# E-cigarette use is associated with subsequent cigarette use among young adult non-smokers, over and above a range of antecedent risk factors: a propensity score analysis

Marina Epstein<sup>1</sup>, Jennifer A. Bailey<sup>1</sup>, Rick Kosterman<sup>1</sup>, Isaac C. Rhew<sup>2</sup>, Madeline Furlong<sup>1</sup>, Sabrina Oesterle<sup>3</sup> & Sean Esteban McCabe<sup>4</sup>

Social Development Research Group, School of Social Work, University of Washington, Seattle, WA, USA,<sup>1</sup> Department of Psychiatry and Behavioral Sciences, University of Washington, Seattle, WA, USA,<sup>2</sup> Southwest Interdisciplinary Research Center, School of Social Work, Arizona State University, Tempe, AZ, USA<sup>3</sup> and Center for the Study of Drugs, Alcohol, Smoking and Health, School of Nursing, Institute for Research on Women and Gender, and Center for Human Growth and Development, University of Michigan, Ann Arbor, MI, USA<sup>4</sup>

#### ABSTRACT

Background and Aims There is a public health concern that the use of e-cigarettes among non-smoking young adults could be associated with transition to combustible cigarette use. The current study is a quasi-experimental test of the relationship between e-cigarette use and subsequent combustible cigarette use among young adult non-smokers, accounting for a wide range of common risk factors. Design Logistic regression was used to predict combustible cigarette use on three or more occasions at age 23 years based on age 21 e-cigarette use. Inverse probability weighting (IPW) was used to account for confounding variables. Setting Data were drawn from the Community Youth Development Study (CYDS), a cohort study of youth recruited in 2003 in 24 rural communities in seven US. states Participants Youth in the CYDS study (n = 4407) were surveyed annually from ages 11 to 16, and at ages 18, 19, 21 and 23 years (in 2016). The sample was gender balanced (50% female) and ethnically diverse (20% Hispanic, 64% white, 3% black and 12% other race or ethnicity). The current study was limited to participants who had never used combustible cigarettes by age 21 (*n* = 1825). **Measurements** Age 21 use of e-cigarettes and age 23 use of combustible cigarettes (three or more occasions) were included in the regression analysis. Age 11-19 measures of 22 common predictors of both e-cigarette and combustible cigarette use (e.g. pro-cigarette attitudes, peer smoking, family monitoring) were used to create IPWs. Findings After applying IPW, e-cigarette use at age 21 was associated with a twofold increase in odds of combustible cigarette use on three or more occasions 2 years later (odds ratio = 2.16, confidence interval 1.23, 3.79). **Conclusions** Among previously never-smoking US young adults, e-cigarette use appears to be strongly associated with subsequent combustible cigarette smoking, over and above measured preexisting risk factors.

**Keywords** Addiction, combustible cigarettes, electronic cigarettes, propensity score analysis, risk factors for smoking, young adulthood.

Correspondence to: Marina Epstein, Social Development Research Group, School of Social Work, University of Washington, 9725 3rd Avenue NE, Ste. 401, Seattle, WA 98115, USA. E-mail: marinaep@uw.edu

Submitted 20 November 2019; initial review completed 18 February 2020; final version accepted 23 October 2020

# INTRODUCTION

While cigarette use rates in the United States have declined due to successful public health campaigns promoting awareness of harm and reducing pro-smoking norms [1,2], current use of electronic cigarettes (e-cigarettes) among US adolescents has increased from 3% in 2012 to 28% in 2019 [1,3,4]. Among young adults (aged 18–25 years), 8% reported current e-cigarette use in 2018 [5]. Despite containing fewer carcinogenic chemicals than combustible cigarettes [6,7], e-cigarette devices deliver nicotine—the highly addictive principal component in cigarettes that has been linked to chronic and persistent smoking [8,9]. The 2016 Surgeon General's Report on e-cigarettes among youth and young adults [10] suggested that e-cigarette use could independently lead to nicotine addiction and may encourage combustible cigarette use. This new avenue to combustible cigarettes among young adults is particularly concerning, because the risk for initiating smoking past the age of 18 has been low [9]. Further, young adults who did not experience the rapid rise of e-cigarette availability as adolescents and who had not started smoking cigarettes have been a low-risk group. However, if e-cigarette initiation in this age group poses a risk for transition to use of combustible cigarettes, increased intervention efforts may be required.

Although a number of studies have shown that non-smoking youth who engage in e-cigarette use are at an increased risk of reporting later cigarette use, recent reviews have stressed that (a) the number of longitudinal studies are still limited, and more are needed to adequately address this critical question; (b) little is known about the transition from e-cigarette to cigarette use among young adults in particular; and (c) most existing studies do not adequately control for common risk factors that drive both electronic and combustible cigarette use [11,12].

# PREVIOUS RESEARCH ON THE TRANSITION FROM ELECTRONIC TO COMBUSTIBLE CIGARETTES

Investigations into the transition from e-cigarette to combustible cigarette use among youth and young adults, including several reviews and meta-analyses, showed that e-cigarette use was associated with increased risk of initiating combustible cigarette smoking in the future, from 6 months to 2.5 years later [11-15]. We are aware of no study that found no longitudinal association between e-cigarette initiation and later combustible cigarette use among non-smokers, although the strength of the association varied. In their meta-analysis, Aladeokin & Haighton [11] estimated that adolescent e-cigarette users in the United Kingdom were six times more likely to initiate combustible cigarette use compared to non-smokers who did not use e-cigarettes. An earlier study by Soneji and colleagues [13] found that the risk of initiation of combustible use for US adolescents was almost four times higher for e-cigarette users versus non-users, although it is worth noting that each meta-analysis included fewer than 10 studies that met the researchers' criteria; many were excluded because they were cross-sectional or lacked adequate control variables. Studies of young adults are far fewer: Glasser and colleagues [12] note that of 26 studies included in their review, only three had young adult samples. The three studies showed that young adult non-smokers were two to three times as likely to smoke cigarettes after using e-cigarettes.

However, finding that e-cigarette use occurred before the use of combustible cigarettes is not enough to determine a causal relationship. Antecedent shared risk and

protective factors for e-cigarette and combustible cigarette use may explain the initiation of both e-cigarette and combustible cigarette use among adolescent and young adult non-smokers [12]. Previous studies have varied in the number and breadth of common risk factors included in the analyses, relatively few have included comprehensive arrays across multiple domains [16-19] and we are aware of no study that has included antecedent risk factors measured longitudinally. In their review, Glasser and colleagues [12] named three major domains of shared risk factors for youth and young adults: demographic (e.g. education, ethnicity), interpersonal (e.g. parents who smoke), and intrapersonal (e.g. sensation-seeking, other substance use). Glasser et al. note that only five of the 26 studies in the review controlled for at least one variable in each domain, and that without including controls in each of those areas, the question remains open as to whether or not those who transitioned from e-cigarette use to cigarette use would have started to smoke in the absence of e-cigarettes.

In addition, studies testing the transition from electronic to combustible cigarettes almost universally use multiple regression approaches (e.g. [16,20-22]). This is problematic, because including multiple covariates in a regression to obtain a partial effect may result in multicollinearity, and may also skew the true value of the effect. Quasi-experimental approaches, such as propensity score methods, are designed to account for multiple related predictors and have been widely used in the social sciences [23,24]. Previous applications of propensity score approaches to account for overlapping risk factors for electronic and combustible cigarettes are limited, and none have been conducted with young adults. For example, a recent cross-sectional study of 10th and 12th graders using propensity score analysis found that accounting for common risk factors significantly reduced (and in one case fully explained) the relationship between e-cigarette and combustible cigarette use [25]. The adjusted odds ratio (OR) using the propensity score method was also lower than the OR obtained using multiple regression analysis. A longitudinal study using the Population Assessment of Tobacco and Health (PATH) study found that non-smokers who used e-cigarettes were 3.21 times as likely to report later cigarette smoking than those who had not used e-cigarettes [26]. More studies are needed in this area, especially those with longitudinal samples and those focused on young adults.

#### Current study

The current study tested whether e-cigarette use at age 21 is associated with combustible cigarette smoking at age 23 among non-smokers, using propensity score approaches to account for multiple shared risk factors. We based the selection of covariates on Glasser *et al.*'s [12]

recommendations, as well as on theories of deviance [27,28] and social influence [29], and extant literature [17,30–32]. Antecedent factors were measured prospectively, between ages 11 and 21. We expected that young adult non-smokers who engaged in e-cigarette use would have higher levels of risk factors (e.g. smoking peers) than youth who did not use e-cigarettes, and that e-cigarette use would be associated with a greater risk of later combustible cigarette use, regardless of prior levels of risk.

## METHODS

#### Participants

The current study used data from the Community Youth Development Study (CYDS) [33], a communityrandomized trial of the Communities That Care prevention system in 24 small towns in seven states (Colorado, Illinois, Kansas, Maine, Oregon, Utah and Washington). Communities were matched in pairs based within state on population size, racial diversity, economic indicators and crime rates and randomly assigned to the control or intervention condition. Since 2003, the study has followed 4407 youth (2205 from experimental and 2002 from control communities), representative of all 5th-grade public school students at the time in the 24 study communities. Parents of 76% of eligible students consented to their child's participation. During the first wave of data collection, 16 students whose parents consented to participation did not assent. The sample was gender balanced (50% female) and ethnically diverse (20% Hispanic, 64% white, 3% black and 12% other race/ethnicity). Fewer than half of participants' parents (44%) had a college degree.

Participants have been surveyed annually from ages 11 to 16 (grades 5-10), and at ages 18 (grade 12), 19, 21, and 23 (in 2016). E-cigarette use was assessed at ages 21 and 23. The survey was completed by more than 90% of participants each year to age 21. At age 23, 88% (n = 3833) of the active sample (still-living participants) who had not requested to be dropped from the study) completed the survey; participants were dispersed throughout 48 US states. In grades 5-12, participants completed a paper-and-pencil questionnaire during a class period. After high school, the questionnaire was offered on-line or mailed. Participants received completion incentives of \$5-10 to grade 12 and \$25-45 at ages 19-23. The University of Washington Human Subjects Review Committee approved this protocol. Because the current study is focused on the association between e-cigarette use at age 21 and age 23 combustible cigarette use among nonsmokers, only those who had not reported combustible cigarette use to age 21 (n = 1825, 42% of the full sample) were included in the current study. Included participants were from both intervention and control group

communities (although see Sensitivity analysis section for subgroup analysis).

#### Measures

#### Inclusion criteria for non-smokers

Lifetime combustible cigarette use was reported at each wave starting at age 11. Participants were asked: 'Have you ever smoked cigarettes?'. Response options were 1 = 'never' 2, = 'once or twice', 3 = 'once in a while', 4 = 'regularly in the past' and 5 = 'regularly now'. Beginning with age 13, participants also reported whether they had ever used 100 cigarettes in their lifetime. Non-smokers were defined as those participants who never reported smoking cigarettes more than 'once or twice' and who never used 100 cigarettes in their lifetime at any wave to age 21. Sensitivity analyses tested a more stringent definition of 'non-smoker' that also excluded those who ever reported smoking cigarettes 'once or twice'.

#### Main analyses

At age 23, participants reported on how many occasions in the past year that they smoked cigarettes. Response options ranged from 0 = 0 occasions', 1 = 1-2 occasions' and 2 = '3-5 occasions' to 6 = '40 or more occasions'. Using on three or more occasions in the past year was coded as having used combustible cigarettes. At ages 21 and 23 participants were asked: 'On how many occasions (if any) have you used electronic cigarettes or e-cigarettes ('vapes'), such as Ruyan or NJOY, in the past 12 months?'. Similar to questions about cigarette use, response options were 0 = 0 occasions', 1 = 1-2 occasions', 2 = 3-5 occasions, and up to 6 = 40 or more occasions'. Because relatively few people reported frequent use of e-cigarettes, any use (one or more occasions and higher) at age 21 was coded as having used e-cigarettes (1). A sensitivity analysis used a classification parallel to combustible cigarette use where reporting 0 occasions or one to two occasions was coded as 0 (no use).

#### Shared risk factors

Shared stress factors included in the propensity score creation were measured from ages 11 to 18 and combined over time by averaging normally distributed predictors and summing categorical variables (see Table 1 for means and ranges). Supporting information, Table S1, lists all the items, their response options, and notes how scales were created.

#### Interpersonal risk factors

Interpersonal risk factors included poor family management, family conflict, parent smoking attitudes, sibling smoking, and peer smoking.

Table 1	Descriptives of	f propensity score	e covariates by e-cigarette use
---------	-----------------	--------------------	---------------------------------

Risk factors	Range	Mean (SD) Did not use e-cigarettes	Mean (SD) Used e-cigarettes	Р
Interpersonal risk factors				
Family management	1-4	1.51 (0.37)	1.60 (0.37)	0.000
Family conflict	1-4	2.00 (0.57)	2.07 (0.57)	0.064
Parent pro-cigarette attitudes	0–6	0.12 (0.40)	0.12 (0.37)	0.830
Sibling smokes	0-7	0.88 (1.50)	1.04 (1.56)	0.065
Peer smoking	0-7	0.99 (1.27)	1.35 (1.43)	0.000
Intrapersonal risk factors				
Perception of cigarettes as not harmful	0-7	0.63 (1.16)	0.58 (0.98)	0.519
Perception that cigarette use is ok	0-7	0.18 (0.50)	0.22 (0.55)	0.144
Never used a cigarette	0-1	0.51 (0.50)	0.39 (0.49)	0.000
Smokeless tobacco use	0-1	0.10 (0.30)	0.15 (0.36)	0.025
Alcohol use frequency	1-7	1.77 (1.14)	2.18 (1.29)	0.000
Marijuana use ever	0-1	0.20 (0.40)	0.36 (0.48)	0.000
Antisocial behavior	0-15	1.12 (2.06)	1.58 (2.42)	0.000
Rebelliousness	0-4	1.69 (0.55)	1.85 (0.56)	0.000
Depression	1-4	1.80 (0.57)	1.88 (0.56)	0.020
Demographic variables				
Gender $(1 = male)$	0-1	0.46 (0.50)	0.57 (0.49)	0.000
Black	0-1	0.03 (0.18)	0.04 (0.20)	0.583
Other	0-1	0.28 (0.45)	0.28 (0.45)	0.674
Hispanic	0-1	0.19 (0.39)	0.22 (0.41)	0.197
Experimental condition	0-1	0.58 (0.49)	0.55 (0.50)	0.538
Family financial hardship	0–6	1.55 (1.67)	1.55 (1.56)	0.901
Parent education	1-6	4.61 (1.22)	4.40 (1.18)	0.013
College attendance (age 21)	0-1	0.39 (0.49)	0.29 (0.46)	0.104
Marital status (age 21)	0-1	0.13 (0.34)	0.09 (0.29)	0.211

Community pairs were also included in the propensity score estimation to account for nesting within community. The largest community was omitted as a referent. White is the referent category for race. SD = standard deviation.

#### Intrapersonal risk factors

Intrapersonal risk factors included personal perception of cigarette harm and normative perception of cigarette use. Participants reported ever use of smokeless tobacco products, their average lifetime alcohol use frequency, ever use of marijuana during high school, anti-social behavior, rebelliousness, and depression.

#### Demographic variables

Demographic variables included gender, race (white, black, other), Hispanic ethnicity, experimental condition, parents' level of education (measured in adolescence), and a retrospective account of family financial hardship during middle and high school (measured at age 23). At age 21, participants reported on their college attendance and whether they were married.

#### Analysis

In the current study, the propensity score was the conditional probability of using e-cigarettes given a set of common risk factors that predict both e-cigarette and

cigarette use. In order to reduce potential bias in estimating the relationship between e-cigarette use and later use of combustible cigarettes, we chose inverse probability weighting (IPW) to account for non-random assignment. IPW is an extension of propensity score methods and has been commonly used in observational studies [23,34] to strengthen causal inference. It is preferable over other propensity score approaches, such as matching pairs of intervention and control groups (here users and non-users of e-cigarettes) on covariates, because matching often leads to exclusion of observations where no match is available, whereas with IPW all observations are generally used. Using IPW, weights are applied that are equal to the inverse of the propensity of one's observed exposure status (e-cigarette use or nonuse) according to covariates [24,34-36]. Applying weights to the study sample yields a 'pseudo-population' where the distribution of potential confounders is balanced across those who did and did not use e-cigarettes, thus reducing potential for biased effect estimates.

IPW analyses were estimated in Mplus version 8.3 [37]. Missing data on the outcome variables was handled using full information maximum likelihood in all analyses. When calculating IPWs, 95 cases were excluded due to missing data on the x (predictor) variables. Those with missing data on the x variables were as likely as those with complete data to use e-cigarettes at age 21 and cigarettes at age 23. Dummy-coded communities of origin (at the pair level) at age 11 were included in the IPW weights to account for clustering. IPW was performed in four steps. First, weights were calculated by regressing e-cigarette use on the risk factors and saving a score for propensity to use e-cigarettes. For those who used e-cigarettes, the calculated score is the propensity. For participants who had not used e-cigarettes, the propensity is equal to 1 minus the score [34]. The distribution of propensity scores was then compared between those who did and did not use e-cigarettes to check if there was an overlap in risk and protective factors between the two groups that would make IPW viable. The propensity scores among those who used e-cigarettes is expected to be higher than among those who did not, but the distributions need to overlap. To account for outlying values in the propensity, propensity scores were stabilized by including a numerator to the weight that was equivalent to the unconditional likelihood of one's exposure status (e-cigarette use or non-use) in the sample. That is, the final weight for those who used e-cigarettes was 1/propensity; for nonusers the final weight was 1/(1-propensity). Thus, the mean of the stabilized weights was approximately 1.

Secondly, to assess whether IPW achieved balance in covariates by exposure status, the relationship between the covariates and e-cigarette use was compared between those who did and did not use e-cigarettes, before and after applying IPWs. This was performed by regressing e-cigarette use on the full set of covariates using the MODEL = NONCOVARIANCES command in Mplus and examining standardized output. The NOCOVARIANCES command set the covariance of all predictors to zero, yielding an estimate of the effect of each predictor on the likelihood of e-cigarette use independently of the other covariates. Covariates were expected to differentiate e-cigarette users from non-users in the unweighted model, and be 'balanced' or not differentiate users from non-users once the weights are applied.

Thirdly, the association between e-cigarette use and later cigarette use was tested using the maximum likelihood estimator (logistic regression) in Mplus. IPWs were applied to the regression model to estimate ORs for cigarette use at age 23 based on e-cigarette use at age 21. With n = 1825, there is 80% power to detect effects as small as OR = 1.2. Lastly, the robustness of the model was tested through sensitivity analyses, where the effect of theory-driven addition or subtraction of covariates on the model was examined.

#### RESULTS

#### Propensity score calculation and covariate balance

Among the 1825 participants in the analytical sample, 12% reported using e-cigarettes (n = 226) at age 21. At age 23, 9% reported e-cigarette use only (n = 160), 5% (n = 90) reported combustible cigarette use (either alone or dual use with e-cigarettes), and the remaining 86% (n = 1579) reported no use of combustible or electronic cigarettes. Approximately half of e-cigarette users at age 21 (n = 89) reported using three or more times in the past year, 16 of whom reported combustible cigarette use. Distribution of the IPWs showed an overlap between the two groups, suggesting successful application of IPW (see Supporting information, Fig. S1). Table 2 shows covariate mean differences between those who did and did not use e-cigarettes at age 21. Table S2 in the Supporting information shows balance in the risk and protective factors before and after application of IPWs. Prior to the application (Supporting information, Table S2, left side), the two groups differed substantially on almost every factor. After the weighting (Supporting information, Table S2, right side) there were no significant differences on risk factors between users and nonusers of e-cigarettes, effectively balancing the sample.

# Association between e-cigarette use and later use of combustible cigarettes

Table 2 shows the ORs and confidence intervals (CIs) of the relationship between age 21 e-cigarette use and age 23 combustible cigarette use among non-smokers with and without IPW. In Model 1, using the full analytical sample, 4% of participants who did not use e-cigarettes at age 21 reported combustible cigarette use at age 23, compared to 11% of those who used e-cigarettes (OR = 3.13, CI = 1.93, 5.03). After applying IPW, using e-cigarettes at age 21 was associated with double the odds of using combustible cigarettes 2 years later (OR = 2.16, CI = 1.23, 3.79).

#### Sensitivity analyses

To test the robustness of the model, we conducted three sensitivity analyses. IPWs using the same set of risk and protective factors were recalculated in each of the sensitivity models. First, we accounted for any prior tobacco experience, even if very limited, by omitting participants who had ever used even a single cigarette in their lifetime or had reported non-combustible tobacco use (e.g. chewing tobacco; Table 2, Model 2, n = 932). Among those with no history of any tobacco use (Model 2), e-cigarette use was associated with nearly a threefold increase in combustible tobacco use (OR = 2.95, CI = 1.11, 7.85). Secondly,

Table 2 Prevalence of combustible us	e at age 23 by e-cigarette	use at age 21 before and af	ter adjusting for propensity
--------------------------------------	----------------------------	-----------------------------	------------------------------

	Prevalence of combustible cigarette use		OR (95% CI)	
	Subgroup n % did not use e-cigarettes	Subgroup n % used e-cigarettes	Before propensity weighting	After propensity weighting
Model 1: full analytical sample	n = 1604 4%	n = 227 11%	3.13 (1.93, 5.03)	2.16 (1.23, 3.79)
Model 2: sensitivity analysis, no prior tobacco use	<i>n</i> = 822 3%	<i>n</i> = 87 11%	4.12 (1.88, 9.04)	2.95 (1.11, 7.85)
Model 3: sensitivity analysis, control group only	<i>n</i> = 673 4%	<i>n</i> = 100 13%	3.20 (1.61, 6.37)	1.97 (0.86, 4.53)
Model 4: sensitivity analysis, 3+ use of e-cigarettes	<i>n</i> = 1726 4%	<i>n</i> = 105 15%	4.01 (2.25, 7.18)	2.24 (0.96, 5.25)

OR = odds ratios; CI = confidence interval.

because the CYDS study has found significant intervention effects on smoking behavior and on level differences in risk and protective factors [38], we re-examined Model 1 with participants from only the control communities (Table 2, Model 3, n = 813). Finally, we recoded the use of e-cigarettes to match the coding for combustible cigarettes (using three or more times) in order to test whether the threshold for e-cigarettes affected the results (Model 4, n = 1825). Results from Models 3 and 4 were similar to the results from the full-sample Model 1 (OR<sub>model3</sub> = 1.97, CI = 0.86, 4.53; OR<sub>model4</sub> = 2.24, CI = 0.96, 5.25), although they did not to reach significance at P < 0.05 level.

## DISCUSSION

The current study is a pseudo-experimental test of the relationship between e-cigarette use among young adult non-smokers and later use of combustible cigarettes. The results indicate that e-cigarette use among 21-year-olds without a history of previous smoking (measured prospectively) was associated with a twofold increase in risk of combustible cigarette use 2 years later, and that this relationship was not solely explained by measured pre-existing interpersonal, intrapersonal, or demographic factors. As e-cigarette use increases in popularity among adolescents and young adults, there is significant concern that the novelty of the devices, coupled with the variety of flavor options may lead non-smokers to use e-cigarettes, which may lead to nicotine addiction and combustible cigarette use.

One of the barriers to this type of analysis is that large longitudinal samples are required, as only a minority of youth use e-cigarettes, and an even smaller minority will later use combustible cigarettes. For example, in the current study of more than 4400 participants, only 25 non-smoking young adults reported combustible cigarette use at age 23 after using e-cigarettes at age 21. In fact, findings from large studies such as PATH and the National Youth Tobacco Survey with 12 000–25 000 participants showed cell sizes as small as 16–50 when examining the

transition from electronic to combustible cigarettes [39,40]. A related study limitation was that because analyses result in small cell sizes, we were not able to examine whether e-cigarette use was associated with regular use (more than three times in the past year) of combustible cigarettes. Smaller cell sizes were also likely to have contributed to two sensitivity tests failing to reach significance, despite a pattern of results that matched the full model. A further limitation was that we were not able to include some of the other relevant risk factors, including parental smoking or intention to smoke, nor e-cigarette-specific risk factors, such as exposure to advertising, attraction to flavoring, and the perception that e-cigarette use is safe [41-44]. Finally, measures of e-cigarette use prior to age 21 or between ages 21 and 23 were not available in the present study. It is possible that some youth tried e-cigarettes before age 21 and already transitioned to combustible use, a pattern we were unable to capture. However, as those participants would not have been included in the current analysis, it probably makes our analysis a conservative estimate. That is, it is likely that the association between e-cigarette use and later combustible use would be higher than reported here if those youth who initiated e-cigarette use earlier had been included. The sample is representative of the communities that were included in the intervention, with high recruitment and retention rates. However, the majority of youth lived in small rural communities; future studies need to replicate this with different and non-US samples, and also investigate the association between regular e-cigarette use and continued use of combustible cigarettes over time. Two recent studies suggest that youth who initiate nicotine use (in any form) over time increasingly report use of combustible cigarettes over e-cigarettes [45,46]. Finally, the e-cigarette marketplace has evolved significantly since the data were collected, now including higher potency e-liquid and greater marketing of products, such as Juul. The relationship between electronic and combustible cigarettes needs to be replicated with more current samples.

Study strengths include a large, diverse sample, excellent retention, longitudinal data, a broad range of risk and protective factors included in the IPW analyses, and a prospectively measured history of cigarette and other tobacco use going back to age 10. A focus on non-smoking young adults, a selective and relatively low-risk sample, showcases that e-cigarette initiation even among this group may be associated with combustible cigarette initiation. In fact, even reporting ever use was associated with a twofold increase in the likelihood of combustible cigarette use. This suggests that interventions aimed at this age group are needed to prevent transition to combustible cigarette smoking, which carries worse health risks than e-cigarette use [47].

The current findings challenge the notion forwarded by e-cigarette manufacturers that youth can continue to use e-cigarettes in lieu of combustible cigarettes and benefit from the probably lower health risks of e-cigarettes [48]. Inasmuch as e-cigarette use is associated with combustible cigarette use, a portion of e-cigarette users are likely to face all the risks posed by combustible cigarettes. As antecedent risk factors do not fully explain the relationship between e-cigarette and combustible cigarette use, subsequent smoking may then be directly attributable to the power of e-cigarettes to not only attract young users, but to lead youth to combustible cigarette use. Thus, stronger regulations on flavor, internet sales, age limits, and advertising are needed to reduce the appeal of e-cigarettes. For example, as youth and young adults continue to name flavor as one of the most common reasons for use [43], eliminating flavored products should make a sizeable impact on the appeal of these products. In addition, health providers may seek to screen youth and young adults for e-cigarette use in order to identify an opportunity to prevent initiation of combustible cigarettes. Finally, preventive interventions may also be useful to disrupt the transition from electronic to combustible cigarettes [49].

#### Declaration of interests

None.

### Acknowledgements

This work was supported by research grants from the National Cancer Institute under awards R37CA225690 and R01CA203809, and the National Institute on Drug Abuse of the National Institutes of Health under awards R01DA015183 and R01DA044522, with co-funding from the National Institute of Child Health and Human Development, the National Institute of Mental Health, the Center for Substance Abuse Prevention and the National Institute on Alcohol Abuse and Alcoholism. The content is solely the responsibility of the authors and does not necessarily represent the official views of the funding agencies.

S.S.McC. is a paid consultant for award R37CA225690. ClinicalTrials.gov identifier: NCT01088542

#### Author Contributions

Marina Epstein: Conceptualization; formal analysis; funding acquisition; investigation; methodology; project administration. Jennifer Bailey: Conceptualization. Rick Kosterman: Methodology, Conceptualization. Isaac Rhew: Methodology. Madeline Furlong: Project administration; resources. Sabrina Osterle: Conceptualization; project administration. Sean Esteban McCabe: Conceptualization.

#### References

- Singh T., Marynak K., Arrazola R. A., Cox S., Rolle I. V., King B. A. Vital signs: exposure to electronic cigarette advertising among middle school and high school students—United States, 2014. *Morb Mortal Wkly Rep* 2016; 64: 1403–8.
- Clarke T. C., Ward B. W., Freeman G., Schiller J. S. Early Release of Selected Estimates Based on Data From the January–March 2015 National Health Interview Survey Atlanta, GA: National Center for Health Statistics. Available at: http://www.cdc. gov/nchs/nhis.htm (accessed 17 April 2020).
- Cullen K. A., Gentzke A., Sawdey M. D. E-cigarette use among youth in the United States, 2019. *JAMA* 2019; 322: 2095–103.
- Miech R., Johnston L., O'Malley P. M., Bachman J. G., Patrick M. E. Adolescent vaping and nicotine use in 2017–2018—US national estimates. *N Engl J Med* 2019; 380: 192–3.
- 5. Substance Abuse and Mental Health Services Administration (SAMHSA) Key Substance Use and Mental Health Indicators in the United States: Results From the 2018 National Survey on Drug Use and Health. Rockville, MD: Center for Behavioral Health Statistics and Quality, Substance Abuse and Mental Health Services Administration; 2019.
- Jensen R. P., Luo W., Pankow J. F., Strongin R. M., Peyton D. H. Hidden formaldehyde in e-cigarette aerosols. N Engl J Med 2015; 372: 392–4.
- Allen J. G., Flanigan S. S., LeBlanc M., Vallarino J., MacNaughton P., Stewart J. H., *et al.* Flavoring chemicals in e-cigarettes: diacetyl, 2, 3-pentanedione, and acetoin in a sample of 51 products, including fruit-, candy-, and cocktailflavored e-cigarettes. *Environ Health Perspect* 2016; 124: 733–9.
- Benowitz N. L. Emerging nicotine delivery products. Implications for public health. Ann Am Thor Soc 2014; 11: 231–5.
- 9. US Department of Health and Human Services *The Health Consequences of Smoking—50 Years of Progress: A report of the Surgeon General.* Atlanta, GA: US Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health; 2014.
- 10. US Department of Health and Human Services. E-Cigarette Use Among Youth and Young Adults. A Report of the Surgeon General. Atlanta, GA: US Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health; 2016.
- 11. Aladeokin A., Haighton K. Is adolescent e-cigarette use associated with smoking in the United Kingdom? A systematic

review with meta-analysis. *Tob Prev Cessat* 2019; https://doi. org/10.18332/tpc/108553

- Glasser A., Abudayyeh H., Cantrell J., Niaura R. Patterns of e-cigarette use among youth and young adults: review of the impact of e-cigarettes on cigarette smoking. *Nicotine Tob Res* 2019; 21: 1320–30.
- 13. Soneji S., Barrington-Trimis J. L., Wills T. A., Leventhal A. M., Unger J. B., Gibson L. A., *et al.* Association between initial use of e-cigarettes and subsequent cigarette smoking among adolescents and young adults: a systematic review and meta-analysis. *JAMA Pediatr* 2017; **171**: 788–97.
- Grana R. A., Benowitz N., Glantz S. A. E-cigarettes: a scientific review. *Contemp Rev Cardiovasc Med* 2014; 129: 1972–86.
- Siddiqui F., Mishu M., Marshall A.-M., Siddiqi K. E-cigarette use and subsequent smoking in adolescents and young adults: a perspective. *Expert Rev Respir Med* 2019; 13: 403–5.
- Watkins S. L., Glantz S. A., Chaffee B. W. Association of noncigarette tobacco product use with future cigarette smoking among youth in the population assessment of tobacco and health (PATH) study, 2013–2015. *JAMA Pediatr* 2018; 172: 181–7.
- Leventhal A. M., Strong D. R., Kirkpatrick M. G., Unger J. B., Sussman S., Riggs N. R., *et al.* Association of electronic cigarette use with initiation of combustible tobacco product smoking in early adolescence. *JAMA* 2015; **314**: 700–7.
- Chaffee B. W., Watkins S. L., Glantz S. A. Electronic cigarette use and progression from experimentation to established smoking. *Pediatrics* 2018; 141: e20173594.
- Conner M., Grogan S., Simms-Ellis R., Scholtens K., Sykes-Muskett B., Cowap L., *et al.* Patterns and predictors of ecigarette, cigarette and dual use uptake in UK adolescents: evidence from a 24-month prospective study. *Addiction* 2019; **114**: 2048–55.
- Wills T. A., Knight R., Sargent J. D., Gibbons F. X., Pagano I., Williams R. J. Longitudinal study of e-cigarette use and onset of cigarette smoking among high school students in Hawaii. *Tob Control* 2016; 26: 34–9.
- 21. Kinnunen J., Ollila H., Minkkinen J., Lindfors P., Rimpelä A. A longitudinal study of predictors for adolescent electronic cigarette experimentation and comparison with conventional smoking. *Int J Environ Res Public Health* 2018; 15: E305.
- 22. Best C., Haseen F., Currie D., Ozakinci G., MacKintosh A. M., Stead M., *et al.* Relationship between trying an electronic cigarette and subsequent cigarette experimentation in Scottish adolescents: a cohort study. *Tob Control* 2018; 27: 373–8.
- Austin P. C. An introduction to propensity score methods for reducing the effects of confounding in observational studies. *Multivar Behav Res* 2011; 46: 399–424.
- Rosenbaum P., Rubin D. B. The central role of the propensity score in observational studies for causal effects. *Biometrika* 1983; 70: 41–55.
- 25. Kim S., Selya A. S. The relationship between electronic cigarette use and conventional cigarette smoking is largely attributable to shared risk factors. *Nicotine Tob Res* 2019; https://doi.org/10.1093/ntr/ntz157
- Spindle T. R., Hiler M. M., Cooke M. E., Eissenberg T., Kendler K. S., Dick D. M. Electronic cigarette use and uptake of cigarette smoking: a longitudinal examination of U.S college students. *Addict Behav* 2017; 67: 66–72.
- Hirschi T. Causes of Delinquency. Berkeley, CA: University of California Press; 1969.
- Jessor R. Risk behavior in adolescence: a psychosocial framework for understanding and action. *J Adolesc Health* 1991; 12: 597–605.

- Catalano R. F., Hawkins J. D. The social development model: a theory of antisocial behavior. In: Hawkins J. D., editor. *Delinquency and Crime: Current Theories*. New York, NY: Cambridge University Press; 1996, pp. 149–97.
- Hawkins J. D., Catalano R. F., Miller J. Y. Risk and protective factors for alcohol and other drug problems in adolescence and early adulthood: implications for substance abuse prevention. *Psychol Bull* 1992; 112: 64–105.
- Stone A. L., Becker L. G., Huber A. M., Catalano R. F. Review of risk and protective factors of substance use and problem use in emerging adulthood. *Addict Behav* 2012; 37: 747–75.
- 32. Wills T. A., Knight R., Williams R. J., Pagano I., Sargent J. D. Risk factors for exclusive e-cigarette use and dual e-cigarette use and tobacco use in adolescents. *Pediatrics* 2015; 135: e43–e51.
- 33. Hawkins J. D., Catalano R. F., Arthur M. W., Egan E., Brown E. C., Abbott R. D., *et al.* Testing communities that care: the rationale, design and behavioral baseline equivalence of the community youth development study. *Prev Sci* 2008; 9: 178–90.
- Leite W. L., Stapleton L. M., Bettini E. F. Propensity score analysis of complex survey data with structural equation modeling: a tutorial with Mplus. *Struct Equat Model* 2019; 26: 448–69.
- Shadish W. R., Steiner P. M. A primer on propensity score analysis. Newborn Infant Nurs Rev 2010; 10: 19–26.
- Benedetto U., Head S. J., Angelini G. D., Blackstone E. H. Statistical primer: propensity score matching and its alternatives. *Eur J Cardiothorac Surg* 2018; 53: 1112–7.
- Muthén L. K., Muthén B. O. Mplus User's Guide, 8th edn. Muthén & Muthén: Los Angeles, CA; 1998-2017.
- Oesterle S., Kuklinski M. R., Hawkins J. D., Skinner M. L., Guttmannova K., Rhew I. C. Long-term effects of the communities that care trial on substance use, antisocial behavior, and violence through age 21 years. *Am J Public Health* 2018; 108: 659–65.
- 39. Stanton C. A., Bansal-Travers M., Johnson A. L., Sharma E., Katz L., Ambrose B. K., *et al.* Longitudinal e-cigarette and cigarette use among US youth in the PATH study (2013–2015). *J Natl Cancer Inst* 2019; 111: 1088–96.
- 40. Shahab L., Beard E., Brown J. Association of initial e-cigarette and other tobacco product use with subsequent cigarette smoking in adolescents: a cross-sectional, matched control study. *Tob Control* 2020; doi: tobaccocontrol-2019-055283.
- 41. Cooper M., Loukas A., Case K. R., Marti C. N., Perry C. L. A longitudinal study of risk perceptions and e-cigarette initiation among college students: interactions with smoking status. *Drug Alcohol Depend* 2018; 186: 257–63.
- 42. Hampson S. E., Andrews J. A., Severson H. H., Barckley M. Prospective predictors of novel tobacco and nicotine product use in emerging adulthood. *J Adolesc Health* 2015; 57: 186–91.
- Bold K. W., Kong G., Cavallo D. A., Camenga D. R., Krishnan-Sarin S. Reasons for trying e-cigarettes and risk of continued use. *Pediatrics* 2016; 138: e20160895.
- 44. Carey F. R., Rogers S. M., Cohn E. A., Harrell M. B., Wilkinson A. V., Perry C. L. Understanding susceptibility to e-cigarettes: a comprehensive model of risk factors that influence the transition from non-susceptible to susceptible among e-cigarette naïve adolescents. *Addict Behav* 2019; **91**: 68–74.
- 45. Niaura R., Rich I., Johnson A. L., Villanti A. C., Romberg A. R., Hair E. C., *et al.* Young adult tobacco and e-cigarette use

transitions: examining stability using multistate modeling. *Nicotine Tob Res* 2019; **22**: 647–54.

- Vogel E. A., Prochaska J. J., Ramo D. E., Andres J., Rubinstein M. L. Adolescents' e-cigarette use: increases in frequency, dependence, and nicotine exposure over 12 months. *J Adolesc Health* 2019; 64: 770–5.
- 47. National Academies of Sciences Engineering and Medicine *Public health consequences of e-cigarettes.* Washington, DC: The National Academies Press; 2018.
- Grana R. A., Ling P. M. 'Smoking revolution': a content analysis of electronic cigarette retail websites. *Am J Prev Med* 2014; 46: 395–403.
- 49. Conner M., Grogan S., Simms-Ellis R., Flett K., Sykes-Muskett B., Cowap L., *et al.* Evidence that an intervention weakens the relationship between adolescent electronic cigarette use and tobacco smoking: a 24-month prospective study. *Tob Control* 2020; 29: 425–31.

#### **Supporting Information**

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Table S1 Variable Description and Response Options.

Figure S1 Overlap Between Propensity Scores By E-cigarette Use Status.

**Table S2** Association of Propensity Score Covariates withE-cigarette Use Before and After Propensity Weighting.