying demographic, psychosocial, and behavioral risk factors, although the potential exists for omitted variable bias. The overall quality of 6 studies[6–8,10,22,24] was reduced because of loss to follow-up that each exceeded 20%. The association between e-cigarette use and cigarette smoking may be biased if respondents lost to follow-up were more or less likely to smoke cigarettes at follow-up than respondents not lost to follow-up. Of the 6 studies, 4 studies[6–8,10] with high loss to follow-up compared complete case and full information analysis, assessed whether the association between e-cigarette use and cigarette smoking differed by characteristics associated with attrition (eg, highest parental educational level), and either stratified analysis based on characteristics associated with attrition or reweighted the sample based on attrition. The substantive conclusions remained the same. Second, we do not know the type of e-cigarette used by respondents or the proportion of respondents who used nicotine-containing e-cigarettes. Later-generation e-cigarettes (eg, “mods”) deliver higher blood nicotine levels than first-generation e-cigarettes (eg, “cig-a-likes”).[36–38] Third, although we conducted an international literature search, all included studies were US based; therefore, our results may not apply to youth in other countries. Fourth, 2 studies[5,8] sampled students from Los Angeles–area high schools, although there was no overlap in the cohorts.

Finally, the studies ascertained mainly early phases of the adolescent smoking process. No study followed up youth long enough to determine the proportion of onset cases who became regular or nicotine-dependent cigarette smokers during the follow-up period.[5–8,22] However, it should be noted that studies[39–44] of smoking transitions have consistently found that early symptoms of nicotine dependence (eg, craving a cigarette) can emerge only a short time after onset, sometimes after an adolescent has smoked only a few cigarettes, and that these early symptoms are strong predictors of subsequent transition to full nicotine dependence. Therefore, from a public health standpoint, there does not seem to be a clear lower threshold for concern with respect to frequency or quantity smoked. For example, DiFranza et al noted that based on their data “First inhalation [of a cigarette] is the most important tobacco use milestone.”[41(p208)]

Conclusions

Our systematic review and meta-analysis of 9 longitudinal studies found consistent and strong evidence thate-cigarette use is associated with increased odds of subsequent cigarette smoking initiation and current cigarette smoking among adolescents and young adults after adjusting for known demographic, psychosocial, and behavioral risk factors. To minimize the potential public health harm from e-cigarette use, the US Food and Drug Administration, as well as state and local agencies, will need to engage in regulatory actions to discourage

youth use of e-cigarettes and prevent the transition from e-cigarettes to other combustible tobacco products. In addition to the currently enacted age limitations on in-store sales, regulatory actions could include restrictions on advertising campaigns that may be viewed by adolescents, limits to characterizing flavors (eg, fruit- and candy-flavored e-cigarettes), strict standards for reporting actual nicotine content in e-liquid, and requirements for age verification for online and retail sales of these products. Such strong regulation of e-cigarettes could curb use among youth and limit the future population-level burden of tobacco.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

Funding/Support: This study was supported by grants R21-CA197912 (Dr Soneji), R01-CA077026 (Dr Sargent), R01-CA140150 (Dr Primack), R21-CA185767 (Dr Primack), and R01-CA153154 and P30-CA071789-16S2 (Dr Wills) from the National Cancer Institute (NCI) at the National Institutes of Health (NIH); grants P50-CA180905 (Drs Barrington-Trimis and Unger) and P50-CA179546 (Drs Gibson and Hornik) from the NCI and the US Food and Drug Administration Center for Tobacco Products; and grants P50-DA036105 (Mr Spindle and DrEissenberg),R01-DA033296 (Dr Leventhal), R01-DA10767 (Dr Andrews), and R01-DA016310 (Dr Unger) from the National Institute on Drug Abuse at the NIH.

Role of the Funder/Sponsor: The funders had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

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Key Points

Question

Is there an association between e-cigarette use and cigarette smoking among adolescents and young adults?

Finding

A systematic review and meta-analysis showed strong and consistent evidence of an association between initial e-cigarette use and subsequent cigarette smoking initiation, as well as between past 30-day e-cigarette use and subsequent past 30-day cigarette smoking.

Meaning

To minimize the potential public health harm from e-cigarette use, the US Food and Drug Administration, as well as state and local agencies, will need to engage in effective regulatory actions to discourage youths' use of e-cigarettes and prevent the transition from e-cigarettes to other combustible tobacco products.

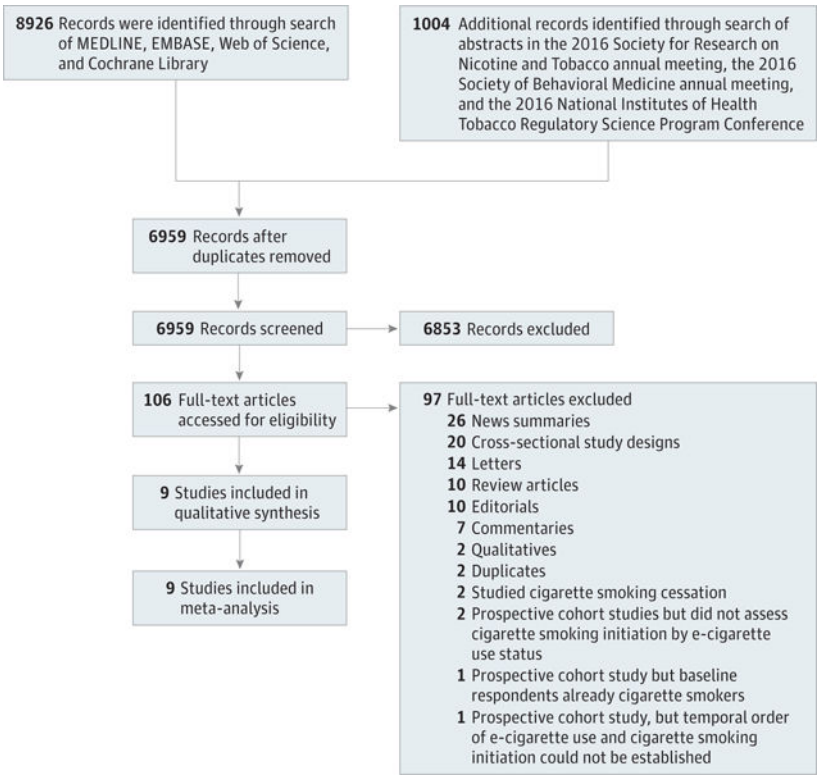

Figure 1. PRISMA Diagram of Study Selection

PRISMA indicates Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

Source	Probability of Cigarette Smoking Initiation, %		Unadjusted OR (95% CI)	Adjusted OR (95% CI)	Weight, %
	Ever e-Cigarette Users	Never e-Cigarette Users			
Miech et al,[10] 2017	31.1	6.8	6.23 (1.57-24.63)	4.78 (1.91-11.96)	11.4
Spindle et al,[9] 2017	29.4	10.6	3.50 (2.41-5.09)	3.37 (1.91-5.94)	17.9
Primack et al,[22] 2016	37.5	9.0	6.06 (2.15-17.10)	8.80 (2.37-32.69)	7.0
Barrington-Trimis et al,[8] 2016	40.4	10.5	5.76 (3.12-10.66)	6.17 (3.29-11.57)	16.6
Wills et al,[7] 2016	19.5	5.4	4.25 (2.74-6.61)	2.87 (2.03-4.05)	23.0
Primack et al,[6] 2015	37.5	9.6	5.66 (1.99-16.07)	8.30 (1.19-58.00)	3.7
Leventhal et al,[5] 2015	31.8	5.6	7.78 (6.15-9.84)	1.75 (1.10-2.78)	20.3
Total	**30.4**	**7.9**	**5.12 (4.41-5.95)**	**3.62 (2.42-5.41)**	**100**

Heterogeneity: $\tau^2 = 0.15$; $Q_6 = 15.04$; $P = .02$; $I^2 = 60\%$
Test for overall effect: $z = 6.25$; $P < .001$

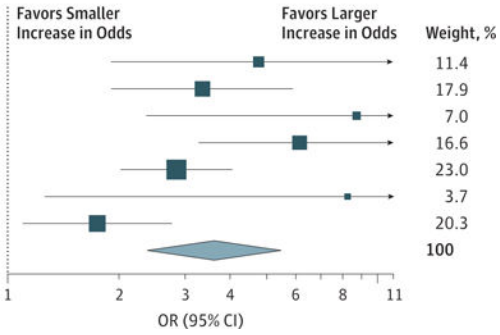

Figure 2. Meta-analysis of Adjusted Odds of Cigarette Smoking Initiation Among Never Cigarette Smokers at Baseline and Ever e-Cigarette Users at Baseline Compared With Never e-Cigarette Users at Baseline

The odds ratios (OR) for the studies[5–10,22] are adjusted for a study-specific set of demographic, psychosocial, and behavioral risk factors. The size of the point estimate (black square) is proportional to the weight of the study in the random-effects meta-analysis model. The weights addto99.9% and not 100% because of rounding. Q indicates Cochrane Q.

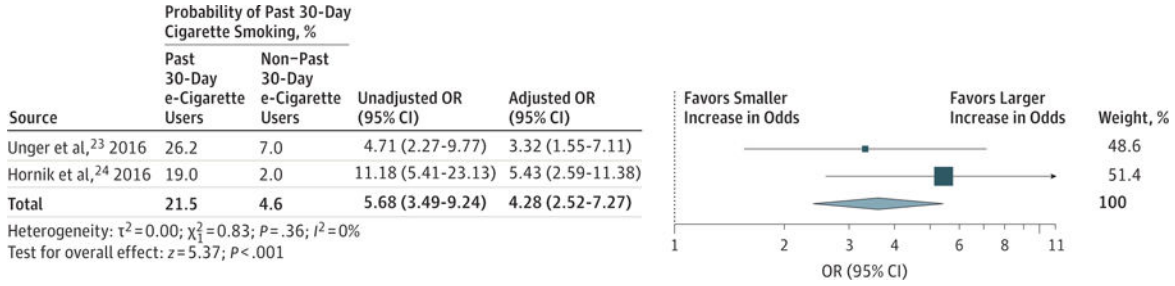

Figure 3. Meta-analysis of Adjusted Odds of Current (Past 30-Day) Cigarette Smoking at Follow-up Among Noncurrent Cigarette Smokers at Baseline and Current e-Cigarette Users at Baseline Compared With Noncurrent e-Cigarette Users at Baseline

The odds ratios (OR) for the studies[23,24] are adjusted for a study-specific set of demographic, psychosocial, and behavioral risk factors. The size of the point estimate (black square) is proportional to the weight of the study in the random-effects meta-analysis model.

Table 1

Summary of Studies

Source	Study Design and Population	Method of Survey	Objective	Age of Sample, Mean (Range), y	Study Period	Follow-up Period, mo	Loss to Follow-up, %	Baseline Sample	Exposure/ Outcome	Covariates	ROBINS-I/NOS
Leventhal et al,[5] 2015	Longitudinal repeated assessment of school-based cohort of 9th graders recruited from high schools in Los Angeles, California	Paper-based questionnaire	"To evaluate whether e-cigarette use among 14-year-old adolescents who have never tried combustible tobacco is associated with risk of initiating use of 3 combustible tobacco products (ie, cigarettes, cigars, and hookah)."[5(P700)]	14.1 (14–14)	2013–2014	12	1.1	Never cigarette smokers (n = 2558)	Ever use of e-cigarettes/ever cigarette smoking	Demographic: age, sex, race/ethnicity, parental educational level Psychosocial: depressive symptoms, impulsivity Behavioral: delinquent behavior, substance use Other: lives with biological parents, family history of smoking, peer smoking, smoking susceptibility, smoking expectancies	Moderate/6
Primack et al,[6] 2015	Longitudinal repeated assessment of a national study of adolescents and young adults (from the Dartmouth Media, Advertising, and Health Study) recruited via random-digit dialing using Landline (66.7%) and cellular telephone numbers (33.3%)	Internet-based visual survey	"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."[6(p1018)]	20.0(16–26)	2012–2013 to 2013–2014	12	30.4	Nonsusceptible never cigarette smokers (n = 694)[a]	Ever use of e-cigarettes/ever cigarette smoking	Demographic: age, sex, race/ethnicity, maternal educational level Psychosocial: sensation seeking Other: parental smoking, peer smoking	Moderate/5
Wills et al,[7] 2016	Longitudinal repeated assessment of 9th, 10th, and 11th graders from high schools on the island of Oahu, Hawaii (4 public, 2 private)	Paper-based questionnaire	"We examined, longitudinally, how e-cigarette use among adolescents is related to subsequent smoking behaviour."[7(p34)]	14.7(14–16)	2013–2014	12	44.3	Never cigarette smokers (n = 1141)	Ever use of e-cigarettes/ever cigarette smoking	Demographic: age, sex, race/ethnicity, family structure, parental educational level Psychosocial: parental support, parental monitoring, rebelliousness	Moderate/5
Barrington-Trimis et al,[8] 2016	Longitudinal repeated assessment of 11th and 12th graders enrolled in the Southern California Children's Health Study	Paper-based questionnaire at baseline Internet-based questionnaire at follow-up	To examine "whether e-cigarette use increases the risk of cigarette initiation among adolescents in the transition to adulthood when the sale of cigarettes becomes legal."[8(p2)]	17.4(16–18)	2014 to 2015–2016	16	28.9	Never cigarette smokers (n = 298)	Ever use of e-cigarettes/ever cigarette smoking	Demographic: grade level, sex, race/ethnicity, parental educational level Other: cigarette use in the home, peer smoking, peer acceptability of smoking	Moderate/5
Primack et al,[22] 2016	Longitudinal repeated assessment of participants recruited from a nationally	Internet-based survey	"To determine the association between baseline e-cigarette use and	23.5 (18–30)	2013–2014	18	39.2	Never cigarette smokers (n = 1506)	Ever use of e-cigarettes/ever	Demographic: age, sex, race/ethnicity, educational level,	Moderate/5

Source	Study Design and Population	Method of Survey	Objective	Age of Sample, Mean (Range), y	Study Period	Follow-up Period, mo	Loss to Follow-up, %	Baseline Sample	Exposure/ Outcome	Covariates	ROBINS-I/NOS
	representative probability-based online nonvolunteer access panel (Knowledge Panel) recruited and maintained by Growth from Knowledge		subsequent initiation of cigarette smoking among young adults who initially never smoked cigarettes."[22(p2)]						cigarette smoking	household income Psychosocial: self-esteem, sensation seeking, rebelliousness Other: relationship status, residing with parents/guardian or a significant other	
Unger et al,[23] 2016	Longitudinal repeated assessment of Hispanic participants in Project RED[b] who attended 1 of 7 high schools in the Los Angeles, California, area in 2005	Internet-based survey	To determine "whether e-cigarette use is associated with subsequent cigarette or marijuana use over a one-year period."[23(p261)]	22.7(22–24)	2014–2015	12	7.8	Non-past 30-d cigarette smokers (n = 1056)	Past 30-d e-cigarette use/ past 30-d cigarette smoking	Demographic: age, sex Other: past-month use of alcohol, past-month use of other tobacco products[c]	Moderate/6
Hornik et al,[24] 2016	Longitudinal repeated assessment of a nationally representative sample of adolescents and young adults recruited via an ongoing, rolling cross-sectional survey based on list-assisted and random-digit dialing using Landline (19%) and cellular telephone numbers (81%)	Internet-based survey	To determine "whether e-cigarette use predicts cigarette use reported 6 months later, in a nationally representative US sample of youth and young adults"[24(p1)]	18.3 (13–25)	2014–2015	6	65.0	Non-past 30-d cigarette smokers (n = 1028)	Past 30-d e-cigarette use/ past 30-d cigarette smoking	Demographic: age, sex, race/ethnicity, parental educational level Psychosocial: sensation seeking, grades Other: ever cigarette use, cigarette use in the home, peer smoking	Moderate/5
Spindle et al,[9] 2017	Longitudinal repeated assessment of a subset of the Spit for Science project, a university-wide longitudinal study aimed at assessing genetic and environmental influences on substance use and emotional health in college students	Internet-based survey	To examine "extent that e-cigarette use is associated with the onset of cigarette smoking and the factors that lead to the uptake of e-cigarettes in college students."[9(p66)]	18.5 (18–25)	2014–2015	12	17.8	Never cigarette smokers (n = 2316)	Ever use of e-cigarettes/ever cigarette smoking	Demographic: age, sex, race/ethnicity Psychosocial: depression, anxiety, impulsivity (5 subscales: positive and negative urgency, lack of premeditation, lack of perseverance, sensation seeking) Other: stressful life events, peer deviance, other tobacco use	Moderate/6
Miech et al,[10] 2017	Longitudinal repeated assessment of 12th graders sampled in the nationally representative Monitoring the Future Study (2014) in 122 schools (105 public, 17 private)	Initial evaluation questionnaire completed in the classroom Follow-up questionnaire completed online	"To prospectively examine vaping as a predictor of future cigarette smoking among youth with and without previous cigarette smoking experience."[10(p1)]	18.0(17–20)	2014–2015	13.4	57.8	Never cigarette smokers (n = 246)	Past 30-d e-cigarette use/ ever cigarette smoking	Demographic: female, race (white, non-white) Other: binge drinking in the past 2 wk, marijuana use in the past 30 d	Moderate/5

Abbreviations: NOS, Newcastle-Ottawa Scale (score range, 0–9); ROBINS-I, Risk of Bias in Non-randomized Studies of Interventions.

[a]Nonsusceptible respondents answered “definitely not” to both of the following survey questions: (1) “If one of your friends offered you a cigarette, would you try it?” and (2) “Do you think you will smoke a cigarette sometime in the next year?”

[b]Project RED (*Reteniendo y Entendiendo Diversidad para Salud* [Retaining and Understanding Diversity for Health]) is a school-based longitudinal study of cultural factors and substance abuse in the Los Angeles, California, area.

[c]Other tobacco products included hookah, cigars, little cigars, and smokeless tobacco.

Table 2

Subgroup Analysis of Cigarette Smoking Initiation

Studies Included in Analysis	No. of Studies	No. of Respondents	Pooled Adjusted OR (95% CI)	I^2,%	*P* Value for Test of Heterogeneity
All	7	8936	3.62 (2.42–5.41)	60	.02
Mean age of sample at baseline, y					
<18	3	4765	3.03 (1.65–5.55)	80	.01
≥18	4	4171	4.27 (2.74–6.63)	0	.50
Baseline year of study					
<2014	4	6076	3.01 (1.70–5.33)	62	.05
≥2014	3	2860	4.48 (3.06–6.57)	0	.37
Sample					
Regional	4	5011	3.08 (1.96–4.84)	71	.02
National	3	3925	6.11 (3.03–12.33)	0	.72

Abbreviation: OR, odds ratio.