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Brief report

Dual Users Compared to Smokers: Demographics, Dependence, and Biomarkers

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Abstract

Introduction: The availability of electronic cigarettes (e-cigarettes) has profoundly changed the tobacco product landscape. In the United States, almost 6 million adults use both combustible and e-cigarettes (ie, dual users). The goal of this study was to understand how smokers and dual users differ in terms of demographics, cigarette dependence, and exposure to carcinogens.

Methods: An observational cohort (smokers, $n = 166$, ≥5 cigarettes/day for 6 months and no e-cigarette use in 3 months; dual users, $n = 256$, smoked daily for 3 months and used e-cigarettes at least once/week for the past 3 months) completed baseline assessments of demographics, tobacco use, and dependence. They also provided breath samples for carbon monoxide (CO) assay and urine samples for cotinine, 3-hydroxycotinine, and 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol (NNAL) assays.

Results: Compared to smokers, dual users (mean e-cigarette use = 5.5 days/week [SD = 1.9]) were significantly younger and more likely to be white, have more education, report a history of psychiatric co-morbidity, and smoke fewer cigarettes per day. There were no differences in CO, cotinine, or 3-hydroxycotinine levels; however, dual users had significantly lower levels of NNAL than did smokers. Most smokers and dual users had no plans to quit smoking within the next year; 91% of dual users planned to continue using e-cigarettes for at least the next year.

Conclusions: In this community sample, dual users are supplementing their smoking with e-cigarette use. Dual users, versus smokers, smoked fewer cigarettes per day and delayed their first cigarette of the day, but did not differ in quitting intentions.

Implications: This comparison of a community sample of established dual users and exclusive smokers addresses key questions of dependence and health risks of dual use in real-world settings. Dual users were more likely to be white, younger, have more than a high school education and have a psychiatric history. Dual users also smoked significantly fewer cigarettes and had lower levels of NNAL (a carcinogen), but they did not differ from exclusive smokers in CO or cotinine levels, suggesting that they supplemented their nicotine intake via e-cigarettes.

Introduction

Electronic cigarettes (e-cigarettes), developed to deliver nicotine in a manner that is satisfying but poses less harm than combustible cigarettes, have dramatically changed the landscape of tobacco use. The rapid translation of this product to the marketplace has left scientists and regulators racing to better understand a product whose popularity has increased exponentially. As of 2016, 15.4% adults in the United States had tried an e-cigarette and 3.2% currently

use them every day or some days; less than one in four who have tried e-cigarettes reported being a current user.[1] In 2014, 15.9% of current smokers were also using e-cigarettes,[2] and in 2015, 59% of e-cigarette users were also current cigarette smokers.[3] This illustrates the clear need to understand more about dual users, almost 6 million of the total 37.8 million smokers[4] who use both e-cigarettes and combustible cigarettes.

Most dual use research has been conducted with adolescents and young adults.[5–7] Given the prevalence of dual use among adult smokers, it is critical to understand more about how dual users might differ from smokers who do not use e-cigarettes (exclusive smokers). There have been analyses of national survey data,[8–10] but few studies have linked survey data with biomarkers of use to examine key questions such as: Do dual users smoke fewer cigarettes per day, replacing some cigarettes with e-cigarettes, and is this reflected in biomarkers? Do dual users have reduced health risks or reduced exposure to carcinogens? How do dual users compare to smokers on demographic characteristics[7] and behaviors and beliefs related to product use patterns and beliefs?[11]

The goal of this research was to characterize a community sample of established dual users relative to exclusive smokers with respect to demographic variables, cigarette dependence, and exposure to carcinogens. One critical question addressed by this research is whether an established pattern of dual use is related to a reduction in exposure to carcinogens (eg, tobacco-specific nitrosamines).

Methods

This longitudinal observational cohort study explores use patterns and health indices over a 2-year period. The data reported here are from the baseline assessments.

Participants were recruited from the greater Madison and Milwaukee, WI areas via television and social media (eg, Facebook) advertisements seeking adults who smoke or use e-cigarettes to participate in a study that tracks tobacco use. Interested callers completed a telephone screen, and eligible participants attended an initial study visit where they learned about the study and provided written informed consent. Participants had to be at least 18 years old, able to read and write English, have *no* plans to quit smoking and/or e-cigarette use in the next 30 days, not currently using smoking cessation medication, and not currently in treatment for psychosis or bipolar disorder. Participants also had to be either exclusive smokers (ie, smoked ≥5 cigarettes/day for the past 6 months and have not used e-cigarettes within the last 3 months) or dual users (used nicotine-containing e- cigarettes at least once a week for the past 3 months and smoked daily for the last 3 months). We initially set a minimum of 5 cigarettes/day for dual users but this created difficulty with recruitment (ie, 28% [57 of the 560] of the e-cigarette users were disqualified for smoking fewer than 5 cigarettes/day). Therefore, approximately 6 months into our 2-year recruitment we changed the dual use criteria to require that dual users merely needed to have smoked daily for the last 3 months. The requirement that participants have no plans to quit smoking was intended to increase the likelihood that the participants would engage in cigarette and/or e-cigarette use for some period of time over the 2-year course of the study.

At baseline, participants completed assessments of demographics, smoking and e-cigarette history and use patterns, beliefs about cigarettes and e-cigarettes, cigarette and e-cigarette dependence (eg, Fagerström Test for Cigarette Dependence [FTCD],[12,13] Wisconsin Inventory of Smoking Dependence Motives [WISDM][14]), and motivation to quit cigarettes and e-cigarettes. Participants also provided a breath sample for carbon monoxide assay and a urine sample for cotinine, 3-hydroxycotinine (3HC), and 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol (NNAL) assays. Cotinine is the major proximate metabolite of nicotine, and 3HC is the major metabolite of cotinine.[15] Both cotinine and the sum of cotinine+3HC have been used as biomarkers of daily nicotine intake.[16] NNAL is a metabolite of the tobacco-specific carcinogen nicotine-derived nitrosamine ketone (NNK), a cause of lung and pancreatic cancer in smokers.[17] Urine cotinine, 3HC, and NNAL were measured by liquid chromatography–mass spectrometry in the Clinical Pharmacology Laboratory at the University of California San Francisco.[18,19]

Table 1. Group Differences in Demographic Variables—*N* (%)

		Total (N = 422)	Smokers (n = 166)	Dual users (n = 256)	Group differences
Site	Madison	184 (43.6%)	66 (39.8%)	118 (46.1%)	$X^2 = 1.64$, $p = .20$
	Milwaukee	238 (56.4%)	100 (60.2%)	138 (53.9%)	
Gender	Women	197 (46.7%)	82 (49.4%)	115 (45.1%)	$X^2 = 0.75$, $p = .39$
	Men	224 (53.1%)	84 (50.6%)	140 (54.9%)	
Race	White	269 (63.7%)	88 (53.0%)	181 (71.0%)	$X^2 = 32.3$, $p < .001$
	African-American	92 (21.8%)	58 (34.9%)	34 (13.3%)	
	Multi-racial	32 (7.6%)	9 (5.4%)	23 (9.0%)	
Hispanic		23 (5.5%)	6 (3.8%)	17 (6.9%)	$X^2 = 1.79$, $p = .18$
Education	More than high school	249 (59.0%)	82 (49.4%)	167 (65.7%)	$X^2 = 11.13$, $p = .004$
	High school/GED	137 (32.5%)	67 (40.4%)	70 (27.6%)	
	Less than high school	34 (8.1%)	17 (10.2%)	17 (6.7%)	
Psychiatric history	Any history	228 (54.0%)	72 (43.4%)	156 (61.2%)	$X^2 = 12.84$, $p < .001$
	Depression	183 (43.4%)	59 (35.5%)	124 (48.4%)	$X^2 = 6.82$, $p = .01$
	Anxiety disorder	115 (27.3%)	37 (22.3%)	78 (30.5%)	$X^2 = 3.40$, $p = .07$
	ADD/ADHD	61 (14.5%)	15 (9.0%)	46 (18.0%)	$X^2 = 6.50$, $p = .01$
Lives with partner who smokes		136 (32.2%)	56 (33.9%)	80 (31.4%)	$X^2 = 0.33$, $p = .85$
Lives with partner who vapes		50 (11.8%)	2 (1.2%)	48 (18.9%)	$X^2 = 32.60$, $p < .001$
Age (Mean [SD])		40.4 (14.1)	42.6 (14.4)	39.0 (13.8)	$t = 2.60$, $p = .01$

GED = General Education Diploma; ADD = attention-deficit disorder.

The dual users and exclusive smokers were characterized with respect to demographic characteristics, smoking and/or vaping behavior and dependence, and biomarkers. Differences were analyzed using chi-square for categorical variables and *t* tests for continuous variables. Continuous variables that were not normally distributed were log transformed. Sensitivity analyses were conducted to explore whether outcome differences between the dual use and smoker groups were because of the dual use group having a lower cigarettes per day inclusion criterion or because of group differences in demographic variables. These analyses were conducted by removing participants who smoked less than 5 cigarettes/day from the analysis or by using demographic variables that differed between the two groups as covariates.

Results

We recruited 422 participants (166 exclusive smokers and 256 dual users), deliberately oversampling dual users. Slightly more than half were men (53.1%), 5.5% were Hispanic, and 32.2% lived with a partner who smokes. There were significant differences between exclusive smokers and dual users on race, education, and self-reported psychiatric history measures (Table 1). Dual users were more likely to be white, younger, have more than a high school education, report a psychiatric history (especially depression and/or attention-deficit hyperactivity disorder (ADHD)), and live with someone who used e-cigarettes.

Among the dual users, the most common type of device used was a refillable tank (65.3%), followed by replaceable cartridges (19.2%), and disposables (11.4%). The most commonly used e-liquid flavors were fruit (42.3%) and menthol (19.9%); 9% had no preference, 6.6% preferred candy flavors, and 6.6% used tobacco-flavored liquid. The preferred nicotine content in the e-liquid (listed in order of prevalence) was high nicotine (18–24 mg; 27.8%), very low nicotine (1–6 mg; 26.9%), low-to-medium nicotine (7–12 mg; 23.3%), medium-to-high nicotine (13–17 mg; 14.8%), very high nicotine (>24 mg; 4.5%), and no nicotine (2.7%). Dual users reported vaping a mean of 5.5 days/week (SD = 1.9) and 10.0 times per day (SD = 14.2), taking a mean of 2.2 (SD = 1.1) puffs per vaping occasion (range: 1–5). Almost half of dual users (48%) reported vaping within 30 minutes of waking whereas 23% did not vape in the first 2 hours after waking. The most common reasons for initiating e-cigarette use among dual users were "to reduce my smoking or smoking urges" (63%), "curiosity" (54%), "to quit smoking" (53%), "enjoyed the taste" (44%), and "for my health" (39%). It should be noted that 96% of dual users were smokers before they started vaping, seven dual users began vaping and smoking in the same year, and two dual users vaped 1–2 years before smoking. Although 69% dual users report that e-cigarettes are less satisfying than tobacco cigarettes, 91% dual users reported no plans to quit e-cigarette use within the next year.

We compared smokers and dual users on indices of dependence and smoke exposure, including biomarkers. There were no differences in age of smoking initiation, WISDM scores, expired carbon monoxide, urine cotinine, or cotinine+3HC. Nor was there a significant difference in age of initiation of vaping between the dual users and the 49% of smokers who had tried e-cigarettes. However, dual users smoked significantly fewer cigarettes, were less likely to smoke within 30 minutes of waking, had lower FTCD scores, reported

Table 2. Group Differences in Smoking, Dependence, and Biomarkers

	Smokers (*n* = 166)	Dual users (*n* = 256)	*t* test	*p* Value
Smoking behavior				
Smoking initiation age	14.5 (3.6)	13.9 (3.2)	1.56	.12
Years of daily smoking	25.6 (14.7)	22.1 (13.9)	2.45	.02
Vaping initiation age	36.7 (15.4) *n* = 82	36.1 (13.9)	–0.001	.999
Years of vaping	—	2.7 (2.3)	—	—
Motivation to quit smoking combustible cigarettes (1–10 scale with 10 = extremely)	3.33 (1.79)	3.68 (1.70)	–2.03	.04
Smoking dependence				
Cigarettes/day	15.80 (10.79)	12.50 (7.39)	3.70	<.001
Expired CO	16.73 (9.64)	16.29 (11.02)	0.42	.67
FTCD	4.81 (2.17)	4.15 (2.43)	2.89	.004
Smoke in first 30 min (*N* [%])	131 (79.4%)	171 (67.3%)	$X^2 = 7.24$	.01
WISDM PDM	4.62 (1.46)	4.37 (1.47)	1.71	.09
WISDM SDM	4.12 (1.26)	4.07 (1.19)	0.41	.69
WISMD total	47.36 (13.69)	46.01 (13.08)	1.01	.31
Smoking biomarkers				
3HC (ng/ml)	5495 (5624)	4937 (5378)	1.02	.31
Log transformed 3HC	3.49 (0.55)	3.46 (0.52)	0.65	.52
Cotinine (ng/ml)	1209 (802)	1209 (988)	–0.01	.995
Log transformed cotinine	2.97 (0.35)	2.94 (0.40)	0.69	.49
Cotinine+3HC (micro molar sum)	36.16 (33.30)	32.60 (32.02)	1.06	.29
Log transformed cotinine+3HC	1.37 (0.45)	1.33 (0.44)	0.70	.48
NNAL (pg/ml)	453.31 (410.12)	340.99 (387.86)	2.80	.01
Log transformed NNAL	2.46 (0.46)	2.23 (0.58)	4.36	<.001

Means and standard deviations are presented unless otherwise noted. CO = carbon monoxide; FTCD = Fagerstrom Test for Cigarette Dependence; 3HC = 3-hydroxycotinine; NNAL = 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol; WISDM PDM = Wisconsin Inventory of Smoking Dependence Motives Primary Dependence Motives; WISDM SDM = Wisconsin Inventory of Smoking Dependence Motives Secondary Dependence Motives.

higher motivation to quit smoking, and had lower levels of NNAL (Table 2). Cotinine, 3HC, cotinine+3HC, NNAL, and NNAL/creatinine were all non-normally distributed, but results were consistent using log-transformed values. Results for the NNAL biomarker were similar for both NNAL and NNAL/creatinine, so we only present the NNAL results. Sensitivity analyses that excluded participants who smoked fewer than 5 cigarettes/day (n = 35) did not change any demographic, cigarettes per day, or biomarker findings. However, there were no longer significant differences in FTCD score, time to first cigarette, or motivation to quit. Effects were consistent when baseline demographic variables that differed between the two groups (eg, race, education, age, and psychiatric history) were included as covariates.

Discussion

Among a community sample participating in a longitudinal observational cohort study, we found that in comparison with exclusive smokers, established dual users were more likely to be younger, have more than a high school education, be white, have a psychiatric history (ie, self-reported history of diagnosis or treatment for depression and/or ADHD), and live with someone who uses e-cigarettes. We also found that dual users, on average, were more motivated to quit smoking combustible cigarettes (mean of 3.68 of 10), smoked three fewer cigarettes per day, had a lower cigarette dependence (FTCD) score, and delayed smoking their first cigarette in the morning than exclusive smokers. However, there was no difference in motivation to quit or FTCD score between dual users and exclusive smokers when dual users smoking fewer than 5 cigarettes/day were removed from the sample in the sensitivity analyses. The change in motivation score was small (3.68–3.63), suggesting the change in significance might be a function of reduced sample size. However, the change in FTCD score was more substantial (4.47–4.15), but it could reflect the artifact of the different cigarettes per day inclusion criteria for the two groups.

Dual users' lower levels of NNAL are consistent with significantly less exposure to cigarette smoke. However, dual users did not differ from smokers in their carbon monoxide or nicotine metabolite levels. Expired carbon monoxide may not reflect daily smoke intake as it has a short half-life and is very sensitive to the time from the last cigarette. However, urine cotinine and the cotinine+3HC are strong indicators of daily nicotine intake.[16] Our results indicate that smokers and dual users take in approximately the same amount of nicotine per day, suggesting that dual users may compensate for smoking fewer cigarettes by obtaining supplemental nicotine from e-cigarettes. Another recent study found that saliva cotinine levels were similar in dual users and in exclusive e-cigarette users, suggesting a similar average desired daily level of nicotine intake among users of tobacco products that can be satisfied by any combination of conventional and e-cigarettes.[20]

The dual users used e-cigarettes at a sufficiently high frequency so that such compensation seems possible (on average, near daily use and 10 uses/day), even though the mean puffs/use event (2.2) was low compared to other survey studies of dual users.[11,21] Although a laboratory study of puffing behavior did suggest that the majority of vaping sessions involve five or fewer puffs,[22] the self-report data from this study are likely limited by participants' ability to provide a single mean number of puffs/vaping session.

Some of these findings are consistent with the extant literature, such as the finding that dual users are less dependent.[23] Shahab et al.[24] similarly found that dual users smoked approximately 3 cigarettes/day fewer than exclusive smokers but did not differ in cotinine levels. However, in contrast to the present findings, Shahab et al.[24] found that dual users' levels of NNAL were similar to those of exclusive smokers, although their sample size was small (n = 36).

These findings are also consistent with past findings that dual users rate e-cigarettes as less satisfying than combustible cigarettes.[25,26] However, although we found that dual users reported greater motivation to quit smoking than did exclusive smokers, Brose et al.[10] did not find such a difference in a population-based study. Brose et al.[10] also found that daily e-cigarette use was positively related to increased quit attempts. Thus, this research contributes to the mounting evidence that smokers use e-cigarettes to help them quit, and such use is associated with higher quitting motivation.[27] E-cigarette use has also been positively associated with quitting success in large sample studies.[28–30] However, more research, including longitudinal cohort research, is needed[31] to identify the relations of e-cigarette use with smoking cessation since conflicting data exist.[10,32,33] Future analyses of these data will examine whether dual use is related to subsequent smoking cessation activity in this sample.

There was a decrease in total NNAL levels in this study, but the reduction was modest. It is unclear whether a modest reduction in NNK exposure is clinically meaningful with respect to reducing cancer risk.[17] Urine NNAL is highly correlated with exposure to other tobacco smoke toxicants, such as polycyclic aromatic hydrocarbons.[34] Insofar as tobacco-related disease is linearly related to exposure to toxicants, one might expect some reduction in disease risk in dual users. However, this is not likely the case for cardiovascular disease. A recent meta-analysis found that even 1 cigarette/day substantially increases cardiovascular risk,[35] suggesting that a modest reduction in smoke exposure may not meaningfully reduce cardiovascular risk.

The finding of higher levels of psychiatric comorbidity among dual users compared to exclusive smokers agrees with some prior findings. For instance, adults (including smokers and nonsmokers) who had been diagnosed with anxiety, depression, or another mental health condition were significantly more likely to have tried e-cigarettes and be current users of e-cigarettes than were individuals without such psychiatric issues.[9] Further, adults who already smoke combustible cigarettes and had mental health issues were more likely to try e-cigarettes than were smokers without such conditions (60.5% vs. 45.3%).[9] Conversely, though, national survey data show that both exclusive smokers and dual users had elevated psychological distress compared to nonsmokers, but that smokers had higher psychological distress than dual users.[36]

The strength of the inferences permitted by this research is limited by the use of nonrandomized, naturally occurring comparison groups and by different smoking heaviness inclusion criteria for the two groups. The change in inclusion criteria resulted in the inclusion of 30 dual users (11.7%) who smoked fewer than 5 cigarettes/day. Although this may increase the external validity of the sample (ie, it may be that many dual users are not smoking 5 cigarettes/day[20]), it does influence the comparability of the two samples. However, the sensitivity analyses that excluded dual users smoking less than 5 cigarettes/day revealed consistent demographic or biomarker results. Despite these limitations, this study illustrates similarities and differences between exclusive smokers and dual users that should be considered when attempting to anticipate

which smokers are especially likely to use e-cigarettes and when trying to ascribe the effects of e-cigarette/dual use. Future research is needed to better understand the daily use patterns of e-cigarettes and combustible cigarettes among dual users and whether these patterns change over time.

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Declaration of Interests

The authors have no conflicts of interest to declare.

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