

Supplement Article

Cross-Sectional Association Between Exclusive and Concurrent Use of Cigarettes, ENDS, and Cigars, the Three Most Popular Tobacco Products, and Wheezing Symptoms Among U.S. Adults

Liane M. Schneller PhD, MS¹, Zahira Quiñones Tavárez MD¹,
Maciej L. Goniewicz PhD, PharmD², Zidian Xie PhD¹, Scott McIntosh PhD³,
Irfan Rahman PhD⁴, Richard J. O'Connor PhD², Deborah J. Ossip PhD³,
Dongmei Li PhD¹

¹Clinical and Translational Science Institute, University of Rochester Medical Center, Rochester, NY; ²Department of Health Behavior, Roswell Park Comprehensive Cancer Center, Buffalo, NY; ³Department of Public Health Sciences, University of Rochester Medical Center, Rochester, NY; ⁴Department of Environmental Medicine, University of Rochester Medical Center, Rochester, NY

Corresponding Author: Liane M. Schneller, PhD, MS, Clinical and Translational Science Institute, University of Rochester Medical Center, 265 Crittenden Blvd, Rochester, NY 14642, USA. Telephone: 716-845-2300; Fax: 716-845-1265; E-mail: liane_schneller@URMC.Rochester.edu

Abstract

Introduction: This study assessed the association of exclusive and concurrent use of cigarettes, electronic nicotine delivery systems (ENDS), and cigars with ever and past 12-month wheezing symptoms among a nationally representative sample of US adult current tobacco users.

Methods: Cross-sectional data from the Population Assessment of Tobacco and Health (PATH) Study Wave 3 (W3) were used. The weighted prevalence of self-reported ever and past 12-month wheezing symptoms for noncurrent users compared with users of cigarettes, ENDS, cigars, and any combination of these products (polytobacco use of these tobacco products) were presented for 28 082 adults. The cross-sectional association of tobacco use with self-reported wheezing symptoms was assessed using weighted multivariable and ordinal logistic regression with consideration of complex sampling design.

Results: Significantly higher odds of ever had wheezing or whistling in the chest at any time in the past were observed among current cigarette (adjusted odds ratio: 2.62, 95% confidence intervals [CI]: 2.35, 2.91), ENDS (1.49, 95% CI: 1.14, 1.95), and polytobacco users (2.67, 95% CI: 2.26, 3.16) compared with noncurrent users. No associations were seen for cigar use. Polytobacco use was associated with a higher odds of ever wheezing when compared with exclusive ENDS (1.61, 95% CI: 1.19, 2.17) and exclusive cigar use (2.87, 95% CI: 1.93, 4.26), but not exclusive use of cigarettes.

Conclusions: Ever wheezing is associated with the use of cigarettes, ENDS, and polytobacco use of cigarettes, ENDS, and/or cigars, but not cigar use. The association of polytobacco use and wheezing appears to be driven by cigarette use.

Implications: Cross-sectional associations with ever and past 12-month wheezing symptoms were found to be the strongest among cigarette users, exclusively or in combination. Future longitudinal research is needed to better understand how cigarette use interacts with other tobacco and nicotine products and contributes to respiratory symptoms.

Introduction

In 2018, about 49.1 million adults in the United States (19.7%) currently used tobacco products.¹ The most popular products reported included cigarettes (13.7%), cigars (3.9%), and electronic nicotine delivery systems (ENDS or e-cigarettes; 3.2%).¹ In addition, nearly 19% of current tobacco users reported using two or more tobacco products.¹ Tobacco use is the leading cause of preventable disease, disability, and death in the United States.² More than \$300 billion is spent each year on smoking-related illnesses in the United States.³ Smoking affects nearly every organ of the body and increases the risk of developing lung disease and other respiratory symptoms (eg, wheezing).² Use of cigarettes and ENDS, independently, has been shown to be associated with an increased risk of developing respiratory diseases,^{2,4-6} including wheezing symptoms.^{2,7} Furthermore, our study team conducted a cross-sectional analysis of nationally representative data and found that dual use of cigarettes and ENDS is associated with self-reported wheezing symptoms.⁷

Wheezing is characterized by a high-pitched whistling sound during expiration or inspiration due to the narrowing of airway walls, obstruction, or constriction.⁸ Wheezing can be experienced in the lower airways, as well as the upper, and usually can be heard by the naked ear.⁸ However, further tests are usually required to determine the cause of wheezing.⁸ Many conditions are known to cause wheezing, including gastroesophageal reflux disease, cardiac disease, respiratory infections, asthma, chronic obstructive pulmonary disease, airway compression (intrinsic or extrinsic), inflammation due to the inhalation of a foreign body,⁸ and high body mass index (BMI).^{9,10}

To our knowledge, there is no research on the association of wheezing symptoms with the current use of cigars alone, nor with the use of any combination of cigarettes, ENDS, and cigars, compared with noncurrent users. The inhalation of noxious chemicals and gases in cigarette smoke is known to cause an increase in mucus production and viscosity causing an obstruction as well as airway inflammation.^{11,12} This has also been shown to be true for ENDS aerosol^{13,14} and may potentially be true for cigar smoke. Therefore, the use of any of these three tobacco products, alone or in combination with each other, may increase the likelihood of reporting wheezing symptoms compared with noncurrent users. Using data from Wave 3 (W3) of the Population Assessment of Tobacco and Health (PATH) Study, this study assessed the association of cigarette, cigar, ENDS, or polytobacco use of these top three products with ever and past 12-month wheezing symptoms when compared with noncurrent users among a nationally representative sample of US adults.

Methods

Study Design and Population

The PATH Study is a nationally representative, longitudinal cohort study of tobacco use behaviors, attitudes and beliefs, and its health

effects among noninstitutionalized adults and youth in the United States, through the National Institute of Health and the US Food and Drug Administration (FDA).¹⁵ Data from W3 of the PATH Study were collected between October 19, 2015 and October 23, 2016 among 28 148 adult and 13 651 youth respondents. The PATH study was conducted by Westat (Rockville, MD), approved by the Westat Institutional Review Board, and informed consent was obtained from participants. More information about the PATH study design and methods are published elsewhere.¹⁶ This analysis provides W3 cross-sectional, self-reported ever and past 12-month wheezing symptoms prevalence estimates from 28 082 US adults who were noncurrent users and users of the top three tobacco products in the United States (cigarette, ENDS, and cigars) using the PATH study public-use files.

Tobacco Product Use

This analysis focused on five mutually exclusive categories of tobacco product use (1) cigarette use, (2) ENDS use, (3) cigar use, (4) any combination of these products, and (5) noncurrent users of these tobacco products. Variables of current established tobacco use are derived and provided by Westat.¹⁵ Current, established, exclusive cigarette smokers were those who had smoked 100 or more cigarettes in their lifetime, smoked every day or some days at W3, and were not current established ENDS or cigar users (referred to as cigarette smokers from here on). Current, exclusive ENDS users were those who had ever used any ENDS, had ever used them fairly regularly, used them every day or some days at W3, and were not current established cigarette or cigar users (referred to as ENDS users from here on). Current, exclusive cigar users were those who had ever smoked a cigar (traditional cigars, cigarillos, or filtered cigars), had smoked at least one cigar product fairly regularly, smoked every day or some days at W3, and were not current established cigarette or ENDS users (referred to as cigar users from here on). Polytobacco users were those who were current established users of any combination of cigarettes, ENDS, and/or cigars at W3 (cigar and ENDS, cigarette and ENDS, cigarette and cigar, as well as cigarette, ENDS, and cigar, referred to as polytobacco users from here on). Noncurrent users were not currently using cigarettes, ENDS, or cigars some days or every day at W3 (see [Supplementary Table 1](#)).

Wheezing Symptoms

Self-reported wheezing symptoms were examined. Questions included (1) Have you ever had wheezing or whistling in the chest at any time in the past (Yes/No), (2) Have you had wheezing or whistling in the chest in the past 12 months (Yes/No), (3) How many attacks of wheezing have you had in the past 12 months (None/1-3/4-12/More than 12), (4) In the past 12 months, how often, on average has your sleep been disturbed due to wheezing (Never woken with wheezing/Less than one night per week/One or more nights per week), (5) In the past 12 months, has wheezing ever been severe enough to limit your speech to only one or two words between breaths (Yes/No), and (6) In the past 12 months, has

your chest sounded wheezy during or after exercise (Yes/No)? Each wheezing symptom variable was assessed individually. Due to small sample sizes for the variable “number of wheezing attacks you have had in the past 12 months,” the categories were collapsed to three levels (None/1–12 attacks/More than 12).

Statistical Analysis

Self-reported ever and past 12-month wheezing symptoms were individually assessed for differences across five levels of tobacco use (no use, current exclusive use of cigarettes, current exclusive use of ENDS, current exclusive use of cigar, or any combination of these products). Weighted cross-sectional prevalence and adjusted odds ratios (aORs) with 95% confidence intervals (95% CI) are reported. Pearson’s chi-square tests were used to assess observed differences between the top three products in the United States and the six dependent variables of self-reported ever and past 12-month wheezing symptoms, as well as demographic and secondhand smoke exposure characteristics. Multivariable logistic regression and multinomial logistic regression models were conducted individually for each of the six dependent variables of self-reported ever and past 12-month wheezing symptoms. Based in part by previous research,⁷ models were adjusted for age, gender, race/ethnicity, BMI, insurance, asthma, and secondhand smoke exposure (lived with a smoker during childhood, currently live with a smoker, rules about smoking combustible product inside their home, and rules about using ENDS inside their home).

Exploratory analyses assessed the association of the four polytobacco use combinations (cigar and ENDS, cigarette and ENDS, cigarette and cigar, as well as cigarette, ENDS, and cigar) with ever and past 12-month wheezing symptoms. In addition, an exploratory analysis assessed the effects of past cigarette use (eg, never smokers versus former smokers for each product category) on the association of current use of the three most popular tobacco products and self-reported ever and past 12-month wheezing symptoms. Former established cigarette smokers were defined as those who have smoked at least 100 cigarettes in their lifetime and have not smoked in the past 12 months or currently do not smoke at all, and never smokers were those who have not smoked 100 cigarettes in their lifetime. However, statistical power was limited for some of the past 12-month wheezing outcomes. Both exploratory analyses consisted of multivariable logistic regression and multinomial logistic regression models that were adjusted for age, gender, race/ethnicity, BMI, insurance, asthma, and secondhand smoke exposure (lived with a smoker during childhood, currently live with a smoker, rules about smoking combustible product inside their home, and rules about using ENDS inside their home).

Analyses were conducted using Stata 16 software (StataCorp LLC, College Station, TX) with W3 replicate weights and balanced repeated replication methods with Fay’s adjustment of 0.3. A $p < .05$ was considered statistically significant. However, to account for multiple comparisons, an adjusted alpha level ($p < .008$) using the Bonferroni method was considered when interpreting the results.

Results

Cross-sectional Association of Wheezing Symptoms and Tobacco Product Use

Ever and past 12-month wheezing symptoms were more prevalent among exclusive cigarette and polytobacco users than noncurrent,

cigar, and ENDS users (see [Supplementary Table 2](#)). Furthermore, ever and past 12-month wheezing symptoms were associated with many of the demographic and secondhand smoke exposure characteristics of interest. In general, ever and past 12-month wheezing symptoms were more prevalent with increasing age, among females, non-Hispanic Whites, those who were overweight or obese, those having private insurance, Medicare, or some other form of insurance, those who did not have asthma, those who were not a former smoker, and those who lived with a regular smoker who smoked inside the home during childhood. Furthermore, ever and past 12-month wheezing symptoms were more prevalent among those who did not live with someone who smoked at W3, as well as those who did not allow smoking a combustible tobacco product, e-cigarettes, or other electronic nicotine products inside their home. However, no association was found between wheezing in the past 12 months and former smoking, sleep disturbed due to wheezing and gender, race/ethnicity and former smoking, speech limited to only one or two words between breaths due to wheezing and race/ethnicity, and chest has sounded wheezy during or after exercise and age, gender, and former smoking. Significantly higher odds of ever had wheezing or whistling in the chest at any time in the past (hereafter “ever wheezing”) was observed among current cigarette (aOR: 2.62, 95% CI: 2.35, 2.91), ENDS (aOR: 1.49, 95% CI: 1.14, 1.95), and polytobacco users (aOR: 2.67, 95% CI: 2.26, 3.16) compared to noncurrent users ([Figure 1A](#)). Cigarette use was associated with a significantly higher odds of ever wheezing when compared to ENDS (aOR: 1.75, 95% CI: 1.333, 2.32) and cigars (aOR: 3.45, 95% CI: 2.38, 4.99). ENDS users were significantly more likely to report ever wheezing in the past when compared to cigar users (aOR: 1.97, 95% CI: 1.16, 3.32). Polytobacco use was associated with a higher odds of ever wheezing when compared with ENDS (aOR: 1.61, 95% CI: 1.19, 2.17) and cigar use (aOR: 2.87, 95% CI: 1.93, 4.26), but not cigarettes. Similar associations were seen for wheezing in the past 12 months (cigarette: aOR: 3.93, 95% CI: 3.45, 4.49; polytobacco: aOR: 3.67, 95% CI: 3.06, 4.40; see [Figure 1B](#)). Although the association for wheezing in the past 12 months with ENDS was significant at an alpha of .05 ($p = .043$), the association was not interpreted as significant due to the multiple comparisons (Bonferroni alpha = .008). Pairwise comparisons for wheezing in the past 12 months mirrored those of ever wheezing (data not shown).

Cigarette and polytobacco use was associated with number of wheezing attacks in the past 12 months (cigarette: 1–12 attacks vs none: aOR: 3.60, 95% CI: 3.12, 4.15; cigarette: ≥ 12 attacks vs none: aOR: 6.28, 95% CI: 4.72, 8.35; polytobacco: 1–12 attacks vs none: aOR: 3.22, 95% CI: 2.62, 3.95; polytobacco: ≥ 12 attacks vs none: aOR: 6.27, 95% CI: 4.34, 9.07; see [Figure 1C](#)) and having sleep disturbed due to wheezing in the past 12 months (cigarette: less than one night per week vs never: aOR: 2.87, 95% CI: 2.28, 3.59; cigarette: one or more nights per week vs never: aOR: 3.48, 95% CI: 2.63, 4.61; polytobacco: less than one night per week vs never: aOR: 3.25, 95% CI: 2.43, 4.34; polytobacco: one or more nights per week vs never: aOR: 4.91, 95% CI: 3.51, 6.85; see [Figure 1D](#)). ENDS users had a significantly higher odds of having more than 12 wheezing attacks versus none in the past 12 months when compared with noncurrent users (aOR: 2.70, 95% CI: 1.43, 5.11), but ENDS use was not associated with sleep being disturbed due to wheezing in the past 12 months. Cigarette and polytobacco use was associated with significantly higher odds of speech limited to one or two words between breaths due to wheezing in

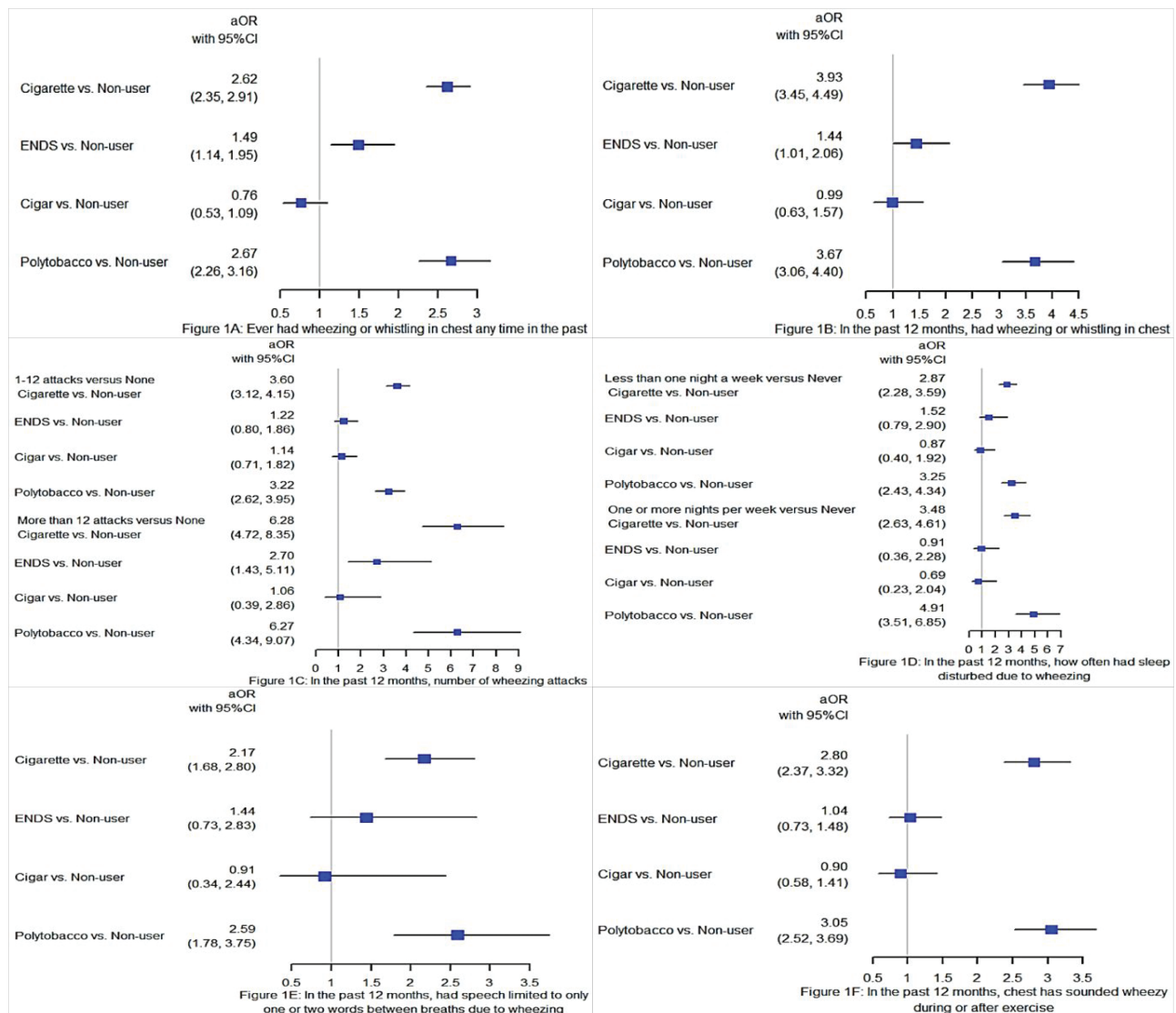


Figure 1. Association of wheezing symptoms with the top three tobacco products among adults in the United States—The Population Assessment of Tobacco and Health Wave 3. Results for ever wheezing (A), past 12-mo wheezing (B), past 12-mo limited speech due to wheezing (E), and past 12-mo wheezing during or after exercise (F) are from multivariable logistic regression and results for past 12-mo number of wheezing attacks (C) and past 12-mo frequency of sleep disturbed due to wheezing (D) are from multinomial logistic regressions models. Adjusted odds ratios and their 95% confidence intervals are reported. Models are adjusted for age, gender, race/ethnicity, body mass index, insurance, asthma, and secondhand smoke exposure (lived with smoker during childhood, currently live with a smoker, rules about smoking combustible product inside home, and rules about using ENDS inside home).

the past 12 months (cigarette: aOR: 2.17, 95% CI: 1.68, 2.80; polytobacco: aOR: 2.59, 95% CI: 1.78, 3.75; see [Figure 1E](#)), and chest has sounded wheezy during or after exercise in the past 12 months (cigarette: aOR: 2.80, 95% CI: 2.37, 3.32; polytobacco: aOR: 3.05, 95% CI: 2.52, 3.69; see [Figure 1F](#)) when compared with noncurrent users. There was no association between ever nor past 12-month wheezing symptoms and cigar use (see [Figure 1](#)). There were no significant differences in odds of reporting ever nor past 12-month wheezing symptoms among the four polytobacco use levels (see [Table 1](#)). When stratified by age and BMI, similar trends were observed for reporting ever and past 12-month wheezing. However, there were no significant differences between the age groups (see [Supplementary Table 3](#)) or BMI groups (see [Supplementary Table 4](#)).

Effects of Past Smoking on the Association of Wheezing and Tobacco Use

About 32% of noncurrent users were identified as a former established smoker, whereas 74% of ENDS users and about 53% of cigar users were former established smokers (see [Supplementary Table 2](#)). There was about 1% of polytobacco users who were currently using ENDS and cigars that have never used cigarettes (data not shown). The following models were suppressed due to insufficient sample size: “In the past 12 months, number of wheezing attacks,” “In the past 12 months, had sleep disturbed due to wheezing,” and “In the past 12 months, had speech limited to only one or two words between breaths due to wheezing.” When compared with noncurrent users who never smoked, significantly higher odds of reporting ever and past 12-month wheezing symptoms was associated with

Table 1. Polytobacco Users of Cigarettes, ENDS, and Cigars and Their Prevalence of Wheezing Symptoms Adults in the United States ($n = 1622$)—The Population Assessment of Tobacco and Health Wave 3

Dependent wheezing symptom variables	Product combinations used by polytobacco users											
	ENDS and cigars (referent)			Cigarettes and ENDS			Cigarettes and cigars			ENDS, cigarettes, and cigars		
	N (%)	N (%)	aOR (95% CI) ^a	N (%)	N (%)	aOR (95% CI) ^a	N (%)	N (%)	aOR (95% CI) ^a	N (%)	N (%)	aOR (95% CI) ^a
	N = 72			N = 827			N = 580			N = 143		
Ever had wheezing or whistling in chest at any time in the past												
No	47 (66.4)	450 (54.5)	Ref	325 (55.9)	Ref	81 (53.6)	Ref	62 (46.4)	1.40 (0.52, 3.79)			
Yes	25 (33.6)	377 (45.5)	1.03 (0.42, 2.54)	255 (44.2)	1.19 (0.45, 3.15)	62 (46.4)	1.19 (0.45, 3.15)					
In the past 12 mo, had wheezing or whistling in chest												
No	16 (18.7)	279 (33.9)	Ref	207 (36.1)	Ref	46 (34.3)	Ref	46 (34.3)	Ref			
Yes	56 (81.3)	548 (66.1)	1.52 (0.53, 4.32)	373 (63.9)	1.95 (0.62, 6.08)	96 (65.7)	1.95 (0.62, 6.08)					
In the past 12 mo, number of wheezing attacks												
None	59 (84.0)	583 (70.6)	Ref	391 (67.0)	Ref	102 (68.2)	Ref	102 (68.2)	Ref			
1–12	13 (16.0)	195 (23.7)	0.70 (0.08, 5.96)	147 (25.7)	0.79 (0.07, 9.39)	33 (24.3)	0.79 (0.07, 9.39)	33 (24.3)	1.86 (0.19, 18.02)			
More than 12	0	48 (5.7)		40 (7.3)		7 (7.6)		7 (7.6)				
In the past 12 mo, how often had sleep disturbed due to wheezing												
Never	62 (86.7)	725 (87.7)	Ref	481 (83.0)	Ref	121 (82.5)	Ref	121 (82.5)	Ref			
Less than one night a week	8 (10.2)	59 (7.1)	0.57 (0.12, 2.73)	55 (9.4)	0.57 (0.12, 2.73)	12 (9.0)	1.02 (0.19, 5.36)	12 (9.0)	0.77 (0.19, 3.05)			
One or more nights per week	2 (3.1)	41 (5.2)	0.70 (0.08, 5.96)	42 (7.6)	0.70 (0.08, 5.96)	9 (8.6)	0.79 (0.07, 9.39)	9 (8.6)	1.86 (0.19, 18.02)			
In the past 12 mo, had speech limited to only one or two words between breaths due to wheezing												
No	67 (91.9)	787 (95.6)	Ref	537 (93.1)	Ref	133 (93.8)	Ref	133 (93.8)	Ref			
Yes	5 (8.1)	39 (4.4)	0.63 (0.04, 10.31)	41 (6.9)	0.63 (0.04, 10.31)	9 (6.2)	1.18 (0.06, 21.81)	9 (6.2)	1.05 (0.06, 20.02)			
In the past 12 mo, chest has sounded wheezy during or after exercise												
No	58 (86.2)	610 (74.8)	Ref	435 (75.5)	Ref	103 (68.6)	Ref	103 (68.6)	Ref			
Yes	13 (13.9)	213 (25.2)	2.32 (0.53, 10.04)	144 (24.5)	2.32 (0.53, 10.04)	40 (31.4)	2.20 (0.45, 10.77)	40 (31.4)	3.20 (0.72, 14.29)			

Polytobacco use included cigarette, ENDS, and cigar use. Results for ever wheezing, past 12-mo wheezing, past 12-mo limited speech due to wheezing, and past 12-mo wheezing during or after exercise are from multivariable logistic regression, and results for past 12-mo number of wheezing attacks and past 12-mo frequency of sleep disturbed due to wheezing are from multinomial logistic regressions models. Adjusted odds ratios and their 95% confidence intervals are reported. Bolded point estimates indicates statistical significance at $p < .05$. The model for number of wheezing attacks could not reach convergence (grayed out cells). aOR = adjusted odds ratio; CI = confidence interval; ENDS = electronic nicotine delivery system; ref = referent category.

^aAdjusted for age, gender, race/ethnicity, body mass index, insurance, asthma, and secondhand smoke exposure (lived with smoker during childhood, currently live with a smoker, rules about smoking combustible product inside home, and rules about using ENDS inside home).

noncurrent users who were former smokers (ever wheezing: aOR: 1.70, 95% CI: 1.49, 1.95; past 12-month wheezing: aOR: 1.58, 95% CI: 1.33, 1.87; wheezing during or after exercise: aOR: 1.48, 95% CI: 1.22, 1.80), cigarette smokers (ever wheezing: aOR: 3.11, 95% CI: 2.74, 3.53; past 12-month wheezing: aOR: 4.55, 95% CI: 3.85, 5.39; wheezing during or after exercise: aOR: 3.12, 95% CI: 2.55, 3.81), and polytobacco users who were former smokers (ever wheezing: aOR: 3.15, 95% CI: 2.62, 3.79; past 12-month wheezing: aOR: 4.24, 95% CI: 3.37, 5.33; wheezing during or after exercise: aOR: 3.42, 95% CI: 2.72, 4.29). On the other hand, ENDS users who never smoked, cigar users who never smoked, cigar users who were former smokers, and polytobacco users who were former smokers did not show a statistically significant association with ever and past 12-month wheezing symptoms when compared with noncurrent users who never smoked. ENDS users who were former smokers had a significantly higher odds of reporting ever wheezing in the past, as well as in the past 12 months, but not during or after exercise in the past 12 months (ever wheezing: aOR: 1.99, 95% CI: 1.47, 2.69; past 12-month wheezing: aOR: 1.94, 95% CI: 1.29, 2.90) when compared with noncurrent users who never smoked (see Table 2). When conducting a pairwise comparison of ENDS users who were former smokers and ENDS users who were never smokers, those who were former smokers had a significantly higher odds of reporting ever wheezing in the past (aOR: 2.73, 95% CI: 1.25, 5.95; data not shown), but this was not true when looking at wheezing in the past 12 months or wheezing during or after exercise in the past 12 months. When looking at the association of past smoking among exclusive cigar and polytobacco users, there was no statistical difference in reporting ever nor past 12-month wheezing symptoms.

Discussion

Using nationally representative PATH Study data from 2015 to 2016, six questions on ever and past 12-month wheezing symptoms were assessed for differences according to the use of the top three most popular tobacco products in the United States (cigarettes, ENDS, and cigars). Ever wheezing was found to be associated with the use of cigarettes, ENDS, or any combination of cigarettes, ENDS, and cigars among the adult population when compared with noncurrent users, after adjustment for demographic and secondhand smoke exposure. Our findings for cigarette and ENDS use aligns with previous research.⁷ One potential explanation for this association is that wheezing or whistling in the chest is a result of inflammation and obstruction from the inhalation of noxious chemicals and gases found in the smoke of cigarettes and ENDS.¹² However, future longitudinal research is needed to better understand how cigarette smoking interacts with other tobacco and nicotine and contributes to respiratory symptoms. When stratifying by past smoking among ENDS users, the observed association of ENDS with ever wheezing appears to be, at least in part, attributable to past smoking. However, we cannot infer causality. In addition, cigarette use appeared to be accounting for the association between polytobacco use and wheezing symptoms due to similar point estimates. However, further analyses of each polytobacco category were inconclusive, potentially due to small sample sizes. Assessment of the four individual polytobacco groups indicated potential differences in effect size, but no significant pairwise comparisons with ever nor past 12-month wheezing symptoms were observed. In addition, when assessing the effects of past cigarette

use on ever and past 12-month wheezing symptoms, polytobacco users who have never used cigarettes (current cigar and ENDS users who have never used cigarettes) were not significantly different than their counterparts who have ever used cigarettes. However, it is important to note that there were few current users of cigars and ENDS who had never used cigarettes.

We did not observe a significant association between cigar use and ever nor past 12-month wheezing symptoms. Cigar smoke can have a higher concentration of noxious chemicals and gases compared with cigarette smoke due to the nonporous cigar wrapper, which makes the cigar tobacco burn less complete than cigarette tobacco, and many cigars are larger than cigarettes.¹⁷ However, cigar smokers report that they do not inhale the smoke into their lungs, likely due to the alkaline pH, which allows the nicotine to be readily absorbed across the oral mucosa.^{17,18} In comparison, cigarette smoke is more acidic and thus less readily absorbed in the oral mucosa.^{17,18} Therefore, inhalation into the lungs provides a larger surface area for the nicotine in cigarette smoke to be absorbed.¹⁷ Cigarette smoke has a lower pH than mini-cigarillos, filtered cigars, cigarillos, and large cigars.¹⁸ In addition, the frequency of cigarette and ENDS use has been shown to affect toxicant exposure,¹⁹ which may be true for cigar use. Furthermore, cigars have been shown to differ between cigar types and when compared to cigarettes.²⁰ Findings from Corey et al.²⁰ showed that everyday usage of cigars is less prevalent compared to cigarettes. Also, the prevalence of everyday usage among the various cigar types differs from 6.7% to 37.3%.²⁰ Finally, cigarette users have reported using 5–20 cigarettes per day, whereas users of cigars reported no more than 10 cigars per day, but was also dependent on the cigar type.²⁰ In the future, these factors should be assessed when examining the association of wheezing symptoms and the top three tobacco products in the United States.

In this study, we also assessed the association of ever and past 12-month wheezing and tobacco use stratified by age (18–34 years vs 35 years and older) and BMI (underweight or normal BMI vs overweight or obese). The stratified analyses showed the same trends as the adjusted analysis, but there were no statistically significant differences in the effect size between the age or BMI groups. However, our findings may be underestimating the association in some instances in part due to the small sample size. For example, wheezing is a broad descriptor for airway restriction that could have many causes, which could also vary by age. Wheezing can be experienced at any age, but in younger people, it is probably due to more transient conditions, while in older people it may indicate more chronic ones. In our stratified analysis, the younger (18–34 years) cigarette and polytobacco users had a smaller effect size than those of their older (35 years and older) counterparts. Given more statistical power, this association may be significantly different and likely due to the length of exposure in that older users have been using tobacco products longer than the younger users. ENDS only entered the market about 14 years ago,²¹ and have evolved rapidly in that time.²² Therefore, the association of ENDS with respiratory health may still be emerging. Furthermore, we assessed the association of BMI, as it is known to be positively correlated with wheezing. It has been shown that cigarette smokers are less likely to exercise compared with ENDS users,²³ but BMI may not be the best proxy for exercise. Future research should take additional factors into account to better understand the relationship between the use of the top three products in the United States and wheezing during or after exercise.

Research has assessed the association of cigarette and ENDS with self-reported ever and past 12-month wheezing symptoms.^{2,7}

Table 2. Association of Tobacco Product Use and Past Smoking With Wheezing Among Adults in the United States – The Population Assessment of Tobacco and Health Wave 3

Dependent wheezing symptom variables	Never smoker (ref)	Use of tobacco products										
		Former smoker	Cigarette users	ENDS users who never smoked	ENDS users who were former smokers	Cigar users who never smoked	Cigar users who were former smokers	Polytobacco users who never smoked	Polytobacco users who were former smokers			
	N (%)	aOR (95% CI) ^a	N (%)	aOR (95% CI) ^a	N (%)	aOR (95% CI) ^a	N (%)	aOR (95% CI) ^a	N (%)	aOR (95% CI) ^a	N (%)	aOR (95% CI) ^a
Ever had wheezing or whistling in chest at any time in the past												
No	8905 (82.0)	Ref	4099 (55.5)	Ref	199 (81.9)	Ref	297 (65.4)	Ref	222 (83.1)	Ref	177 (80.3)	Ref
Yes	1928 (18.0)	1.70 (1.49, 1.95)	3333 (44.5)	3.11 (2.74, 3.53)	38 (18.1)	0.73 (0.34, 1.54)	162 (34.6)	1.99 (1.47, 2.69)	44 (16.9)	0.90 (0.51, 1.58)	57 (19.7)	0.98 (0.63, 1.52)
In the past 12 mo, had wheezing or whistling in chest												
No	9774 (90.0)	Ref	4778 (64.8)	Ref	214 (87.6)	Ref	366 (80.6)	Ref	241 (91.5)	Ref	192 (85.4)	Ref
Yes	1052 (10.0)	1.58 (1.33, 1.87)	2649 (35.2)	4.55 (3.85, 5.39)	23 (12.5)	0.74 (0.28, 1.96)	93 (19.4)	1.94 (1.29, 2.90)	25 (8.5)	0.80 (0.38, 1.69)	42 (14.6)	1.49 (0.87, 2.56)
In past 12 mo, chest has sounded wheezy during or after exercise												
No	9774 (90.0)	Ref	4778 (64.8)	Ref	214 (87.6)	Ref	366 (80.6)	Ref	241 (91.5)	Ref	192 (85.4)	Ref
Yes	1052 (10.0)	1.48 (1.22, 1.80)	2649 (35.2)	3.12 (2.55, 3.81)	23 (12.5)	0.55 (0.23, 1.31)	93 (19.4)	1.40 (0.93, 2.09)	25 (8.5)	1.02 (0.56, 1.86)	42 (14.6)	1.06 (0.55, 2.04)

Results for ever wheezing, past 12-mo wheezing, and past 12-mo wheezing during or after exercise are from multivariable logistic regression. Adjusted odds ratios and their 95% confidence intervals are reported. Bolded point estimates indicates statistical significance at $p < .05$. Other models were suppressed due to low statistical power. aOR = adjusted odds ratio; CI = confidence interval; ENDS = electronic nicotine delivery system; ref = referent category.

^aModels are adjusted for age, gender, race/ethnicity, body mass index, insurance, asthma, and secondhand smoke exposure (lived with smoker during childhood, currently live with a smoker, rules about smoking combustible product inside home, and rules about using ENDS inside home).

However, as of 2018, cigar use was more prevalent than ENDS use in the United States (3.9% vs 3.2%).¹ Therefore, to our knowledge, this was the first study to assess the exclusive and polytobacco use of the top three products used in the United States. However, despite the strong external validity, internal validity, and retention rates of the PATH Study, there are still some limitations to note. First, the statistical power to assess all tobacco products was limited. Second, the data are self-reported and subject to recall bias. Third, this is a cross-sectional analysis, and therefore causality cannot be assessed. Fourth, the information for some potential confounders, such as diet and physical activity, may not be available or as robust. In addition, the nicotine dependence (eg, quantity, frequency of use, time since last cigarette among former smokers) of current and former consumers should be assessed as a potential confounder, which calls for a need of a cross-tobacco product nicotine dependence measure. Fifth, asthma was included in the models as a potential confounder to account for childhood asthma. However, the data do not allow us to separate childhood- from adult-onset asthma and may have masked the association. The removal of asthma from the models did not significantly change the point estimates, but future studies should assess childhood asthma versus adult-onset asthma as a potential confounder. Final, the data were collected in 2015–2016, at which point pod-based ENDS (eg, JUUL) that dominate the market today were not yet widely available. It is possible that these pod-based products, particularly those using higher concentration salt-based nicotine solutions, could have a differential impact on respiratory health. Therefore, future research should assess more recent data that reflect consumers of pod-based models, who may also differ in use characteristics that could affect respiratory outcomes.

This study aligns with previous findings⁷ and adds to the body of literature assessing the association of tobacco use and ever and past 12-month wheezing symptoms. Cigarette smoking and polytobacco use showed consistent and strong associations with ever and past 12-month wheezing. ENDS use, particularly in former cigarette smokers, was also associated with ever and past 12-month wheezing. This may be a function of the relative newness of the ENDS market. Therefore, future longitudinal studies should follow wheezing symptoms over time to assess changes in wheezing symptoms as the use of tobacco changes. Final, although cigar use did not show a clear association with wheezing, the composition of cigar smoke is comparable to that of cigarettes, and cigar use has other clear negative health impacts.²⁴ Eliminating the use of tobacco products remains a clear benefit to health.

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>.

Funding

This work was supported by the US Food and Drug Administration and National Cancer Institute (U54CA238110) and by the University of Rochester CTSA award number TL1 TR002000 from the National Center for Advancing Translational Sciences of the National Institutes of Health. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health or the US Food and Drug Association.

Declaration of Interests

MLG received research grant from Pfizer and served as a member of scientific advisory board to Johnson & Johnson. All other authors did not have any conflicts to report.

References

1. Creamer MR, Wang TW, Babb S, et al. Tobacco product use and cessation indicators among adults – United States, 2018. *MMWR Morb Mortal Wkly Rep*. 2019;68(45):1013–1019.
2. US Department of Health and Human Services. *The Health Consequences of Smoking – 50 Years of Progress: A Report of the Surgeon General*. Atlanta, GA: US Department of Health and Human Services; 2014.
3. Xu X, Bishop EE, Kennedy SM, Simpson SA, Pechacek TF. Annual healthcare spending attributable to cigarette smoking: an update. *Am J Prev Med*. 2015;48(3):326–333.
4. Perez MF, Atuegwu NC, Mead EL, Oncken C, Mortensen EM. Adult e-cigarettes use associated with a self-reported diagnosis of COPD. *Int J Environ Res Public Health*. 2019;16(20):3938–3948. doi:10.3390/ijerph16203938
5. Wills TA, Pagano I, Williams RJ, Tam EK. E-cigarette use and respiratory disorder in an adult sample. *Drug Alcohol Depend*. 2019;194:363–370.
6. Bhatta DN, Glantz SA. Association of E-cigarette use with respiratory disease among adults: a longitudinal analysis. *Am J Prev Med*. 2020;58(2):182–190.
7. Li D, Sundar IK, McIntosh S, et al. Association of smoking and electronic cigarette use with wheezing and related respiratory symptoms in adults: cross-sectional results from the Population Assessment of Tobacco and Health (PATH) Study, Wave 2. *Tob Control*. 2020;29(2):140–147.
8. Patel PH, Mirabile VS, Sharma S. *Wheezing*. Treasure Island, FL: StatPearls; 2019.
9. Colak Y, Afzal S, Lange P, Nordestgaard BG. Obese individuals experience wheezing without asthma but not asthma without wheezing: a Mendelian randomisation study of 85,437 adults from the Copenhagen General Population Study. *Thorax*. 2016;71(3):247–254. doi:10.1136/thoraxjnl-2015-207379
10. Wandalsen GF, Borges LV, Barroso N, et al. Gender differences in the relationship between body mass index (BMI) changes and the prevalence and severity of wheezing and asthma in the first year of life. *Allergol Immunopathol (Madr)*. 2015;43(6):562–567.
11. Heijink IH, de Bruin HG, van den Berge M, et al. Role of aberrant WNT signalling in the airway epithelial response to cigarette smoke in chronic obstructive pulmonary disease. *Thorax*. 2013;68(8):709–716.
12. Garmendia J, Morey P, Bengoechea JA. Impact of cigarette smoke exposure on host-bacterial pathogen interactions. *Eur Respir J*. 2012;39(2):467–477.
13. Muthumalage T, Prinz M, Ansah KO, Gerloff J, Sundar IK, Rahman I. Inflammatory and oxidative responses induced by exposure to commonly used e-cigarette flavoring chemicals and flavored e-liquids without nicotine. *Front Physiol*. 2017;8:1130.
14. Kaur G, Muthumalage T, Rahman I. Mechanisms of toxicity and biomarkers of flavoring and flavor enhancing chemicals in emerging tobacco and non-tobacco products. *Toxicol Lett*. 2018;288:143–155.
15. Population Assessment of Tobacco and Health (PATH) Study. doi:10.3886/Series606.
16. Hyland A, Ambrose BK, Conway KP, et al. Design and methods of the Population Assessment of Tobacco and Health (PATH) Study. *Tob Control*. 2017;26(4):371–378.
17. National Cancer Institute. Smoking and Tobacco Control Monograph 9: Cigars: Health Effects and Trends. <https://cancercontrol.cancer.gov/brp/tcrb/monographs/9/index.html>. Published 1998. Accessed January 28, 2020.
18. Lawler TS, Stanfill SB, deCastro BR, et al. Surveillance of nicotine and pH in cigarette and cigar filler. *Tob Regul Sci*. 2017;3(suppl 1):101–116.

19. Goniewicz ML, Smith DM, Edwards KC, et al. Comparison of nicotine and toxicant exposure in users of electronic cigarettes and combustible cigarettes. *JAMA Netw Open*. 2018;1(8):e185937.
20. Corey CG, Holder-Hayes E, Nguyen AB, et al. US adult cigar smoking patterns, purchasing behaviors, and reasons for use according to cigar type: findings from the Population Assessment of Tobacco and Health (PATH) Study, 2013–2014. *Nicotine Tob Res*. 2018;20(12):1457–1466. doi:10.1093/ntr/ntx209
21. US Department of Health and Human Services. *E-Cigarette Use Among Youth and Young Adults: 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; 2016.
22. National Academy of Sciences Engineering and Medicine. *Public Health Consequences of E-Cigarettes*. In: Eaton DL, Kwan LY, Stratton K, eds. Washington, DC: National Academy Press; 2018.
23. Miller C, Smith DM, Goniewicz ML. Physical activity among adolescent tobacco and electronic cigarette users: cross-sectional findings from the population assessment of tobacco and health study. *Prev Med Rep*. 2019;15:100897.
24. Chang CM, Corey CG, Rostron BL, Apelberg BJ. Systematic review of cigar smoking and all cause and smoking related mortality. *BMC Public Health*. 2015;15:390.