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Effectiveness of e-cigarettes as aids for smoking cessation: evidence from the PATH Study cohort, 2017–2019

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ABSTRACT

Objective To assess the effectiveness of e-cigarettes in smoking cessation in the USA from 2017 to 2019, given the 2017 increase in high nicotine e-cigarette sales.

Methods In 2017, the PATH Cohort Study included data on 3578 previous year smokers with a recent quit attempt and 1323 recent former smokers. Respondents reported e-cigarettes or other products used to quit cigarettes and many covariates associated with e-cigarette use. Study outcomes were 12+ months of cigarette abstinence and tobacco abstinence in 2019. We report weighted unadjusted estimates and use propensity score matched analyses with 1500 bootstrap samples to estimate adjusted risk differences (aRD).

Results In 2017, 12.6% (95% CI 11.3% to 13.9%) of recent quit attempters used e-cigarettes to help with their quit attempt, a decline from previous years. Cigarette abstinence for e-cigarette users (9.9%, 95% CI 6.6% to 13.2%) was lower than for no product use (18.6%, 95% CI 16.0% to 21.2%), and the aRD for e-cigarettes versus pharmaceutical aids was -7.3% (95% CI -14.4 to -0.4) and for e-cigarettes versus any other method was -7.7% (95% CI -12.2 to -3.2). Only 2.2% (95% CI 0.0% to 4.4%) of recent former smokers switched to a high nicotine e-cigarette. Subjects who switched to e-cigarettes appeared to have a higher relapse rate than those who did not switch to e-cigarettes or other tobacco, although the difference was not statistically significant.

Conclusions Sales increases in high nicotine e-cigarettes in 2017 did not translate to more smokers using these e-cigarettes to quit smoking. On average, using e-cigarettes for cessation in 2017 did not improve successful quitting or prevent relapse.

INTRODUCTION

Electronic cigarettes (e-cigarettes), which were first sold in the USA in 2007, had become a popular cessation aid for US smokers by 2014–2016.^{1,2} From 2013 to 2017 US sales of e-cigarettes almost doubled,³ which was associated with rapid uptake among adolescents.⁴ If there was a similar increase in e-cigarette usage attributed to smoking cessation (either as a cessation aid or an alternative nicotine source) and effectiveness was demonstrated, we would expect that successful cigarette cessation would increase in the population.

Randomised clinical trials (RCTs) are the optimal design to assess the efficacy of e-cigarettes as

smoking cessation aids. To date, a number of RCTs have addressed the role of e-cigarettes as an aid to quitting cigarettes, and a recent systematic review concluded, with moderate certainty, that e-cigarettes improve cessation by an estimated four additional successful quitters per 100 quit attempters when compared with nicotine replacement therapy (NRT).⁵ However, RCTs are usually conducted under optimal conditions, which means that they may not translate to the effectiveness of the product in community settings.⁶ Analyses of the Population Assessment of Tobacco and Health (PATH) Study⁷ have not found that e-cigarettes improve cessation.^{8,9}

To date, no trials have been reported that test the hypothesis that cigarette smokers are able to switch to e-cigarettes and maintain their nicotine habit without relapsing to cigarette smoking. A recent PATH Study analysis found that those who switched to e-cigarettes between 2014 and 2016 were more likely to relapse to cigarette smoking by 2017 than those who were free from all tobacco including e-cigarettes between 2014 and 2016.¹⁰ However, the e-cigarette market has changed dramatically since 2016. JUUL Labs introduced nicotine salt technology in 2015 and high nicotine concentration pods (ie, 5% nicotine by weight).¹¹ On the back of an innovative marketing campaign, JUUL became the most popular US e-cigarette in 2017^{12,13} when over 50% of all e-cigarette products sold had high (>4%) nicotine concentrations.³ Increasing the nicotine concentration in e-cigarette liquid increases nicotine exposure for users,^{14–16} and high nicotine JUUL users have blood nicotine concentrations similar to cigarette smokers, which some argue may be a prerequisite for successfully switching to e-cigarettes.¹⁷ Thus, in 2017, recent former smokers had the opportunity to switch to e-cigarettes with a much higher nicotine concentration than was possible for those in earlier years, which could reduce relapse to cigarette smoking.

The PATH Study is a nationally representative longitudinal study that can address questions on the effectiveness of e-cigarettes in reducing cigarette smoking. However, for longitudinal studies to address whether a product may cause an outcome such as smoking cessation requires careful analysis. The critical point is that groups must be as comparable as possible across variables that might be related to the study outcome.¹⁸ In RCTs, randomisation of product usage usually achieves this effect.

In observational studies it is necessary to control for the variables associated with using e-cigarettes, particularly those that are also associated with longer term cigarette cessation (eg, motivation to quit). Some published analyses of PATH Study data^{19–21} have not required that the control group has a recent quit attempt. Given that e-cigarettes are seen as a popular way to quit cigarettes,¹ such an analytical decision means that the control group will be very different from the e-cigarette user group as it will include many people who are not trying to quit, thus significantly biasing the conclusions in favour of an e-cigarette effect.²²

In this paper, our starting population are PATH Study respondents who were established smokers in 2016. To address the hypothesis that e-cigarettes are an effective cigarette cessation aid, we limit our consideration to those who reported a quit attempt in the year prior to the 2017 (W4) survey and compare how cessation aids used were associated with 12+ months of cigarette/tobacco abstinence at the 2019 (W5) survey (see study flowchart in online supplemental file 1). To address whether switching to e-cigarettes improves maintenance of cigarette abstinence, we focus on those who were recent former smokers in 2017 (W4) and compare relapse to cigarette smoking in 2019 (W5) among those who switched to e-cigarettes versus those who did not use any tobacco or e-cigarette product.

METHODS

Data sources

The PATH Study is a US nationally representative cohort study. A screener survey of a stratified address-based sample of households oversampled tobacco users, young adults aged 18–24 and African Americans for the adult cohort.⁷ The first four survey waves (W1–4) were at annual intervals starting in 2013–14 (W1), and W5 (2019) was conducted ~2 years after W4 (2017). The initial household screener had a 54% response rate and the adult survey response rates were 74.0%, 83.2%, 78.4% and 73.5% for W1–4, respectively. Among initial screened households, 27 757 adults were interviewed at W4 and an additional new replenishment sample of 6065 adults were added to the cohort to adjust for attrition and reset the cohort sample size, thus reducing the magnitude of weighting required to provide population estimates.²³ The weighted response rate for W4 replenishment household screener was 52.8% and the response rate of the adult survey was 68.0% at W4 and 88.0% at W5. The Westat Institutional Review Board approved the study and all respondents provided written informed consent. Data were obtained from available restricted use files.²³

Study sample

The W4 (2017) total sample included both a continuing cohort and an added refreshment sample (see online supplemental file 1). For longitudinal analyses requiring earlier data we are limited to the continuing cohort subset (those with W1–W3 data). For each PATH survey, lifetime 100+ cigarette smokers were asked if they “currently smoke every day, some days, or not at all”.²³ Thus, in this paper the continuing cohort are drawn from those who were current daily or some-day smokers at W3 (2016). For the added refreshment sample at W4 (2017), we assessed previous year smoking from: “Around this time 12 months ago, did you smoke cigarettes every day, some days or not at all?”

To investigate whether e-cigarettes are an effective cigarette cessation aid, we identified recent quit attempters from the W4 question: “In the past 12 months, have you tried to quit cigarettes completely?” A positive response was made by 3578 previous year established smokers. To investigate whether switching to

e-cigarettes helps prevent relapse to cigarettes, we identified recent former smokers at W4 from a “not at all” response to the current cigarette smoking question among previous year established smokers (n=1323).

Use of e-cigarette or other products

To identify products used to help quit attempts, W4 quit attempters were asked: “Thinking back to the last time you tried to quit cigarettes in the past 12 months”, followed by three separate types of questions: “did you use an e-cigarette/ (other non-cigarette tobacco product) to help you quit?”; “did you use a nicotine patch, gum, inhaler, nasal spray, lozenge or pill?”; and “did you use Chantix, varenicline, Wellbutrin, Zyban or bupropion?”.

To identify recent former smokers who had switched to an alternative nicotine source, we used the current use question (responses of every day, some days or not at all) for each of the following products: e-cigarettes, cigars, cigarillo, filtered cigars, pipes, hookah, snus and smokeless products. E-cigarette users were asked: “What concentration of nicotine do you usually use?” with eight response categories ranging from 0% to 4+%, as well as don't know.

Study outcome

At W5 (2019) current cigarette and other tobacco use was assessed from responses to the current use question for each product. To assess duration of abstinence from cigarettes, recent former smokers were asked: “In the past 12 months, have you smoked a cigarette/(used product), even one or two puffs/times?” Cigarette abstinence includes those who were using e-cigarettes or other tobacco products. Tobacco abstinence requires abstinence from all tobacco and e-cigarettes. This question was asked for all tobacco products as well as e-cigarettes. Duration of abstinence came from the question: “About how long has it been since you last smoked a cigarette/puffed from an electronic nicotine product?”

Study covariates

PATH Study investigators identified and measured potential confounders for e-cigarette and cessation analyses and demonstrated that these were mismatched between e-cigarette users and control participants.⁹ Most of these variables were best measured when participants were still smokers at W3 (2016) and are only available for the continuing cohort. They include sociodemographic variables (age, sex, education, race, ethnicity, income), cigarette smoking status (daily or non-daily), tobacco dependence index,²⁴ time since last quit attempt, cigarette consumption, e-cigarette use status (any use or no use), interest in quitting cigarettes, self-efficacy about quitting, smoke-free home, exposure to smoking, perceived harm of cigarettes and e-cigarettes, cigarette pack-years, age began regular smoking, insurance status and health-related covariates (external/internal mental health symptoms, existence of smoking-related disease). Questions for each covariate and univariate distributions by product used in the quit attempt are shown in online supplemental file 2,3.

To test whether switching to e-cigarettes prevented relapse, we used the same set of covariates with the following exceptions: (1) we added duration of cigarette abstinence at W4 (2017); (2) we changed the source of the smoke-free home measure from W3 (2016) to W4 (2017). Details of these covariates with univariate distributions by product used are shown in online supplemental file 4,5.

Statistical analyses

All analyses were conducted in R (version 3.6.1). For unadjusted analyses using total samples (continuing + refreshment), estimates were weighted using W4 single wave weights²³ and variance estimates for confidence intervals were calculated using replicate weights constructed using a balanced repeated replication procedure with Fay adjustment ($\rho=0.3$).⁷ Sample characteristics were explored using weighted proportions with 95% confidence limits. The adjusted analyses were restricted to the continuing cohort only and used W1–W5 longitudinal survey weights.²³

For the adjusted propensity score matching analysis we created 1500 bootstrap samples for each hypothesis test. Within each bootstrap sample we used simple imputation (R package ‘Mice’) for missing data from all the covariates, and we identified the optimal set of covariates prior to estimating the propensity score as follows. To select variables we used the LASSO with the Akaike Information Criterion (AIC).^{25 26} The optimal set of covariates was the one that returned the smallest AIC. Then, for each exposure separately, we calculated a propensity score for each participant by estimating the unweighted probability of membership in the e-cigarette use group using logistic regression adjusting for the optimised set of covariates. Using the estimated propensity score, we matched up to two controls for each case (nearest neighbour matching using R package ‘Matchit’)²⁷ within the a priori calliper distance of 0.1. Cases that did not have a match meeting these criteria were omitted from the sample (<10% for each matching). For each matched bootstrap sample we used logistic regression with survey weights (R package ‘survey’) to estimate the average risk difference between the two matched groups for each outcome. The model included an indicator of the matched pair (or triple) and an indicator of use of e-cigarettes or not. The risk difference was estimated by the bootstrap mean estimate and the confidence intervals were calculated using

the 95% bootstrap quantiles. To assess e-cigarettes as a cigarette cessation aid we compared 12+ months of cigarette abstinence between (1) any e-cigarette for quit attempt versus anyone who did not use an e-cigarette; and (2) any e-cigarette versus NRT or pharmaceutical aid only for quit attempt. We also compared those who used e-cigarettes only versus NRT or pharmaceutical aid only in a sensitivity analysis. To assess if e-cigarettes prevent relapse to cigarettes, we estimated the risk difference in rates of relapse to cigarette smoking between any e-cigarette versus no e-cigarette at W4. Current use of NRT and pharmaceutical aids was only collected in relation to the last quit attempt.

RESULTS

Characteristics of tobacco use among recent quit attempters

There were no differences between the continuing cohort and the combined continuing cohort and refreshment sample (ie, total W4 sample) in any of the following key measures (table 1). In 2017 (W4), 32.8% (95% CI 31.8% to 33.9%) of previous year established smokers reported a recent quit attempt in the year prior to W4 and 12.4% (95% CI 11.6% to 13.3%) were recent former smokers at W4. Among recent quit attempters, 12.6% (95% CI 11.3% to 13.9%) reported using e-cigarettes to help in their last quit attempt (8.7% e-cigarettes only, 3.2% e-cigarettes and NRT/pharmaceutical aid, 0.5% e-cigarettes and other tobacco products, 0.2% used 3+ products); 2.5% (95% CI 1.9% to 3.1%) used non-e-cigarette tobacco products (2.1% non-e-cigarette tobacco products only); 20.6% (95% CI 18.9% to 22.3%) used NRT or a pharmaceutical aid only and 64.3% (95% CI 62.4% to 66.1%) did not use any product.

Among recent former cigarette smokers in 2017 (W4), 15.3% had switched to e-cigarettes (daily: 9.1% (95% CI 7.1% to 11.0%); non-daily: 6.2% (95% CI 4.7% to 7.7%); 10.4% e-cigarettes only) and 15.9% (95% CI 13.6% to 18.2%) reported

Table 1 Characteristics of PATH Study Wave 4 tobacco use

	W4 continuing cohort*			W4 continuing cohort+refreshment sample†		
	n	Wtd%	95% CI (%)	n	Wtd%	95% CI (%)
W4 population	24 905			30 970		
Smoking prevalence 12 months before W4	8564	19.6	(19.0 to 20.2)	10 614	19.7	(19.2 to 20.3)
Daily cigarette smokers	6286	74.1	(72.9 to 75.3)	7705	73.3	(72.1 to 74.4)
Non-daily cigarette smokers	2278	25.9	(24.7 to 27.1)	2909	26.7	(25.6 to 27.9)
Recent quit attempters (in year prior to W4)	2870	32.8	(31.6 to 33.9)	3578	32.8	(31.8 to 33.9)
Product used in quit attempt						
Any e-cigarettes	363	11.6	(10.2 to 13.0)	488	12.6	(11.3 to 13.9)
Non e-cigarette tobacco product‡	67	2.3	(1.7 to 2.9)	91	2.5	(1.9 to 3.1)
No tobacco product but any NRT§ or pharmaceutical aid¶	566	20.7	(18.9 to 22.5)	700	20.6	(18.9 to 22.3)
No product	1874	65.4	(63.4 to 67.4)	2299	64.3	(62.4 to 66.1)
Recent former smokers (RFS) at W4	1035	11.9	(10.9 to 12.8)	1323	12.4	(11.6 to 13.3)
Product used by RFS at W4						
Daily e-cigarettes	110	9.3	(7.1 to 11.5)	136	9.1	(7.1 to 11.0)
Non-daily e-cigarettes	61	5.3	(3.7 to 6.9)	94	6.2	(4.7 to 7.7)
Non-e-cigarette tobacco product‡	188	15.6	(13.0 to 18.1)	240	15.9	(13.6 to 18.2)
Tobacco-free	676	69.8	(66.5 to 73.1)	853	68.8	(65.9 to 71.8)

*The continuing cohort were interviewed on each of the previous PATH waves (W1, W2, W3).

†The W4 continuing cohort + refreshment sample includes all people interviewed for the PATH Study in 2017 (W4). The purpose of the refreshment sample (those first interviewed at W4) was to reset the size of the cohort and reduce the weighting needed to make estimates that were nationally representative of the US population.

‡Other products used by recent former smokers were those from the cigar family (traditional cigars, cigarillos and filtered cigars) and the smokeless family (snus pouches, loose snus, moist snuff, dip, spit and chewing tobacco).

§NRT (nicotine replacement therapy) includes nicotine patch, gum, inhaler, nasal spray, lozenge or pill.

¶Pharmaceutical aid includes Chantix, varenicline, Wellbutrin, Zyban or bupropion.

W4, Wave 4; Wtd, weighted US population estimate (W4 single-wave weights were used).

Table 2 Characteristics of recent quit attempters reported at PATH Wave 4 by use of non-cigarette tobacco products on last quit attempt prior to Wave 4

Variable	No tobacco product use (n=2999)		Any e-cigarette use (n=488)		Other non-cigarette tobacco use* (n=91)	
	Wtd%	95% CI	Wtd%	95% CI	Wtd%	95% CI
Age						
18–34	81.0	79.1 to 83.0	15.4	13.3 to 17.5	3.5	2.2 to 4.9
35–50	84.0	81.3 to 86.7	13.7	11.3 to 16.2	2.3	1.4 to 3.2
50+	89.7	87.8 to 91.5	8.8	7.1 to 10.4	1.6	0.7 to 2.4
Sex						
Male	84.6	82.7 to 86.5	12.0	10.3 to 13.8	3.4	2.5 to 4.3
Female	85.2	83.3 to 87.0	13.3	11.6 to 14.9	1.6	0.8 to 2.3
Education						
<High school	86.9	84.8 to 89.0	10.6	8.7 to 12.5	2.5	1.6 to 3.5
High school graduate	86.6	84.4 to 88.7	9.8	7.8 to 11.7	3.6	2.2 to 5.1
Some college+	82.9	81.0 to 84.9	15.3	13.4 to 17.1	1.8	1.0 to 2.6
Race/ethnicity						
Non-Hispanic white	82.5	80.5 to 84.4	15.3	13.4 to 17.2	2.2	1.6 to 2.9
Others	89.0	87.4 to 90.6	8.0	6.5 to 9.4	3.0	1.8 to 4.2
Income (US\$)						
<35 000	86.5	84.7 to 88.3	10.6	9.0 to 12.1	2.9	2.0 to 3.8
≥35 000	82.7	80.3 to 85.1	15.6	13.2 to 17.9	1.7	1.0 to 2.4
Cigarette smoking status at W3						
Daily	83.4	81.7 to 85.1	13.9	12.3 to 15.5	2.7	1.9 to 3.4
Non-daily	88.2	86.3 to 90.1	9.7	7.7 to 11.7	2.1	1.1 to 3.0
E-cigarette use at W3						
Marked	66.0	61.5 to 70.5	30.8	26.4 to 35.1	3.2	1.4 to 5.1
Not marked	89.1	87.8 to 90.3	8.6	7.5 to 9.7	2.3	1.7 to 3.0
Time since last quit attempt						
<90 days	83.4	81.0 to 85.9	14.3	11.9 to 16.8	2.3	1.2 to 3.3
≥90 days	82.4	80.1 to 84.6	14.9	12.6 to 17.1	2.8	1.7 to 3.9

*Other non-cigarette tobacco: any use of cigar, cigarillo, filtered cigar, pipe, hookah, snus or smokeless tobacco.

PATH, Population Assessment of Tobacco and Health; W3, Wave 3; W4, Wave 4; Wtd, weighted US population estimate (W4 single-wave weights were used).

use of another tobacco product (11.5% cigar family, 2.9% smokeless, 3.6% other or multiple products) and 68.8% (95% CI 65.9% to 71.8%) reported not using any tobacco or e-cigarette. Among those who had switched to e-cigarettes, only 2.2% (95% CI 0.0% to 4.4%) reported using e-cigarettes with concentration >4% (see online supplemental file 6) and 1.9% (95% CI 0.4% to 3.4%) reported using JUUL e-cigarettes. This supplement also presents the 2019 (W5) data for recent former smokers who switched to e-cigarettes as this proportion increased to 22.0% (95% CI 19.6% to 24.5%) compared with the 15.3% observed at W4, with 19.9% of them using high nicotine content e-cigarettes.

Characteristics of recent quit attempters who used e-cigarettes

The use of e-cigarettes to aid a quit attempt was higher in 18–50-year-old subjects than in those aged 50+ years, higher in those who had attended college than in those who did not complete high school, higher in non-Hispanic white people than in other race ethnicities, higher in those with incomes >\$35 000 than in those with lower incomes, higher in 2016 (W3) daily smokers than in non-daily smokers and higher in 2016 (W3) e-cigarette users (table 2). Similar use patterns were observed for recent former smokers (see online supplemental file 3, 5), although the lower sample size of recent former smokers resulted in some wide confidence intervals.

Successful quitting at W5 among quit attempters in year prior to W4

Unadjusted successful quitting in the total samples (continuing + refreshment)

Among those who used e-cigarettes in their last quit attempt prior to W4 (2017), 9.9% (95% CI 6.6% to 13.2%) were abstinent from cigarettes for 12+ months but not all tobacco at W5, which was lower than those who used NRT or pharmaceutical aid only (15.2%, 95% CI 12.3% to 18.1%) or those who did not use any product in the quit attempt (18.6%, 95% CI 16.0% to 21.2%), with similar patterns between the total sample and the continuing cohort (table 3). Considering abstinence for 12+ months from all tobacco including e-cigarettes, the proportion who used e-cigarettes for the quit attempt (3.5%, 95% CI 1.5% to 5.5%) was considerably lower than those who used NRT or pharmaceutical aid only (12.5%, 95% CI 9.6% to 15.4%) or who did not use any product when attempting to quit (13.9%, 95% CI 11.4% to 16.5%). For both abstinence from cigarettes and abstinence from all tobacco (including e-cigarettes), our data suggest that those who used e-cigarettes to help them quit had a similar outcome to those who used another non-cigarette combustible (eg, cigar) or smokeless tobacco product (eg, snus) (table 3).

Among recent former smokers who had switched to daily use of e-cigarettes in 2017 (W4), 43.2% (95% CI 32.5% to 54.0%) had successfully quit cigarette smoking by 2019 (W5), which

Table 3 Abstinence for 12+ months at Wave 5 among smokers who tried to quit prior to Wave 4 according to products used to assist during last quit attempt prior to Wave 4

Product used to assist during last quit attempt prior to W4	W4 sample type	Sample size	Abstinent* all tobacco (including e-cigarettes) at W5		Abstinent cigarettes, not all tobacco at W5†	
			Wtd%	95% CI	Wtd%	95% CI
E-cigarette	Continuing cohort‡	319	2.5	(0.5 to 4.5)	8.5	(5.1 to 11.8)
	Continuing cohort + refreshment sample§	401	3.5	(1.5 to 5.5)	9.9	(6.6 to 13.2)
Other tobacco product¶ but no e-cigarettes	Continuing cohort	58	2.8	(0 to 6.0)	13.5	(1.5 to 25.4)
	Continuing cohort + refreshment sample	77	2.5	(0.5 to 4.5)	14.1	(4.4 to 23.9)
No tobacco product or e-cigarettes but any NRT** or pharmaceutical aid††	Continuing cohort	489	13.2	(9.6 to 16.8)	16.2	(12.7 to 19.6)
	Continuing cohort + refreshment sample	582	12.5	(9.6 to 15.4)	15.2	(12.3 to 18.1)
No product	Continuing cohort	1613	14.7	(11.8 to 17.6)	19.2	(16.3 to 22.1)
	Continuing cohort + refreshment sample	1923	13.9	(11.4 to 16.5)	18.6	(16.0 to 21.2)
Total	Continuing cohort	2479	12.6	(10.6 to 14.7)	17.1	(15.0 to 19.2)
	Continuing cohort + refreshment sample	2983	12.0	(10.2 to 13.8)	16.7	(14.9 to 18.5)

*Abstinence = 12+ months, reported at Wave 5.

†Those abstinent from cigarettes could be using e-cigarettes or other tobacco products.

‡The continuing cohort were W4 respondents who had been surveyed at previous PATH Study waves (W1–W3).

§The W4 continuing cohort + refreshment sample includes all people interviewed for the PATH Study in 2017 (W4). The purpose of the refreshment sample (those first interviewed at W4) was to reset the size of the cohort and reduce the weighting needed to make estimates that were nationally representative of the US population.

¶Other products used by recent former smokers were those from the cigar family (traditional cigars, cigarillos and filtered cigars) and the smokeless family (snus pouches, loose snus, moist snuff, dip, spit and chewing tobacco).

**NRT (nicotine replacement therapy) includes nicotine patch, gum, inhaler, nasal spray, lozenge or pill.

††Pharmaceutical aid includes Chantix, varenicline, Wellbutrin, Zyban or bupropion.

W4, Wave 4; W5, Wave 5; Wtd, weighted US population estimate (W4 single-wave weights).

was similar to those who used e-cigarettes on a non-daily basis or to those who switched to another tobacco product, whether daily or non-daily (table 4). All estimates of successful quitting for those who switched to another nicotine source were below the lower confidence bound for those who reported no tobacco use in 2017 (W4) (52.9%, 95% CI 47.8% to 58.0%), although confidence intervals overlapped. Among those who had relapsed between 2017 (W4) and 2019 (W5), 15–20% had made another quit attempt (re-quit) and were abstinent at the time of the 2019 (W5) survey, although there were no differences across categories in the duration of these re-quit attempts.

Adjusted successful quitting in the continuing cohort

Propensity score matching achieved comparable study groups for variables associated with e-cigarette use at W4 (2017) (see online supplemental file 7-9). However, the perception that e-cigarettes were less harmful than cigarettes fell from 23.8% (95% CI 23.1% to 24.5%) in 2016 (W3) to 16.4% (95% CI 15.9% to 17.0%) in 2019 (W5) (see online supplemental file 10). Among quit attempters, those who used an e-cigarette as an aid had a lower 12+ month cigarette abstinence rate than those who did not (adjusted risk difference (aRD) -7.7 , 95% CI -12.2 to -3.2). Similarly, using an e-cigarette as an aid resulted in a lower 12+ month cigarette abstinence rate than using NRT or a pharmaceutical aid (aRD -7.3 , 95% CI -14.4 to -0.4) (figure 1A). When the outcome was 12+ months abstinence from cigarettes, e-cigarettes or any other tobacco product, these results were essentially the same with the aRD showing that e-cigarette use had between 7.4% and 6.4% lower abstinence than either not using e-cigarettes or using a pharmaceutical aid

(figure 1B). The sensitivity analysis estimating the aRD between e-cigarette only users and NRT or pharmaceutical aid only users produced similar results.

Propensity score matching achieved highly comparable groups among recent former smokers who had switched to e-cigarettes compared with those who had not (online supplemental file 7). The e-cigarette group appeared to have a higher relapse rate by W5 (2019) than those who did not use any tobacco or e-cigarette product (aRD 9.4%, 95% CI -5.0% to 22.8%); however, this did not reach statistical significance.

DISCUSSION

In this analysis of the most recent PATH Study data, smokers who reported using e-cigarettes to help them in their most recent cigarette quit attempt were less rather than more likely than other quit attempters to achieve either successful cigarette cessation or to become tobacco and e-cigarette free. Rather than e-cigarettes adding four additional successful cigarette quitters per 100 quit attempters compared with pharmaceutical aid users as concluded by a systematic review of RCT data,⁵ in this study e-cigarette use was associated with seven fewer successful quitters per 100 quit attempters. Furthermore, switching to e-cigarettes did not reduce the risk of relapse to cigarette smoking compared with other recent former smokers. Instead, nearly 60% of recent former smokers who were daily e-cigarette users had relapsed to cigarette smoking by 2019 (W5).

Between 2013 and 2018 there was a rapid increase in both the number of e-cigarette products available in the USA (now >800) and in the total unit sales, with over 40% sales growth between 2016 and 2017 alone.³ This rapid growth has been attributed to

Table 4 Unadjusted cigarette smoking status at Wave 5 among recent former cigarette smokers* by use of non-cigarette tobacco products assessed at Wave 4

Exposure as RFS assessed in 2017 (W4)			Cigarette smoking status in 2019 (W5)							
			Successfully quit		Relapsed					
Sample type	Sample size	12+ months, no puff		Significant re-quit† (3–12 months)		Re-quit (0–3 months)		Current smoker		
		Wtd%	95% CI	Wtd%	95% CI	Wtd%	95% CI	Wtd%	95% CI	
Daily e-cigarette use	Continuing cohort‡	96	45.3	34.1 to 56.5	14.9	8.4 to 21.3	2.9	0.0 to 6.1	36.9	24.0 to 49.9
	Total W4 population§	115	43.2	32.5 to 54.0	17.4	11.0 to 23.7	3.0	0.1 to 5.9	36.4	24.9 to 47.9
Non-daily e-cigarette use	Continuing cohort	52	29.3	14.7 to 43.9	15.3	4.9 to 25.8	12.4	4.9 to 25.8	43.0	26.4 to 59.6
	Total W4 population	74	34.6	21.2 to 48.1	14.1	4.8 to 23.4	14.2	6.6 to 21.7	37.1	22.4 to 51.7
Daily use of other tobacco products¶	Continuing cohort	65	38.4	23.8 to 52.9	9.2	0.7 to 17.7	9.6	0.0 to 20.4	42.9	27.1 to 58.7
	Total W4 population	78	43.6	30.5 to 56.6	7.7	0.6 to 14.8	11.5	1.2 to 21.7	37.3	23.4 to 51.2
Non-daily use of other tobacco products	Continuing cohort	99	42.7	31.8 to 53.7	18.1	9.2 to 26.9	5.9	0 to 12.0	33.3	22.5 to 44.2
	Total W4 population	121	44.7	34.2 to 55.2	15.9	8.5 to 23.2	7.9	0.9 to 14.9	31.5	22.1 to 40.9
Any cigar use**	Continuing cohort	156	44.0	34.9 to 53.1	13.3	6.7 to 19.9	7.5	1.7 to 13.3	35.2	25.8 to 44.7
	Total W4 population	194	44.1	36.0 to 52.1	13.6	7.7 to 19.6	8.5	3.2 to 13.8	33.8	25.6 to 42.1
Any combusted tobacco product use††	Continuing cohort	178	40.9	32.2 to 49.5	13.8	7.7 to 19.9	8.5	2.4 to 14.6	36.7	27.4 to 46.1
	Total W4 population	224	42.6	34.1 to 51.2	13.9	8.5 to 19.2	9.2	3.9 to 14.6	34.3	25.6 to 43.0
No tobacco use	Continuing cohort	576	52.8	47.5 to 58.0	9.8	7.3 to 12.4	4.3	2.0 to 6.6	33.1	28.1 to 38.1
	Total W4 population	701	52.9	47.8 to 58.0	10.7	8.1 to 13.4	5.2	2.8 to 7.6	31.2	26.8 to 35.7

Other tobacco product use: any use of other e-products, cigar, cigarillo, filtered cigar, pipe, hookah, snus or smokeless tobacco.

*Recent former cigarette smoker: those who were not smoking cigarettes at Wave 4 but who were established smokers 1 year earlier.

†Re-quit is a relapse to smoking since the previous survey followed by an additional quit attempt (we classify 3+ months off as a significant re-quit attempt).

‡The continuing cohort were W4 respondents who had been surveyed at previous PATH Study waves (W1–W3).

§The total W4 population is the continuing cohort + refreshment sample and includes all people interviewed for the PATH Study in 2017 (W4). The purpose of the refreshment sample (those first interviewed at W4) was to reset the size of the cohort and reduce the weighting needed to make estimates that were nationally representative of the US population.

¶Other tobacco use includes all other tobacco products including the combusted tobacco products and smokeless products, but not e-cigarettes.

**Any cigar use includes traditional cigars, cigarillo and filtered cigars.

††Any combusted tobacco product use: any use of cigar, cigarillo, filtered cigar, pipe or hookah.

RFS, recent former smokers; Wtd, weighted US population estimate;.

the introduction and effective marketing of high nicotine e-cigarettes, initially by JUUL Labs.²⁸ The high nicotine JUUL e-cigarette has been noted as the closest match to cigarettes in both nicotine delivery and user satisfaction,²⁹ which should make it one of the best candidates as a product to which smokers could switch in order to maintain their nicotine habit.³⁰ Thus, it was surprising that, just as sales for JUUL were surging in the marketplace, the use of e-cigarettes as a cessation aid fell from 17.4% of recent quit attempters in PATH W3⁸ to 12.4% at PATH W4. However, by 2019 this situation had changed, at least among recent former smokers, with 22% switching to e-cigarettes and ~4% using high nicotine concentration e-cigarettes. Our analysis suggests that the 2017 JUUL marketing campaigns were not effective in encouraging smokers to use JUUL products to help with quit attempts, unlike their effectiveness in encouraging young people to initiate nicotine use with their products.^{4 31 32} However, when we looked ahead to 2019, recent

former smokers had started using high nicotine e-cigarettes. The effectiveness of high nicotine e-cigarettes at preventing relapse will require another follow-up PATH survey.

This study has both advantages and limitations. The PATH Study is a large cohort of a representative sample of the US population with a rigorous methodology, including biological samples to validate self-reported cigarette smoking.⁷ In previous reports, biomarker concentrations indicate that self-reporting is valid.³³ This study included a large group of potential confounders that were measured prior to the target quit attempt and propensity score matching was used to achieve highly comparable groups. Each PATH survey collects detailed current use of a comprehensive set of tobacco products and detailed duration of abstinence of recently used products, allowing a comparison of the effectiveness of a wide range of potential products to help smokers quit. However, this study is observational and the exposure variable was not under experimental control. While our analytical

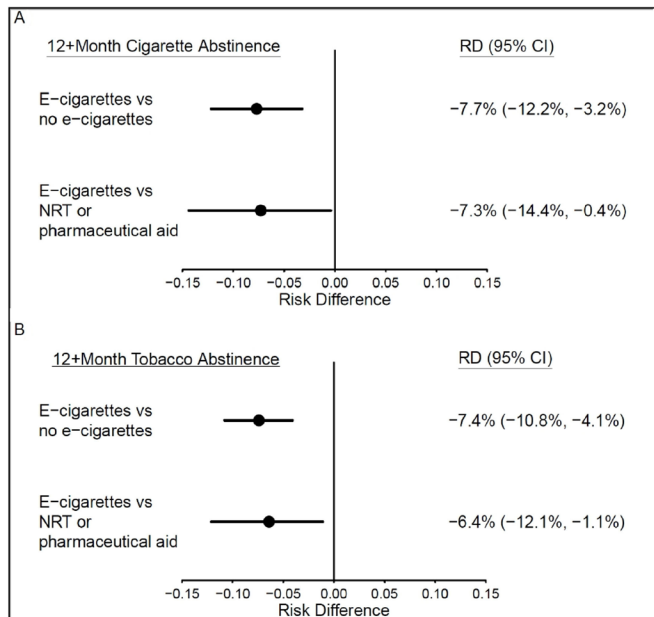


Figure 1 The adjusted risk difference (RD) in the rate of 12+ months of cigarette/tobacco abstinence for quit attempters by comparing the use of e-cigarettes versus no product use and the use of e-cigarettes versus use of nicotine replacement therapy (NRT) or pharmaceutical aid only during the last quit attempt in the year prior to Wave 4. (A) 12+ months of cigarette abstinence; (B) 12+ months of tobacco abstinence. Analyses using propensity score matching followed by logistic regression adjustment. Bootstrap samples were created to make statistical inference (details given in the section on Statistical Analyses). Covariates used for propensity score matching include: age, sex, education, race, ethnicity, income, cigarette smoking status at W3, time since last quit attempt, tobacco dependence index, cigarette consumption at W3, duration of previous quit attempt reported at W4, interest in quitting cigarettes, self-efficacy about quitting, smoke-free home, exposure to smoking, perceived harm of cigarettes and e-cigarettes, cigarette pack-years, age began regular smoking, insurance status, external mental health symptoms, internal mental health symptoms and existence of smoking-related disease. Missing data were imputed using simple imputation for each bootstrap sample. Cigarette abstinence does not include abstinence from e-cigarettes or other tobacco products. Tobacco abstinence includes no use of e-cigarette, cigar, cigarillo, filtered cigar, pipe, hookah, snus and smokeless tobacco.

design adjusted for potential confounding variables, other variables that were unmeasured confounders limit causal inference.

CONCLUSION

In 2017, a time of rapid growth in e-cigarette sales in the USA and increasing nicotine content in e-cigarette liquids, no such growth was seen in the use of e-cigarettes for cessation. In this study, smokers trying to quit or interested in switching to another nicotine delivery system were not early adopters of the high nicotine e-cigarettes such as JUUL, which have been reported as the closest products to resembling the experience of cigarette smoking. This analysis did not show a cessation benefit from using e-cigarettes either to help a cessation attempt or as a substitute for cigarette smoking. However, there is evidence that cigarette smokers were starting to use high nicotine e-cigarettes by 2019 and further follow-up in PATH is needed to see whether these changes result in future cessation benefit.

What this paper adds

What is already known on this subject?

- ▶ Randomised clinical trials indicate e-cigarettes have efficacy in helping smokers quit
- ▶ US cohort studies have not demonstrated effectiveness in the real world
- ▶ Starting in 2017, JUUL high nicotine e-cigarettes became the most popular e-cigarette brand and overall e-cigarette sales increased markedly

What important gaps in knowledge exist on this topic?

- ▶ The influence of the increased nicotine content of e-cigarettes on US smokers' ability to quit cigarette smoking is not known

What this study adds

- ▶ Despite a large increase in e-cigarette sales, the proportion who used e-cigarettes to help quit cigarettes declined and in 2017 only 2.2% of recent former smokers were using high nicotine e-cigarettes
- ▶ Those who used e-cigarettes to aid their cigarette quit attempt in the year prior to the 2017 survey were less likely to have successfully quit by 2019 compared with those who used a pharmaceutical aid or no product at all
- ▶ E-cigarette use did not prevent recent former smokers from relapsing to cigarettes
- ▶ However, the usage of high nicotine e-cigarettes for cessation increased in 2019, suggesting that this question needs to be addressed again in the 2021 PATH survey

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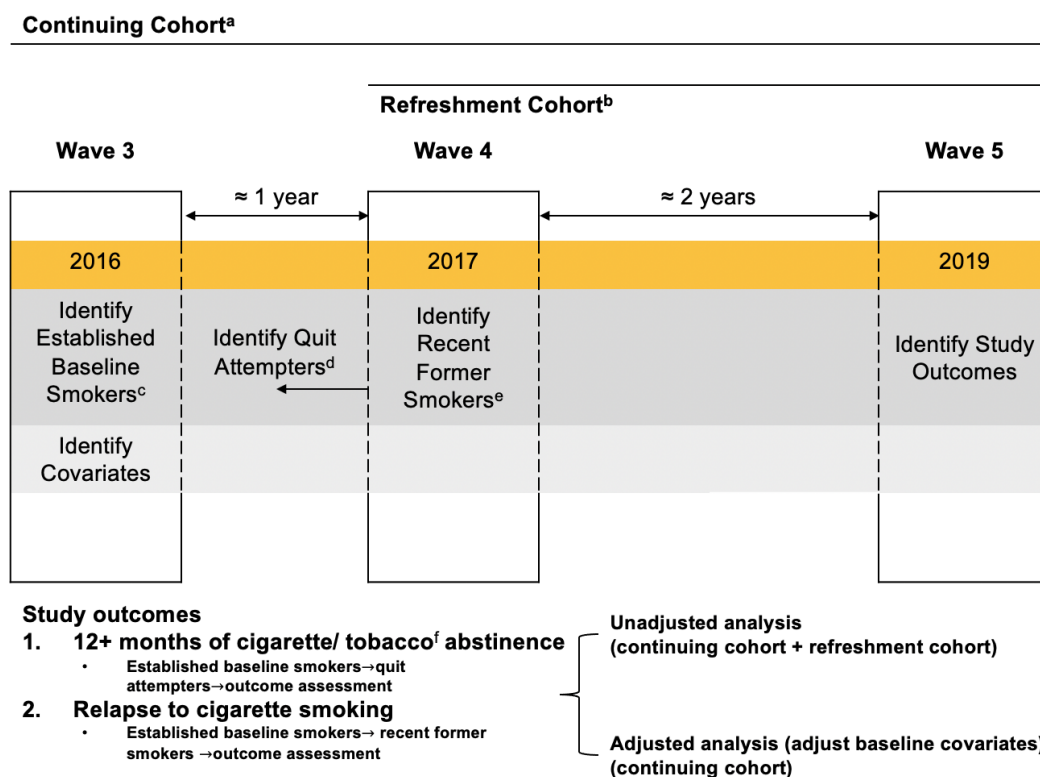
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Supplements for Chen et al. Effectiveness of e-cigarettes as aids for smoking cessation: evidence from the PATH Study, 2017-19

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Supplement 1. PATH Smoking Cessation Study (2017-2019) Flowchart



Abbreviations: PATH, Population Assessment of Tobacco and Health.

^a Continuing Cohort: those who were interviewed at each of the three waves.

^b Refreshment Cohort: who were first interviewed at Wave 4.

^c Established Baseline Smokers: those who smoked cigarettes at Wave 3.

^d Quit attempters: those who made at least 1 quit attempt in the year prior to Wave 4.

^e Recent Former Smokers: those who smoked cigarettes at Wave 3 but didn't smoke cigarettes at Wave 4.

^f Tobacco: any of e-cigarettes, cigar, cigarillo, filtered cigar, pipe, hookah, snus or smokeless tobacco.

Supplement 2. Measurement Detail for Pre-identified Study Covariates for Adjusted Analysis of Use of E-cigarettes on 12+ Months Cigarette/Tobacco Abstinence among Quit Attempters (in PATH Study [with variable names])

Socio-demographics: Use standard derived variables for age, sex, education, race, ethnicity, and income (R03R_A_AGE, R03R_A_SEX, R01R_A_EDUC, R04R_A_EDUC4, R03R_A_RACE, R03R_A_HISP, R03_AM0030; Note the variable of education comes from PATH Wave 4 database since it was not asked in Wave 3. If R04R_A_EDUC4 is missing but R01R_A_EDUC is not, we replaced the value of R04R_A_EDUC4 by R01R_A_EDUC.

Cigarette smoking status at W3: Smoked cigarettes daily or non-daily at W3 (R03_AC1003).

Time since last quit attempt: This was calculated as the date of W4 survey completed minus the end date of the most recent quit attempt reported in W4 (R04R_A_INTERVIEW_MMYR, R04R_A_INTERVIEW_WK, R04_AN0135).

Tobacco dependence index: (R03_AN0025, R03_AN0030, R03_AN0065, R03_AN0035, R03_AN0045, R03_AN0085, R03_AN0090, R03_AN0060, R03_AN0095, R03_AN0100, R03_AN0055, R03_AN0050, R03_AN0070, R03_AN0075, R03_AN0080). Variables are combined to derive the variable tobacco dependence index by calculating the mean of the non-missing scores. Tobacco dependence items take the form of a series of statements on emotional and physical responses to tobacco products (e.g. "I frequently crave {product}", "I usually want to {use product} right after I wake up", "I [would] feel alone without my {product}"). Respondents are asked to rate their level of agreement with each statement on a 5-point scale, where 1="Not true of me at all" and 5="Extremely true of me". Respondents can also answer "don't know" or refuse to answer the question; these are treated as missing responses. Responses are rescaled to a 3-point scale, where 1 (not at all) = 0, 2 or 3 = 50 and 4 or 5 = 100, summed and divided by the number of non-missing values.

Cigarette consumption at W3: Average number of cigarettes now smoked each day (R03_AC1021UN, R03_AC1021NN). Responses could be reported as cigarettes or packs. For respondents with missingness in those variables, we replaced their cigarette consumption by multiplying average number of cigarettes smoked per day among non-current 30-day smokers (R03_AC1023UN, R03_AC1023NN) with the number of days smoked in the past 30 days (R03_AC1022) and divided by 30 days.

E-cigarettes use at W3: Derived with variables R03_AV1003EC.

Interest in quitting cigarettes: On a scale of 1-10 where 1=Not at all interested and 10=Extremely interested (R03_AN0230).

Self-efficacy about quitting: "If you did try to quit {product} altogether in the next 6 months, how likely do you think you would be to succeed?" on a 4-point scale from 1=Not at all likely and 4=Very likely (R03_AN0245).

Smoke-free home: Variables (R03_AR1045) were used to identify the variable smoke-free home when participants became recent former cigarette smokers. Statement that best describes rules about smoking a combustible tobacco product inside home. It's a 3-point scale from 1 (not allowed anywhere or anytime at all) to 3 (allowed anywhere or anytime at all).

Exposure to smokers: "In the past 7 days, number of hours that you were in close contact with others when they were smoking." (R03_AX0068).

Perceived harmfulness of cigarettes: Respondents were asked "How harmful do you think cigarettes are to health?" and could reply on a 5-point scale from 1 (not at all harmful) to 5 (extremely harmful) (R03_AC9050).

Relative perceived harmfulness of e-cigarettes: Respondents were asked "Is using e-cigarettes less harmful, about the same, or more harmful than smoking cigarettes?" and could reply on a 3-point scale, where 1=Less harmful, 2=About the same and 3=More harmful (R03_AE1099).

Cigarette pack-years: Calculated by multiplying the number of packs smoked per day by the number of years the respondent smoked regularly, missing values in the number of packs smoked per day were completed by cigarette consumptions calculated above.

Age began regular smoking: (R01_AC1007, R02_AC1007_NB and R03_AC1007_NB). If it's still missing, using (R01_AC1020, R02_AC1020_NB and R03_AC1020_NB) to replace it.

Insurance status: (R03_AM0026_01 to R03_AM0026_08) Respondents who reported currently being covered by at least one type of health insurance, including insurance purchased directly or through an employer or union, Medicare, Medicaid, VA, TRICARE or other military health care and Indian Health Insurance, were scored as having insurance coverage. Missing data on all of these variables were coded to "did not have insurance".

External mental health symptoms: Respondents were asked the last time they had experienced any of 7 externalizing (e.g., had a hard time paying attention or listening to instructions at school, work or home, bullied or started physical fights). The number of reports of experiencing such symptoms in the past month or the past 2-12 months was summed and coded into a 3-level severity indicator, with those reporting 0 or 1 symptom scored as Low, 2-3 symptoms scored as Moderate and 4 or more scored as High.

Internal mental health symptoms: Respondents were asked the last time they experienced any of 4 internalizing disorder symptoms: feeling very trapped, lonely, sad, blue, depressed, or hopeless about the future, feeling very anxious, nervous, tense, scared, panicked, or like something bad was going to happen, had sleep problems. The number of reports of experiencing such symptoms in the past month or the past 2-12 months was summed and coded into a 3-level severity indicator, with those reporting 0 or 1 symptom scored as Low, 2-3 symptoms scored as Moderate and 4 or more scored as High.

Existence of smoking-related disease: Respondents were asked if they had ever been told by a doctor or health professional that they had any of the listed diseases.

Group A: Heart Disease: High blood pressure (R01_AX0111_01, R02_AX0111_NB_01 and R03_AX0111_NB_01), High cholesterol (R01_AX0111_02, R02_AX0111_NB_02 and R03_AX0111_NB_02) Congestive heart failure (R01_AX0111_03, R02_AX0111_NB_03 and R03_AX0111_NB_03); a stroke (R01_AX0111_04, R02_AX0111_NB_04 and R03_AX0111_NB_04); A heart attack (R01_AX0111_05, R02_AX0111_NB_05 and R03_AX0111_NB_05); Some other heart condition (R01_AX0111_06, R02_AX0111_NB_06 and R03_AX0111_NB_06)

Group B: Respiratory Disease: COPD (R01_AX0119_01, R02_AX0119_NB_01 and R03_AX0119_NB_01); chronic bronchitis (R01_AX0119_02, R02_AX0119_NB_02 and R03_AX0119_NB_02); emphysema (R01_AX0119_03, R02_AX0119_NB_03 and R03_AX0119_NB_03); asthma (R01_AX0119_04, R02_AX0119_NB_04 and R03_AX0119_NB_04); some other lung or respiratory condition (R01_AX0119_05, R02_AX0119_NB_05 and R03_AX0119_NB_05)

Group C: Cancer: (R01_AX0144, R02_AX0144_NB and R03_AX0144_NB)

Supplement 3. Full Sample Characteristics of Adjusted Analysis of Use of E-cigarettes on 12+ Months Cigarette/ Tobacco Abstinence among Quit Attempters^a in PATH Study, According to Use of Non-cigarette Tobacco Products in Last Quit Attempt prior to Wave 4

Wtd % is the population in row category (for example, among those aged 18-34, 83.0% didn't use tobacco at the exposure assessment, 14.0% used e-cigarette and 3.0% used other non-cigarette tobacco product etc.).

Variable	Category	Non-cigarette Tobacco Product Use by Recent Former Smokers					
		No tobacco use (n=2054)		Any e-cigarette use(n=311)		Other non-cigarette tobacco use ^c (n=54)	
		Wtd %	95% CL	Wtd %	95% CL	Wtd %	95% CL
Age	18-34	83.0	80.2, 85.7	14.0	11.3, 16.8	3.0	1.6, 4.4
	35-50	84.1	81.0, 87.2	13.4	10.6, 16.2	2.5	1.3, 3.6
	50+	90.0	87.7, 92.3	8.2	6.1, 10.4	1.8	0.8, 2.8
Sex	Male	85.1	82.7, 87.4	11.6	9.3, 13.9	3.3	2.2, 4.4
	Female	86.2	83.8, 88.5	12.3	10.2, 14.3	1.6	0.5, 2.7
Education	Less than high school	87.2	84.5, 89.8	9.9	7.6, 12.3	2.9	1.7, 4.1
	High school graduate	87.3	84.5, 90.2	9.4	6.8, 12.1	3.2	1.3, 5.1
	Some college or higher	83.9	81.4, 86.4	14.3	12.0, 16.6	1.8	0.8, 2.8
Race	White	84.0	81.9, 86.1	13.8	11.8, 15.7	2.3	1.5, 3.0
	Others	89.5	87.2, 91.8	7.4	5.3, 9.4	3.2	1.5, 4.9
Ethnicity	Hispanic	92.2	89.5, 94.9	5.5	3.0, 8.1	2.2	0.3, 4.1
	Non-Hispanic	84.3	82.4, 86.2	13.2	11.3, 15.1	2.5	1.8, 3.2
Income (US\$)	< 35000	85.7	83.7, 87.8	11.0	9.2, 12.7	3.3	2.2, 4.4
	>= 35000	85.1	82.2, 88.0	13.8	11.0, 16.5	1.2	0.4, 1.9
Cigarette smoking status at W3	Daily	84.6	82.6, 86.5	12.7	10.8, 14.6	2.7	1.7, 3.7
	Non-daily	87.9	85.3, 90.5	10.3	7.9, 12.7	1.8	0.9, 2.7
Time since last quit attempt (months)	<=6	84.2	81.8, 86.7	13.9	11.5, 16.2	1.9	1.1, 2.7
	>6	82.7	79.6, 85.7	13.7	10.5, 16.9	3.6	1.5, 5.8
Tobacco dependence index ^b	0-33.3	89.5	86.1, 92.8	9.1	6.1, 12.1	1.4	0.0, 2.8

	33.4-66.7	86.5	84.0, 89.1	11.0	8.5, 13.4	2.5	1.3, 3.7
	66.8-100	82.3	79.0, 85.5	14.7	11.7, 17.8	3.0	1.7, 4.3
Cigarette consumption at W3 (pack)	< 1	87.0	85.3, 88.7	10.9	9.2, 12.6	2.1	1.4, 2.8
	>= 1	80.4	76.6, 84.3	15.8	12.2, 19.3	3.8	1.8, 5.8
E-cigarettes use at W3	Marked	67.2	61.0, 73.3	29.6	23.9, 35.4	3.2	0.7, 5.6
	Not marked	89.3	87.8, 90.9	8.4	7.1, 9.7	2.3	1.5, 3.1
Interest in quitting cigarettes	1-7	87.5	85.0, 89.9	10.5	8.3, 12.8	2.0	1.0, 3.0
	8-9	83.2	79.2, 87.2	14.0	10.7, 17.4	2.7	0.6, 4.8
	10	85.7	83.2, 88.3	11.8	9.4, 14.1	2.5	1.4, 3.6
Self-efficacy about quitting (in the next 6 months)	Not at all likely	91.6	81.2, 100.0	3.6	0.0, 11.0	4.8	0.0, 11.8
	A little likely	84.5	78.3, 90.7	12.6	7.2, 17.9	2.9	0.1, 5.8
	Somewhat likely	86.5	82.7, 90.2	11.5	8.0, 15.1	2.0	0.5, 3.5
	Very likely	90.3	86.7, 93.9	7.8	4.5, 11.1	1.9	0.6, 3.3
Smoke-free home	Yes	85.8	81.9, 89.7	11.4	7.9, 15.0	2.7	0.8, 4.7
	No	85.6	83.9, 87.3	12.1	10.4, 13.8	2.3	1.5, 3.1
Exposure to smokers (in the past 7 days)	<=10 hours	87.2	85.3, 89.1	10.5	8.7, 12.4	2.3	1.4, 3.2
	>10 hours	81.9	78.5, 85.3	15.5	12.2, 18.8	2.6	1.1, 4.1
Perceived harmfulness of cigarettes	Not to somewhat harmful	89.1	85.9, 92.3	8.8	5.9, 11.7	2.1	0.5, 3.6
	Very/extremely harmful	84.7	82.9, 86.4	12.8	11.0, 14.5	2.6	1.7, 3.4
Relative perceived harmfulness of e-cigarettes	1 = Less harmful	75.9	72.0, 79.7	22.1	18.3, 25.8	2.0	1.1, 3.0
	2 = About the same	89.8	87.8, 91.7	7.6	5.9, 9.3	2.6	1.6, 3.6
	3 = More harmful	90.4	86.4, 94.4	8.1	4.3, 11.8	1.6	0.2, 2.9
Cigarette pack-years	<= 20	84.4	82.1, 86.7	13.2	10.9, 15.5	2.4	1.4, 3.4
	21-35	83.5	79.0, 88.1	14.2	10.3, 18.2	2.3	0.4, 4.1
	> 35	84.0	79.3, 88.7	12.4	8.3, 16.5	3.7	1.0, 6.3
Age began regular smoking	18+	85.2	82.9, 87.5	11.6	9.2, 14.1	3.2	1.8, 4.6
	< 18	83.1	80.5, 85.8	14.9	12.3, 17.4	2.0	1.0, 2.9
Insurance Status	Yes	85.3	83.4, 87.2	12.5	10.7, 14.3	2.2	1.4, 3.0
	No	87.1	83.0, 91.2	9.7	6.4, 13.0	3.2	1.1, 5.4
External mental health symptoms	Low	89.2	87.0, 91.3	9.1	7.1, 11.0	1.8	1.1, 2.4
	Moderate	81.6	78.0, 85.2	15.0	12.0, 18.1	3.4	1.5, 5.3

	High	78.9	74.9, 83.0	17.5	13.6, 21.5	3.5	1.1, 6.0
Internal mental health symptoms	Low	88.8	86.7, 91.0	9.3	7.3, 11.4	1.8	1.1, 2.6
	Moderate	83.5	79.8, 87.1	13.9	10.7, 17.1	2.7	1.2, 4.2
	High	80.7	77.1, 84.3	15.7	12.1, 19.3	3.6	1.8, 5.4
Existence of smoking-related disease	Yes	87.2	85.0, 89.4	10.3	8.2, 12.4	2.5	1.6, 3.5
	No	84.1	81.7, 86.5	13.6	11.2, 15.9	2.4	1.3, 3.5

Abbreviations: PATH, Population Assessment of Tobacco and Health; Wtd, Weighted US population estimate (W1-W5 longitudinal weights were used); CL, Confidence Limit; W3, Wave 3, etc.

^a Quit Attempters: those who made at least 1 quit attempt in the year prior to W4.

^b Tobacco Dependence Index tertiles based on Strong et al²⁰

^c Other non-cigarette tobacco use include any use of cigar, cigarillo, filtered cigar, pipe, hookah, snus or smokeless tobacco.

Supplement 4. Measurement Detail for Pre-identified Study Covariates for Adjusted Analysis of Use of E-cigarettes on Relapse to Cigarettes Smoking among Recent Former Cigarette Smokers (in PATH Study [with variable names])

Socio-demographics: Use standard derived variables for age, sex, education, race, ethnicity, and income (R03R_A_AGE, R03R_A_SEX, R01R_A_EDUC, R04R_A_EDUC4, R03R_A_RACE, R03R_A_HISP, R03_AM0030; Note the variable of education comes from PATH Wave 4 database since it was not asked in Wave 3. If R04R_A_EDUC4 is missing but R01R_A_EDUC is not, we replaced the value of R04R_A_EDUC4 by R01R_A_EDUC.

Cigarette smoking status at W3: Smoked cigarettes daily or non-daily at W3 (R03_AC1003).

Tobacco dependence index: (R03_AN0025, R03_AN0030, R03_AN0065, R03_AN0035, R03_AN0045, R03_AN0085, R03_AN0090, R03_AN0060, R03_AN0095, R03_AN0100, R03_AN0055, R03_AN0050, R03_AN0070, R03_AN0075, R03_AN0080). Variables are combined to derive the variable tobacco dependence index by calculating the mean of the non-missing scores. Tobacco dependence items take the form of a series of statements on emotional and physical responses to tobacco products (e.g. "I frequently crave {product}", "I usually want to {use product} right after I wake up", "I [would] feel alone without my {product}"). Respondents are asked to rate their level of agreement with each statement on a 5-point scale, where 1="Not true of me at all" and 5="Extremely true of me". Respondents can also answer "don't know" or refuse to answer the question; these are treated as missing responses. Responses are rescaled to a 3-point scale, where 1 (not at all) = 0, 2 or 3 = 50 and 4 or 5 = 100, summed and divided by the number of non-missing values.

Cigarette consumption at W3: Average number of cigarettes now smoked each day (R03_AC1021UN, R03_AC1021NN). Responses could be reported as cigarettes or packs. For respondents with missingness in those variables, we replaced their cigarette consumption by multiplying average number of cigarettes smoked per day among non-current 30-day smokers (R03_AC1023UN, R03_AC1023NN) with the number of days smoked in the past 30 days (R03_AC1022) and divided by 30 days.

E-cigarettes use at W3: Derived with variables R03_AV1003EC.

Duration of cigarette abstinence reported at W4: Questions about "How long since you completely quit smoking cigarettes" were identified to derive time of quitting cigarettes (R04_AC1009UN, R04_AC1009NN).

Interest in quitting cigarettes: On a scale of 1-10 where 1=Not at all interested and 10=Extremely interested (R03_AN0230).

Self-efficacy about quitting: "If you did try to quit {product} altogether in the next 6 months, how likely do you think you would be to succeed?" on a 4-point scale from 1=Not at all likely and 4=Very likely (R03_AN0245).

Smoke-free home: Variables (R04_AR1045) were used to identify the variable smoke-free home when participants became recent former cigarette smokers. Statement that best describes rules about smoking a combustible tobacco product inside home. It's a 3-point scale from 1 (not allowed anywhere or anytime at all) to 3 (allowed anywhere or anytime at all).

Exposure to smokers: "In the past 7 days, number of hours that you were in close contact with others when they were smoking." (R03_AX0068).

Perceived harmfulness of cigarettes: Respondents were asked "How harmful do you think cigarettes are to health?" and could reply on a 5-point scale from 1 (not at all harmful) to 5 (extremely harmful) (R03_AC9050).

Relative perceived harmfulness of e-cigarettes: Respondents were asked "Is using e-cigarettes less harmful, about the same, or more harmful than smoking cigarettes?" and could reply on a 3-point scale, where 1=Less harmful, 2=About the same and 3=More harmful (R03_AE1099).

Cigarette pack-years: Calculated by multiplying the number of packs smoked per day by the number of years the respondent smoked regularly, missing values in the number of packs smoked per day were completed by cigarette consumptions calculated above.

Age began regular smoking: (R01_AC1007, R02_AC1007_NB and R03_AC1007_NB). If it's still missing, using (R01_AC1020, R02_AC1020_NB and R03_AC1020_NB) to replace it.

Insurance status: (R03_AM0026_01 to R03_AM0026_08) Respondents who reported currently being covered by at least one type of health insurance, including insurance purchased directly or through an employer or union, Medicare, Medicaid, VA, TRICARE or other military health care and Indian Health Insurance, were scored as having insurance coverage. Missing data on all of these variables were coded to “did not have insurance”.

External mental health symptoms: Respondents were asked the last time they had experienced any of 7 externalizing (e.g., had a hard time paying attention or listening to instructions at school, work or home, bullied or started physical fights). The number of reports of experiencing such symptoms in the past month or the past 2-12 months was summed and coded into a 3-level severity indicator, with those reporting 0 or 1 symptom scored as Low, 2-3 symptoms scored as Moderate and 4 or more scored as High.

Internal mental health symptoms: Respondents were asked the last time they experienced any of 4 internalizing disorder symptoms: feeling very trapped, lonely, sad, blue, depressed, or hopeless about the future, feeling very anxious, nervous, tense, scared, panicked, or like something bad was going to happen, had sleep problems. The number of reports of experiencing such symptoms in the past month or the past 2-12 months was summed and coded into a 3-level severity indicator, with those reporting 0 or 1 symptom scored as Low, 2-3 symptoms scored as Moderate and 4 or more scored as High.

Existence of smoking-related disease: Respondents were asked if they had ever been told by a doctor or health professional that they had any of the listed diseases.

Group A: Heart Disease: High blood pressure (R01_AX0111_01, R02_AX0111_NB_01 and R03_AX0111_NB_01), High cholesterol (R01_AX0111_02, R02_AX0111_NB_02 and R03_AX0111_NB_02) Congestive heart failure (R01_AX0111_03, R02_AX0111_NB_03 and R03_AX0111_NB_03); a stroke (R01_AX0111_04, R02_AX0111_NB_04 and R03_AX0111_NB_04); A heart attack (R01_AX0111_05, R02_AX0111_NB_05 and R03_AX0111_NB_05); Some other heart condition (R01_AX0111_06, R02_AX0111_NB_06 and R03_AX0111_NB_06)

Group B: Respiratory Disease: COPD (R01_AX0119_01, R02_AX0119_NB_01 and R03_AX0119_NB_01); chronic bronchitis (R01_AX0119_02, R02_AX0119_NB_02 and R03_AX0119_NB_02); emphysema (R01_AX0119_03, R02_AX0119_NB_03 and R03_AX0119_NB_03); asthma (R01_AX0119_04, R02_AX0119_NB_04 and R03_AX0119_NB_04); some other lung or respiratory condition (R01_AX0119_05, R02_AX0119_NB_05 and R03_AX0119_NB_05)

Group C: Cancer: (R01_AX0144, R02_AX0144_NB and R03_AX0144_NB)

Supplement 5. Full Sample Characteristics of Adjusted Analysis of Use of E-cigarettes on Relapse to Cigarettes Smoking among Recent Former Cigarette Smokers^a in PATH Study, According to Use of Non-cigarette Tobacco Products at Wave 4

Wtd % is the population in row category (for example, among those aged 18-34, 60.1% didn't use tobacco at the exposure assessment, 17.9% used e-cigarette and 22.0% used other non-cigarette tobacco product etc.).

Variable	Category	Non-cigarette Tobacco Product Use by Recent Former Smokers					
		No tobacco use (n=560)		Any e-cigarette use(n=142)		Other non-cigarette tobacco use ^c (n=160)	
		Wtd %	95% CL	Wtd %	95% CL	Wtd %	95% CL
Age	18-34	60.1	56.0, 64.1	17.9	13.5, 22.3	22.0	18.0, 26.0
	35-50	71.8	63.6, 80.1	18.4	11.7, 25.1	9.7	5.2, 14.3
	50+	84.6	78.7, 90.6	5.4	2.3, 8.5	10.0	4.9, 15.1
Sex	Male	63.1	58.0, 68.3	15.9	12.1, 19.8	20.9	16.5, 25.4
	Female	75.4	70.1, 80.6	13.7	9.4, 18.0	10.9	7.5, 14.4
Education	Less than high school	71.0	63.2, 78.8	11.9	6.7, 17.2	17.1	10.6, 23.5
	High school graduate	70.1	62.9, 77.3	11.8	7.2, 16.3	18.2	11.7, 24.6
	Some college or higher	67.8	63.1, 72.5	17.1	13.0, 21.2	15.1	11.8, 18.5
Race	White	68.0	63.7, 72.2	17.4	13.8, 21.1	14.6	11.1, 18.2
	Others	71.2	64.4, 78.1	8.1	4.7, 11.4	20.7	15.1, 26.3
Ethnicity	Hispanic	77.9	70.8, 85.0	10.9	5.2, 16.6	11.2	6.4, 16.0
	Non-Hispanic	66.8	62.7, 70.8	16.0	12.5, 19.4	17.2	14.0, 20.5
Income (US\$)	< 35000	71.9	67.4, 76.4	12.1	8.8, 15.4	16.0	12.4, 19.6
	>= 35000	65.1	59.3, 71.0	18.9	14.3, 23.5	16.0	11.6, 20.4
Cigarette smoking status at W3	Daily	72.9	67.7, 78.2	16.4	11.6, 21.1	10.7	7.3, 14.1
	Non-daily	66.1	61.2, 71.1	13.8	10.6, 17.1	20.0	16.3, 23.8
Tobacco dependence index ^b	0-33.3	69.9	63.7, 76.0	11.8	7.9, 15.6	18.4	13.6, 23.2
	33.4-66.7	66.0	58.2, 73.9	19.8	13.7, 26.0	14.1	8.6, 19.7
	66.8-100	65.2	55.2, 75.2	20.9	12.1, 29.7	13.9	6.7, 21.2
Cigarette consumption at W3 (pack)	< 1	67.6	63.7, 71.5	16.5	13.0, 19.9	15.9	13.2, 18.7
	>= 1	74.9	65.4, 84.3	12.9	5.4, 20.4	12.3	4.2, 20.3
E-cigarettes use at W3	Marked	41.3	32.9, 49.7	48.5	40.2, 56.9	10.1	5.78, 14.4

	Not marked	74.7	71.1, 78.4	7.8	5.6, 9.9	17.5	14.3, 20.7
Duration of cigarette abstinence reported at W4 (days)	<=90	62.2	56.9, 67.5	20.1	14.7, 25.5	17.7	13.3, 22.0
	>90	73.3	68.5, 78.1	11.4	8.2, 14.7	15.2	11.9, 18.5
	1-7	64.9	58.4, 71.4	14.8	10.7, 18.9	20.3	14.8, 25.8
Interest in quitting cigarettes	8-9	66.1	58.5, 73.6	16.2	8.4, 24.1	17.7	10.7, 24.7
	10	72.9	65.2, 80.6	16.7	10.8, 22.7	10.4	5.4, 15.4
Self-efficacy about quitting (in the next 6 months)	Not at all likely	83.6	47.7, 100.0	0	0.0, 0.0	16.4	0.0, 52.3
	A little likely	64.6	41.2, 88.0	26.3	3.7, 49.0	9.0	0.0, 21.6
	Somewhat likely	75.2	63.8, 86.7	12.0	3.8, 20.3	12.7	4.7, 20.7
	Very likely	70.6	62.1, 79.0	15.7	9.9, 21.4	13.8	8.0, 19.6
Smoke-free home	Yes	61.2	48.1, 74.2	9.6	4.5, 14.7	29.2	18.2, 40.3
	No	69.8	66.0, 73.5	15.5	12.3, 18.7	14.8	11.8, 17.7
Exposure to smokers (in the past 7 days)	<=10 hours	71.2	67.0, 75.4	13.8	10.4, 17.2	15.0	12.0, 17.9
	>10 hours	59.3	50.9, 67.7	19.6	12.6, 26.6	21.1	13.8, 28.4
Perceived harmfulness of cigarettes	Not to somewhat harmful	67.1	59.2, 75.1	15.6	10.1, 21.0	17.3	10.9, 23.7
	Very/extremely harmful	69.5	65.2, 73.7	14.8	11.3, 18.2	15.7	12.4, 19.1
Relative perceived harmfulness of e-cigarettes	1 = Less harmful	53.5	46.5, 60.4	28.8	22.6, 35.1	17.7	12.0, 23.5
	2 = About the same	76.3	72.2, 80.4	8.4	5.7, 11.1	15.3	11.7, 18.8
	3 = More harmful	77.3	68.1, 86.5	8.6	2.2, 15.0	14.1	7.0, 21.3
Cigarette pack-years	<= 20	65.7	60.8, 70.5	20.9	16.2, 25.7	13.4	10.0, 16.8
	21-35	76.7	64.3, 89.1	12.4	2.0, 22.8	10.9	2.7, 19.2
	> 35	78.3	66.8, 89.7	7.3	1.1, 13.5	14.4	5.2, 23.6
Age began regular smoking	18+	70.7	63.4, 78.1	16.5	10.6, 22.3	12.8	8.1, 17.5
	< 18	67.0	60.3, 73.6	18.2	14.0, 22.4	14.8	9.4, 20.2
Insurance Status	Yes	69.2	65.2, 73.2	15.5	12.5, 18.5	15.3	12.0, 18.5
	No	68.3	60.7, 76.0	11.9	6.2, 17.6	19.8	13.5, 26.0
External mental health symptoms	Low	72.2	67.8, 76.5	11.2	8.5, 14.0	16.6	12.9, 20.4
	Moderate	65.9	58.2, 73.5	18.5	11.9, 25.0	15.7	10.1, 21.2

	High	61.8	53.4, 70.3	22.7	15.7, 29.7	15.5	8.8, 22.2
Internal mental health symptoms	Low	69.5	65.0, 74.0	11.8	8.7, 14.9	18.7	14.9, 22.6
	Moderate	71.2	63.7, 78.7	14.7	9.1, 20.3	14.1	8.5, 19.7
	High	65.2	56.6, 73.7	23.2	16.4, 30.1	11.6	6.5, 16.7
Existence of smoking-related disease	Yes	75.0	70.3, 79.6	12.1	8.7, 15.5	12.9	9.0, 16.8
	No	64.7	60.0, 69.3	16.8	12.6, 21.1	18.5	14.8, 22.2

Abbreviations: PATH, Population Assessment of Tobacco and Health; Wtd, Weighted US population estimate (W1-W5 longitudinal weights were used); CL, Confidence Limit; W3, Wave 3, etc.

^a Recent Former Cigarette Smokers: those who smoked cigarettes at W3 and didn't smoke cigarettes at W4.

^b Tobacco Dependence Index tertiles based on Strong et al²⁰

^c Other non-cigarette tobacco use includes any use of cigar, cigarillo, filtered cigar, pipe, hookah, snus or smokeless tobacco.

Supplement 6. Nicotine Concentration in E-cigarettes Used by Recent Former Smokers

Abbreviations: Wtd, weighted US population estimate; CL, confidence limit.

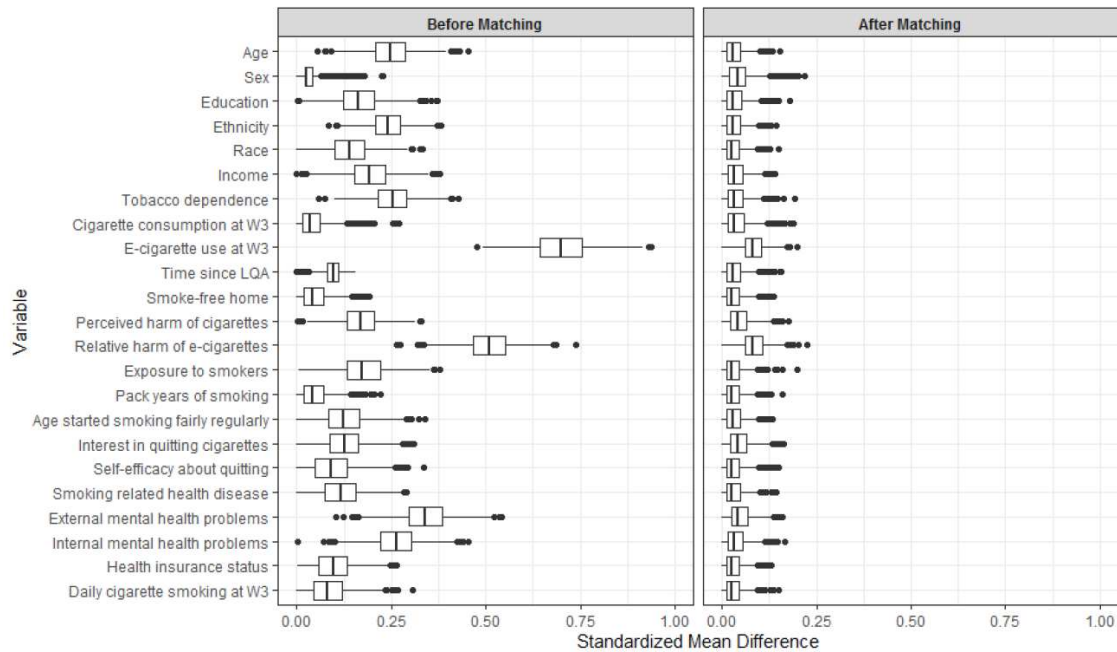
^a. Recent Former Smoker: those who were not smoking cigarettes but who were established smokers at baseline (one year before).

	Wave 4 (2017)			Wave 5 (2019)		
	n	Wtd %	95% CL	n	Wtd %	95% CL
Previous Year Established Smokers ^a	10614			9053		
Recent former smokers (RFS) ^b	1323	12.4	11.6,13.3	1595	17.0	15.8,18.2
RFS who had switched to e-cigarettes	230	15.3	12.9,17.7	399	22.0	19.6,24.5
Nicotine concentration in e-cigarettes						
I don't know the concentration	30	11.9	6.8, 16.9	46	9.7	6.5, 13.0
0-6mg or 0.0-0.6%	110	48.5	40.3, 56.6	170	44.6	38.8, 50.4
7-12mg or 0.7-1.2%	16	7.3	3.6, 11.1	14	3.1	1.3, 5.0
13-17mg or 1.3-1.7%	3	1.7	0.0, 3.8	7	2.9	0.4, 5.3
18-24mg or 1.8-2.4%	19	8.1	4.1, 12.2	10	2.9	0.7, 5.1
25-39mg or 2.5-3.9%	6	2.7	0.4, 5.0	22	5.9	3.1, 8.7
40+mg or 4.0+%	5	2.2	0.0, 4.4	83	19.9	15.1, 24.6
Missing	41	17.6	11.5, 23.8	47	11	7.3, 14.8

^a In the year prior to the survey, this was the population of established smokers

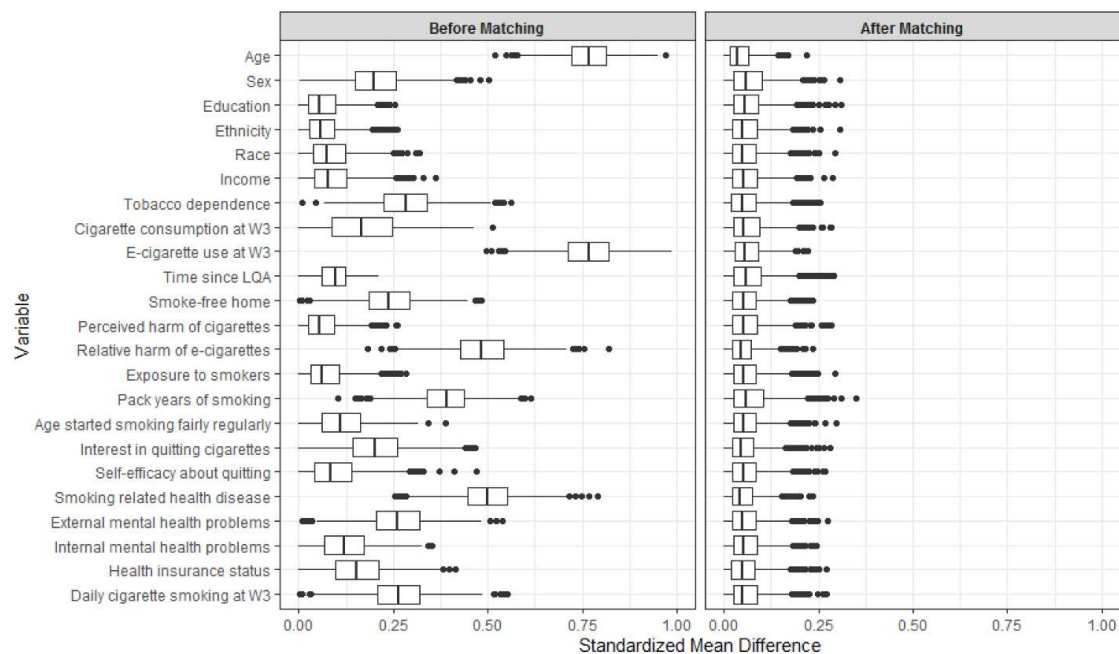
^b these were the previous year established smokers who were quit at the time of the survey

Supplement 7. Standardized Differences in 23 Important Covariates between Those Who Used Any E-cigarettes to Quit in 2016-2017 and Those Who Did Not among Quit Attempters, before and after Matching



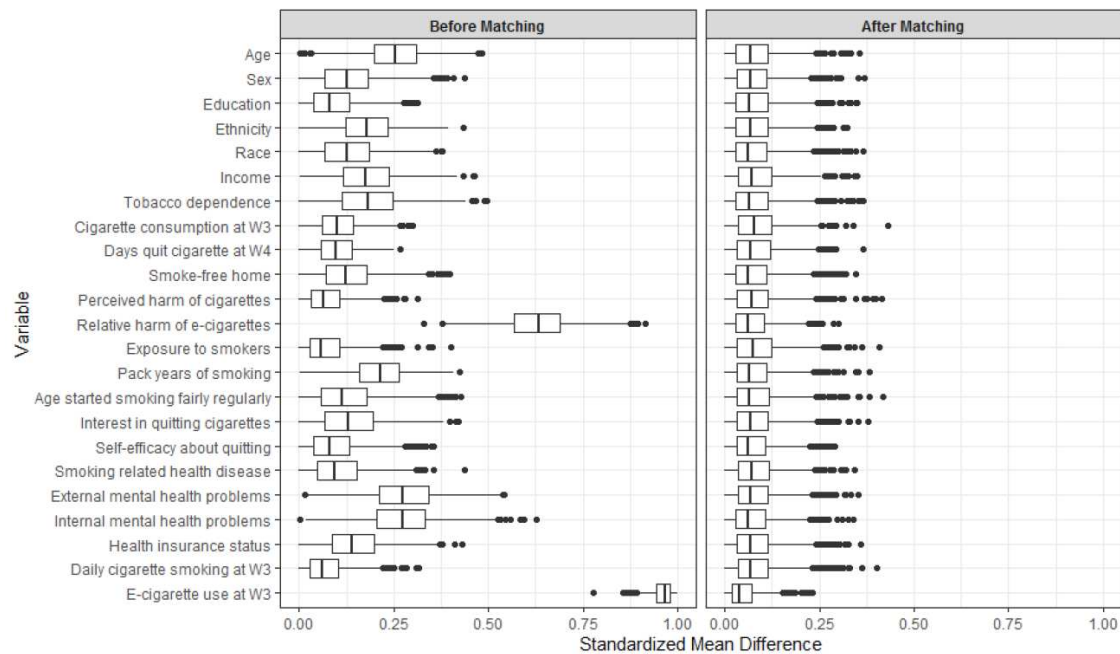
This boxplot presents the bootstrap distribution of the weighted standardized mean difference between baseline smokers who used e-cigarettes to aid their most recent quit attempt prior to PATH Wave 4, and those who did not among quit attempters, on the indicated variable. We consider an optimal match to be a covariate with a standardized median difference of $< |0.1|$. Before matching, 15 of the 23 covariates had less than optimal comparability between study groups (standardize mean difference $> |0.1|$). After matching, none of the 23 covariates had less than optimal comparability between study groups. 1500 bootstrap samples were used. For a given covariate, we define “a marked improvement in covariate balance from matching” as a decrease of at least 0.1 units in the median absolute difference of the standardized covariate between exposed and non-exposed subjects, comparing the bootstrap distribution before and after matching. These comparisons do not use the survey weights. For this comparison, the following 12 covariates below achieved a marked improvement in covariate balance from the matching procedure (ordered by size of the difference in medians: E-cigarette use at W3, Relative perceived of harmfulness of e-cigarettes, External mental health symptoms, Internal mental health symptoms, Tobacco dependence index, Age, Ethnicity, Income, Exposure to smokers, Perceived harmfulness of cigarettes, Education and Race).

Supplement 8. Standardized Differences in 23 Important Covariates between Those Who Used Any E-cigarettes to Quit in 2016-2017 and Those Who Used NRT or Pharmaceutical Aid Only among Quit Attempters, before and after Matching



This boxplot presents the bootstrap distribution of the weighted standardized mean difference between baseline smokers who used e-cigarettes to aid their most recent quit attempt prior to PATH Wave 4, and those who used NRT or pharmaceutical aid only among quit attempters, on the indicated variable. We consider an optimal match to be a covariate with a standardized median difference of $< |0.1|$. Before matching, 15 of the 23 covariates had less than optimal comparability between study groups (standardized mean difference $> |0.1|$). After matching, none of the 23 covariates had less than optimal comparability between study groups. 1500 bootstrap samples were used. For a given covariate, we define “a marked improvement in covariate balance from matching” as a decrease of at least 0.1 units in the median absolute difference of the standardized covariate between exposed and non-exposed subjects, comparing the bootstrap distribution before and after matching. These comparisons do not use the survey weights. For this comparison, the following 13 covariates below achieved a marked improvement in covariate balance from the matching procedure (ordered by size of the difference in medians: E-cigarette use at W3, Age, Smoking related health disease, Relative perceived of harmfulness of e-cigarettes, Pack years of smoking, Tobacco dependence index, Daily cigarette smoking status at W3, External mental health symptoms, Smoke-free home, Interest in quitting cigarettes, Sex, Cigarette consumption at W3, Insurance status.

Supplement 9. Standardized Differences in 23 Important Covariates between Those Who Used Any E-cigarettes and Those Did Not Use E-cigarettes at Wave 4 among Recent Former Smokers, before and after Matching



This boxplot presents the bootstrap distribution of the weighted standardized mean difference between those who used any e-cigarettes and those who didn't use e-cigarettes among recent former smokers at PATH Wave 4, on the indicated variable. We consider an optimal match to be a covariate with a standardized median difference of $< |0.1|$. Before matching, 16 of the 23 covariates had less than optimal comparability between study groups (standardize mean difference $> |0.1|$). After matching, none of the 23 covariates had less than optimal comparability between study groups. 1500 bootstrap samples were used. For a given covariate, we define "a marked improvement in covariate balance from matching" as a decrease of at least 0.1 units in the median absolute difference of the standardized covariate between exposed and non-exposed subjects, comparing the bootstrap distribution before and after matching. These comparisons do not use the survey weights. For this comparison, the following 9 covariates below achieved a marked improvement in covariate balance from the matching procedure (ordered by size of the difference in medians: E-cigarette use at W3, Relative perceived of harmfulness of e-cigarettes, External mental health symptoms, Internal mental health symptoms, Age, Pack years of smoking, Tobacco dependence index, Ethnicity and Income).

Supplement 10. The Change of Perception of Harmfulness of Cigarettes and Relative Harmfulness of E-cigarettes, PATH Study Wave 3 to Wave 5

Variable	Wave 3 (n=28148)		Wave 4 (n=33644)		Wave 5 (n=32687)	
	Wtd %	95% CL	Wtd %	95% CL	Wtd %	95% CL
Perceived harmfulness of cigarettes						
Not to somewhat harmful	9.3	8.9, 9.7	10.1	9.7, 10.6	9.5	9.1, 9.9
Very/extremely harmful	90.4	90.1, 90.8	89.6	89.1, 90.0	90.2	89.8, 90.6
Missingness	0.2	0.2, 0.3	0.3	0.2, 0.4	0.3	0.2, 0.4
Relative perceived harmfulness of e-cigarettes						
1 = Less harmful	23.8	23.1, 24.5	20.7	20.0, 21.3	16.4	15.9, 17.0
2 = About the same	62.9	62.1, 63.7	67.1	66.5, 67.8	68.6	67.9, 69.4
3 = More harmful	11.0	10.5, 11.5	10.5	10.1, 11.0	13.7	13.1, 14.3
Missingness	2.3	2.0, 2.6	1.7	1.4, 1.9	1.2	1.0, 1.4

Abbreviations: PATH, Population Assessment of Tobacco and Health; Wtd, weighted US population estimate; CL, confidence limit.