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E-cigarettes and Tobacco Exposure Biomarkers among American Indian Smokers

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Abstract

Objectives: We assessed associations between electronic cigarette (e-cigarette) use and smoking-related measures among American Indians (AIs) who smoke.

Methods: We collected baseline survey and smoking biomarker data in a cohort of 375 adult AI smokers at a Cherokee Nation healthcare facility in Oklahoma. We used multivariate logistic and linear regression analyses to determine associations between e-cigarette use and smoking-related characteristics, including biomarkers.

Results: Current e-cigarette users were more likely than never users to report a quit attempt in the past 12 months (current vs never adjusted odds ratio (AOR) = 2.24 [95% CI 1.20–4.16]). Current and past e-cigarette users were more likely than never users to report a likelihood to quit smoking (current vs never AOR = 2.97 [95% CI 1.34–6.56]; past vs never AOR = 1.77 [95% CI

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Conflict of Interest Statement

The authors have no conflicts of interest to report.

1.08–2.91)). E-cigarette use was not significantly associated with confidence to quit smoking, cigarette packs smoked per day, or cotinine levels.

Conclusions: E-cigarette use was associated with previous and future quit attempts, but not with reductions in cigarette smoking or confidence in quitting. This suggests that many dual users might benefit from the addition of evidence-based smoking cessation treatments.

Keywords

American Indians; electronic cigarettes; cigarette smoking

Electronic cigarettes (e-cigarettes) have become popular among adults who smoke.^{1,2} Many individuals use e-cigarettes to help them reduce or quit smoking,^{3,4} but the effectiveness of e-cigarettes as smoking cessation aids remains unproven⁵ and these products are not approved by the FDA for smoking cessation.⁶ American Indians and Alaska Natives (AIs/ANs) have the highest prevalence of cigarette smoking nationwide;⁷ yet, few studies report or evaluate e-cigarette use among AIs/ANs.^{2,8} In one such study, in 2014, adult AIs/ANs had more than twice the prevalence of e-cigarette use than the general population (10.7% vs 3.7%).²

E-cigarette use is a rapidly evolving phenomenon, and patterns of use have been studied previously. Some studies have shown associations between e-cigarette use and sex^{9–11} but not all.^{12,13} E-cigarette use is also associated with younger age^{1,14} and other studies have found differences in e-cigarette use by sociodemographic groups, including by education and income levels.^{1,11} Additional studies have evaluated health-related characteristics such as depression and overall general health.^{12,15} Despite higher prevalence of e-cigarette use among AIs/ANs, patterns of use among AIs/ANs have not been reported previously.

Upon initial e-cigarette use, most people who smoke do not switch completely to e-cigarettes. Instead, they use e-cigarettes and cigarettes concurrently.² Such “dual use” may impact the user’s intentions and attempts to quit tobacco use. Some studies have shown that dual users have an increased number of previous quit attempts^{9,13,16} and smoke fewer cigarettes per day.^{17–20} However, other studies have found no difference between dual users and cigarette-only users in cotinine levels,²¹ the predominate metabolite of nicotine.²² This suggests that e-cigarette use may reduce exposure to harmful by-products of cigarette combustion but may not reduce nicotine intake.

None of these studies, however, evaluated these aspects of e-cigarette use among AIs/ANs who smoke. Understanding the concurrent use of e-cigarettes and cigarettes in AIs/ANs populations is particularly important because of the persistently higher prevalence of cigarette use^{23,24} and e-cigarette use² in this population. AIs also have a lower smoking cessation and higher smoking relapse rates when compared to other populations.^{23,25,26} Furthermore, racial minority groups have been found to be less likely to use nicotine replacement therapy compared to non-Hispanic Whites.^{27,28} Specifically, AI/AN current smokers have been found to report the lowest utilization of quit aids including the use of nicotine gum, patch or spray, inhaler or lozenge, smoking cessation medication, telephone quit lines, support groups or the Internet compared to other racial groups.²⁵ Thus, the impact

of e-cigarette use on smoking patterns among AIs may not be comparable to other populations previously studied and exploration of e-cigarette use in this group is warranted.

The primary objective of this study was to assess associations between e-cigarette use (current, past, and never) and smoking-related measures in a sample of adult AIs who currently use combustible cigarettes. We hypothesized that current and past e-cigarette users would be more likely to report prior quit attempts, more confidence in quitting cigarette use, higher intentions to quit, and smoking fewer cigarette packs per day compared to e-cigarette never users.

METHODS

Design

This study is a cross-sectional analysis of survey and biomarker data collected at the baseline of an ongoing observational 18-month cohort study of adult AIs who smoke.

Setting

Oklahoma has one of the highest numbers of e-cigarette retailers in the nation and 27% of all Oklahomans have tried e-cigarettes at least once in their life.^{29,30} The state is also home to 39 tribes and has one of the largest AI populations in the US.³¹

Headquartered in Tahlequah, Oklahoma, Cherokee Nation encompasses 14 predominantly rural counties in northeastern Oklahoma. Approximately 135,000 Cherokee citizens reside in the area under tribal administration.

Cherokee Nation operates the Cherokee Nation Health Services (CNHS), the largest tribally-operated healthcare system in the US. Patients must show proof of AI/AN descent, such as possession of a Certificate of Degree of American Indian or Alaska Native Blood (CDIB) card from a federally-recognized tribe, to receive services at CNHS. Whereas Cherokee Nation citizens comprise the largest group of patients seen in the CNHS, patients from more than 300 AI tribes are seen at CNHS facilities.

Sample

Research staff recruited study participants from a high-traffic waiting area within the W.W. Hastings primary care outpatient facility in Tahlequah, Oklahoma. On recruitment days, study staff set up a table with information about the study. The table contained a sign announcing the study and inviting potentially eligible persons to participate. Unless approached first by patients, research staff approached potential participants and invited them to hear more about the study. In addition, handbills were printed and available at clinic registration desks. Most participants presented themselves at the table after reading the sign or handbill, or by hearing of it by word-of-mouth. Individuals were eligible for the study if they were age 18 years or older and answered affirmatively to both of the following questions: “Are you American Indian?” and “Do you have a CDIB card?” In addition, individuals were eligible if they indicated that they had smoked at least 100 cigarettes in their lifetime and smoked at least one day during the previous 30 days. Research staff

obtained informed consent from all participants and participants received a \$20.00 department store gift card.

Survey Design and Implementation

Research staff used validated measures, when possible, to develop the survey instrument. Research staff used survey questions from the American Indian Adult Tobacco Survey, the Population Assessment of Tobacco and Health (PATH) Study, and the National Tobacco Survey.^{32–34} The research staff carefully considered the length of the questionnaire to ensure that the participants could complete the survey within approximately 30 minutes. The survey consisted of questions relating to sociodemographic measures, smoking measures, e-cigarette use measures, other tobacco use, nicotine dependence, tobacco and e-cigarette knowledge and attitude, and health history.

Research staff recruited participants over a 3-month period. The research coordinator, who has extensive experience with research regarding this population, was primarily tasked with data collection. Additionally, a research assistant, who also was experienced in research studies with AIs, occasionally assisted with data collection. The 2 lead investigators also participated in and oversaw recruitment during the beginning of the study to ensure adherence to protocol. Finally, this project included opportunities for undergraduate and graduate students to participate in research activities under the direct supervision of the research coordinator. All research staff involved in recruitment were trained in data collection methods, human subjects training, and approved by all appropriate institutional review boards.

Participants completed this self-administered paper-and-pencil survey and provided biomarker samples at the time of study enrollment. All respondents were instructed not to include ceremonial tobacco use in their responses because patterns of ceremonial tobacco use has been shown to be different compared to commercial tobacco use.³²

Measures: Dependent Variables

Past 12 months quit attempts.—Past 12 months quit attempts were assessed by self-report and were dichotomized as *no* versus *yes*.

Confidence to quit smoking.—Confidence to quit smoking was based on the question, “*How confident are you that you will quit smoking within the next month?*” Responses consisted of a range on a ladder scale with 0 = Not at all confident and 10 = very confident, as modified by Boudreaux et al.³⁵

Likelihood to quit smoking.—Likelihood to quit smoking was based on the question, “*How soon are you likely to quit smoking?*” Individuals who reported a likelihood of quitting within the next 30 days, within the next 6 months, within a year, or more than a year were classified as likely to quit. Individuals who reported: “I am not likely to quit smoking” were classified as not likely to quit.

Cigarette packs smoked per day.—Cigarette packs smoked per day were based on self-reported number of cigarettes smoked per day; we dichotomized this measure as 1

pack (≥ 20 cigarettes) versus <1 pack (<20 cigarettes) per day, due to clustering of responses at 20 cigarettes and 10 cigarettes per day.

Salivary cotinine levels.—Participants provided saliva samples by spitting directly into Cryovial collection tubes.³⁶ Research staff immediately stored all samples in a cooled container on site to minimize bacterial overgrowth and transferred samples to a −80 °C freezer within 72 hours after collection. Cotinine is stable in unfrozen saliva within this time frame and comparable to samples that are immediately frozen.³⁷ Salivary cotinine was measured using a Salimetrics Salivary Cotinine ELISA kit (Salimetrics, State College, PA).

We conducted the assays using the standard protocol provided by the manufacturer, with the assay having a reported lower limit of sensitivity of 0.15ng/mL. Research staff thawed samples in a room temperature water bath, and then centrifuged them at 1500 g for 15 minutes. A 10 µL supernatant was diluted 1:10 in the provided loading buffer. Research staff loaded 20 µL of sample or standard into each well. All samples and standards were run in duplicate, with results reported as mean values of each duplicate set. Data were analyzed using BioTek Gen5 software. Results were calculated from a 4-parameter logistic curve fit produced using absorbance readings from known cotinine standards (0, 0.8, 2.5, 7.4, 22.2, 66.7, 200 ng/mL).

Measures: Independent Variables

Status of e-cigarette use.—Status of e-cigarette use was assessed with the following questions: “*Have you ever vaped or used an e-cig, even one or 2 times?*” and, “*On how many of the past 30 days did you use an e-cig or vape even one or 2 times?*” Individuals were considered current e-cigarette users if they reported e-cigarette use within the past 30 days. Individuals were considered past e-cigarette users if they ever used e-cigarettes but did not use within the past 30 days. Individuals were considered never e-cigarette users if they had never used e-cigarettes, even one or 2 times.

Measures: Covariates

Among US smokers, e-cigarettes are used most often to reduce or quit smoking^{3,4} and, historically, smoking cessation patterns and motivations vary by age, sex, and income^{38–41} including among AIs/ANs.^{42–45} Some studies show associations between electronic cigarette use and sex^{9,10} but not all.^{12,13} Use of electronic cigarettes is also associated with younger age, even among smokers.¹⁴ Therefore, to control for potential confounding variables, we included the variables described below.

Demographics.—Age groupings were categorized as years 18–44 and 45+. Sex was categorized as male or female. Education was defined as the highest level of school completed and categorized as less than high school, high school graduate/GED, and more than high school. Household income was defined as annual household income from all sources and was categorized as \$0 – \$15,000; \$15,001 – \$30,000; and \$30,001+. Respondents self-reported their health status as excellent, very good, good, fair, or poor. Those reporting excellent, very good, or good were grouped for analysis to compare with

fair or poor. Marital status was categorized as married, unmarried living with a partner, single, and divorced/separated/widowed.

Health-related variables.—Chronic medical history was dichotomized (no/yes) based on respondent's self-reported history of having any one or more of the following: cancer, cardiovascular or heart disease, diabetes, chronic obstructive pulmonary disease, or emphysema. Depression was dichotomized (no/yes) based on self-reported history of having had a diagnosis of depression.

Other tobacco use.—Other tobacco use (current, past, or never) was based on use of smokeless tobacco, cigars, cigarillos, filtered cigars, hookahs, or dissolvable tobacco. Never use was defined as having never tried any of the aforementioned tobacco products. Past use was defined as either having tried or yearly use of any of the aforementioned tobacco products. Current use was defined as daily, weekly, or monthly use of any of these or other tobacco products.

Data Analysis

The sample size for this study was based on preliminary unpublished data by one of the co-authors of this study. Results of the unpublished study showed that the proportion of AI smokers using e-cigarettes in the past 30 days was 26%. For our study, assuming a prevalence of 26%, a margin of error in a 95% confidence interval of 4.4% yielded a baseline sample of 375 individuals. Categorical data were represented by count (%). Continuous data were represented by median (inter-quartile range) or mean (SD). Comparisons among e-cigarette use groups were performed by χ^2 test for categorical variables, and a Kruskal-Wallis or ANOVA test was used for continuous variables.

In building the initial multivariate models, we considered age, sex, education, income, general health, marital status, chronic medical history, depression, and other tobacco use status as covariates. Because age, sex, and income are associated with the use of electronic cigarettes^{1,9–11} and also with smoking cessation,⁴⁶ we also considered 2-way interactions between e-cigarette use and age, sex, and income. Final multivariate models were formed using the backward selection method. Past 12 months quit attempts, likelihood to quit smoking, and cigarette packs smoked per day were modeled by logistic regression. Confidence to quit smoking, and salivary cotinine levels were modeled by linear regression. We also re-ran the multivariate logistic and linear models to explore whether forcing in other potentially confounding variables (age, sex, income, and education) would change the results of the backward selection method. All tests were 2-sided with a p-value of < .05 defined as being statistically significant. We used SAS software (version 9.3, Cary, NC).

RESULTS

Table 1 presents the sociodemographic and tobacco-related characteristics by e-cigarette use status of the study population. Of the 375 adult AI cigarette smokers, approximately 37% never used e-cigarettes, 47% were past e-cigarettes users, and 16% were current e-cigarette users. Current and past e-cigarette users were younger ($p = .02$) and more likely to have had a depression diagnosis ($p = .001$) than never users.

Past and current e-cigarette users were more likely to have made a quit attempt in the past 12 months ($p = .03$) and were more likely to indicate a likelihood to quit smoking ($p = .008$) than those who never used e-cigarettes. However, there were no statistically significant differences in confidence to quit smoking ($p = .10$), cigarette packs smoked per day ($p = .40$), or salivary cotinine levels ($p = .24$) by e-cigarette category.

Multivariate analyses were subsequently performed, adjusting for potential confounders and effect modifiers as outlined in the data analysis section. E-cigarette use was significantly associated ($p = .04$) with having made a quit attempt in the past 12 months. The odds of having made one or more quit attempts in the past 12 months was 2.24 (95% confidence interval (CI) = 1.20–4.16) times greater among current e-cigarette users compared to never e-cigarette users (Table 2). Current and past e-cigarette users were at greater odds of reporting a likelihood to quit smoking (current vs never OR = 2.97 (95% CI 1.34–6.56); past vs never OR = 1.77 (95% CI 1.08–2.91) ($p = .01$, Table 2). There was no statistically significant association between e-cigarette use and confidence to quit ($p = .10$, Table 2), number of cigarette packs smoked per day ($p = .34$, Table 3), and salivary cotinine levels ($p = .20$, Table 3). Multivariate analyses were performed again to force age, sex, income, and education into the linear and logistic regression models (data not shown). Re-running the analyses with these variables did not affect the point estimates or p-values for variables of interest.

DISCUSSION

To our knowledge, this is the first study to characterize e-cigarette use among AI adults who smoke. More than 63% of our study population reported use of e-cigarettes either currently or in the past. This prevalence of past or current use is higher than reported among current US smokers in 2014 (47.6%).² The data from this study show that current e-cigarette users were more likely to report a quit attempt in the past 12 months and that they were likely to indicate intention to quit smoking. However, consumption of less than a pack of cigarettes per day did not vary by e-cigarette group. Furthermore, there were no statistically significant differences in confidence to quit smoking, or salivary cotinine levels by e-cigarette use status.

Our finding that e-cigarette users were more likely to report previous 12 months quit attempts is consistent with previous research in non-AI populations.^{9,13,16} The association between e-cigarette use and previous quit attempts and intentions to quit smoking may indicate smoking cessation readiness. Inquiring about current e-cigarette use may help clinicians and public health professionals identify AIs who intend to quit smoking. Notably, we cannot infer from this study whether smoking prevention and control efforts should or should not include electronic cigarettes. However, because clinician screening of e-cigarette use is not universally done,^{8,12} such inquiry could open avenues for engaging these patients in discussions of existing evidence-based smoking cessation interventions.

Although e-cigarettes may be used to reduce or quit cigarette smoking, our results do not suggest that e-cigarette use is associated with a reduction of cigarette consumption to less than a pack per day. Other research has shown that e-cigarette use may lower the number of

cigarettes smoked per day in the short term but these effects were no longer seen after one year of e-cigarette use.⁴⁷ These conflicting results, plus the fact that the current study summarizes only the baseline patterns of dual use in a cohort of adult AI smokers, justifies further investigation into the effects of e-cigarette use on smoking cessation among AIs. In particular, how the role, if any, of e-cigarettes might be coupled with other interventions to increase cigarette cessation rates merits exploration.

This study has some limitations. First, this was a cross-sectional analysis so causality and temporal relationship of associations cannot be determined. Second, participants consisted of a clinic-based convenience sample and not a sample of the general population. Therefore, selection bias for those who more frequently use healthcare may have been introduced and may affect the generalizability of our results. However, the advantage of the clinic-based sampling performed for this study is that this primary care setting could serve as an important platform for smoking cessation services among dual users. The clinic setting may be an ideal setting for future follow-up research and tobacco cessation interventions. Survey data were self-reported and subject to recall bias, and the small sample size of current e-cigarette users limits our ability to conduct more in-depth analyses such as stratified models based on pack years of smoking. We did not survey former cigarette smokers and could not assess whether or not former smokers used e-cigarettes as a cessation aid. Surveying this group could provide valuable insight as to whether e-cigarettes could be successfully used as a cessation aid.

Despite these limitations, this is the first study to evaluate e-cigarette use among AIs who smoke in a region with a high prevalence of e-cigarette use. This population also has a high prevalence of smoking-related mortality;^{48,49} which increases the need for understanding the effects of e-cigarette use on AI health. Our longitudinal study will help increase understanding of the effect of e-cigarette use on markers of tobacco use and nicotine dependence, once our 18-month follow-up data have been collected and analyzed.

In conclusion, current use of cigarettes and e-cigarettes was associated with past 12 months quit attempts and a self-reported likelihood of future tobacco cessation. This may be an indication that e-cigarette use may signify a greater interest in smoking cessation. However, e-cigarette use was not associated with confidence to quit in the next month, cigarette packs smoked per day, or salivary cotinine levels. For this population of AIs who smoke, use of e-cigarettes may be associated with intentions to quit but the effect on reducing cigarette consumption is limited.

Human Subjects Statement

The human subjects' protection protocol for this study was approved by the University of Oklahoma Health Sciences Center Institutional Review Board and the Cherokee Nation Institutional Review Board.

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Table 1

Sociodemographic and Tobacco-related Characteristics of Study Population

	Overall N (%)	Never E-Cig User N (%)	Past E-Cig User N (%)	Current E-Cig User N (%)	p-value
Age					.02
18–44	215 (57.3%)	65 (47.4%)	108 (60.7%)	42 (70.0%)	
45+	160 (42.7%)	72 (52.6%)	70 (39.3%)	18 (30.0%)	
Sex					.80
Male	145 (38.7%)	54 (39.4%)	66 (37.1%)	25 (41.7%)	
Female	230 (61.3%)	83 (60.6%)	112 (62.9%)	35 (58.3%)	
Education					.14
Less than high school	76 (20.4%)	35 (25.7%)	27 (15.3%)	14 (23.3%)	
High school grad/GED	146 (39.1%)	54 (39.7%)	72 (40.7%)	20 (33.3%)	
More than high school	151 (40.5%)	47 (34.6%)	78 (44.1%)	26 (43.3%)	
Income					.76
\$0 – \$15,000	173 (47.3%)	67 (50.4%)	77 (44.3%)	29 (49.2%)	
\$15,001 – \$30,000	114 (31.1%)	37 (27.8%)	60 (34.5%)	17 (28.8%)	
\$30,001	79 (21.6%)	29 (21.8%)	37 (21.3%)	13 (22.0%)	
Health Status					.40
Excellent/very good/good	230 (62.2%)	84 (62.2%)	105 (59.7%)	41 (69.5%)	
Fair/poor	140 (37.8%)	51 (37.8%)	71 (40.3%)	18 (30.5%)	
Marital Status					.15
Married	128 (34.6%)	57 (42.2%)	54 (30.7%)	17 (28.8%)	
Unmarried with partner	71 (19.2%)	20 (14.8%)	38 (21.6%)	13 (22.0%)	
Single	90 (24.3%)	36 (26.7%)	39 (22.2%)	15 (25.4%)	
Divorced/separated/widowed	81 (21.9%)	22 (16.3%)	45 (25.6%)	14 (23.7%)	
Chronic Medical History					.29
No	225 (61.1%)	79 (58.5%)	104 (60.1%)	42 (70.0%)	
Yes	143 (38.9%)	56 (41.5%)	69 (39.9%)	18 (30.0%)	
Depression					.001
No	210 (58.7%)	92 (71.3%)	87 (51.2%)	31 (52.5%)	

	Overall N (%)	Never E-Cig User N (%)	Past E-Cig User N (%)	Current E-Cig User N (%)	p-value
Yes	148 (41.3%)	37 (28.7%)	83 (48.8%)	28 (47.5%)	
Other Tobacco Use					
Current	64 (17.1%)	19 (13.9%)	33 (18.5%)	12 (20.0%)	.05
Past	237 (63.2%)	80 (58.4%)	119 (66.9%)	38 (63.3%)	
Never	74 (19.7%)	38 (27.7%)	26 (14.6%)	10 (16.7%)	
Past 12 Months Quit Attempts					
No	225 (60.6%)	92 (67.6%)	92 (59.4%)	29 (48.3%)	
Yes	146 (39.4%)	44 (32.4%)	44 (40.6%)	31 (51.7%)	.10
Confidence to Quit					
Smoking: Mean (SD)	2.8 (2.8)	3.0 (2.9)	2.5 (2.7)	3.4 (2.7)	
Likelihood to Quit Smoking					
Not likely	97 (26.1%)	47 (34.8%)	41 (23.25)	9 (15.3%)	.008
Likely	274 (73.9%)	88 (65.2%)	136 (76.8%)	50 (84.7%)	
Cigarette Packs per Day					
<1	230 (62.7%)	90 (67.2%)	104 (59.8%)	36 (61.0%)	
1	137 (37.3%)	44 (32.8%)	70 (40.2%)	23 (39.0%)	.40
Cotinine Levels (ng/mL)					
mean (SD)	375.6 (350.9)	348.6 (364.0)	399.2 (352.7)	367.8 (315.0)	.24

Table 2

Multivariate Analysis of Smoking Cessation-related Variables among Adult American Indian Smokers

	Past 12 Months Quit Attempts	Confidence to Quit Smoking	Likelihood to Quit Smoking
	OR (95%CI)	Diff. (SE)	OR (95% CI)
E-Cig Use	p = .04	p = .10	p = .01
Current	2.24 (1.20, 4.16)	0.40 (0.43)	2.97 (1.34, 6.56)
Past	1.43 (.89, 2.28)	-0.44 (0.32)	1.77 (1.08, 2.91)
Never	REF	REF	REF

Multivariate Analysis of Smoking-related Behaviors and Exposure Biomarkers among Adult American Indian Smokers

Table 3

	Cigarette Packs per Day		Cotinine Levels ng/mL
	OR (95%CI)	Diff. (SE)	
E-Cig Use	p = .34	p = .20	
Current	1.47 (0.74, 2.89)	64.2 (53.8)	
Past	1.43 (0.86, 2.38)	68.3 (39.6)	
Never	REF	REF	
Age	p = .005	p < .001	
18-44	REF	REF	
45+	1.94 (1.23, 3.07)	156.7 (36.8)	
General Health	--	p = .008	
Excellent/very good/good		REF	
Fair/poor		99.7 (37.3)	
Depression	p = .002	--	
No	REF		
Yes	2.05 (1.30, 3.24)		

Not included in final model