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Original Investigation

Exposure to Nicotine and Toxicants Among Dual Users of Tobacco Cigarettes and E-Cigarettes: Population Assessment of Tobacco and Health (PATH) Study, 2013–2014

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Abstract

Introduction: Concurrent use of tobacco cigarettes and e-cigarettes ("dual use") is common among tobacco users. Little is known about differences in demographics and toxicant exposure among subsets of dual users.

Aims and Methods: We analyzed data from adult dual users (current every/some day users of tobacco cigarettes and e-cigarettes, $n = 792$) included in the PATH Study Wave 1 (2013–2014) and provided urine samples. Samples were analyzed for biomarkers of exposure to nicotine and selected toxicants (tobacco-specific nitrosamine NNK [NNAL], lead, cadmium, naphthalene [2-naphthol], pyrene [1-hydroxypyrene], acrylonitrile [CYMA], acrolein [CEMA], and acrylamide [AAMA]). Subsets of dual users were compared on demographic, behavioral, and biomarker measures to exclusive cigarette smokers ($n = 2411$) and exclusive e-cigarette users ($n = 247$).

Results: Most dual users were *predominant cigarette smokers* (70%), followed by *daily dual users* (13%), *non-daily concurrent dual users* (10%), and *predominant vapers* (7%). Dual users who smoked daily showed significantly higher biomarker concentrations compared with those who did not smoke daily. Patterns of e-cigarette use had little effect on toxicant exposure. Dual users with high toxicant exposure were generally older, female, and smoked more cigarettes per day. Dual

users who had low levels of biomarkers of exposure were generally younger, male, and smoked non-daily.

Conclusions: In 2013–2014, most dual users smoked cigarettes daily and used e-cigarettes occasionally. Cigarette smoking appears to be the primary driver of toxicant exposure among dual users, with little-to-no effect of e-cigarette use on biomarker levels. Results reinforce the need for dual users to stop smoking tobacco cigarettes to reduce toxicant exposure.

Implications: With considerable dual use of tobacco cigarettes and e-cigarettes in the United States, it is important to understand differences in toxicant exposure among subsets of dual users, and how these differences align with user demographics. Findings suggest most dual users smoke daily and use e-cigarettes intermittently. Low exposure to toxicants was most common among younger users, males, and intermittent smokers; high exposure to toxicants was most common among older users, females, and heavier cigarette smokers. Results underscore the heterogeneity occurring within dual users, and the need to quit smoking cigarettes completely in order to reduce toxicant exposure.

Introduction

In 2013–2014, approximately 5.5% of adults in the United States were current e-cigarette users. Among them, 70% were current cigarette smokers.[1] Dual use of tobacco cigarettes and e-cigarettes ("dual use") is the most common poly-tobacco use behavior in the United States, with nearly 23% of adult multiple tobacco product users engaging in this use pattern.[1] Commonly indicated reasons for dual use include reducing health risks associated with smoking, circumventing smoke-free policies, reducing the number of cigarettes smoked per day (CPD), and as aids to quit cigarettes.[2] While dual use may represent a transitional behavior to wean smokers from tobacco cigarettes, it may also sustain continued cigarette use while substituting e-cigarettes in circumstances where smoking is prohibited.[3] Data indicate that for most dual users, concurrent use of these products is a persistent behavior, or results in continued use of tobacco cigarettes alone.[4]

However, "dual use" is a broad label applied to a heterogeneous group who engage in a wide range of behaviors, including variable frequency of smoking and vaping. Recent data from an observational study identified four distinct groups of dual users based on frequency of product use: "*daily dual users*" (concurrent users who report daily use of both products), "*predominant smokers*" (those who smoke cigarettes daily but use e-cigarettes non-daily), "*predominant vapers*" (those who use e-cigarettes daily but smoke cigarettes non-daily), and "*non-daily concurrent dual users*" (those who use both cigarettes and e-cigarettes non-daily). These groups differed in nicotine dependence, attitudes toward smoking and vaping, and quit behaviors.[5] Considering these behavioral differences among dual users, other domains of study merit examination.

Although a significant proportion of dual users state that their primary reason for using e-cigarettes is to reduce harm from smoking tobacco cigarettes,[2] at aggregate, studies have shown that dual users tend to exhibit similar levels of exposure to nicotine and toxicants when compared with exclusive cigarette smokers.[6,7] However, different patterns of dual use (ie, *daily dual users*, *predominant smokers*, *predominant vapers*, *non-daily concurrent dual users*)[5] may result in differing levels of exposure to nicotine and toxicants.[6] In a small international study of daily dual users, those who smoked fewer than five CPD exhibited lower levels of exposure to nicotine and toxicants when compared with daily dual users who smoked 10 CPD or more.[8] Many biomarker studies employ small samples recruited using convenience-driven methods.[7–12] It is important to examine the frequency and quantity of smoking and e-cigarette use among a nationally representative sample of dual users to better characterize tobacco-related exposures, and to understand the potential public health benefits and harms of e-cigarette use and dual use.[4]

Using data from Wave 1 (2013–14) of the Population Assessment of Tobacco and Health (PATH) Study, we performed an analysis of dual users addressing two aims. First, we sought to characterize dual users based on their demographic, behavioral, and biomarker levels, with a focus on their frequency and intensity of smoking. Then, we compared the degree to which these dual users were similar to, or different from, exclusive users of e-cigarettes or tobacco cigarettes in terms of their demographics, use behaviors, and exposure to tobacco-specific biomarkers.

Methods

Data Source

Data are from Wave 1 Restricted Use Files (RUF) and Biomarker Restricted-Use Files (BRUF) of the PATH Study (2013–14), a nationally representative, longitudinal cohort study designed to assess tobacco use patterns and associated health behaviors. Details on the study interview procedures, questionnaires, sampling, weighting, and data access are available at https://doi.org/10.3886/Series606.[13] At Wave 1, 32 320 adults aged 18 or older participated in the study. The weighted response rate for the household screener was 54.0%; among those who completed the adult interview, the weighted response rate for those providing a urine sample was 63.6%.[13] Among adults who provided a urine sample, a stratified probability sample of 11 522 adults were selected for laboratory analysis to ensure respondents represented diverse tobacco product use patterns, including users of multiple tobacco products and never users of any tobacco product; details are provided in the BRUF User Guide (http://doi.org/10.3886/ICPSR36840.userguide). Westat's Institutional Review Board approved the study design and data collection protocol.

Biospecimen Collection and Laboratory Procedures

Consenting participants self-collected full-void spot urine samples in 500 mL polypropylene containers at the time of their interview, or at a subsequently scheduled visit. Samples were immediately placed in

a Crēdo Cube shipper, which transported samples between 2°C and 8°C, and were shipped overnight to the PATH Study biorepository for storage and processing. Biomarkers were measured using highly selective mass spectrometric methods under a rigorous quality control/quality assurance program at the CDC Division of Laboratory Sciences.[14–25]

Analytic Sample

Our analysis built upon previous work[6] and focused on "current product users." To be included in the sample, respondents had to: (1) provide a urine sample for analysis, (2) use tobacco cigarettes and/or e-cigarettes every day or some days, (3) use no other tobacco products, and (4) use no nicotine replacement therapies within the last 3 days. The main group under study was "*dual users*" of tobacco cigarettes and e-cigarettes (n = 792), stratified into four distinct groups developed by Borland et al.[5] based on self-reported frequency of product use: daily cigarette smokers and daily e-cigarette users ("*daily dual users*," n = 90), daily cigarette smokers and non-daily e-cigarette users ("*predominant smokers*," n = 560), non-daily cigarette smokers and daily e-cigarette users ("*predominant vapers*," n = 55), and non-daily users of both products ("*non-daily concurrent dual users*," n = 87).

We compared the four subgroups of dual users to current exclusive cigarette smokers (n = 2411) and current exclusive e-cigarette users (n = 247). In addition to the criteria above, exclusive cigarette smokers and dual users had to smoke at least 100 cigarettes in their lifetime. The final analytic sample size was 3450. In calculating adjusted geometric mean (GM) values, current exclusive e-cigarette users with urinary NNAL values in excess of 14.5 pg/mg creatinine were excluded (n = 66) in order to rule out potential misclassification related to cigarette smoking status.[26]

User Characteristics and Tobacco Use Behaviors

User-related variables of interest included demographic information (age, sex, race/ethnicity, and education level) and patterns of product use (frequency, intensity, and time to first product). Frequency of use was classified according to every day or some days use of cigarettes/e-cigarettes. Cumulative monthly exposure measures indicating intensity of cigarette/e-cigarette consumption were calculated by multiplying the number of cigarettes/e-cigarettes used per day by 30 (every day product users) or by the number of days the product was used in the past 30 days (some days product users). This resulted in measures for the number of cigarettes smoked per month (CPM) and the number of e-cigarettes used per month (EPM). Time to first cigarette/e-cigarette use was also examined as an indicator of nicotine dependence. Due to missing data for EPM (23%) and time to first e-cigarette (53%), these measures were categorized to allow the missing data to be considered in modeling to minimize the extent of bias on results. Both CPM/EPM measures were categorized using quartiles, with EPM having an additional category to indicate missing information. Time to first product was classified based on categories used in the Fagerström Test for Nicotine Dependence (FTND),[27] with e-cigarette measures having an additional category to indicate missing information. Tests were performed to assess correlation between the predictors for potential collinearity issues and were determined to be within acceptable ranges.

Main Outcomes

Data for nine biomarkers of exposure selected from several classes of known tobacco constituents, including nicotine metabolites, tobacco-specific nitrosamines, metals, polycyclic aromatic hydrocarbons, and volatile organic compounds served as primary outcomes. References to analytic limits of detection have been published elsewhere.[6] Nicotine exposure was assessed using total nicotine equivalents-2, calculated as the molar sum of urinary cotinine and trans-3′-hydroxycotinine. Other biomarkers included those for tobacco-specific nitrosamine NNK (total NNAL), lead, cadmium, naphthalene (2-naphthol), pyrene (1-hydroxypyrene), acrylonitrile (CYMA), acrolein (CEMA), and acrylamide (AAMA). While CEMA is the minor metabolite of acrolein and is detected at lower concentrations relative to the major metabolite (3HPMA), CEMA holds value in measuring exogenous exposure via tobacco smoke due to greater endogenously produced levels of 3HPMA. Both markers are highly correlated with one another, self-reported tobacco smoking, and with serum cotinine concentrations measured in the US population.[28] Representative biomarkers were chosen due to their documented association with tobacco-attributable illnesses or other adverse health effects, and their ability to discriminate between cigarette and e-cigarette use. The clinical significance of these biomarkers has been described elsewhere.[6] We estimated dual users' likelihood of group membership into "*low exposure*," "*average exposure*," and "*high exposure*" groups. To create these measures, the person-weighted creatinine-adjusted biomarker distributions among dual users were split into quartiles. The lowest quartile (Q1) served as the "*low exposure*" group. The second and third quartiles (Q2 and Q3) were combined to represent "*average*" exposure. The highest quartile (Q4) represented the "*high exposure*" group.

Statistical Analysis

Data were examined using univariate and bivariate statistical procedures. We analyzed demographic and tobacco use characteristics according to dual use categories developed by Borland et al.[5] For biomarker comparisons, preliminary analyses revealed that frequency of cigarette smoking appeared to be the primary driver of toxicant exposure. Therefore, adjusted GMs were calculated for each biomarker among dual users who smoked daily (ie, *predominant smokers* and *daily dual users*) versus those who smoked non-daily (ie, *predominant vapers* and *non-daily concurrent dual users*); these were compared with adjusted GMs for exclusive e-cigarette users and exclusive cigarette smokers with similar frequency of product use. Adjusted GMs were derived using multiple linear regression using log-transformed biomarker values as outcomes, with controls for urinary creatinine, age, sex, race/ethnicity, exposure to secondhand smoke, and past 30-day cannabis use. For all biomarkers other than nicotine, GMs also adjusted for TNE-2. TNE-2 was selected as a proxy adjustment variable for intensity of product use due to its ubiquitous presence across different nicotine-containing products and its documented relation to daily nicotine intake, the number of cigarettes smoked, nicotine intake from e-cigarettes, and smoking topography (ie, the frequency, volume, and duration of individual puffing behaviors).[29–31] Post-estimation procedures were run to obtain the adjusted marginal mean values of the natural log of the biomarker of interest and their respective 95% confidence intervals for each group; these were exponentiated to produce the adjusted GM. Adjusted GMs were compared using Bonferroni-corrected pairwise contrasts following adjusted models.

Multinomial logistic regression modeling was used to characterize dual users having low (Q1), average (Q2 + Q3), and high (Q4) biomarker levels according to demographic and behavioral characteristics. Three parallel sets of models were run to

test associations: (1) among high and low dual users only (base referent category = average (Q2 + Q3) exposure dual users), (2) among all dual users compared with exclusive e-cigarette users (base referent category = exclusive e-cigarette users), and (3) among all dual users compared with exclusive cigarette smokers (base referent category = exclusive cigarette smokers). Models were adjusted for relevant variables for the tobacco product of interest, ie, dual users were compared with each other on both tobacco cigarette and e-cigarette metrics, dual users versus exclusive e-cigarette users were compared on e-cigarette metrics, and dual users versus exclusive cigarette smokers were compared on tobacco cigarette metrics. Models were adjusted for age (continuous), sex, and race/ethnicity (White, non-Hispanic; non-White, non-Hispanic; Hispanic). Covariables for tobacco use behaviors included cigarettes/e-cigarettes used per month, frequency of cigarette/e-cigarette use (every day or some days), and time to first cigarette/e-cigarette.

Analyses were completed using *svy* commands in Stata version 14.0, and were weighted using urine weights for the analyses of the PATH biomarker data.[32] Variance estimation was approached using balanced, repeated replications with Fay's adjustment set to 0.3 to enhance estimate precision. Estimates with relative standard errors greater than 30% have been flagged due to concerns of estimate stability. p values <.05 were considered statistically significant.

Results

Demographic Characteristics

Demographic characteristics for dual users, exclusive cigarette smokers, and exclusive e-cigarette users have been described elsewhere.[6] On average, all dual users tended to be similar in age to exclusive cigarette smokers and older than exclusive e-cigarette users (weighted χ^2 $F(2.91, 287.61) = 6.35$, $p = .0004$), were more likely to be female than exclusive cigarette smokers ($F(1, 99) = 9.20$, $p = .003$), identify as White compared with exclusive e-cigarette users and exclusive cigarette smokers (both $p < .05$), and were generally more well educated than exclusive cigarette smokers ($F(2.81, 278.30) = 8.80$, $p < .001$). All dual users and exclusive users were statistically similar in terms of cigarette and e-cigarette consumption.[6]

Cigarette Smoking and E-Cigarette Use Patterns Among Dual Users

The distribution of dual users according to frequency of product use was: *predominant smokers* (70%), followed by *daily dual use* (13%), *non-daily concurrent dual use* (10%), and *predominant vapers* (7%). Dual users who smoked daily (including *predominant smokers* and *daily dual users*) had similar cigarette and e-cigarette consumption to each other.[6] *Predominant smokers* smoked 16.2 CPD on average and used 1.02 e-cigarettes per day on the days they used e-cigarettes, while *daily dual users* smoked 16.0 CPD and used 1.22 e-cigarettes per day. *Predominant smokers* and *daily dual users* exhibited small-medium positive associations with their CPD and urinary TNE-2 (Spearman $\rho = 0.24$, $p < .001$), NNAL (Spearman $\rho = 0.28$, $p < .001$), cadmium (Spearman $\rho = 0.17$, $p < .001$), 2-naphthol (Spearman $\rho = 0.14$, $p = .002$), CYMA (Spearman $\rho = 0.30$, $p < .001$), and CEMA (Spearman $\rho = 0.21$, $p < .001$) concentrations. These users differed in their history of e-cigarette use, with *predominant vapers* exhibiting the greatest propensity to have used e-cigarettes the previous year (20%). *Daily dual users* and *predominant smokers* exhibited the greatest propensity for smoking daily the previous year (84% and 94%, respectively), with 69% of *predominant vapers*, and 32% of *non-daily concurrent users* smoking every day during the previous year.

Biomarkers of Exposure Among Dual Users

Figure 1 depicts the distribution of the four dual user subgroups into the low and high exposure categories for all nine biomarkers; *average exposure* dual users were omitted for presentation clarity. In general, classification into *low* and *high exposure* groups for each of the nine biomarkers followed a dose–response pattern correlated with frequency (daily/non-daily) of tobacco cigarette use.

Comparisons of adjusted GMs for dual users in contrast to exclusive e-cigarette users and exclusive cigarette smokers can be viewed in Supplementary Figure 1. GM toxicant concentrations for dual users mirrored those of exclusive cigarette smokers with the same frequency of smoking for biomarkers of exposure to NNK, naphthalene, pyrene, acrylonitrile, and acrolein. Urinary lead and cadmium were statistically equivalent across all users. Nicotine exposure was significantly greater among dual users when compared with exclusive cigarette smokers with similar smoking frequency. There were no differences in nicotine exposure between dual users who were non-daily cigarette smokers and exclusive daily e-cigarette users. Dual users who smoked non-daily had significantly greater levels of biomarkers for NNK, naphthalene, pyrene, acrylonitrile, acrolein, and acrylamide than exclusive daily e-cigarette users. With few exceptions, dual users who smoked daily exhibited greater adjusted GMs when compared with dual users who smoked non-daily.

Association Between Demographics, Patterns of Use, and Biomarker Levels

Table 1 depicts a summary of results from 27 multinomial logistic regression models comparing demographic characteristics of dual users falling into low (Q1), average (Q2 + Q3), and high (Q4) biomarker concentration groups. The full set of significant findings can be viewed in Supplementary Table 1. When comparing *low* and *high exposure* dual users to those with *average exposure* across all biomarkers, *low exposure* dual users were consistently younger, less likely to be female, tended to identify as racial/ethnic minorities (non-White, non-Hispanic, or Hispanic), tended to smoke cigarettes some days rather than every day, and were less likely to consume a greater number of CPM. By contrast, *high exposure* dual users tended to be older, female, engage in moderate EPM consumption, and smoked a high number of CPM.

Compared with exclusive e-cigarette users, *low exposure* dual users tended to be younger and used e-cigarettes some days rather than every day. *Average exposure* dual users tended to be older than exclusive e-cigarette users, were less likely to be non-White, non-Hispanic, or Hispanic rather than White, non-Hispanic, and were more likely to use e-cigarettes some days rather than every day. On average, *high exposure* dual users tended to be older than exclusive e-cigarette users, female, were less likely to be non-White, non-Hispanic, or Hispanic rather than White, non-Hispanic, and were more likely to use e-cigarettes some days rather than every day. No statistically significant differences in intensity of e-cigarette use or time to first e-cigarette were detected between dual users and exclusive e-cigarette users.

Similar findings emerged when comparing dual users to exclusive cigarette smokers. *Low exposure* dual users tended to be younger

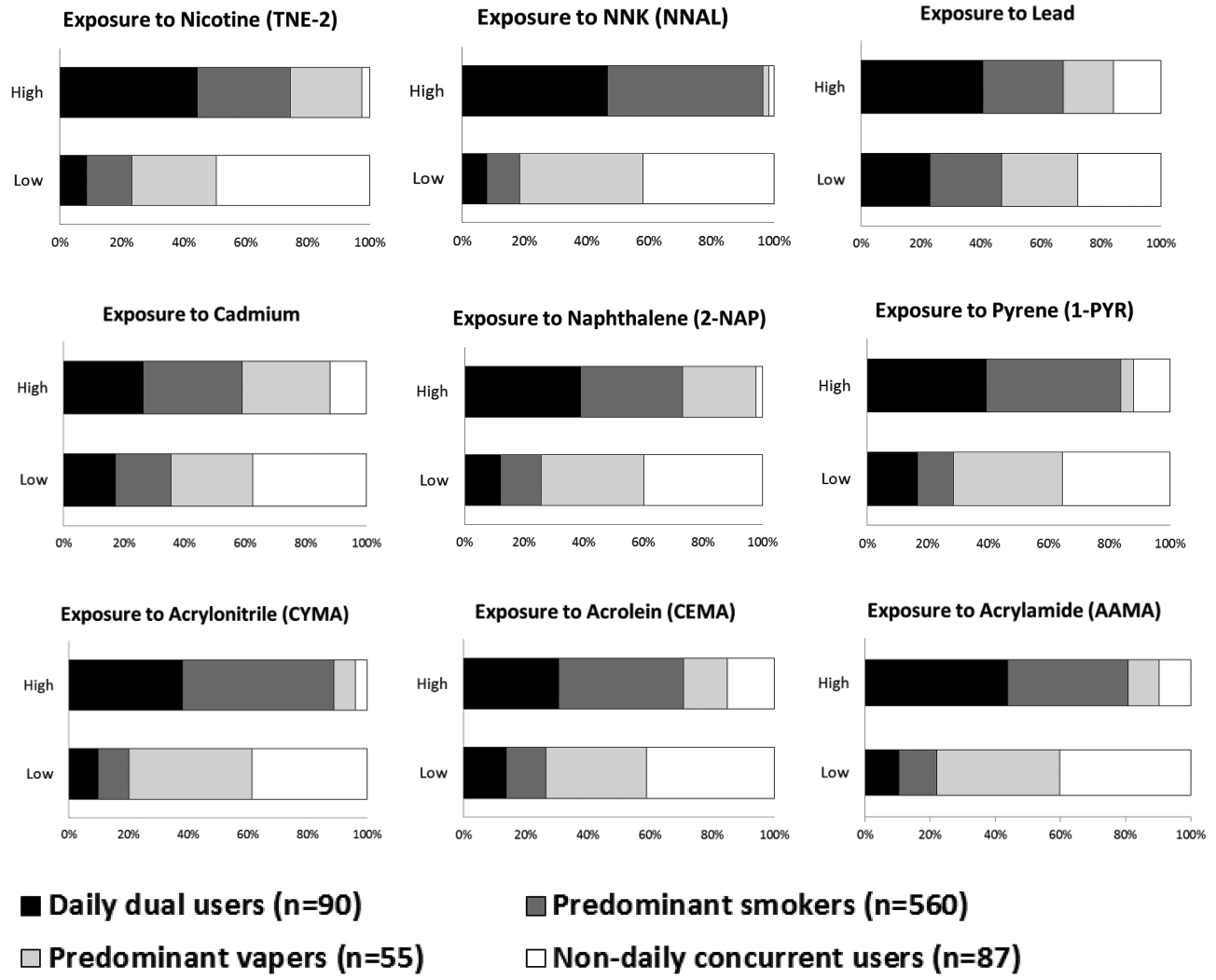

Figure 1. Weighted proportions of dual user subgroups accounting for low and high biomarker concentrations for total nicotine equivalents††, tobacco-specific nitrosamine NNK††, lead, cadmium, naphthalene, pyrene, acrylonitrile††, acrolein, and acrylamide (n = 792). ††An estimate of the precision has been made, however it and the estimated statistic may not be valid due to skewness in the data. The analytic sample size varies based on the specific biomarker (range: 761–792).

than exclusive cigarette smokers, smoke some days rather than every day, and have high levels of monthly smoking. *Average exposure* dual users tended to be less likely to identify as non-White, non-Hispanic, or Hispanic compared with exclusive cigarette smokers, were more likely to smoke some days rather than every day and were more likely to engage in moderate monthly smoking. *High exposure* dual users tended to be older than exclusive smokers, female, exhibit moderate-heavy levels of CPM, were more likely to smoke within the first hour of the day, and were more likely to smoke some days.

Discussion

This study sought to characterize differences in tobacco-related constituent exposure profiles among dual users of tobacco cigarettes and e-cigarettes, and examine how these exposures, demographic characteristics, and tobacco-related behaviors compare with those of exclusive users of either product. Our findings suggest significant variability in nicotine and toxicant exposure among dual users, with continued, frequent cigarette smoking appearing to drive greater exposure to toxicants. Dual users with high toxicant exposure tended to be older, female, exhibited behaviors related to nicotine dependence and engrained cigarette smoking behaviors (including greater quantity of monthly smoking, infrequent vaping, and compared with exclusive cigarette smokers, a shorter time to first cigarette). By contrast, compared with dual users with average or high levels of toxicant exposure, dual users with lower levels of toxicant exposure tended to be younger in age, male, and to exhibit less frequent and lower quantity product use. These findings reinforce that dual users are a diverse group, which is evidenced not simply through behaviors, but also by toxicant exposure profiles.

Taken as a whole, our findings suggest that the majority of dual users mirror exposure profiles of exclusive cigarette smokers with similar smoking frequency.[6] This reinforces findings by Borland et al. that point toward the importance of product use frequency as a marker of delineation in subsets of dual users.[5] Our findings extend on this concept to note that, at the time of data collection, frequency of cigarette smoking served as an important demarcation for toxicant exposure and select demographic characteristics. Select

Table 1. Summary of Findings From Weighted Multinomial Logistic Regression Models Comparing Demographics and Tobacco Use Behaviors Among (1) Low and High Exposure to Average Exposure Dual Users, (2) Low, Average, and High Exposure Dual Users to Exclusive E-Cigarette Users, and (3) Low, Average, and High Exposure Dual Users to Exclusive Cigarette Smokers

	"*Low Exposure*" (Q1)	"*Average exposure*" (Q2 + Q3)	"*High exposure*" (Q4)
1: *Low* and *high exposure* dual users (base referent: *average exposure* dual users)	• Younger age (8/9 biomarkers) • Less likely to engage in low level monthly cigarette smoking (6/9 biomarkers) • Less likely to be female (5/9 biomarkers) • More likely to smoke cigarettes "some days" (4/9 biomarkers) • More likely to belong to a racial/ethnic minority group (2/9 biomarkers) • More likely to use moderate EPM (1/9 biomarkers) • Less likely to smoke 6–30 min after waking (1/9 biomarkers)	Base reference category for the outcome for multinomial model series 1	• Older in age (7/9 biomarkers) • More likely to be female (6/9 biomarkers) • More likely to engage in moderate-heavy monthly cigarette smoking (6/9 biomarkers) • More likely to engage in moderate EPM (3/9 biomarkers) • More likely to be skipped out of EPM measures (2–9 biomarkers) • More likely to smoke first cigarette within first 30 min of the day (2/9 biomarkers) • Less likely to vape e-cigarettes "some days" (2/9 biomarkers) • Less likely to smoke cigarettes "some days" (1/9 biomarkers) • Less likely to have first e-cigarette within first 5 min of the day (1/9 biomarkers)
2: *Low, average, and high exposure* dual users (base referent: *exclusive e-cigarette users*)	• More likely to use an e-cigarette "some days" (9/9 biomarkers) • Younger in age (5/9 biomarkers) • Less likely to be female (1/9 biomarkers)	• Older in age (9/9 biomarkers) • Less likely to identify as racial/ethnic minority (9/9 biomarkers) • More likely to use e-cigarettes "some days" (9/9 biomarkers)	• Older in age (9/9 biomarkers) • Less likely to identify as racial/ethnic minority (8/9 biomarkers) • More likely to use e-cigarettes "some days" (8/9 biomarkers) • More likely to be female (3/9 biomarkers)
3: *Low, average, and high exposure* dual users (base referent: *exclusive cigarette smokers*)	• Younger in age (9/9 biomarkers) • More likely to smoke cigarettes "some days" (8/9 biomarkers) • Less likely to use high CPM (4/9 biomarkers) • Less likely to identify as racial/ethnic minority (3/9 biomarkers)	• Less likely to identify as a racial/ethnic minority (9/9 biomarkers) • More likely to use moderate CPM (9/9 biomarkers) • More like to smoke cigarettes "some days" (3/9 biomarkers) • More likely to be female (2/9 biomarkers)	• More likely to be female (9/9 biomarkers) • More likely to engage in moderate-heavy monthly cigarette smoking (9/9 biomarkers) • Older in age (5/9 biomarkers) • More likely to smoke cigarettes within first hour of waking (3/9 biomarkers) • More likely to smoke cigarettes "some days" (3/9 biomarkers)

CPM = cigarettes per month; EPM = e-cigarettes per month.

characteristics of low exposure dual users (ie, younger, smoked fewer tobacco cigarettes) tended to mirror those for intermittent smokers. Akin to previous calls for research related to intermittent smoking,[33] these data suggest the importance of conducting within-group assessments of dual users based on smoking frequency, as subsets of dual users with different smoking frequency likely exhibit distinct motives, quit intentions, and beliefs about their use that may correlate with exposure profiles and thus, potential negative health consequences arising from dual use.

The question of whether dual use serves as a bridge to cessation, or as a means to sustained tobacco cigarette smoking, remains important in light of increasing proliferation of e-cigarette use and popularity among current smokers. Despite the significant, public emphasis toward the unknown long-term health effects of e-cigarette use, the health effects from cigarette smoking are well documented.[34] The majority of dual users in our study continued daily cigarette smoking in combination with their e-cigarette use; as such, many dual users exhibited high levels of toxicant exposure similar to exclusive cigarette smokers. However, a small group of dual users who smoked some days exhibited lower toxicant concentrations than the majority of daily dual users, suggesting that exposure related to dual use differs by the level of cigarette smoking. It is important to communicate the need to completely quit using tobacco cigarettes to achieve any exposure reduction that e-cigarettes may provide, as even low levels of cigarette smoking introduce significant health risks to users.[33] Recent data indicate that cigarette smokers who used e-cigarettes daily had 77% increased odds of achieving smoking cessation 1–2 years later relative to cigarette smokers who did not use e-cigarettes.[35] Conversely, the odds of cigarette smoking relapse were higher among former smokers who continued to use e-cigarettes more than 1 year after quitting cigarettes.[36] The role of e-cigarettes as agents for cigarette smoking cessation warrants continued examination via longitudinal and randomized controlled trial designs, studies of contextual situations that may facilitate use of either product, and studies developing interventions to minimize negative health consequences among dual users.

Advantages of this study include use of a nationally representative sample of never, former, and current tobacco product users

from the US noninstitutionalized population to derive estimates of exposure and related demographic and behavioral correlates. The PATH Study includes detailed information related to tobacco use, including the ability to control for confounders such as secondhand smoke exposure and cannabis use. Limitations include the time period for analysis (2013–2014), which reflected widespread use of first generation e-cigarette devices among our sample, including blu, NJOY, Logic, Mistic, and eGo brand devices. These earlier generation devices had low power outputs (which have been linked to lower toxicant exposure than later generation "box mod" style products),[3] and served as inferior sources of nicotine delivery. Due to changes in the nicotine formulations (eg, nicotine salts) and power outputs used in later generation e-cigarettes, it is important to consider whether, and how, these changes may shift cigarette smoking behaviors and toxicant exposure among dual users. Further, limitations in the administration of measures to assess nicotine concentration and flavor use precluded our ability to examine these as potential contributors to toxicant exposure in this study. As the market continues to advance with newer-generation e-cigarette products (such as nicotine salt-based "pod-mod" products) and an array of e-cigarette flavors, continued surveillance of dual use patterns involving toxicant exposure, demographic characteristics, and related tobacco use behaviors will help inform whether and how the evolution of the e-cigarette market may facilitate or hinder continued dual use or cessation. Additional work examining associations between toxicant exposure profiles and other important demographic indicators (such as sexual and gender minority status) will also enhance understanding of these connections among dual users.

Further, several measured toxicant biomarkers have exposure sources other than tobacco smoke. For example, acrylamide is found in carbohydrate-rich foods that are cooked at high temperatures, as well as in tobacco smoke, which may explain observations among non-daily e-cigarette users in Supplementary Figure 1. Along these same lines, biomarkers of exposure to metals (lead and cadmium) accumulate in the body over years resulting from tobacco smoking and environmental exposures, and are slowly released in the urine over many years. Therefore, urinary metal concentrations are driven by historical exposures (most typically from previous cigarette smoking) than from current tobacco use. Full-void spot urine sample collection procedures may limit the interpretation of some biomarkers due to the absence of additional data on individual metabolism or other dietary exposures that can impact biomarker levels. Future studies may consider similar tobacco-related biomarker assessments using alternative biospecimen collection procedures (eg, overnight fasting from food and/or tobacco). Finally, there are currently no validated biomarkers specific to e-cigarette use, resulting in our analysis characterizing the presence of cigarette biomarkers in e-cigarette users and dual users. While new potential biomarkers of e-cigarette use have been proposed,[37] those constituents were not measured in this study. Despite these limitations, these data add to our understanding of the diversity of exposures that occur among dual users, and can serve as a basis for other work that is required to improve understanding of toxicant exposures this large and important group of e-cigarette users may experience.

Conclusions

Most dual users smoke cigarettes daily and use e-cigarettes occasionally. Cigarette smoking appears to be the primary driver of toxicant exposure among dual users, with little-to-no effect of e-cigarette use on biomarker levels. Exclusive e-cigarette users have lower toxicant levels than exclusive cigarette smokers. Results reinforce the need for dual users to stop smoking tobacco cigarettes to reduce toxicant exposure.

Supplementary Material

A Contributorship Form detailing each author's specific involvement with this content, as well as any supplementary data, are available online at https://academic.oup.com/ntr.

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Declaration of Interests

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