

Sex differences in tobacco use, attempts to quit smoking, and cessation among dual users of cigarettes and e-cigarettes: Longitudinal findings from the US Population

Assessment of Tobacco and Health Study

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ABSTRACT (250/250 words)

Significance: A growing number of adults use more than one tobacco product, with dual use of cigarettes and e-cigarettes being the most common combination. Monitoring sex disparities in tobacco use is a public health priority. However, little is known regarding whether dual users differ by sex.

Methods: Data came from Waves 4-6 (12/2016-11/2021) of the Population Assessment of Tobacco and Health Study, a US nationally-representative longitudinal survey. This analysis included current adult dual users of cigarettes and e-cigarettes. We used weighted generalized estimating equations to assess the association between sex and (1) making a cigarette quit attempt (n=1,882 observations from n=1,526 individuals) and (2) smoking cessation (n=2,081 observations from n=1,688 individuals) across two wave pairs, adjusting for age, education, ethnicity, time-to-first cigarette after waking, and e-cigarette use frequency.

Results: Among US dual users, 14.1% (95% **Confidence Intervals [CI]**=11.9-16.4) of females and 23.4% (20.0-26.9) of males were young adults (aged 18-24), 11.7% (9.2-14.2) of females and 14.4% (11.6-17.2) of males had <high school education, and 82.2% (79.4-84.5) of females and 78.7% (75.1-82.4) of males were white. Overall, 44.9% (41.6-48.1) of females compared with 37.4% (33.5-41.3) of males made an attempt to quit smoking between a baseline and follow-up wave (**Adjusted Risk Ratio [ARR]**=1.23, 1.05-1.45). In contrast, there were no apparent differences between females (22.1%, 19.0-25.2) and males (24.3%, 21.5-27.1) in smoking cessation (ARR=1.06, 0.84-1.35).

Conclusion: US females who dual use e-cigarettes and cigarettes were more likely to attempt to quit smoking, but not more likely to succeed at quitting, than males.

Keywords: Cigarette Smoking; E-Cigarette; Electronic Nicotine Delivery Systems; Dual Use; Smoking Cessation; Quit Attempt; Nicotine Dependence; Sex Differences; Cohort Studies

Introduction

Monitoring sex differences in behavioral health is a public health priority and important for addressing disparities in the United States (US) (National Institutes of Health, 2019; The White House, 2024). Sex disparities in cigarette smoking are well-documented and have led to two US Surgeon General's Reports dedicated to smoking among women (Centers for Disease Control and Prevention, 2002; US Office on Smoking, 1980). Though the prevalence of cigarette smoking remains higher among men (Cornelius et al., 2022), the decline in smoking over time is slower among women, leading to increases in the proportion of remaining smokers who are women (Higgins et al., 2015; Warren et al., 2006). Further, women who smoke are less likely to achieve long term abstinence than men (Smith et al., 2016). Sex differences may be influenced, at least in part, by the rise of tobacco marketing campaigns targeting women (Brown-Johnson et al., 2014) as well as differences in the effects of nicotine. Women metabolize nicotine more rapidly than men (Benowitz et al., 2006), appear to find nicotine *per se* less rewarding, and appear more affected by non-nicotine factors (Perkins, 2009; Perkins and Karelitz, 2016; Sofuoglu and Mooney, 2009). Collectively, these factors may contribute to the overall lower rate of smoking cessation among women compared to men who smoke cigarettes.

Though cigarette smoking remains the most preventable cause of premature death in the US (US Department of Health and Human Services, 2014), the tobacco landscape is shifting, with a rapidly growing number of adults using multiple tobacco products (Taylor et al., 2020). Dual use of cigarettes and e-cigarettes is the most common combination of tobacco products (Rubenstein, Pacek and McClernon, 2022). Though not without risk, the potential harm from e-cigarettes is substantively less than cigarettes (Balfour et al., 2021; National Academies of Sciences, Engineering, and Medicine, 2018). Randomized clinical trials (RCTs) demonstrate that e-cigarettes can be used to quit smoking (Hartmann-Boyce et al., 2022). Population-based cohort studies suggest that, compared to no e-cigarette use, daily e-cigarette use is associated

with greater smoking cessation while non-daily e-cigarette use is associated with decreased smoking cessation (Wang, Bhadriraju and Glantz, 2021). Importantly, while completely switching from cigarettes to e-cigarettes greatly reduces harm (Warner, 2018), continued smoking among dual users, even at low levels, represents a perpetuation of the immense health harm related to combusted tobacco use (Holt et al., 2023; Smith et al., 2021). Thus, dual use has the potential to reduce harm (by promoting smoking cessation) or perpetuate harm (by promoting continued smoking), with the critical difference between the two likely dependent upon how the tobacco products are used. However, little is known regarding whether or how sex is associated with differences in the dual use of cigarettes and e-cigarettes and subsequent smoking cessation (Coleman et al., 2022).

With regard to e-cigarette use, prior research indicates US women compared to men are less likely to have tried (Lee and Oh, 2019) or regularly use (Boakye et al., 2022) e-cigarettes. Further, women appear to prefer sweet flavored e-cigarettes (Dawkins et al., 2013) and report different reasons for use, including for mood management and weight-control (Piñeiro et al., 2016). Importantly, one analysis of Waves 1-2 of the Population Assessment of Tobacco and Health (PATH) Study identified that while women were overall less likely to quit smoking than men, e-cigarette use did not impact women's ability to achieve smoking cessation or the likelihood of returning to smoking (Verplaetse et al., 2019). A separate cross-sectional analysis found US women were more likely to report using e-cigarettes to try to quit smoking than men, but men who used e-cigarettes were more likely to be former smokers (Abrams, Kalousova and Fleischer, 2020).

The aims of this study were to first describe sex differences in the demographic and tobacco use characteristics of dual users, and second, to examine sex differences in cigarette quit attempts and smoking cessation among dual users using longitudinal US nationally representative data from the PATH Study.

Methodology

Data are from the PATH Study, a nationally representative **longitudinal cohort** survey of the civilian non-institutionalized US **population**, collected in Wave 4 (W4; December 2016 to January 2018), Wave 5 (December 2018 to November 2019), and Wave 6 (March 2021 to November 2021). We used Waves 4, 5, and 6 because data were collected after the introduction of nicotine salt e-cigarettes (e.g., Juul and Vuse) in the US (Romberg et al., 2019), which differ substantially from older e-cigarette generations (Leventhal et al., 2021). The PATH Study was approved by the Westat IRB (Hyland et al., 2017). The study methods and data are publicly available (Piesse et al., 2021; Tourangeau et al., 2019). Briefly, the starting sample for this study includes adults (n=33,822; ≥ 18 years) at the time of the Wave 4 survey; a probability replenished cohort of adults accounting for aging of Wave 1 participants and sample attrition. Participants who were ≥ 18 years old in any wave were included, which allowed individuals who were not 18 in an earlier wave to “age in” to the sample. This analysis (described in detail below) tested outcomes across two wave pairs (Wave 4-Wave 5 and Wave 5-Wave 6), with the former Wave in each pair serving as baseline for the latter. The protocol for this analysis was pre-registered on Open Science Framework (Klemperer and Kock, 2024).

Measures

Sample-Defining Measures

For this study, the analytic sample was restricted to adults (≥ 18 years) who participated in all three waves and who, at a baseline wave, reported current regular dual use of cigarettes and e-cigarettes (n=1,738). Current regular cigarette smoking was defined as ever having smoked ≥ 100 lifetime cigarettes and currently smoke cigarettes every day or some days. Current regular e-cigarette use was defined as ever having used e-cigarettes (including use of vape pens, personal vaporizers and mods, e-cigars, e-pipes, e-hookahs, and hookah pens) fairly regularly, and currently uses e-cigarettes every day or some days (Hyland et al., 2017).

Baseline Characteristics

Cigarette and e-cigarette dependence. The PATH Study assessed cigarette and e-cigarette dependence using the Tobacco Dependence Index and the E-cigarette Dependence Index (sTable 1), respectively, which are well-validated measures (Strong et al., 2020; Strong et al., 2022; Strong et al., 2017) that each use 16 questions from previously validated dependence measures (American Psychiatric Association, 2013; Shiffman et al., 2004; Smith et al., 2010). Additionally, participants were asked how soon they smoke their first cigarette and first use their e-cigarette after waking, which are important dependence indicators with good predictive validity (Fagerstrom, 2003; Piper et al., 2020).

Frequency of cigarette and e-cigarette use. Respondents were asked whether they currently smoke cigarettes daily or non-daily and whether they currently use e-cigarettes daily or non-daily and were categorized as daily vs non-daily users of each product. Additionally, respondents were categorized according to Borland and colleagues' (2019) recommended dual use categories: dual daily user (i.e., uses both cigarettes and e-cigarettes daily), predominant smoker (i.e., smokes cigarettes daily and uses e-cigarettes non-daily), predominant vaper (i.e., smokes cigarettes non-daily and uses e-cigarettes daily), or dual non-daily user (i.e., uses both cigarettes and e-cigarettes non-daily).

E-cigarette flavors. Respondents were asked to identify the e-cigarette flavor(s) most regularly or last used, including tobacco; menthol or mint; clove or spice; fruit; chocolate; an alcoholic drink; a non-alcoholic drink; candy, desserts, other sweets; or other.

E-cigarette device type. Respondents were asked to identify whether the e-cigarette they most often use is a refillable tank, prefilled cartridge, a mod system, disposable, or something else. E-cigarette device types were reported at Wave 5 only.

Reasons for e-cigarette use. Respondents were asked to confirm (yes or no) whether they used electronic nicotine products for each of the following reasons: they are affordable;

they might be less harmful to me than smoking cigarettes; they come in flavors I like; they help people quit smoking cigarettes; they don't smell; they feel like smoking a regular cigarette; they are more acceptable to non-tobacco users; they might be less harmful to people around me than cigarettes; I can use them at times or in places where smoking cigarettes is not allowed; as a way of cutting down on my cigarette smoking. In addition, at Wave 5 only, respondents were asked to confirm (yes or no) whether they used electronic nicotine products as a way to quit smoking.

Sex. Respondents were asked "What is your sex?" with response options Male or Female.

Sociodemographic covariates. Age (time-varying categorical variable: 18-24, 25-34, 35-44, 45-54, 55-64, ≥ 65), race/ethnicity (time invariant categorical variable: **non-Hispanic** white alone, **non-Hispanic** black alone, other) and education (time varying categorical variable: < High School, GED, High School Graduate, Some college/associates degree, Bachelor's or advanced degree) were included as sociodemographic covariates.

Outcomes

Cigarette quit attempt. Respondents were classified as having made a quit attempt if, at follow-up, they either reported making an attempt to quit smoking cigarettes in the past 12 months, or they reported that they are not smoking cigarettes at all (versus not having made an attempt to quit smoking in the past 12 months).

Smoking cessation. **Smoking cessation** refers to the proportion of respondents who achieved cigarette abstinence among all included respondents. Specifically, using the predefined PATH variable for former established cigarette smoking, respondents who, at a follow-up wave, reported that they have not smoked cigarettes within the past 12 months or currently do not smoke them at all were classified as having quit smoking.

Recent quit success. Recent quit success refers to the proportion of respondents who achieved cigarette abstinence among respondents who attempted to quit smoking in the past 12 months. Specifically, respondents who reported making a quit attempt (as defined above) were classified as having quit if they reported that they currently do not smoke cigarettes at all.

Analysis

Weighted percentages and 95% confidence intervals (CIs) were computed for baseline wave demographic and tobacco use characteristics as well as for cigarette quit attempts and cessation overall and according to sex. The prevalence estimates were weighted using the recommended Wave 6 all-waves weight (and 100 replicate weights) for the Wave 4 cohort, which addresses issues of attrition and non-response and permits estimation of characteristics across the three waves of data between Wave 4 to Wave 6 (Hyland et al., 2017; Piesse et al., 2021; US Department of Health and Human Services, 2023).

Generalized estimating equation (GEE) poisson regression models were used to assess the association between sex as a time-invariant explanatory variable and the time-varying outcomes of 1) having made a cigarette quit attempt between a baseline and follow-up wave and 2) complete smoking cessation at a follow-up wave, using variables constructed across Waves 4-5 and Waves 5-6. Importantly, unlike standard regression methods, GEE accounts for within-participant correlation (Hanley et al., 2003) which is inherent in the PATH Study's longitudinal design. We conducted both unadjusted univariate models as well as models adjusting for age, race/ethnicity, and educational attainment values at the baseline wave of each wave pair. Additionally, adjusted models included baseline tobacco use characteristics (time to first cigarette and e-cigarette use frequency) as time-varying covariates. Analyses were weighted using the PATH study Wave 6 all-waves weight for the Wave 4 cohort to provide nationally representative estimates. All analyses were computed in R using the PATH study recommended balance replication method, with Fay's adjustment set to 0.3.

A sensitivity analysis exploring the outcome of **recent** quit success (i.e., the percent of those who made a quit attempt that achieved smoking cessation) was also conducted using the same model structure as indicated above for the analysis of complete cessation.

Results

Baseline demographic characteristics

Based on 2,142 observations from 1,738 adults across Waves 4 to 6, US adult dual users were overall less likely to be female (46.1%, 95% **Confidence Interval [CI]**=43.4, 48.8) than male (53.9%, 95% CI=51.2, 56.6). The majority of dual users were white (80.3%, 95% CI=77.9, 82.7) and 37.5% (95% CI=35.2, 39.7) had some college education, with no **significant** differences by sex (Table 1). However, compared with males, a lower proportion of female dual users were young adults aged 18 to 24 (females: 14.1%, 95% CI=11.9, 16.4; males: 23.4%, 95% CI=20.0, 26.9), and a greater proportion of female dual users were widowed, divorced or separated (females: 32%, 95% CI=28.8, 36.5; males: 17.5%, 95% CI=14.8, 20.2), and lesbian, gay or bisexual (females: 21.6%, 95% CI=17.6, 25.6; males: 11.2%, 95% CI=6.9, 15.5). Finally, compared with males, a lower proportion of females were Hispanic (females: 8.2%, 95% CI=6.4, 10.0; males: 14.1%, 95% CI=11.3, 7.0).

Baseline cigarette and e-cigarette characteristics

Female dual users reported significantly greater cigarette dependence than males (female mean Tobacco Dependence Index=2.89 (SD=1.17); male mean=2.59 (SD=1.15); $p<.001$; Table 2). Similarly, more females reported smoking their first cigarette of the day within 30 minutes of waking compared to males (females: 60.5%, 95% CI=57.1, 63.8; males: 54.1%, 95% CI=50.0, 58.3; $p<0.05$). There were no apparent sex differences in e-cigarette dependence. There were significant differences in combined cigarette and e-cigarette use frequencies ($p<0.001$; Table 2). Specifically, the prevalence of predominant smoking (i.e., use cigarettes daily and e-cigarettes non-daily) was higher among females (54.2%, 95% CI=50.6,

57.9) than males (47.1%, 95% CI=43.4, 50.8) while the prevalence of predominant vaping (i.e., use cigarettes non-daily and e-cigarettes daily) was lower among females (13.2%, 95% CI=10.6, 15.8) than males (20.0%, 95% CI=16.5, 23.5).

There were no significant sex differences in e-cigarette flavor (sTable 2) or device type (sTable 3) most often used. With regard to flavor, fruit flavored e-cigarettes were the most popular (33.6%, 95% CI=30.8, 36.4) followed by tobacco (22.3%, 95% CI=19.4, 25.2), menthol or mint (21.6%, 95% CI=18.7, 24.5), and candy, desserts or other sweets (17.3%, 95% CI=15.0, 19.6). With regard to device type, refillable tank e-cigarettes were the most popular device type (49.6%, 95% CI=46.3, 52.8) followed by prefilled cartridges (26.7%, 95% CI=23.6, 29.8), mod systems (13.7%, 95% CI=11.3, 16.1), disposables (8.8%, 95% CI=6.9, 10.8), and some other device (1.2%, 95% CI=0.5, 1.9). Of note, mod systems appeared to be used less often among females (10.3%, 95% CI=7.4, 13.2) than males (16.5%, 95% CI=12.9, 20.0), though confidence intervals were overlapping.

The most common reasons for using e-cigarettes were because *they might be less harmful to people around me than cigarettes* (79.8%, 95% CI=77.3, 82.4), *can use them at times or in places where smoking cigarettes is not allowed* (78.4%, 95% CI=76.2, 80.5), and *they come in flavors I like* (78.0%, 95% CI=75.8, 80.2), with no significant differences by sex (sTable 2). However, compared to males, females were more likely to endorse using e-cigarettes because *they are more acceptable to non-tobacco users* (females=73.9%, 95% CI=70.8, 77.0; males=69.1, 95% CI=65.4, 72.7; p<0.05), *they don't smell* (females=71.9%, 95% CI=68.8, 75.0; males=65.0%, 95% CI=61.2, 68.8; p<0.01), and *they are affordable* (females=61.9%, 95% CI=58.5, 65.2; males=57.0%, 95% CI=53.4, 60.6; p<0.05). Of note, the majority of dual users reported using e-cigarettes *as a way of cutting down on my cigarette smoking* (69.1, 95% CI=66.6, 71.7; sTable 2) and *as a way to quit smoking cigarettes* (59.7%, 95% CI=56.4, 63.0; sTable 3), with no differences by sex.

Cigarette Quit Attempts and Smoking Cessation

After adjusting for demographic and tobacco use characteristics, female dual users were significantly more likely to **have made a cigarette quit attempt** than males (Females=44.9%, 95% CI=41.6, 48.1; Males=37.4%, 95% CI=33.5, 41.3; **Adjusted Risk Ratio [ARR]=1.23, 95% CI=1.05, 1.45**; Tables 3 and 4). **Age was a significant covariate in our fully adjusted model**, such that respondents aged 35-44 were less likely to make a cigarette quit attempt than those aged 18-24 (Table 4). There were no apparent sex differences in the likelihood of achieving smoking cessation (Females=22.1%, 95% CI=19.0, 25.2; Males=24.3%, 95% CI=21.5, 27.1; ARR=1.06, 95% CI=0.84, 1.35). **Age was also significant covariate**, such that respondents aged 25 or older were less likely to achieve smoking cessation than those aged 18-24. Additionally, smoking within 30 minutes of waking was associated with decreased smoking cessation while daily e-cigarette use was associated with increased smoking cessation (Table 4). A sensitivity analysis exploring **recent** quit success (i.e., the percent of those who made a quit attempt that achieved smoking cessation) yielded similar results (sTable 4).

Rates of cigarette quit attempts, smoking cessation, and recent quit success by sex were **explored separately by wave pair** in Supplemental Table 5. There were no apparent sex differences in the likelihood of a cigarette quit attempt between Waves 4 to 5, but females were significantly more likely than males to attempt to quit between Waves 5 to 6 (females=44.7%, 95% CI=40.6, 48.9; males=36.2%, 95% CI=31.0, 41.4; $p=0.011$). In contrast, between Waves 4 to 5, females were significantly less likely than males to have achieved smoking cessation (females=15.8%, 95% CI=12.0, 19.6; males=21.8%, 95% CI=18.5, 25.1; $p=0.011$) or recent quit success (females=22.7%, 95% CI=17.1, 28.3; males=35.4%, 95% CI=28.5, 42.3; $p=0.003$), though there were no apparent sex differences for either outcome between Waves 5 to 6.

Discussion

To our knowledge this longitudinal analysis is the first to explore sex differences in demographics, use characteristics, cigarette quit attempts, and smoking cessation among dual users of cigarettes and e-cigarettes in a US nationally representative sample. Overall, we found that more US adult dual users are male than female. There were a number of important sex differences including that, compared to males, female dual users were older, more likely to be non-Hispanic, and more likely to identify as lesbian, gay or bisexual. With regard to tobacco use characteristics, females were more dependent on cigarettes, more likely to predominantly smoke cigarettes, less likely to predominantly vape e-cigarettes, and more likely to use e-cigarettes for reasons related to social acceptability, smell and affordability. Perhaps most important, female dual users were more likely to attempt to quit, but no more likely to achieve, smoking cessation compared to males. **Of note, our exploratory analyses indicate variability in findings between the two included wave pairs, suggesting a need for future research to explore time trends by sex when more PATH Waves which reflect use patterns after the rise of nicotine salt e-cigarettes (Romberg et al, 2019; Leventhal et al., 2023) become available.**

In addition to **describing cessation outcomes at the population level, sex differences in demographic and tobacco use characteristics identified in this analysis could help to inform ongoing efforts to develop smoking cessation treatment for adult dual users.** A number of characteristics we found to be associated with being a female dual user have been shown to predict decreased **access to or effectiveness of** tobacco treatment in prior research among people who exclusively smoke cigarettes, including older age (Messer et al., 2008; **Steinberg et al., 2006**) and greater cigarette dependence (Fagerstrom, 2003). Female dual users were also more likely to identify as belonging to a sexual minority group, which experience disproportionately **more** barriers to tobacco treatment in the US (Wheldon and Wiseman, 2021). Further, our findings that females were more likely to try to quit but no more likely to achieve smoking cessation than males suggest overall more failed cigarette quit attempts among female

dual users and indicate a need to address sex differences with interventions to improve quit success among female dual users. Combined, findings from this analysis demonstrate the importance of developing treatment for dual users with these differences in mind to ensure equity in efficacy and access across sexes. Finally, despite finding no significant sex differences in overall smoking cessation, our finding that female dual users were more likely to predominantly smoke and less likely to predominantly vape is concerning and warrants further investigation given that meta-analyses demonstrate predominant vaping is associated with increased smoking cessation while predominant smoking is associated with decreased smoking cessation (Wang, Bhadriraju and Glantz, 2021).

The US Food and Drug Administration (FDA)-proposed nicotine-limiting standard for cigarettes (US Food and Drug Administration, 2022) is a policy intervention that has the potential to improve cigarette quit success among all dual users, despite the sex differences identified in this analysis. Prior randomized controlled trials (RCTs) of a nicotine-limiting standard for cigarettes demonstrate that switching to very low nicotine content cigarettes reduces smoking, decreases nicotine dependence, and increases cigarette abstinence among adults who exclusively smoke cigarettes (Donny et al., 2015; Higgins et al., 2020; Klemperer et al., 2022). However, compared to exclusive smokers, dual users may be particularly responsive to the effects of a national nicotine limiting standard for cigarettes given that they already have experience with e-cigarettes, which, though not without risk, most experts agree are substantially less harmful than cigarettes (Balfour et al., 2021; National Academies of Sciences, Engineering, and Medicine, 2018). Dual users who are not able to quit nicotine altogether may be more likely to completely switch from cigarettes to e-cigarettes if a nicotine limiting standard for cigarettes is imposed. For female dual users in particular, a nicotine limiting standard for cigarettes could help to surmount their higher cigarette dependence relative to males identified

in this analysis. As such, future research is needed to experimentally test very low nicotine content cigarettes among dual users and examine effects separately by sex.

Limitations

This analysis was limited to exploring female versus male sex differences, but there is a need to examine differences in dual use according to gender, including transgender and non-binary individuals. **Time between PATH Waves varied (11 months between Waves 4 to 5 vs 15 months between Waves 5 to 6) which may have influenced findings.** The e-cigarette market in the US is changing rapidly and thus there is a need to continue monitoring sex differences in e-cigarette use characteristics that may have developed after Wave 6 data collection for the PATH Study was completed in November 2021. Finally, consistent with prior research (Borland et al., 2019), we categorized cigarette and e-cigarette use frequency as daily or non-daily use of each. However, patterns of dual use are likely dynamic and far more complex, including differences in use within a given day. Future research is needed to explore sex differences in more nuanced patterns of dual use and clinical implications.

Conclusions

This analysis identified a number of important sex differences in demographic characteristics, tobacco use characteristics, and attempts to quit smoking among US adult dual users. Combined, key tobacco use findings indicate that female dual users are more cigarette dependent, less likely to use their e-cigarette daily, and, though more likely to attempt, no more likely to succeed at quitting cigarette smoking compared to males. These nationally representative findings underscore the importance of ongoing surveillance of sex differences and provide support for the development of treatment and policy interventions that account for differences between female and male dual users.

Declaration of Interests: The authors have nothing to disclose.

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Table 1: Demographic characteristics of dual users overall and according to sex in a baseline wave.

| Characteristic | Overall (n _{obs} =2,142) Weighted % (95% CI) | Female (n _{obs} =1,099) Weighted % (95% CI) | Male (n _{obs} =1,043) Weighted % (95% CI) | Test statistic |
|-------------------------------|---|--|--|--------------------------------------|
| Age | | | | |
| 18-24 | 19.2 (17.2-21.2) | 14.1 (11.9-16.4) | 23.4 (20.0-26.9) | |
| 25-34 | 30.7 (28.1-33.3) | 25.9 (22.7-29.0) | 34.9 (30.7-39.0) | |
| 35-44 | 20.7 (18.5-22.9) | 21.0 (17.9-24.1) | 20.6 (17.0-24.0) | |
| 45-54 | 16.0 (13.5-18.5) | 20.2 (16.3-24.0) | 12.5 (9.4-15.6) | X ² (5)=101.6, p<0.001 |
| 55-64 | 9.3 (7.8-10.7) | 12.6 (10.1-15.0) | 6.4 (4.5-8.3) | |
| 65+ | 4.1 (2.8-5.4) | 6.3 (3.9-8.8) | 2.2 (1.0-3.4) | |
| Marital Status | | | | |
| Married | 28.4 (25.9-30.9) | 28.9 (25.4-32.5) | 27.9 (24.6-31.3) | |
| Widowed, divorced, separated | 24.5 (19.5-20.8) | 32.7 (28.8-36.5) | 17.5 (14.8-10.2) | X ² (2)=79.8, p<0.001 |
| Never married | 47.1 (44.3-49.9) | 38.4 (34.5-42.3) | 54.5 (50.8-58.3) | |
| Education level | | | | |
| <High School | 13.2 (11.2-15.1) | 11.7 (9.2-14.2) | 14.4 (11.6-17.2) | |
| GED | 10.4 (8.7-12.2) | 9.2 (6.8-11.6) | 11.5 (9.2-13.7) | |
| High School Graduate | 27.5 (25.2-29.7) | 26.4 (23.4-29.6) | 28.2 (24.8-31.6) | |
| Some college/associate degree | 37.4 (35.2-39.7) | 40.7 (37.5-44.0) | 34.7 (31.2-38.2) | X ² (4)=8.0, p=0.50 |
| Bachelors/advanced degree | 11.5 (9.8-13.2) | 11.8 (9.7-13.9) | 11.2 (8.9-13.6) | |
| Race | | | | |
| White alone | 80.3 (77.9-82.7) | 82.2 (79.4-84.5) | 78.7 (75.1-82.4) | |
| Black alone | 10.4 (8.8-12.1) | 10.5 (8.1-12.8) | 10.4 (8.0-12.9) | X ² (2)=8.1, p=0.09 |
| Other | 9.3 (7.5-11.1) | 7.3 (5.4-9.2) | 10.9 (8.1-13.6) | |
| Hispanic origin | | | | |
| Hispanic | 11.4 (9.5-13.3) | 8.2 (6.4-10.0) | 14.1 (11.3-17.0) | X ² (1)=18.7, p<0.001 |
| Non-Hispanic | 88.6 (86.7-90.5) | 91.8 (90.0-93.6) | 85.9 (83.0-88.7) | |
| Sexual Orientation | | | | |
| Lesbian, Gay, Bisexual, Other | 16.0 (13.0-19.1) | 21.6 (17.6-25.6) | 11.2 (6.9-15.5) | X ² (1)=42.7, p<0.001 |
| Heterosexual | 84.0 (80.9-87.0) | 78.4 (74.4-82.4) | 88.8 (84.5-93.1) | |

Note: Number of observations (n_{obs}) are not weighted. Sample is weighted using the Wave 6 all-waves weight for the Wave 4 cohort.

Table 2. Dependence characteristics of dual users overall and according to sex in a baseline wave.

| Characteristic | Overall (n _{obs} =2,142) Weighted % (95% CI) | Female (n _{obs} =1,099) Weighted % (95% CI) | Male (n _{obs} =1,043) Weighted % (95% CI) | Test statistics t=3.6(df=98), p<0.001 |
|---|--|---|---|---|
| | | | | |
| Cigarette dependence | | | | |
| Tobacco Dependence Index, mean (SD) | 2.73 (1.17) | 2.89 (1.17) | 2.59 (1.15) | |
| First cigarette after waking | | | | |
| ≤ 30 minutes, % | 57.0 (54.4-59.7) | 60.5 (57.1-63.8) | 54.1 (50.0-58.3) | |
| > 30 minutes, % | 43.0 (40.3-45.6) | 39.5 (36.2-42.9) | 45.9 (41.7-50.0) | $\chi^2(1)=5.2$, p<0.05 |
| E-cigarette dependence | | | | |
| E-cigarette Dependence Index, mean (SD) | 1.78 (0.93) | 1.75 (0.95) | 1.81 (0.92) | t=-0.9(df=98), p=0.4 |
| First e-cigarette after waking | | | | |
| ≤ 30 minutes | 43.3 (40.9-45.8) | 44.8 (41.0-48.5) | 42.1 (38.5-45.6) | |
| > 30 minutes | 56.7 (54.2-59.1) | 55.2 (51.5-59.0) | 57.9 (54.4-61.5) | $\chi^2(1)=1.6$, p=0.3 |
| Use frequency | | | | |
| Dual daily user | 12.3 (10.3-14.2) | 14.0 (11.2-16.7) | 10.8 (8.2-13.4) | |
| Predominant smoker | 50.4 (47.6-53.1) | 54.2 (50.6-57.9) | 47.1 (43.4-50.8) | $\chi^2(3)=27.4$, p<0.001 |
| Predominant vaper | 16.8 (14.6-19.1) | 13.2 (10.6-15.8) | 20.0 (16.5-23.5) | |
| Dual non-daily user | 20.5 (18.2-22.8) | 18.6 (15.7-21.5) | 22.1 (18.8-25.3) | |

Note: Number of observations (n_{obs}) are not weighted. Sample is weighted using the Wave 6 all-waves weight for the Wave 4 cohort. Tobacco Dependence Index range: 1=least to 5=most dependent. Use frequency definitions: Dual daily user=uses both cigarettes and e-cigarettes daily; Predominant smoker=Uses cigarettes daily and e-cigarettes non-daily; Predominant vaper=uses e-cigarettes daily and cigarettes non-daily; Dual non-daily user=uses both cigarettes and e-cigarettes non-daily.

Table 3: Unadjusted associations between making a cigarette quit attempt and smoking cessation between a baseline and follow-up wave and sex, among those who were dual using in a baseline wave.

| Sex | Cigarette Quit Attempt | | Smoking Cessation | |
|------------|-------------------------------|-------------------------------|--------------------------|-------------------------------|
| | % (95% CI) | Unadjusted RR (95% CI) | % (95% CI) | Unadjusted RR (95% CI) |
| Male (ref) | 37.4 (33.5-41.3) | 1.00 | 24.3 (21.5-27.1) | 1.00 |
| Female | 44.9 (41.6-48.1) | 1.19 (1.01-1.40) | 22.1 (19.0-25.2) | 0.91 (0.72-1.13) |

Note:

Percentages reflect *overall* quit attempts or quit success among respondents between any baseline and follow-up wave.

Percentages and models are computed using the Wave 6 all-waves weight for the Wave 4 cohort.

Number of observations in quit attempt model: n=1,930

Number of observations in smoking cessation model: n=2,142

Table 4: Full model output for adjusted associations between making a cigarette quit attempt and smoking cessation between a baseline and follow-up wave and sex, among those who were dual using in a baseline wave.

| Sex | Cigarette Quit Attempt Adjusted RR (95% CI) | Smoking Cessation Adjusted RR (95% CI) |
|-------------------------------------|--|---|
| Male (ref) | 1.00 | 1.00 |
| Female | 1.23 (1.05-1.45) | 1.06 (0.84-1.35) |
| Age | | |
| 18-24 | 1.00 | 1.00 |
| 25-34 | 0.83 (0.65-1.07) | 0.70 (0.52-0.95) |
| 35-44 | 0.68 (0.49-0.94) | 0.44 (0.27-0.71) |
| 45-54 | 0.72 (0.51-1.03) | 0.41 (0.24-0.70) |
| 55-64 | 0.69 (0.47-1.00) | 0.44 (0.24-0.79) |
| 65+ | 0.86 (0.45-1.64) | 0.55 (0.19-1.63) |
| Education | | |
| <High School | 1.00 | 1.00 |
| GED | 0.67 (0.43-1.04) | 1.12 (0.58-2.15) |
| High School graduate | 0.85 (0.62-1.17) | 1.32 (0.80-2.18) |
| Some college/associate degree | 1.09 (0.85-1.40) | 1.85 (1.15-2.97) |
| Bachelors/advanced degree | 1.16 (0.82-1.63) | 2.46 (1.40-4.32) |
| Race/ethnicity | | |
| White alone | 1.00 | 1.00 |
| Black alone | 1.05 (0.78-1.41) | 1.13 (0.76-1.69) |
| Other | 1.17 (0.91-1.51) | 0.88 (0.58-1.33) |
| First cigarette after waking | | |
| More than 30 minutes | 1.00 | 1.00 |
| Within 30 minutes | 0.96 (0.81-1.12) | 0.64 (0.47-0.88) |
| E-cigarette use frequency | | |
| Some days | 1.00 | 1.00 |
| Every day | 1.19 (0.99-1.44) | 1.64 (1.29-2.09) |

Note: Models are weighted using the Wave 6 all-waves weight for the Wave 4 cohort.

Number of observations in quit attempt model: n=1,894

Number of observations in smoking cessation model: n=2,081

References

- Abrams, L.R., Kalousova, L., Fleischer, N.L., 2020. Gender differences in relationships between sociodemographic factors and e-cigarette use with smoking cessation: 2014–15 current population survey tobacco use supplement. *J. of Public Health* 42:e42-e50.
- American Psychiatric Association, 2013. *Diagnostic and Statistical Manual of Mental Disorders*, 5th ed. American Psychiatric Association, Washington.
- Balfour, D.J., Benowitz, N.L., Colby, S.M., Hatsukami, D.K., Lando, H.A., Leischow, S.J., Lerman, C., Mermelstein, R.J., Niaura, R., Perkins, K.A., 2021. Balancing Consideration of the Risks and Benefits of E-Cigarettes. *Am. J. Public Health*:e1-e12.
- Benowitz, N.L., Lessov-Schlaggar, C.N., Swan, G.E., Jacob III, P., 2006. Female sex and oral contraceptive use accelerate nicotine metabolism. *Clin. Pharm. Therap.* 79:480-88.
- Boakye, E., Osuji, N., Erhabor, J., Obisesan, O., Osei, A.D., Mirbolouk, M., Stokes, A.C., Dzaye, O., El Shahawy, O., et al., 2022. Assessment of Patterns in e-Cigarette Use Among Adults in the US, 2017-2020. *JAMA Netw. Open* 5:e2223266-e66.
- Borland, R., Murray, K., Gravely, S., Fong, G.T., Thompson, M.E., McNeill, A., O'Connor, R.J., Goniewicz, M.L., Yong, H.H., et al., 2019. A new classification system for describing concurrent use of nicotine vaping products alongside cigarettes (so-called 'dual use'): findings from the ITC-4 Country Smoking and Vaping wave 1 Survey. *Addiction* (Abingdon, England) 114 Suppl 1:24-34.
- Brown-Johnson, C.G., England, L.J., Glantz, S.A., Ling, P.M., 2014. Tobacco industry marketing to low socioeconomic status women in the USA. *Tob. Control* 23:e139-e46.
- Centers for Disease Control and Prevention, 2002. Women and smoking: a report of the Surgeon General. Executive summary. *MMWR Recomm Rep* 51:i-iv; 1-13.
- Coleman, S.R., Piper, M.E., Byron, M.J., Bold, K.W., 2022. Dual Use of Combustible Cigarettes and E-cigarettes: a Narrative Review of Current Evidence. *Curr. Addict. Rep.*:1-10.
- Cornelius, M.E., Loretan, C.G., Wang, T.W., Jamal, A., Homa, D.M., 2022. Tobacco Product Use Among Adults - United States, 2020. *MMWR Morb Mortal Wkly Rep* 71:397-405.
- Dawkins, L., Turner, J., Roberts, A., Soar, K., 2013. 'Vaping' profiles and preferences: an online survey of electronic cigarette users. *Addiction* (Abingdon, England) 108:1115-25.
- Donny, E.C., Denlinger, R.L., Tidey, J.W., Koopmeiners, J.S., Benowitz, N.L., Vandrey, R.G., al'Absi, M., Carmella, S.G., Cinciripini, P.M., et al., 2015. Randomized Trial of Reduced-Nicotine Standards for Cigarettes. *NEJM* 373:1340-9.
- Fagerstrom, K.-O., 2003. Time to first cigarette; the best single indicator of tobacco dependence? *Monaldi Arch Chest Dis* 59:95-98.
- Hanley, J.A., Negassa, A., Edwardes, M.D.D., Forrester, J.E., 2003. Statistical analysis of correlated data using generalized estimating equations: An orientation. *Am J Epidemiol* 157(4):364-375. doi:10.1093/aje/kwf215
- Hartmann-Boyce, J., Lindson, N., Butler, A.R., McRobbie, H., Bullen, C., Begh, R., Theodoulou, A., Notley, C., Rigotti, N.A., Turner, T., 2022. Electronic cigarettes for smoking cessation. *Cochrane Database of Systematic Reviews*.
- Higgins, S.T., Kurti, A.N., Redner, R., White, T.J., Gaalema, D.E., Roberts, M.E., Doogan, N.J., Tidey, J.W., Miller, M.E., et al., 2015. A literature review on prevalence of gender differences and

- intersections with other vulnerabilities to tobacco use in the United States, 2004-2014. *Prev. Med.*
- Higgins, S.T., Tidey, J.W., Sigmon, S.C., Heil, S.H., Gaalema, D.E., Lee, D., Hughes, J.R., Villanti, A.C., Bunn, J.Y., et al., 2020. Changes in Cigarette Consumption With Reduced Nicotine Content Cigarettes Among Smokers With Psychiatric Conditions or Socioeconomic Disadvantage: 3 Randomized Clinical Trials. *JAMA Netw Open* 3:e2019311.
- Holt, N.M., Shiffman, S., Black, R.A., Goldenson, N.I., Sembower, M.A., Oldham, M.J., 2023. Comparison of biomarkers of exposure among US adult smokers, users of electronic nicotine delivery systems, dual users and nonusers, 2018–2019. *Scientific Reports* 13:7297.
- Hyland, A., Ambrose, B.K., Conway, K.P., Borek, N., Lambert, E., Carus, C., Taylor, K., Crosse, S., Fong, G.T., Cummings, K.M., 2017. Design and methods of the Population Assessment of Tobacco and Health (PATH) Study. *Tob. Control* 26:371-78.
- Klemperer, E., Kock, L., 2024. Sex differences in dual cigarette and e-cigarette use and smoking cessation in the United States: longitudinal analyses. *Open Science Framework*. DOI: 10.17605/OSF.IO/F6K4W https://osf.io/f6k4w?mode=&revisionId=&view_only=
- Klemperer, E.M., Luo, X., Jensen, J., Al'Absi, M., Cinciripini, P.M., Robinson, J.D., Drobis, D.J., McClernon, J., Strasser, A.A., Strayer, L.G., 2022. Smoking abstinence and cessation-related outcomes one month after an immediate versus gradual reduction in nicotine content of cigarettes. *Prev. Med.* 165:107175.
- Lee, J., Oh, M., 2019. The moderating effect of gender on the association between E-cigarette use and smoking status: A cross-sectional study. *Addict. Behav.* 93:108-14.
- Leventhal, A.M., Madden, D.R., Peraza, N., Schiff, S.J., Lebovitz, L., Whitted, L., Barrington-Trimis, J., Mason, T.B., Anderson, M.K. and Tackett, A.P., 2021. Effect of exposure to e-cigarettes with salt vs free-base nicotine on the appeal and sensory experience of vaping: a randomized clinical trial. *JAMA Netw Open*, 4(1), pp.e2032757-e2032757.
- Messer, K., Trinidad, D.R., Al-Delaimy, W.K., Pierce, J.P., 2008. Smoking cessation rates in the United States: a comparison of young adult and older smokers. *Am. J. Public Health*. 98:317-22.
- National Academies of Sciences, Engineering, and Medicine, 2018. Public health consequences of e-cigarettes. National Academies Press. <https://nap.nationalacademies.org/catalog/24952/public-health-consequences-of-e-cigarettes>
- National Institutes of Health, 2019. Advancing science for the health of women: The Trans-NIH strategic plan for women's health research. <https://orwh.od.nih.gov/about/trans-nih-strategic-plan-womens-health-research>
- Perkins, K.A., 2009. Acute responses to nicotine and smoking: implications for prevention and treatment of smoking in lower SES women. *Drug Alcohol Depend.* 104:S79-S86.
- Perkins, K.A., Karelitz, J.L., 2016. Potential sex differences in the pattern of sensory reinforcers enhanced by nicotine. *Exp. Clin. Psychopharmacol.* 24:156-61.
- Piesse, A., Opsomer, J., Dohrmann, S., DiGaetano, R., Morganstein, D., Taylor, K., Carus, C., Hyland, A., 2021. Longitudinal Uses of the Population Assessment of Tobacco and Health Study. *Tob. Regul. Sci.* 7:3-16.
- Piñeiro, B., Correa, J.B., Simmons, V.N., Harrell, P.T., Menzie, N.S., Unrod, M., Meltzer, L.R., Brandon, T.H., 2016. Gender differences in use and expectancies of e-cigarettes: Online survey results. *Addict. Behav.* 52:91-97.

- Piper, M.E., Baker, T.B., Benowitz, N.L., Smith, S.S., Jorenby, D.E., 2020. E-cigarette Dependence Measures in Dual Users: Reliability and Relations With Dependence Criteria and E-cigarette Cessation. *Nicotine Tob. Res.* 22:756-63.
- Romberg, A.R., Lo, E.J.M., Cuccia, A.F., Willett, J.G., Xiao, H., Hair, E.C., Vallone, D.M., Marynak, K. and King, B.A., 2019. Patterns of nicotine concentrations in electronic cigarettes sold in the United States, 2013-2018. *Drug Alcohol Depend.* 203, pp.1-7.
- Rubenstein, D., Pacek, L.R., McClernon, F.J., 2022. Multiple Tobacco Product Use Conceptual Framework: A 2021 Update on Evidence. *Nicotine Tob. Res.*
- Shiffman, S., Waters, A.J., Hickcox, M. 2004. The nicotine dependence syndrome scale: a multidimensional measure of nicotine dependence. *Nicotine Tob. Res.* 2004 Apr 1;6(2):327-48.
- Smith, D.M., Christensen, C., Van Bemmel, D., Borek, N., Ambrose, B., Erives, G., Niaura, R., Edwards, K.C., Stanton, C.A., Blount, B.C., 2021. Exposure to nicotine and toxicants among dual users of tobacco cigarettes and e-cigarettes: Population Assessment of Tobacco and Health (PATH) study, 2013–2014. *Nicotine Tob. Res.* 23:790-97.
- Smith, P.H., Bessette, A.J., Weinberger, A.H., Sheffer, C.E., McKee, S.A., 2016. Sex/gender differences in smoking cessation: a review. *Prev. Med.* 92:135-40.
- Smith, S., Piper, M., Bolt, D., Fiore, M., Wetter, D., Cinciripini, P., Baker, T., 2010. Development of the Brief Wisconsin Inventory of Smoking Dependence Motives. *Nicotine Tob. Res.* 12:489-99.
- Sofuoglu, M., Mooney, M., 2009. Subjective responses to intravenous nicotine: greater sensitivity in women than in men. *Exp. Clin. Psychopharmacol.* 17:63-9.
- Steinberg, M.B., Akincigil, A., Delnevo, C.D., Crystal, S., Carson, J.L., 2006. Gender and age disparities for smoking-cessation treatment. *Am. J. Prev. Med.* 30(5):405-12.
- Strong, D.R., Leas, E., Noble, M., White, M., Frissell, K.C., Glasser, A., Katz, L., Taylor, K., Compton, W.M., Conway, K.P., 2020. Predictive validity of the adult tobacco dependence index: Findings from waves 1 and 2 of the Population Assessment of Tobacco and Health (PATH) study. *Drug Alcohol Depend.* 214:108134.
- Strong, D.R., Leas, E., Noble, M., White, M., Glasser, A., Taylor, K., Edwards, K.C., Frissell, K.C., Compton, W.M., Conway, K.P., 2022. Validation of the wave 1 and wave 2 Population Assessment of Tobacco and Health (PATH) study indicators of tobacco dependence using biomarkers of nicotine exposure across tobacco products. *Nicotine Tob. Res.* 24:10-19.
- Strong, D.R., Pearson, J., Ehlke, S., Kirchner, T., Abrams, D., Taylor, K., Compton, W.M., Conway, K.P., Lambert, E., Green, V.R., 2017. 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.* 178:257-66.
- Taylor, K.A., Sharma, E., Edwards, K.C., Halenar, M.J., Kissin, W., Kasza, K.A., Day, H., Anic, G., Gardner, L.D., et al., 2020. Longitudinal pathways of exclusive and polytobacco cigarette use among youth, young adults and adults in the USA: findings from the PATH Study Waves 1–3 (2013–2016). *Tob. Control.* 29:s139-s46.
- Tourangeau, R., Yan, T., Sun, H., Hyland, A., Stanton, C.A., 2019. Population Assessment of Tobacco and Health (PATH) reliability and validity study: selected reliability and validity estimates. *Tob. Control.* 28:663-68.
- The White House, 2024. Executive Order on Advancing Women's Health Research and Innovation. <https://www.whitehouse.gov/briefing-room/presidential-actions/2024/03/18/executive-order-on-advancing-womens-health-research-and-innovation/>

US Department of Health and Human Services, 2014. The health consequences of smoking—50 years of progress: A report of the surgeon general. Atlanta, GA: US Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health 17.

US Department of Health and Human Services, 2023. National Institutes of Health. National Institute on Drug Abuse, and United States Department of Health and Human Services. Food and Drug Administration. Center for Tobacco Products. Population Assessment of Tobacco and Health (PATH) Study [United States] Public-Use Files. Inter-university Consortium for Political and Social Research [distributor], 2023-12-15. <https://doi.org/10.3886/ICPSR36498.v19>

US Food and Drug Administration, 2022. FDA News Release: FDA announces plans for proposed rule to reduce addictiveness of cigarettes and other combusted tobacco products.

US Office on Smoking, 1980. The health consequences of smoking for women: A report of the surgeon general. US Department of Health and Human Services, Public Health Service, Office of the Assistant Secretary for Health, Office on Smoking and Health.

Verplaetse, T.L., Moore, K.E., Pittman, B.P., Roberts, W., Oberleitner, L.M., Peltier, M.K.R., Hacker, R., Cosgrove, K.P., McKee, S.A., 2019. Intersection of e-cigarette use and gender on transitions in cigarette smoking status: findings across waves 1 and 2 of the population assessment of tobacco and health study. *Nicotine Tob. Res.* 21:1423-28.

Wang, R.J., Bhadiraju, S., Glantz, S.A., 2021. E-cigarette use and adult cigarette smoking cessation: a meta-analysis. *Am. J. Public Health* 111:230-46.

Warner, K.E., 2018. How to Think—Not Feel—about Tobacco Harm Reduction. *Nicotine Tob. Res.* 21:1299-309.

Warren, C.W., Jones, N.R., Eriksen, M.P., Asma, S., 2006. Patterns of global tobacco use in young people and implications for future chronic disease burden in adults. *The Lancet*. 367:749-53.

Wheldon, C.W., Wiseman, K.P., 2021. Psychological, normative, and environmental barriers to tobacco cessation that disproportionately affect sexual minority tobacco users. *Nicotine Tob. Res.* 23:1030-37.