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Estimating the Population Attributable Fraction of Asthma Due to Electronic Cigarette Use and Other Risk Factors Using Kentucky Behavioral Risk Factor Survey Data, 2016–2017

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ABSTRACT
Introduction: Electronic nicotine delivery systems ENDS have become popular in the United States among both new users of nicotine and those seeking less harmful alternatives to traditional cigarettes. Users often perceive ENDS as being less harmful than traditional cigarettes. This study investigated the relationship between use of ENDS and asthma in a representative sample of adults. *Methods:* For this cross-sectional study, we used data from the Kentucky Behavioral Risk Factor Surveillance System telephone survey data from 2016-2017. Using a weighted multivariable logistic regression analysis, we identified important covariates to adjust for to calculate the population attributable fraction (PAF) of asthma due to ENDS and other modifiable risk factors factors (cigarette use, obesity, education, and employment). The confidence intervals for the PAFs were estimated using bootstrap methods of variance estimation. *Results:* We found that 10.6% of those aged 18-30 reported currently had asthma. After adjusting for noted covariates, ENDS use did not significantly increase the odds of asthma. In the final PAF model, the PAF of asthma due to ENDS was 0.4% (95% CI: -5.41, 6.21). *Conclusion:* While these findings suggest only modest effects of ENDS use on asthma prevalence, future research including older age groups and more long-term users might produce different results.

KEYWORDS
ENDS; e-cigarettes; nicotine; asthma; Kentucky

Introduction

Electronic cigarettes (also known as ENDS [electronic nicotine delivery systems], "e-cigarettes," or "e-cigs") have been rapidly adopted in the United States, perhaps because they have been promoted as a healthy alternative to traditional cigarette consumption and a tool for smoking cessation (Coleman et al., 2017; Ned Sharpless, 2019). Coleman and colleagues found in a recent assessment of PATH data (Population Assessment of Tobacco and Health) that among all user groups (current, former, and never cigarette smokers) the perception of lack of harm was one of the most common reasons for initiation. Former cigarette smokers also reported use of e-cigarettes as a means of smoking cessation, which appears to be a component in their growing popularity (Coleman et al., 2017). McMillen and colleagues found that adult usage increased by over 11% from 2011–2013, with current cigarette smokers being the majority of users, but nonsmokers also experiencing an increase in engagement (Coleman et al., 2017; McMillen et al., 2015; National Center for Chronic Disease P et al., 2016). It is important to note, however, that highest rates of use are among adolescents and young adults (Carroll Chapman & Wu, 2014).

The aerosols ("vapor") from e-cigarettes nevertheless share some chemical components with traditional cigarettes (e.g. nicotine), even though they do not rely on combustion. Specific design elements vary among manufacturers, but ENDS generally include three components—a heating element, a battery (often a rechargeable lithium battery), and a reservoir for the liquid that is aerosolized for the user to inhale (CDC.gov, 2020a; Grana et al., 2014). The liquid typically consists of nicotine, some flavoring, and a solvent (such as propylene glycol or vegetable glycerin) (Goniewicz et al., 2015). Many of the flavoring compounds used in these products, although perhaps noted safe for dermal or oral exposure, may have little to no assessments for inhalation (CDC.gov, 2020b; Grana et al., 2014). Other challenges include labeling inaccuracies—which may not list all substances accurately, or omit them entirely. These inconsistences have been found when evaluating both the e-cigarette solution as well as inhaled chemicals in puff-to-puff assessments (Cheng, 2014; Grana et al., 2014; Lisko et al., 2015; National Center for Chronic Disease P et al., 2016). Limited research suggests that solvent mixture could also impact the physical characteristics of the aerosol, leading to the variation in findings currently seen in the literature (Zhang

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et al., 2013). Many researchers attribute documented variations to lack of quality control in both device and liquid manufacturing (Cheng, 2014; Goniewicz et al., 2013; Grana et al., 2014; McMillen et al., 2015).

Studies comparing nicotine levels in blood plasma (CDC.gov, 2020a) and urine (Grana et al., 2014) of traditional and e-cigarette users have observed lower levels in e-cigarette users. Other studies have found that harmful toxicants often present in traditional cigarettes, such as formaldehyde, acetaldehyde, and toluene, are present in lower concentrations in both e-cigarettes solutions and the users compared to traditional cigarettes and smokers (Grana et al., 2014; Ratajczak et al., 2018). This is due to the combustion process in traditional cigarettes, absent in e-cigarettes, that generates many of the chemicals that are known to be harmful to respiratory health (Ratajczak et al., 2018).

Since e-cigarettes only became available to general consumers in, 2007 (McMillen et al., 2015), little is known about the long-term effects of use. However, cross-sectional studies suggest that e-cigarette usage is associated with higher rates of asthma, or asthma-like symptoms in both adults (Osei et al., 2019; Wang et al., 2018; Wills et al., 2019) and teens (Kim et al., 2017; Schweitzer et al., 2017; Wills et al., 2016). Although some evidence suggests smokers who switch to e-cigarettes improve their respiratory function, preliminary studies in teens indicate those who report asthma symptoms have a higher prevalence of e-cigarette use compared to their peers (Clapp & Jaspers, 2017; Polosa et al., 2014). A recent study by Wills, using data from the Hawaii BRFSS, showed that e-cigarette use in adults is associated with a decline in respiratory health compared to nonsmokers (Wills et al., 2019). Given that asthma prevalence has been increasing, and the evidence suggesting that e-cigarette use is associated with asthma symptoms, this study seeks to quantify what proportion of asthma cases in young adults (18–30) may be due to e-cigarette use—either alone or in combination with combustible tobacco products (Centers for Disease Control (CDC), 2019).

Methods

This retrospective cross-sectional analysis of existing data was evaluated by the University of Kentucky Institutional Review Board and ruled exempt.

Data were obtained directly from the Kentucky Behavioral Risk Factor Surveillance System (BRFSS) for the study period, 2016–2017. The BRFSS is a random-digit-dialed telephone survey, conducted among both mobile phones and land-based telephones annually. It is funded by the Centers for Disease Control and Prevention (CDC) but administered and conducted by the states. Responses are weighted to the population to allow for population-based estimation of the prevalence of health conditions and health-related behaviors. We focused on young adults between the ages of 18–30 because this age group has been shown to have the highest prevalence of e-cigarette use (Coleman et al., 2017; McMillen et al., 2015).

Asthma and cigarette use

Asthma classification was self-reported; those who responded affirmatively to "(Ever told) you that you had asthma?" and "do you still have asthma" were classified as having asthma (CDC, 2018). Current e-cigarette use was ascertained by the question "Do you now use e-cigarettes or other electronic vaping products every day, some days, or not at all?" For traditional cigarettes, participants who reported smoking at least 100 hundred cigarettes, and responded that they smoked "every day" or "some days" were considered current smokers. Those who reported they had not smoking 100 cigarettes or who reported smoking "not at all" were considered nonsmokers.

Other covariates

Employment was classified as employed (self-employed, or employed for wages), non-working (out of work, retired, or unable to work), or other (home-makers or students). Participants with a BMI $\geq$ 30 were classified as obese, otherwise non-obese. Other covariates included education (less than high school education, high school graduate, and some college or above), gender (male, female), marital status (married/long term relationship, divorced/separated, never married), income (<\$25k, \$25–<\$50k, >\$50k), race (white non-Hispanic, black non-Hispanic, and other [including Hispanic]), and age, (continuous).

Statistical analysis

All variables were summarized with counts and percentages for the overall sample and by current asthma status. Statistical differences among groups were assessed with chi-square tests. Unadjusted and adjusted weighted logistic regression models were used to identify key individual factors associated with asthma. To calculate the population attributable fraction (PAF) and variance estimation, adjusting for the survey weights, we used a four-step SAS macro, developed and provided by Herringa and colleagues (2015). First, we identified the risk model, a logistic regression, and entered modifiable and non-modifiable risk factors into the model. Using the macro, we estimated the parameters using BRFSS survey weights. In the third step, the macro calculated the population-weighted estimate of the PAF. In the third step, the macro calculated the standard errors and confidence limits using the bootstrap variance estimation methods. Finally, the confidence limits for the PAF were constructed. This method was repeated for each modifiable risk factor (cigarette smoking, ENDS use, education, and employment). For further detail on the process, please see Heeringa and colleagues published work (Heeringa et al., 2015).

Data management and statistical analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC). We used survey procedures to account for the complex sample survey design when applicable, and statistical significance was based on a p value <0.05.

Table 1. Demographic characteristics and modifiable risk factors for asthma among those 18–30 years old BRFSS—2016–2017.

	Asthma (N =253)	No Asthma (N = 2,107)	Total Participants (N = 2,387)	P-value
Current e-cigarette user				
Not current e-cigarette smoker	222 (90.6%)	1860 (91.5%)	2082 (91.4%)	**0.63**
Current e-cigarette smoker	23 (9.4%)	172 (8.5%)	195 (8.6%)	
Ever used e-cigarettes				
Never used e-cigarettes	143 (58.4%)	1206 (59.4%)	1349 (59.2%)	**0.77**
Ever used e-cigarettes	102 (41.6%)	826 (40.6%)	928 (40.8%)	
Current smoker				
Not current smoker	184 (74.5%)	1597 (78.3%)	1781 (77.9%)	**0.17**
Current smoker	63 (25.5%)	442 (21.7%)	505 (22.1%)	
Ever used cigarettes				
Never used cigarettes	159 (64.4%)	1388 (68.1%)	1547 (67.7%)	**0.24**
Ever used cigarettes	88 (35.6%)	651 (31.9%)	739 (32.3%)	
Obese				
Not obese	149 (66.8%)	1454 (74.5%)	1603 (73.7%)	**0.01**
Obese	74 (33.2%)	498 (25.5%)	572 (26.3%)	
Education				
Less than High School	15 (5.9%)	112 (5.3%)	127 (5.4%)	**0.31**
High School	74 (29.2%)	652 (31.0%)	726 (30.8%)	
Some college or technical degree	106 (41.9%)	770 (36.6%)	876 (37.2%)	
Bachelor's degree or above	58 (22.9%)	570 (27.1%)	628 (26.6%)	
Employment				
Employed (self or otherwise)	149 (59.4%)	1390 (66.7%)	1539 (65.9%)	**0.03**
Non-working	31 (12.4%)	176 (8.4%)	207 (8.9%)	
Student/Homemaker	71 (28.3%)	517 (24.8%)	588 (25.2%)	
Gender				
Female	170 (67.2%)	964 (45.8%)	1134 (48.1%)	**<0.01**
Male	83 (32.8%)	1143 (54.2%)	1226 (51.9%)	
Income				
<$25k	72 (43.4%)	439 (29.1%)	511 (30.5%)	**<0.01**
$25-<$50k	46 (27.7%)	426 (28.3%)	472 (28.2%)	
>$50	48 (28.9%)	642 (42.6%)	690 (41.2%)	
Race/Ethnicity				
White, Non-Hispanic	201 (79.8%)	1767 (84.6%)	1968 (84.1%)	**0.13**
Black, Non-Hispanic	25 (9.9%)	149 (7.1%)	174 (7.4%)	
Hispanic / Other race	26 (10.3%)	173 (8.3%)	199 (8.5%)	
Age				
Mean (SD)	23.7 (3.84)	24.1 (3.78)	24 (3.79)	**0.11**
Median (Q1, Q3)	23 (20, 27)	24 (21, 27)	24 (21, 27)	
Minimum, Maximum	18, 30	18, 30	18, 30	

Results

There were a total of 2387 participants, 253 (10.6%) with current asthma (Table 1). Of the total participants, 22.1% reported currently smoking cigarettes and 8.6% were current e-cigarette users. The majority of the sample was non-obese (73.7%), employed (65.9%), male (51.9%), and white (84.1%).

Of those who currently had asthma, 25.5% were current smokers, 41.6% had used ENDS devices, and 6.9% were dual users. Those with asthma were more likely to be obese (33.2%), female (67.2%), and live in a household with <$25,000 income per year (43.4%). There was also a higher percentage who were not working (12.4%) among those with asthma, compared to those without (8.4%). For those who reported not having asthma, 8.5% reported current ENDS use and 40.6% reported using a device. The majority of those without asthma did not currently smoke (78.3%) and few reported ever trying cigarettes (31.9%).

Table 2 presents the unadjusted and adjusted odds for individual factors associated with asthma. Neither e-cigarettes (AOR = 1.05, $p = 0.9$) nor cigarettes significantly increased the odds (AOR = 1.25, $p = 0.36$), adjusting for other covariates. However, those with a high school education had lower odds of asthma compared to those who had less than high school education (AOR = 0.38, $p = 0.01$). Males had 63% lower odds of asthma compared to females, adjusting for other relative covariates ($p < 0.01$).

Table 3 summarizes the PAF and 95% confidence limits for each modifiable risk factor. After controlling for asthma risk factors (obesity, cigarette smoking, employment status, gender, and education), the PAF of e-cigarettes on asthma was 0.4% (95% CI −5.41, 6.21). The largest modifiable risk factor, cigarette smoking was 2.67% (95% CI: −12.5, 16.6), however it was not significant. Compared to those who did not graduate high school, obtaining a high school degree decreased the PAF of asthma, although this was not significant (PAR = −36.1%, 95% CI: −78.2, 6.01).

Discussion

This study assessed individual characteristics associated with increased odds of asthma and calculated the PAF of asthma cases due to e-cigarette use, cigarette use, obesity, education, and employment using survey weights adjusting for gender. Our study found that a majority of Kentuckians aged 18–30 had ever used traditional cigarettes. A substantial but smaller proportion (~41%) had also tried e-cigarettes, but only 9% reported currently using them. If Kentuckians in this age group had never used ENDS, we estimate that 0.4% of

Table 2. Weighted multivariate logistic regression for current asthma, adjusted for relevant risk factors using the BRFSS 2016–2017.

	Unadjusted OR				Adjusted OR			
	OR	LCL	UCL	*p*-value	OR	LCL	UCL	*p*-value
Current ENDS user								
Not ENDS user	Reference				Reference			
ENDS user	1	0.52	1.91	1	1.06	0.5	2.21	0.89
Current Cigarette Smoker								
Not a smoker	Reference				Reference			
Smoker	1.54	0.98	2.42	0.06	1.13	0.69	1.84	0.63
Obese								
Non-obese	Reference				Reference			
Obese	1.24	0.82	1.87	0.31	0.99	0.62	1.56	0.96
Education								
Less than a high school	Reference				Reference			
High school	0.49	0.24	1.02	0.06	0.37	0.18	0.77	0.01
Some college or technical degree	0.54	0.26	1.11	0.09	0.48	0.24	0.98	0.04
BA or above	0.4	0.19	0.87	<0.01	0.3	0.14	0.66	<0.01
Employment								
Not employed	Reference				Reference			
Employed (self or otherwise)	0.44	0.24	0.82	0.01	0.59	0.32	1.07	0.08
Student/Homemaker	0.44	0.22	0.87	0.02	0.41	0.2	0.84	0.01
Race/Ethnicity								
White	Reference				Reference			
Black, Non-Hispanic	1.2	0.64	2.26	0.57	1.16	0.57	2.39	0.68
Hispanic / Other race	1.04	0.53	2.02	0.91	1.15	0.54	2.45	0.72
Gender								
Female	Reference				Reference			
Male	0.39	0.26	0.59	<.0001	0.36	0.23	0.56	<0.01
Age	1.01	0.96	1.07	0.68	1	0.95	1.06	<0.01

Table 3. Population attributable fraction (%) and 95% Confidence Interval for modifiable risk factors for asthma among those aged 18–30, BRFSS 2016–2017.

	AF	LCL	UCL
Current smoker	2.67	−12.47	16.59
Current e-cigarette smoker	0.40	−5.41	6.21
Obesity	0.04	−9.39	9.48
Education			
Less than High School	*Reference*		
High School	−36.11	−78.23	6.01
Some college or technical degree	−33.31	−73.24	6.63
BA or above	−20.83	−39.52	−2.14
Employment			
Non-Working	*Reference*		
Employed (self or otherwise)	−31.57	−83.57	20.42
Student/Homemaker	−25.61	−43.47	−7.76

asthma cases could have been prevented in those aged 18–30 in Kentucky (95% CI: −5.41, 6.21). This equates to approximately 2890 cases, given the U.S. Census-estimated number of Kentucky adults aged (18–29) range in 2017, and the prevalence of asthma that we estimated for this age range in Kentucky (Bureau USC, 2017).

Although the literature suggests obesity is a major risk factor for asthma (Kim et al., 2017), we did not observe this after adjustment for noted covariates. Furthermore, the PAF of asthma for obesity was very low. We did, however, find a strong negative association between asthma and educational attainment, which does agree with what is already known about associations between asthma and socioeconomic status (Ellison-Loschmann et al., 2007). This might also partially explain why, compared to those who were unemployed, those who worked or were a student/homemaker had lower prevalence of asthma.

Although the asthma PAF we observed for those aged 18–30 was not statistically significant, further work is still needed. This study only included adults 18–30 years old, who may not have been using these products long enough to experience symptoms consistent with asthma. Furthermore, use rates of ENDS might increase in older age groups over the next few decades without substantial intervention. This seems especially likely given research showing that people begin using these products at younger ages (Carroll Chapman & Wu, 2014; Evans-Polce et al., 2020).

Given the noted lack of quality control in product manufacturing, wide variety of compounds used in these products, and lack of inhalation exposure assessment, the long-term health effects of ENDS use are unknown. Studies assessing short-term health effects of ENDS use suggest that, although less harmful than traditional cigarettes, users still experience respiratory symptoms (Osei et al., 2019; Schweitzer et al., 2017; Wang et al., 2018; Wills et al., 2019). Furthermore, those with preexisting asthma may suffer more immediate health effects, such as reduced pulmonary function and airway inflammation, compared to those without asthma (Kotoulas et al., 2020). After adjusting for other covariates, we found that there was an increase in the odds of asthma for those who use e-cigarettes that were quite similar to that for combustible cigarettes, although the association was not statistically significant.

Limitations of this study are inherent in its cross-sectional design and implementation *via* telephone survey. The data were self-reported, and we were unable to confirm asthma diagnosis or obtain other relevant information, such as age of onset. Additionally, we do not know the length of ENDS use, the frequency that respondents consumed these products, or if their use preceded onset of asthma symptoms. There also may be bias in reporting ENDS or cigarette use, as participants from some demographic groups, due to social desirability bias, may not acknowledge use.

Additionally, other risk factors, such as occupational exposures, could not be accounted for, as these questions are not included in the standard BRFSS questionnaire. Additional limitations relate to the exclusion of respondents outside the 18–30 age range, which was necessary due to very low current use rates of ENDS among older adults. Lastly, our results may not be generalizable to other states, as they are derived from a population-based sample of Kentucky adults.

Conclusion

This study found preliminary evidence that ENDS use modestly contributes to asthma burden, but further work exploring this in a larger sample is needed.

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Conflicts of interest

None

Declaration of interest

There are no competing interests to declare.

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