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Can e-Cigarettes and Pharmaceutical Aids Increase Smoking Cessation and Reduce Cigarette Consumption? Findings from a Nationally Representative Cohort of American Smokers

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Running head: e-Cigarettes, Pharmaceutical Aids, and Smoking

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ABSTRACT

Many smokers believe that electronic nicotine delivery systems (ENDS) and pharmaceutical cessation aids can help them quit smoking or reduce cigarette consumption, but the evidence for e-cigarettes to aid quitting is limited. Examining 3,093 quit attempters in the nationally-representative US Population Assessment of Tobacco and Health (PATH) Study between 2013 and 2015, we evaluated the influence of ENDS and pharmaceutical cessation aids on persistent abstinence (≥30 days) from cigarettes, and reduced cigarette consumption, using Propensity Score Matching to balance comparison groups on potential confounders and multiple imputation to handle missing data. At PATH Wave 2, 25.2% of quit attempters reported using ENDS to quit during the previous year, making it the most popular cessation aid in 2014-15. More quit attempters were persistently cigarette abstinent than persistently tobacco abstinent (15.5±0.8% vs 9.6±0.6%). Using ENDS to quit cigarettes increased the probability of persistent cigarette abstinence at Wave 2 (Risk Difference (RD)=6%; 95% CI: 2%;10%), but using approved pharmaceutical aids did not (varenicline RD=2%; 95% CI: -6%,13%; buproprion RD=4%, 95% CI: -6%, 17%; NRT RD=-3%, 95% CI -8%, 2%). Among quit attempters who relapsed, ENDS did not reduce the average daily cigarette consumption (-0.18 cigarettes per day; 95% CI: -1.87;1.51).

Keywords: Cessation; electronic nicotine delivery systems (ENDS); pharmaceutical aids; propensity score matching

INTRODUCTION

Electronic nicotine delivery systems (ENDS) are devices that became commercially available in the United States in 2007 when the rates of smoking cessation had stalled(1). A recent comprehensive National Academies of Sciences Engineering and Medicine report(2) concluded that inhaled aerosol from e-cigarettes has fewer and lower levels of toxicants than smoke from combusted tobacco cigarettes, and experienced adult users of the most recent third generation e-cigarettes (e.g. advanced personal vaporizers) are able to extract similar levels of nicotine to the amounts obtained from cigarette smoking(3). The National Academies of Sciences Engineering and Medicine report also noted that "*For both individuals and for public health, the central potential benefit of e-cigarettes is to promote smoking cessation among established cigarette smokers or at least to reduce a smoker's exposure to combustible tobacco products*" (2) (Chap 17, p. 423). At the same time, there is substantial evidence that e-cigarette use in young people increases the risk of future cigarette smoking(4).

Current prevalence estimates for ENDS usage in the US vary with surveys, with Wave 1 of the US Population Assessment of Tobacco and Health (PATH) Study (2013-14) indicating 5.5% of the population were current users (5) and the 2014-15 Tobacco Use Supplement of the Current Population Survey indicating a lower 2.4%.(1) In the Tobacco Use Supplement of the Current Population Survey current ENDS use rates were 19.0% for recent quitters and 11.5% for current smokers, with the majority being non-daily users. In the PATH Study, 83.5% of current and 76% of former cigarettes smokers(5) agreed that e-cigarettes could substitute in places where cigarettes were proscribed. Similarly, ~75% agreed that e-cigarettes can help people quit smoking cigarettes.

There is a substantial literature of randomized controlled trials (RCTs) showing the efficacy of nicotine replacement, varenicline, and buproprion, as smoking cessation aids(6), but few trials of e-cigarettes. For the latter, meta-analyses(2) consistently identify only 2 international trials that appropriately address the role of e-cigarettes in cessation. Bullen et al.(7)

randomized smokers who wanted to quit to either e-cigarettes, nicotine patches or placebo e-cigarette. Biochemically verified 6-months continuous abstinence was not significantly higher in the e-cigarette group than the nicotine patch group or the placebo control (7.3% vs 5.8% vs 4.1%). Capponetto et al(8) compared e-cigarettes to a placebo e-cigarette, and verified 6-months continuous abstinence was 11% vs 4%, which reached borderline significance.

In contrast to randomized trials, population based longitudinal studies reflect how e-cigarettes are actually being used in the target population. Six longitudinal studies that addressed the potential role of e-cigarettes in cessation(9-14) met the inclusion criteria in both recent systematic reviews that National Academies of Sciences Engineering and Medicine judged to be the most comprehensive and rigorous(15, 16). Two of these(13, 14) focused exclusively on patient populations and as such are not generalizable to the general population. All the others were considered to have significant methodological flaws that limited the quality of conclusions, including lack of identification and control of known prognostic factors for successful cessation. In particular, higher levels of nicotine dependence are known to be positively associated with use of a cessation aid as well as negatively associated with cessation success. Another National Academies of Sciences Engineering and Medicine criticism of studies focused on the inclusion of participants who were using e-cigarettes for reasons other than as a cessation aid. Additionally, there was an expressed concern that relapsed smokers may not have recalled all of their unsuccessful quit attempts or had degraded their significance by recalling them as “not really a quit attempt.” This proposed pattern of differential recall of past quit attempts could lead to a bias towards fewer recalled failures(17, 18). However, the evidence that this recall bias is differential by use of cessation aids has been unconvincing (19).

Understanding the potential role that ENDS products may play in cessation requires direct comparisons with recommended efficacious pharmaceutical products [varenicline, bupropion

and Nicotine Replacement Therapy (NRT)](20). The effectiveness of how these aids have been disseminated at the population level has been questioned(21), and this needs replication.

In this study, we use the first 2 waves from the large nationally representative PATH Study (22, 23) to evaluated the influence of ENDS and pharmaceutical cessation aids on persistent abstinence (≥30 days) from cigarettes as well as reduced cigarette consumption using Propensity Score Matching (PSM) to balance comparison groups on potential confounders.

METHODS

Data source

The federally-funded PATH Study (24) drew an address-based area probability sample of the non-institutionalized US population for Wave 1 and completed in-household audio-computer-assisted self-interviews in English and Spanish in 2013-14. Westat's Institutional Review Board approved the PATH Study design/protocol and the Office of Management and Budget approved the data collection. Over-sampling was undertaken for tobacco users, African Americans, and young adults aged 18-24 years. In this adult sample, the Wave 1 weighted response rate was 74%, and there were 10,851 who reported current smoking (i.e. regularly smoking cigarettes every day or some days). Approximately one year following their Wave 1 interview, a similar in-household self-interview (Wave 2) was undertaken and 8,861 (81.7%) of the above Wave 1 current smokers were re-interviewed. Of these, 5,712 (64.5%) did not report a quit attempt prior to Wave 2, and 56 had incomplete details on their quit attempt, leaving a sample of 3,093 for this analysis.

Measures

Tobacco use status. During the interview at both waves, participants were shown pictures of tobacco products prior to responding to questions about use. At Wave 1, all current cigarette smokers (every day or some days users) were queried on the frequency of use in the past 30 days, number of cigarettes consumed per day, and how old they were when they first started

smoking fairly regularly. For other tobacco products, a regular current user was identified with the questions: “Do you now use [PRODUCT] every day, some days or not at all?” and, “Have you ever used [PRODUCT] fairly regularly?”

At Wave 2, all current regular users from Wave 1 were asked “In the past 12 months, have you tried to quit [PRODUCT]?” Those who responded “not at all” to the current use question at Wave 2 were asked, “About how long has it been since you last [smoked/used PRODUCT]?” As use in the past month indicates current use for some products, we use ≥30 days abstinence at Wave 2 (persistent abstinence) as an early marker of successful cessation for both cigarettes and from all forms of tobacco other than ENDS.

At Wave 2, those who reported a quit attempt in the past year were asked about use of each of the following products during that attempt (allowing multiple product use): ENDS (e-cigarettes); Nicotine Replacement Therapy (NRT: a nicotine patch, gum, inhaler, nasal spray, lozenge or pill); varenicline (Chantix: Pfizer, Groton, Connecticut); buproprion (Wellbutrin or Zyban: GlaxoSmithKline, Brentford, London).

Smoking history. Age of cigarette smoking initiation was assessed with the question, “How old were you when you first started smoking fairly regularly?” (coded: <18 years old; ≥ 18 years old). Quitting history prior to Wave 1 was also queried. All respondents were asked, “Which statement best describes the rules about smoking inside your home?” The response, “It is not allowed anywhere or at any time inside my home” indicated a smoke-free home. Time spent around other smokers was assessed using the question, “During the past seven days, about how many hours were you around others who were smoking [whether or not you were smoking yourself]? Include time in your home, in a car, at work, or outdoors.” Beliefs about the harmfulness of e-cigarettes were assessed using the question “Is using e-cigarettes less harmful, about the same, or more harmful than smoking cigarettes?” (coded: less harmful; all other responses). A psychometrically valid scale of dependence on tobacco products was developed from multiple questions on the PATH survey (25).

Sociodemographic characteristics. The PATH Study contains detailed information on a number of standard sociodemographic characteristics. Respondent's age was queried in individual years, which we reduced to 2 categories for this study: 18–34 years and ≥35 years. We used binary classifications for sex, education status (college graduate vs. less than college graduate), and race/ethnicity (non-Hispanic White vs. other). Our binary classification of educational attainment highlighted college graduates who have a much higher successful cessation rate than other education groups.

Multiple imputations: Missing data were observed on a few of the variables we assessed (Web Table 1). Missing data were imputed using the Amelia II algorithm in R with 5 imputed datasets, and by assuming a missing at random pattern (26). Natural logarithm transformation improved normality of 3 continuous variables and was used for imputation **(**Web Figure 1**).** Imputation diagnostics suggested the Amelia II algorithm provided imputed values well within range of observed values **(**Web Figure 2**)** and accurately predicted the majority of the observed values for the continuous variables **(**Web Figure 3**).**

Statistical analysis

Frequencies of cessation aid usage and cigarette and tobacco abstinence were described across sociodemographic and smoking characteristics, using complete cases for each comparison, and the statistical significance for bivariate differences were tested using a weighted $\boldsymbol{X}^2$ tests. PSM was used to choose a comparison group of respondents for each 'treatment' group (e.g. ENDS, varenicline, bupropion and NRT) that balanced the groups with respect to potential confounders. Matching algorithms were optimized separately for each cessation aid group to assess quitting rates and then again for relapsers at Wave 2 to assess levels of consumption. For each cessation aid product group, we compared users to non-users and also compared the group of ENDS users to the group who used any approved pharmaceutical aids.

To calculate propensity scores, we first obtained imputed datasets, then optimized logistic models and estimated propensity scores and finally averaged the propensity score for each

individual across the datasets (27). Separate logistic models were fit for each of the imputed datasets with each cessation aid group as an outcome and potential confounders entered as covariates in the regression equation. Likelihood ratio tests (28) were used to assess whether continuous model coefficients should be specified as either a quadratic or a linear function depending on the cessation aid of interest (**Web Tables 1, 2**). After identifying the best fitting specifications, we estimated each respondent's propensity to use a product from each of the cessation aid groups, and averaged the final resulting propensity score for each individual across imputations (27).

Using the resulting propensity scores, each cessation aid user was matched to the closest non-user(s) using the nearest-neighbor method with optimizations assessed for choice of matching ratios and caliper.(29) Standardized mean differences of each covariate were used to judge whether the matching improved balance across all imputed datasets **(Web Tables 3-12).** We chose the ratio and caliper that provided the lowest average imbalance across all imputed datasets and assured covariates had standardized mean differences that were <|0.1|. Our final ratio and caliper decisions are provided in **Web Table 13.**

We then estimated differences in cigarette and tobacco abstinence at Wave 2 with pairwise comparisons among each cessation aid user group and subsequently for ENDS users vs. users of any approved pharmaceutical cessation aid. Further, among relapsers, we estimated the association of cessation aid use with cigarette consumption at Wave 2. For the models predicting cigarette and tobacco abstinence, risk differences (RDs) and their corresponding 95% confidence intervals (CIs) were calculated using logistic regression and by using 1,000 draws from the multivariate normal distribution with the mean vector equal to the model coefficients and the variance equal to the coefficient covariance matrix (30). For the models predicting cigarette consumption, mean differences (MDs) and 95% CIs were calculated using ordinary least squares (OLS) regression. We also checked whether assuming a negative binomial distribution altered effect size. All covariate coefficient values were centered at their

mean. All analyses were performed using R version 3.4.3, all tests for descriptive analyses were 2 tailed, and significance tests were adjusted for multiple comparisons ($\alpha = 0.05/12$).

RESULTS

Characteristics of sample

Just over half the population of quit attempters (53%) were male, 43% were under the age of 35 years, 68% were non-Hispanic white and 88.5% did not have a college degree. Of these demographics, only having a college degree was associated with persistent cigarette abstinence at Wave 2 (20.0±2.3% vs 14.9±0.8%) (**Table 1**). Persistent tobacco abstinence (≥30 days) was achieved at Wave 2 by 9.6±0.6% of these quit attempters, however 15.5±0.8% were persistently abstinent from cigarettes. Of these quit attempters, three quarters (76%) were daily smokers, with half smoking between 10-20 cigarettes/d; 41% reported no quit attempt in the year prior to baseline.

In terms of use of cessation aids, 25.2% used ENDS, while 23.5% used at least one approved pharmaceutical cessation aid (NRT=18.7%; varenicline=5.7%; buproprion=3.1%) (**Table 1**). Of those who used a cessation aid, 15.1% reported using more than one product, with the largest proportion of these using ENDS and NRT together (13.5%). Compared to those under age 34 years, a greater proportion of older quit attempters were users of approved pharmaceutical products, while fewer used ENDS as a cessation aid (22.8% ±1.1 vs. 28.3% ±1.4), Overall, 84.5% of this population had relapsed to cigarette smoking by the Wave 2 survey (**Table 1**).

Measures of nicotine dependence at Wave 1 were associated with greater likelihood of using a cessation aid in the quit attempt and a lower chance of being cigarette abstinent at Wave 2. For cigarette consumption, this effect was only seen among those who smoked ≥10 cigarettes/day compared to those who smoked less. The more time spent with other smokers, the higher the use of ENDS as a cessation aid (16.8±2.6% vs 23.9 ±1.1% vs 30.0±1.7%), and those exposed ≥10 hours were less likely to be cigarette abstinent at Wave 2 (12.8±1.1% vs 16.8±1.1% for

those exposed 0.1-10 hours). There was no difference in use of cessation aids among smokers who had a smoke-free home at Wave 1 although those with a smoke-free home were also more likely to be cigarette abstinent at Wave 2 (18.1%±1.0 vs 12.1%± 0.9).

Among quit attempters, one quarter of those who used ENDS for the target quit attempt also used ENDS at Wave 1 (6.6/18.7+6.6) **(Table 2**). Wave 1 use of ENDS made no difference in the proportion who had substituted e-cigarettes for cigarette smoking at Wave 2 follow-up. Persistent abstinence from all tobacco at Wave 2 was lower in those using ENDS to quit than other groups. Of the additional 6% who were persistently cigarette abstinent, but not persistently tobacco abstinent at Wave 2, 73% (4.4/6.0) were ENDS users at Wave 2 including some who reported using other cessation methods in their quit attempt. At Wave 2, there was significant dual use of cigarettes and ENDS among relapsed smokers from all cessation aid user groups, with the highest dual use from those who had used ENDS at Wave 1 (60.7% ±4.6).

Achieving comparable groups with matching

Comparison of the standardized mean differences identified imbalance across the cessation aid user groups on many of the covariates we assessed in the unmatched dataset (**Web Tables 3-12**). However, after matching, the standardized mean differences of each covariate included were systematically below 0.1. Matching improved the comparability of groups. Matched samples were well balanced with respect to the covariates that we assessed (**Web Tables 3-12**).

Helpfulness of cessation aids

In **Figure 1 A)**, we present the association between the use of each of the cessation aids and abstinence from cigarettes. Using ENDS to try to quit use cigarette smoking increased the probability of abstinence from cigarettes (risk difference (RD)= 5%, 95% CI: 1%, 10%). Both varenicline, (RD=3%: 95% CI: -5%, 12%) and bupropion (RD=8%, 95% CI: -2%, 21%) had positive risk differences that were not significant whereas NRT (RD=-3%, 95% CI: -8%, 3%)

had a negative, but non-significant risk difference for persistent abstinence from cigarettes. However, when comparing ENDS users to any pharmaceutical aid (using ENDS, but not varenicline, bupropion or NRT) , we did not detect a difference in abstinence from cigarettes (RD= 3%, 95% CI -3%, 10%).

We also present the association between the use of each of the cessation aids on reduction of cigarette consumption among those who had relapsed to cigarette smoking at Wave 2 (**Figure 1 B**). ENDS use was not associated with lower average daily cigarette consumption at Wave 2 (-0.34 cigarettes/d; 95% CI: -1.42, 0.75). Similarly, the use of varenicline, bupropion, or NRT to aid the quit attempt was not associated with lower average daily cigarette consumption at Wave 2 and ENDS users were not different to pharmaceutical aid users. Assuming a negative binomial distribution did not alter effect size or statistical significance (**Web Figure 4**).

DISCUSSION

In this nationally representative study of the US population, approximately one third of the baseline smokers reported a quit attempt of at least one day during the year prior to the second interview. Of these quit attempters, almost half (48.7%) used a cessation aid to help them quit. The majority of those who chose a cessation aid reported using ENDS to quit (25.2% of all quit attempters) suggesting that smokers may lack confidence in the approved cessation aids. Using a subsample balanced through PSM, we estimated that using ENDS increased the probability of persistent abstinence from cigarettes by 6 %. Both varenicline and buproprion had a positive risk difference for quitting, however, neither was statistically significant. There was also no statistically significant difference when comparing ENDS as a cessation aid to users of approved cessation aids.

The vast majority (79%) of quit attempters had relapsed back to cigarette smoking by the Wave 2 survey. Of those who used ENDS as a cessation aid, over 70% were still using ENDS at Wave 2, the majority of whom were smoking cigarettes as well. Among relapsers at Wave 2, there was no evidence that using ENDS to quit was associated with lower cigarette

consumption. Thus, there is a distinct possibility that a subgroup of dual users at Wave 2 may have higher levels of nicotine intake, which may make it harder for them to quit smoking cigarettes in the future,(31) emphasizing the need for continued monitoring of this population.

A recent study also analyzed data from the PATH Study to evaluate the association of recent e-cigarette use on cigarette abstinence.(32) This paper was different to ours in that it focused on quit attempters without considering the reason for using e-cigarettes. As 75% of smokers believe e-cigarettes help cessation(5), the inclusion of non-quit attempters in the analysis will bias their main findings in favor of e-cigarettes for cessation. Another important difference is that they conducted a traditional multivariable analysis. Given the important improvement in comparability of exposed and unexposed groups through the use of PSM, it is unlikely that the study adequately controlled for the many baseline potential confounders. An interesting finding was that the association between 30-day cigarette abstinence and e-cigarettes was limited to daily use of e-cigarettes, which was an uncommon pattern of use at Wave 2 in this population. A limitation of both of these studies is that abstinence was limited to a relatively short time period (30-day) prior to Wave 2. With relapse to smoking still considerable through 12 months after a quit attempt,(33) these findings need to be confirmed through at least another year (e.g. Wave 3 of the PATH Study).

A strength of our study is that we were able to compare the association of ENDS use to aid a cessation attempt with the use of other recommended cessation aids. While we did not detect an association of use of pharmaceutical cessation aids with cigarette abstinence, we also did not detect a difference in using ENDS as a cessation aid compared to use of a pharmaceutical aid. Part of this issue relates to the paucity of US smokers who used an approved cessation aid as well as with the size of the observed association.

The PATH Study is a large addressed-based sample that is representative of the US population. Our choice of persistent abstinence as our outcome measure is supported as an earlier indicator of success as only 15% of quit attempters in this study achieved this level of

abstinence. As the PATH Study has additional annual data collections, both long-term relapse among those who were persistently abstinent at Wave 2, and developing patterns of ENDS and cigarette use, will be able to be better described in the future. Our study indicates that some key potential predictors of abstinence (such as tobacco dependence measures) are also associated strongly with choice of a cessation aid, including an ENDS product. We used PSM, which offers a way to achieve baseline comparability of study groups (thus mimicking one of the goals of randomized trials)(34) prior to undertaking a analysis on the outcome of interest.

Conclusions

Our results indicate that ENDS are a more popular choice than approved pharmaceutical products as a smoking cessation aid among US quit attempters, over three quarters of whom were daily smokers. In the future, as ENDS products continue to evolve to make nicotine delivery more similar to that obtained from a cigarette,(35) it is possible that they may play a bigger role in assisting smokers to quit combustible tobacco (36). In parallel, using ENDS as a cessation aid resulted in dual use among relapsers; it did not reduce their cigarette consumption but rather appeared to expose them to potential additional risk.

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Conflict of interest: none declared.

Abbreviations

ENDS, electronic nicotine delivery systems

CI, confidence interval

NRT, Nicotine Replacement Therapy

PATH, Population Assessment of Tobacco and Health

PSM, Propensity Score Matching

RD, risk difference

.**References**

1. Zhu S-H, Zhuang Y-L, Wong S, Cummins SE, Tedeschi GJ. E-cigarette use and associated changes in population smoking cessation: evidence from US current population surveys. BMJ. 2017;358.
2. National Academies of Sciences, Engineering, and Medicine. Public Health Consequences of E-Cigarettes. Washington, DC: Health and Medicine Division, National Academies of Sciences, Engineering, and Medicine, 2018.
3. Wagener TL, Floyd EL, Stepanov I, Driskill LM, Frank SG, Meier E, et al. Have combustible cigarettes met their match? The nicotine delivery profiles and harmful constituent exposures of second-generation and third-generation electronic cigarette users. *Tob Control.*2017;26:e23-e28.
4. Soneji S, Barrington-Trimis JL, Wills TA, Leventhal AM, Unger JB, Gibson LA, 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(8):788-97.
5. Coleman BN, Rostron B, Johnson SE, Ambrose BK, Pearson J, Stanton CA, et al. Electronic cigarette use among US adults in the Population Assessment of Tobacco and Health (PATH) Study, 2013–2014. *Tob Control.*2017;26:e117-e126.
6. Fiore M, Jaén C, Baker T, Bailey W, Benowitz N, Curry S, et al. Treating Tobacco Use and Dependence: 2008 Update. Clinical Practice Guideline. Executive Summary. Rockville, MD: U.S. Department of Health and Human Services, Public Health Service, 2008.
7. Bullen C, Howe C, Laugesen M, et al. Electronic cigarettes for smoking cessation: a randomised controlled trial. Lancet. 2013;382(9905):1629-1637.
8. Caponnetto P, Campagna D, Cibella F, Morjaria JB, Caruso M, Russo C, et al. EffiCiency and Safety of an eLectronic cigAreTte (ECLAT) as tobacco cigarettes substitute: A prospective 12-month randomized control design study. *PloS One*. 2013;8(6):e66317.
9. Al-Delaimy WK, Myers MG, Leas EC, Strong DR, Hofstetter CR. E-cigarette use in the past and quitting behavior in the future: a population-based study. *Am J Public Health*. 2015;105(6):1213-9..
10. Brose LS, Hitchman SC, Brown J, West R, McNeill A. Is the use of electronic cigarettes while smoking associated with smoking cessation attempts, cessation and reduced cigarette consumption? A survey with a 1-year follow-up. *Addiction*. 2015; 110(7):1160-8.
11. Hajek P, D Spearing E L. Adding e-cigarettes to Specialist Stop-Smoking Treatment: City of London Pilot Project. *J Addict Res Ther.* 2015; 6:244. doi:10.4172/2155-6105.1000244
12. Manzoli L, Flacco ME, Fiore M, La Vecchia C, Marzuillo C, Gualano MR, et al. Electronic cigarettes efficacy and safety at 12 Months: Cohort study. *PloS One.* 2015;10(6):e0129443.
13. Borderud SP, Li Y, Burkhalter JE, Sheffer CE, Ostroff JS. Electronic cigarette use among patients with cancer: characteristics of electronic cigarette users and their smoking cessation outcomes. *Cancer.* 2014;120(22):3527-35.
14. Prochaska JJ, Grana RA. E-Cigarette Use among smokers with serious mental illness. *PloS One.* 2014;9(11):e113013.
15. El Dib R, Suzumura EA, Akl EA, Gomaa H, Agarwal A, Chang Y, et al. Electronic nicotine delivery systems and/or electronic non-nicotine delivery systems for tobacco smoking cessation or reduction: a systematic review and meta-analysis. *BMJ Open.* 2017;7(2).
16. Hartmann-Boyce J, McRobbie H, Bullen C, Begh R, Stead LF, Hajek P. Electronic cigarettes for smoking cessation. *Cochrane Db Syst Rev.* 2016;9:CD010216.

17. Gilpin E, Pierce JP. Measuring smoking cessation: problems with recall in the 1990 California Tobacco Survey. *Cancer Epidemiol Biomarkers Prev.*1994;3:613-617.
18. Borland R, Partos TR, Cummings KM. Systematic biases in cross-sectional community studies may underestimate the effectiveness of stop-smoking medications. *Nicotine Tob Res.* 2012;14(12):1483-7.
19. Messer K, Pierce JP. Is the lack of effect of smoking cessation aids in population studies explained by recall bias? Comment on the article by Borland et al. (2012). *Nicotine Tob Res*. 2013;15(3):752-3.
20. The Clinical Practice Guideline Treating Tobacco Use, Dependence Update Panel L, Staff. A Clinical Practice Guideline for Treating Tobacco Use and Dependence: 2008 Update: A U.S. Public Health Service Report. *Am J Prev Med.* 2008;35(2):158-76.
21. Leas E, Pierce JP, Benmarhnia T, White MW, Noble ML, Trinidad DR, et al. Effectiveness of pharmaceutical smoking cessation aids in a nationally representative cohort of American smokers. *J Natl Cancer Inst.* 2017. https://doi.org/10.1093/jnci/djx240
22. United States Department of Health and Human Services, National Institutes of Health, National Institute on Drug Abuse, Food and Drug Administration CfTP. Population Assessment of Tobacco and Health (PATH) Study [United States] Restricted-Use Files. Inter-university Consortium for Political and Social Research (ICPSR) [distributor]; 2017.
23. United States Department of Health and Human Services, National Institutes of Health. National Institute on Drug Abuse, United States Department of Health and Human Services, Food and Drug Administration. Population Assessment of Tobacco and Health (PATH) Study 2013-2017 [United States] Restricted-Use Files User Guide. ICPSR36231.: Inter-university Consortium for Political and Social Research 2017.
24. Hyland A, Ambrose BK, Conway KP, Borek N, Lambert E, Carusi C, et al. Design and methods of the Population Assessment of Tobacco and Health (PATH) study. *Tob Control*. 2017;26:371-378.
25. Strong DR, Pearson J, Ehlke S, Kirchner T, Abrams D, Taylor K, et al. Indicators of dependence for different types of tobacco product users: Descriptive findings from Wave 1 (2013-2014) of the Population Assessment of Tobacco and Health (PATH) study. *Drug Alcohol Depend.* 2017;178:257-266.
26. Honaker J, King G, Blackwell M. Amelia II: A program for missing data. 2011;45(7):47.
27. Mitra R, Reiter JP. A comparison of two methods of estimating propensity scores after multiple imputation. *Stat Methods Med Res.* 2016;25(1):188-204.
28. Meng X-L, Rubin DB. Performing Likelihood Ratio Tests with Multiply-Imputed Data Sets. *Biometrika.* 1992;79(1):103-11..
29. Austin PC, Grootendorst P, Anderson GM. A comparison of the ability of different propensity score models to balance measured variables between treated and untreated subjects: a Monte Carlo study. *Stat Med.* 2007;26(4):734-53.
30. King G, Tomz M, Wittenberg J. Making the most of statistical analyses: Improving interpretation and presentation. *Am J Polit Sci.* 2000;44(2):347-61.
31. Selya AS, Dierker LC, Rose JS, Hedeker D, Mermelstein RJ. The role of nicotine dependence in e-Cigarettes' potential for smoking reduction. *Nicotine Tob Res*. 2017. https://doi.org/10.1093/ntr/ntx160
32. Berry KM, Reynolds LM, Collins JM, Siegel MB, Fetterman JL, Hamburg NM, et al. E-cigarette initiation and associated changes in smoking cessation and reduction: the Population Assessment of Tobacco and Health Study, 2013–2015. *Tob Control.* 2018. doi: 10.1136/tobaccocontrol-2017-054108.
33. Gilpin EA, Pierce JP, Farkas AJ. Duration of smoking abstinence and success in quitting. *J Natl Cancer Inst.* 1997;89:572-6.

34. Austin PC. An Introduction to Propensity Score Methods for Reducing the Effects of Confounding in Observational Studies. *Multivariate Behav Res.* 2011;46(3):399-424.
35. Hancock E. Tobacco behemoth Philip Morris just launched a cigarette 'alternative' — but it is far from problem-free. *Business Insider Nordic.* 2016. https://www.businessinsider.in/Tobacco-behemoth-Philip-Morris-just-launched-a-cigarette-alternative-but-it-is-far-from-problem-free/articleshow/55712051.cms
36. Yao XI, Wang X, Speicher PJ, Hwang ES, Cheng P, Harpole DH, et al. Reporting and guidelines in propensity score analysis: A systematic review of cancer and cancer surgical studies. *J Natl Cancer Inst.* 2017;109(8).

Table 1. Use of Cessation Aids and Persistent Abstinence at Wave 2 of PATH Study by Baseline Characteristics in Quit Attempters: United States, 2013-2015

			Products Used to Aid Quit Attempt				Wave 2 ≥30 Day Abstinence	
Wave 1 Characteristics			ENDS	Varenicline	Buproprion	NRT	Cigarettes Only	All Tobacco
	N	% (SE)	% (SE)	% (SE)	% (SE)	% (SE)	% (SE)	% (SE)
Total	3093	100	25.2 (0.9)	5.7 (0.5)	3.1 (0.3)	18.7 (0.7)	15.5 (0.8)	9.6 (0.6)
Sociodemographics								
Age								
18–34 years	1518	43.5 (0.9)	28.3 (1.4)	2.1 (0.4)	1.4 (0.3)	10.3 (0.9)	16.8 (1.1)	9.7 (0.9)
≥35 years	1575	56.5 (0.9)	22.8 (1.1)	8.4 (0.8)	4.4 (0.6)	25.1 (1.4)	14.6 (1.1)	9.5 (0.9)
Sex								
Male	1510	53.0 (1.0)	22.3 (1.4)	4.8 (0.6)	2.1 (0.4)	16.9 (1.2)	15.6 (1.0)	8.5 (0.7)
Female	1583	47.0 (1.0)	28.5 (1.2)	6.7 (0.7)	4.2 (0.5)	20.7 (1.2)	15.4 (1.0)	10.7 (0.8)
Education								
<College Grad	2743	88.5 (0.7)	24.5 (1.0)	5.6 (0.5)	2.9 (0.3)	18.4 (0.9)	14.9 (0.8)	8.9 (0.6)
College Grad	331	11.5 (0.7)	31.8 (2.7)	5.6 (1.4)	4.1 (1.2)	18.2 (2.6)	20.0 (2.3)	14.0 (1.9)
Race								
Non-White	1097	32.0 (1.0)	15.1 (1.3)	2.9 (0.7)	2.2 (0.5)	14.3 (1.3)	14.3 (1.2)	10.5 (1.0)
White	1996	68.0 (1.0)	30.0 (1.2)	7.0 (0.6)	3.5 (0.4)	20.7 (1.1)	16.1 (0.9)	9.2 (0.7)
Nicotine Dependence Variables								
Cigarettes Per Day (cigs/day)								
0–9 cigs/day	1285	41.3 (1.3)	22.2 (1.4)	3.2 (0.7)	3.0 (0.6)	11.8 (1.1)	19.1 (1.2)	12.1 (1.0)
10–20 cigs/day	1560	51.2 (1.5)	27.7 (1.3)	7.4 (0.7)	3.2 (0.5)	23.0 (1.3)	12.8 (1.0)	7.8 (0.8)
>20 cigs/day	199	7.3 (0.5)	29.7 (3.5)	8.7 (2.3)	2.6 (1.2)	28.7 (3.7)	11.5 (2.3)	6.3 (1.7)
Frequency								
Some Days	739	24.0 (0.9)	21.0 (1.9)	2.2 (0.7)	3.4 (0.7)	11.4 (1.3)	12.9 (0.8)	7.5 (0.6)
Every Day	2354	76.0 (0.9)	26.5 (1.0)	6.8 (0.6)	3.0 (0.4)	21.0 (1.1)	24.0 (1.8)	16.3 (1.6)
Tobacco Dependence (0 to 100)								
0–33.3	742	23.6 (0.8)	14.9 (1.4)	1.7 (0.5)	2.0 (0.5)	8.8 (1.1)	24.1 (1.7)	17.9 (1.5)
33.4–66.7	1251	40.5 (1.1)	25.2 (1.5)	6.6 (0.7)	3.1 (0.6)	19.2 (1.3)	13.8 (1.1)	7.7 (0.9)
66.8–100	1100	35.9 (1.0)	32.0 (1.5)	7.3 (1.0)	3.8 (0.7)	24.5 (1.5)	11.9 (1.0)	6.3 (0.8)
Quitting History Prior to Wave 1								
No Previous Y Quit	1235	40.9 (1.2)	23.8 (1.1)	5.2 (0.7)	3.0 (0.5)	17.0 (1.2)	18.0 (1.2)	10.9 (0.9)
<30 day Quit Attempt	1398	44.3 (1.1)	26.4 (1.5)	5.2 (0.8)	3.4 (0.5)	20.0 (1.3)	11.6 (1.1)	7.1 (0.8)
≥30 day Quit Attempt	460	14.8 (0.7)	25.5 (2.3)	5.4 (1.4)	2.5 (0.9)	19.2 (2.5)	20.7 (2.2)	13.2 (2.0)
Wave 1 E-cigarette Use								
Every Day	127	4.3 (0.5)	73.6 (4.1)	4.4 (1.9)	5.1 (2.1)	14.7 (3.3)	18.0 (3.7)	4.2 (2.0)
Some Days	629	19.6 (0.8)	38.2 (2.2)	6.7 (1.1)	3.8 (0.8)	19.0 (1.7)	15.4 (0.9)	10.4 (0.7)
Not at All	2337	76.1 (0.9)	19.1 (0.9)	5.5 (0.6)	2.8 (0.3)	18.8 (1.0)	15.6 (1.8)	7.7 (1.3)
Exposure to Smokers								
0 hours/week	275	9.8 (0.6)	16.8 (2.6)	9.0 (2.7)	4.9 (1.3)	19.2 (3.2)	18.6 (2.9)	12.5 (2.2)
1–10 hours/week	1707	55.1 (1.0)	23.9 (1.1)	5.5 (0.7)	2.9 (0.4)	18.4 (1.2)	16.8 (1.1)	9.7 (0.8)
≥10 hours/week	1068	33.6 (1.0)	30.0 (1.7)	5.1 (0.7)	2.9 (0.5)	19.0 (1.4)	12.8 (1.1)	8.6 (0.9)
Smoke-Free Home								
No	1322	42.0 (1.1)	26.4 (1.3)	5.8 (0.8)	3.2 (0.5)	21.6 (1.3)	12.1 (0.9)	6.9 (0.7)
Yes	1761	58.0 (1.1)	24.2 (1.3)	5.4 (0.6)	3.0 (0.5)	16.4 (1.0)	18.1 (1.0	11.5 (0.9)

Abbreviations: ENDS, electronic nicotine delivery systems; NRT, Nicotine Replacement Therapy; SE, standard error.

Table 2. Tobacco Use Status at Wave 2 of PATH Study by Cessation Method Used, Including ENDS[a] use at Wave 1, United States, 2013-2015

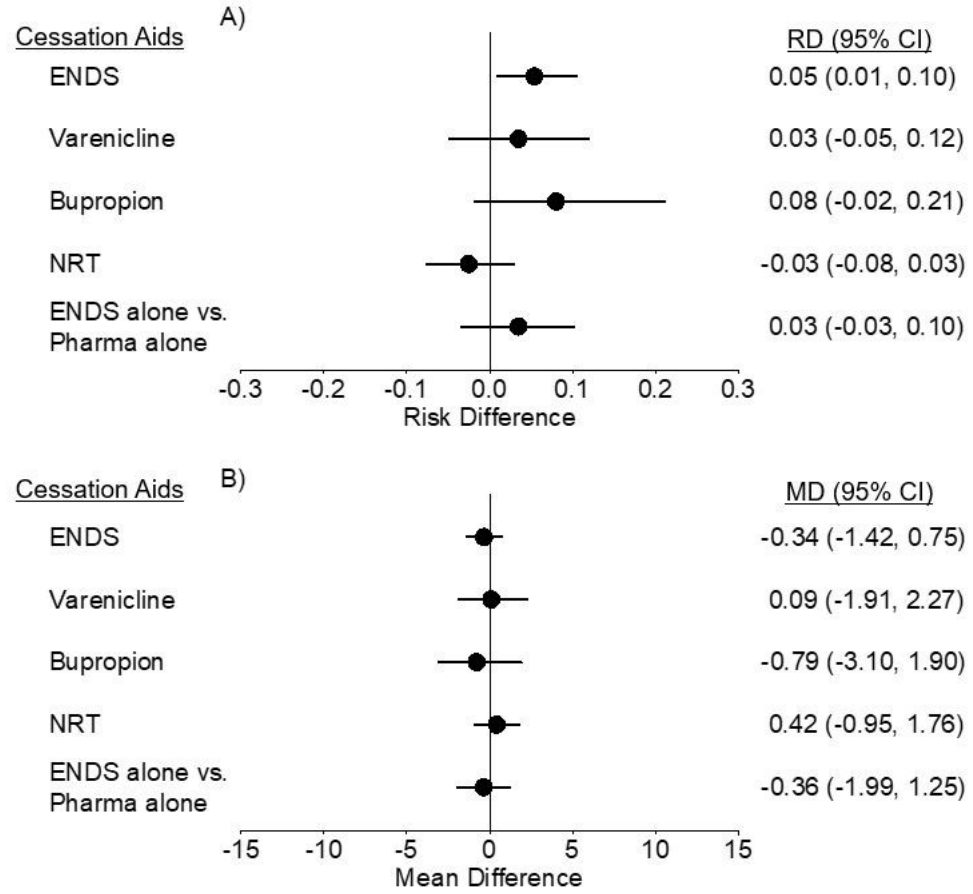
Tobacco Use Status at Wave 2	Cessation Aid Used in Last Quit Attempt[b]						Total (*n* = 3,093)	
	ENDS W1 users (*n* = 200)	ENDS not at W1 (*n* = 569)	NRT (*n* = 533)	Varenicline (*n* = 156)	Buproprion (*n* = 92)	No Aid Used (*n* = 1,820)		
	% (SE)	% (SE)	% (SE)	% (SE)	% (SE)	% (SE)	N	% (SE)
Persistent Abstinence of all Tobacco								
	5.6 (1.7)	3.7 (0.8)	6.1 (1.1)	10.2 (2.8)	10.3 (2.9)	12.5 (0.9)	283	9.6 (0.6)
Persistent Abstinence of Cigarettes Only								
ENDS User	13.9 (2.7)	12.6 (1.8)	3.2 (0.9)	3.1 (1.2)	10.7 (3.8)	1.6 (0.3)	133	4.4 (0.5)
Other User	0.0 (0.0)	0.6 (0.4)	1.2 (0.5)	0.7 (0.5)	0.0 (0.0)	2.2 (0.5)	49	1.6 (0.3)
Cigarette <30 day Abstinence								
Cigarettes Only	0.5 (0.5)	0.6 (0.3)	3.8 (1.0)	2.5 (1.3)	6.0 (3.0)	3.0 (0.5)	80	2.7 (0.3)
Cigarettes+ ENDs	4.2 (1.5)	5.1 (1.1)	1.2 (0.5)	0.0 (0.0)	1.8 (1.9)	0.7 (0.3)	48	1.6 (0.3)
Cigarettes + Other	0.0 (0.0)	0.3 (0.2)	0.4 (0.3)	1.3 (0.9)	2.0 (1.4)	1.2 (0.3)	28	0.9 (0.2)
Cigarette Relapser								
Cigarette Only	10.5 (2.4)	21.7 (1.8)	52.5 (2.3)	53.5 (4.8)	41.5 (7.0)	476 (1.4)	1274	42.3 (1.1)
Cigarette + ENDS	60.7 (4.6)	50.6 (2.6)	20.9 (1.7)	23.8 (3.7)	20.1 (4.8)	13.3 (0.9)	748	23.4 (1.0)
Cigarette + Other	4.6 (1.7)	4.9 (0.9)	10.8 (1.4)	5.0 (2.4)	7.6 (2.6)	17.8 (1.0)	450	13.6 (0.7)

Abbreviations: CI, Confidence Interval; ENDS, electronic nicotine delivery systems; NRT, Nicotine Replacement Therapy;
SE, Standard Error; W1, Wave 1 of PATH Study; W2, Wave 2 of PATH Study.

[a] ENDS users may also use other (non-cigarette) tobacco products.

[b] Cessation Aid Used in Last Quit Attempt, % (SE): ENDS W1 Users, 6.6% (0.5); ENDS not at Wave 1, 18.7% (0.7);
NRT, 18.7% (0.9); Varenicline, 5.7% (0.5); Buproprion, 3.1% (0.3); No Aid Used, 57.3 % (1.0).

Figure 1.



Dot plots illustrating for each cessation aid **A)** the difference in the probability of remaining abstinent from cigarette smoking for at least 30 days and **B)** the difference in cigarette consumption among smokers[a] who had relapsed to using cigarettes in the PATH Study, United States, 2013-14, 2014-15.

[a] Cigarette consumption assessed only among smokers who had relapsed to using cigarettes.

Abbreviations: CI, Confidence Interval; ENDS, Electronic Nicotine Delivery System; ENDS alone, Using ENDS, but not varenicline, bupropion or NRT; MD, median difference; NRT, Nicotine Replacement Therapy; Pharma alone, using either varenicline, bupropion or NRT, but not ENDS; RD, risk difference.