

Original investigation

# Use of Electronic Cigarettes and Self-Reported Chronic Obstructive Pulmonary Disease Diagnosis in Adults

Zidian Xie<sup>1</sup>, Deborah J. Ossip<sup>2</sup>, Irfan Rahman<sup>3</sup>, Dongmei Li<sup>1</sup>

<sup>1</sup>Department of Clinical & Translational Research, University of Rochester Medical Center, Rochester, NY; <sup>2</sup>Department of Public Health Sciences, University of Rochester Medical Center, Rochester, NY; <sup>3</sup>Department of Environmental Medicine, University of Rochester Medical Center, Rochester, NY

Corresponding Author: Dr. Zidian Xie, Department of Clinical & Translational Research, University of Rochester Medical Center, Rochester, NY 14642-0708, USA. Telephone: 585-275-4398; Fax: 585-276-1122; E-mail: [zidian\\_xie@urmc.rochester.edu](mailto:zidian_xie@urmc.rochester.edu)

## Abstract

**Introduction:** Electronic cigarette (e-cigarette) use (vaping) has increased in recent years. Chronic obstructive pulmonary disease (COPD) is the third leading cause of death associated with smoking.

**Aims and Methods:** Based on 2016 and 2017 Behavioral Risk Factor Surveillance System national survey data on 891 242 adult participants who indicated their smoking and vaping status, the cross-sectional association of vaping with self-reported COPD diagnosis was investigated, using univariable and multivariable weighted logistic regression models.

**Results:** Compared to never users, while dual users showed the highest association with self-reported COPD diagnosis (adjusted odds ratio [aOR] = 4.39; 95% confidence interval [CI] = 3.98 to 4.85), current vapers who were either ex-smokers or never smoked showed significantly higher association with self-reported COPD diagnosis (aOR = 3.24; 95% CI = 2.78 to 3.78 and aOR = 1.47; 95% CI = 1.01 to 2.12, respectively). Current vapers who were ex-smokers showed higher association with self-reported COPD diagnosis than ex-smokers who do not vape (aOR = 1.27; 95% CI = 1.09 to 1.48). Dual users showed higher association with self-reported COPD diagnosis than current smokers who do not vape (aOR = 1.16; 95% CI = 1.05 to 1.27). Ex-smokers showed significantly less association with self-reported COPD diagnosis (aOR = 0.67; 95% CI = 0.64 to 0.71) than current smokers. Current vapers who were either ex-smokers or never smoked had less association with self-reported COPD diagnosis compared to current smokers, with aOR = 0.85 (95% CI = 0.73 to 0.99) and aOR = 0.39 (95% CI = 0.27 to 0.56).

**Conclusions:** Vaping is significantly associated with self-reported COPD diagnosis in adults, even among vapers who never smoked. Whether there is a benefit for COPD of switching from smoking to vaping requires study of the long-term effects of vaping.

**Implications:** With the increase of e-cigarette use in recent years, the health effects of e-cigarettes need to be investigated. While several studies have examined the association of vaping with respiratory symptoms among adolescents, little is known about the association of vaping with susceptibility to COPD among US adults. Using cross-sectional national survey data in adults, our study showed that vaping was significantly associated with self-reported COPD diagnosis. Although our data did not

establish the causal relationship between vaping and self-reported COPD diagnosis, this study raises concerns about the observed association between vaping and self-reported COPD diagnosis.

## Introduction

Cigarette smoking, the leading causes of preventable death in the United States, leads to many health risks, including heart disease, stroke, and lung cancer.<sup>1</sup> Chronic obstructive pulmonary disease (COPD) caused by smoke exposure is projected to be the third leading cause of death.<sup>2</sup> Since introduced to the United States in 2007 as a purported safer alternative to traditional cigarettes, electronic cigarette (e-cigarette) use prevalence has increased, especially among youth.<sup>3,4</sup> While most studies have focused on health effects, such as COPD, of cigarette smoking,<sup>5,6</sup> several recent studies have explored the potential effect of e-cigarettes on risk indicators of COPD, mainly in mice and human cells. E-cigarette use has been well shown to cause oxidative stress and inflammation in mice and human bronchial and lung epithelial cells, including in human e-cigarette users,<sup>7-13</sup> and to compromise the immune defense against bacterial and viral infection in the mouse model,<sup>14</sup> which in turn might lead to the development of COPD. One study demonstrated that e-cigarette exposure in mice could induce pathogenic response similar to what occurs in human COPD.<sup>15</sup> However, in vitro cell systems or animal models do not reflect actual health outcomes in human.<sup>16</sup> By measuring the level of innate defense proteins associated with COPD in induced sputum samples, e-cigarette users showed similar changes in innate defense proteins as smokers, suggesting that e-cigarettes might have similar effects on the human airway as traditional cigarettes.<sup>17</sup>

While e-cigarette use is considered as a potential tobacco harm reduction approach,<sup>18</sup> little is known about the health effects of e-cigarettes on humans.<sup>19,20</sup> While one study showed that adolescent current e-cigarette users had elevated but not significant risk of chronic bronchitic symptoms,<sup>21</sup> other studies showed that e-cigarette use significantly increased the risk of respiratory symptoms in Chinese adolescents in Hong Kong who were either never-smokers or ex-smokers,<sup>22</sup> as well as in South Korea adolescents<sup>23</sup> and California high-school students.<sup>21</sup> Although these studies established the possible association of vaping with respiratory symptoms among adolescents, these studies have certain limitations since some important confounding variables were not controlled in their models.<sup>16</sup> For example, smoking history was not carefully controlled for, but past smoking can have long-term effects on respiratory symptoms. There is still little evidence on the association of vaping with respiratory disorder among adults. Vaping has been shown to be associated with an increased risk of wheezing and other related respiratory symptoms in adults.<sup>24</sup> A recent study showed an association between vaping and respiratory disorder (including COPD and asthma) among non-smokers based on Behavioral Risk Factor Surveillance System (BRFSS) data for Hawaii adults.<sup>25</sup>

Due to the limitation of currently available data, some methodological limitations (eg, unstandardized e-cigarette aerosol extraction procedure in cell line studies and unrealistic pattern of e-cigarette use in mouse studies) with previous studies on the association of vaping with respiratory health,<sup>16</sup> as well as varying definitions of smoking and vaping status, there is no clear conclusion about the association of vaping with risk in COPD in adults. Although it might take decades to confirm the long-term health effects of e-cigarettes, it is possible to detect an early change in respiratory symptoms (such as COPD) due to vaping with current

available data. Using 2016 and 2017 BRFSS national survey data, we investigated the cross-sectional association of vaping with self-reported COPD diagnosis among never-smokers, past smokers, and current smokers in US adults.

## Methods

### Data Source and Participants

The open-source BRFSS national survey data from 2016 and 2017 were collected by the Centers for Disease Control and Prevention. BRFSS is a cross-sectional national health-related telephone (including cellular and landlines) survey on health-related risk behaviors and chronic health status among adults (18 years or older) in the United States. Each state determined whether to sample by county, public health districts, or other substate geography. Samples of telephone numbers (landline and cellular) were obtained from the Centers for Disease Control and Prevention. Random selection based on the number of adults living within a residence was used in the landline sample, while cellular telephone participants were weighted as single-adult households.<sup>26</sup> There were 486 303 adult participants in 2016 and 450 016 adult participants in 2017. The combined 2016 and 2017 BRFSS data resulted in a dataset of 936 319 adult participants.

### Vaping and Smoking Status

To eliminate the potential long-term effect of previous smoking on self-reported COPD diagnosis, we distinguished past smokers from never-smokers, therefore grouping the adult participants into six smoking and vaping categories: (1) Current smokers: Have smoked at least 100 cigarettes in your entire life, now smoke every day or some days, and not currently vaping. (2) Dual users: Have smoked at least 100 cigarettes in your entire life, now smoke every day or some days, and currently vaping every day or some days. (3) Ex-smokers: Have smoked at least 100 cigarettes in your entire life, now do not smoke cigarettes at all, and not currently vaping. (4) Current vapers who were ex-smokers: Have smoked at least 100 cigarettes in your entire life, now do not smoke cigarettes at all, currently vaping every day or some days. (5) Current vapers who never smoked: Have smoked fewer than 100 cigarettes in your entire life, and now do not smoke cigarettes at all, currently vaping every day or some days. (6) Never users: Have smoked less than 100 cigarettes in your entire life, now do not smoke cigarettes at all, and not currently vaping.

### Outcome Variable and Covariates

The outcome variable was based on the following item: (Ever told) you have COPD, emphysema, or chronic bronchitis? The outcome variable "self-reported COPD diagnosis" has two levels, "yes" or "no." Only participants who answered either "yes" or "no" to this question were included in our analysis. Covariates controlled for in our analysis included age, sex, race/ethnicity, marital status, employment status, education level, income level, body mass index, and general health categories, which were purposefully selected.<sup>27</sup> Briefly, any variable showing a significant univariate test ( $p$ -value < .25) was included in the multivariate analysis. Starting from the nonsignificant covariate that had the largest  $p$ -value, we removed

the covariates one by one from the model. Every time we removed a covariate, we checked both percentage changes in estimated coefficients of remaining covariates and goodness-of-fit test to determine whether they were important confounding variables. After all significant covariates selected in the first step were tested, a prefinal model was obtained. Then, variables not originally included in the model were added back to the final model to check their significance and possible confounding effects. Through this iterative process of deleting, refitting, and verifying, the final model only included significant confounding variables. To compare the contribution of age to the association of vaping with self-reported COPD diagnosis, we grouped age into three levels: 18–34, 35–64, and over 65 years. We also discretized the income into five levels: “less than \$10 000,” “\$10 000 to \$20 000,” “\$20 000 to \$35 000,” “\$35 000 to \$75 000,” and “\$75 000 or more.”

### Statistical Analysis

To examine the association of smoking and vaping status with covariates, weighted frequency distributions were conducted. Univariable and multivariable weighted logistic regression models were used to examine the association of smoking and vaping status with the outcome variable “self-reported COPD diagnosis.” The covariates were included in multivariable weighted logistic regression models if they significantly contributed to the models ( $p$ -value < .05) and showed no multicollinearity with other variables. Since BRFSS data were collected through landline telephone and cellular telephone, to account for the sampling design, the variable \_LLCPWT assigned to each respondent as final weight was included in our statistical analysis. The variable \_STSTR used for stratification and the variable \_PSU used for clustering were included in our statistical models. Since 2016 and 2017 BRFSS data were combined in our study, the final weight was calculated as dividing each year’s weight by 2.

Unadjusted odds ratios (ORs) from univariable weighted logistic regression models and adjusted ORs (aORs) from multivariable weighted logistic regression models, and their 95% confidence intervals (CIs), were used to quantify the association between vaping and self-reported COPD diagnosis. To stratify the association of vaping with self-reported COPD diagnosis on age, we calculated aORs at three age group levels: 18–34, 35–64, and over 65 years. All analyses were conducted using PROC SURVEY procedure in SAS V.9.4 (SAS Institute, Inc, Cary, NC), accounting for the complex sampling design. The standard deviations were estimated using the Taylor series linearization method. All tests were two-sided with a significance level of 5%.

## Results

### Demographic Characteristics of Smoking and Vaping Status

After combining 2016 and 2017 BRFSS survey data, there were 936 319 adult participants ( $\geq 18$  years old). Of these, 891 242 (95%) indicated their current smoking and vaping status, including 15 986 dual users (1.8%), 115 189 current smokers (12.9%), 245 973 ex-smokers (27.6%), 8876 current vapers who were ex-smokers (1.0%), 3912 current vapers who never smoked (0.4%), and 501 306 never users (56.2%).

While most current smokers were between 35 and 64 years old (58.26%), the majority of current vapers who never smoked were

between 18 and 34 years old (87.86%) (Supplementary Table S1). Except for never users, there were more males than females in other smoking/vaping categories, especially in current vapers who were either ex-smokers or never smoked (62.25% and 66.47%, respectively). For all smoking and vaping statuses, especially for current vapers who were ex-smokers, the majority were White. The prevalence of current vapers who never smoked among different race/ethnicity categories was similar to that of never users, suggesting that the number of current vapers who never smoked (mostly between 18 and 34 years old) in each race/ethnicity category is relatively proportional to their population. The majority of current vapers who never smoked were never married (70.87%), which is consistent with most of them being aged 18–34 years. For both ex-smokers and never users, most current vapers had graduated high school or attended college or technical school. As has been shown previously, adults with the highest education level—graduated from college or technical school—were more likely to be never users or ex-smokers. Among dual users and current smokers, most were at low-income levels (<\$35 000). While a relative high percentage of current vapers who never smoked were at normal weight (44.26%), the population in other smoking and vaping status was evenly distributed among normal weight, overweight, and obesity. Relative higher percentages of dual users and current smokers were in fair or poor general health relative to never-smokers, 20% versus 11% in fair and 8.6% versus 3.2% in poor condition. By comparison, in general, current vapers who never smoked were younger and more likely to be unmarried male compared to never users.

### Cross-Sectional Association of Vaping With Self-Reported COPD Diagnosis

Among 891 242 adults who indicated their smoking and vaping status, 887 182 responded to the question about whether they were

**Table 1.** The Association of Vaping With Self-Reported COPD Diagnosis in Adults

Smoking and vaping status	Unadjusted OR (95% CI)	Adjusted OR (95% CI)
Dual users	5.97 (5.51, 6.47)	4.39 (3.98, 4.85)
Current smokers	5.79 (5.53, 6.05)	3.80 (3.58, 4.02)
Current vapers who were ex-smokers	3.66 (3.14, 4.27)	3.24 (2.78, 3.78)
Current vapers who never smoked	0.71 (0.53, 0.96)	1.47 (1.01, 2.12)
Ex-smokers	3.99 (3.83, 4.16)	2.56 (2.43, 2.69)
Never users	Reference	Reference
Current smokers	1.45 (1.39, 1.51)	1.48 (1.41, 1.56)
Current vapers who were ex-smokers	0.92 (0.79, 1.07)	1.27 (1.09, 1.48)
Ex-smokers	Reference	Reference
Ex-smokers	0.69 (0.66, 0.72)	0.67 (0.64, 0.71)
Dual users	1.03 (0.95, 1.12)	1.16 (1.05, 1.27)
Current vapers who were ex-smokers	0.63 (0.54, 0.74)	0.85 (0.73, 0.99)
Current vapers who never smoked	0.12 (0.09, 0.17)	0.39 (0.27, 0.56)
Current smokers	Reference	Reference

BMI = body mass index; CI = confidence interval; COPD = chronic obstructive pulmonary disease; ORs = odds ratios.

The covariates controlled for the adjusted ORs: age, sex, race/ethnicity, marital status, employment status, education, income, BMI, and general health.

told that they have COPD and were included in our further analysis, including 812 175 (91.55%) who answered “no” and 75 007 (8.45%) who answered “yes.” To examine the association of vaping with self-reported COPD diagnosis, the unadjusted and adjusted ORs based on univariable and multivariable weighted logistic regression models were calculated (Table 1). Compared to never users, all smoking and vaping categories with the exception of current vapers who never smoked showed significantly higher unadjusted ORs for self-reported COPD diagnosis, ranging from 3.66 to 5.97. After adjusting for the confounding variables, dual users, current smokers, current vapers who were ex-smokers, and ex-smokers continued to show significantly higher aORs for self-reported COPD diagnosis than never users, ranging from 2.56 to 4.39. Therefore, either current or past smoking, both with and without vaping, is significantly associated with self-reported COPD diagnosis. Contrary to lower unadjusted OR for self-reported COPD diagnosis (OR = 0.71; 95% CI = 0.53 to 0.96), after adjusting for the confounding variables, current vapers who never smoked had a higher aOR for self-reported COPD diagnosis (aOR = 1.47; 95% CI = 1.01 to 2.12) than never users, suggesting that vaping alone is associated with self-reported COPD diagnosis.

As given in Table 1, compared to ex-smokers, current vapers who were ex-smokers showed significantly higher aOR for self-reported COPD diagnosis (aOR = 1.27; 95% CI = 1.09 to 1.48), which demonstrates that vaping is significantly associated with self-reported COPD diagnosis in ex-smokers. Compared to current smokers, dual users showed slightly higher aOR (aOR = 1.16; 95% CI = 1.05 to 1.27), which suggests that vaping could increase the association with self-reported COPD diagnosis in current smokers. Compared to current smokers, ex-smokers showed significantly lower aOR for self-reported COPD diagnosis (aOR = 0.67; 95% CI = 0.64 to 0.71), indicating quitting smoking can significantly decrease the association with self-reported COPD diagnosis. In addition, compared to current smokers, current vapers who were either ex-smokers or never smoked showed significantly lower aORs, 0.85 (95% CI = 0.73 to 0.99) and 0.39 (95% CI = 0.27 to 0.56) respectively, suggesting that

vaping has significantly lower association with self-reported COPD diagnosis compared to smoking.

### The Association of Vaping With Self-Reported COPD Diagnosis by Age Group

Considering the onset for COPD is in mid-life, and most of the current vapers who never smoked (87.86%) were between 18 and 34 years old (Supplementary Table S1), we decided to examine the association of vaping with self-reported COPD diagnosis at different age groups, 18–34, 35–64, and over 65 years. As given in Table 2, in all three age groups, compared to never users, all smoking/vaping categories showed higher association with self-reported COPD diagnosis as indicated by high aORs, and their aORs increased with the increase in age. Although compared to never users, aORs for current vapers who never smoked were higher, they were not statistically significant, which was likely due to the small sample sizes for current vapers who never smoked and had COPD in all three age groups: 65 participants in the 18–34 age group, 50 participants in the 35–64 age group, and 11 participants in the over 65 age group. However, when the two older age groups were combined, the association with self-reported COPD diagnosis for current vapers who never smoked became statistically significant due to the increase of power, with aOR = 1.78 (95% CI = 1.04 to 3.05).

Compared to ex-smokers, while aOR of current vapers who were ex-smokers in the 18–34 age group was not significant (aOR = 0.99; 95% CI = 0.59 to 1.67), their association with self-reported COPD diagnosis became higher in 35–64 and over 65 age groups, with aOR = 1.22 (95% CI = 1.01 to 1.46) and aOR = 2.11 (95% CI = 1.66 to 2.69), respectively. Similarly, compared to current smokers, although dual users did not show significantly higher association with self-reported COPD diagnosis in 18–34 age group (aOR = 1.22; 95% CI = 0.96 to 1.56), their association with self-reported COPD diagnosis became significant in 35–64 and over 65 age groups, with aOR = 1.15 (95% CI = 1.02 to 1.30) and aOR = 1.57 (95% CI = 1.22 to 2.00), respectively. Together, the association of vaping with

**Table 2.** The Association of Vaping With Self-Reported COPD Diagnosis in Different Age Groups

Smoking and vaping status	Adjusted OR (95% CI)		
	Age: 18–34 ( <i>n</i> = 139 982)	Age: 35–64 ( <i>n</i> = 425 843)	Age: 65+ ( <i>n</i> = 310 826)
Dual users	2.84 (2.22, 3.63)	4.02 (3.54, 4.57)	8.38 (6.57, 10.68)
Current smokers	2.32 (1.95, 2.76)	3.50 (3.24, 3.78)	5.35 (4.87, 5.89)
Current vapers who were ex-smokers	1.79 (1.09, 2.93)	2.76 (2.29, 3.32)	6.77 (5.29, 8.66)
Current vapers who never smoked	1.09 (0.66, 1.79) <sup>a</sup>	1.56 (0.85, 2.85) <sup>b</sup>	2.48 (0.81, 7.53) <sup>c</sup>
Ex-smokers	1.80 (1.42, 2.29)	2.27 (2.10, 2.45)	3.21 (2.98, 3.45)
Never users	Reference	Reference	Reference
Current smokers	1.29 (1.01, 1.63)	1.55 (1.44, 1.66)	1.67 (1.53, 1.82)
Current vapers who were ex-smokers	0.99 (0.59, 1.67)	1.22 (1.01, 1.46)	2.11 (1.66, 2.69)
Ex-smokers	Reference	Reference	Reference
Ex-smokers	0.78 (0.61, 0.99)	0.65 (0.60, 0.70)	0.60 (0.55, 0.65)
Dual users	1.22 (0.96, 1.56)	1.15 (1.02, 1.30)	1.57 (1.22, 2.00)
Current vapers who were ex-smokers	0.77 (0.47, 1.26)	0.79 (0.66, 0.95)	1.26 (0.98, 1.63)
Current vapers who never smoked	0.47 (0.28, 0.78)	0.44 (0.24, 0.81)	0.46 (0.15, 1.41)
Current smokers	Reference	Reference	Reference

BMI = body mass index; CI = confidence interval; COPD = chronic obstructive pulmonary disease; ORs = odds ratios.

The covariates controlled for the adjusted ORs: age, sex, race/ethnicity, marital status, employment status, education, income, BMI, and general health.

<sup>a</sup>65 subjects with COPD out of 3135.

<sup>b</sup>50 subjects with COPD out of 649.

<sup>c</sup>11 subjects with COPD out of 93.



self-reported COPD diagnosis becomes more pronounced with the increase of age.

## Discussion

Although the association between smoking and COPD is well studied previously,<sup>28–30</sup> little has been done to determine the association between vaping and COPD in adults. In this study using national BRFSS survey data, we investigated the cross-sectional association of vaping with self-reported COPD diagnosis in adults. We observed a significant cross-sectional association of vaping with self-reported COPD diagnosis irrespective of their current smoking status (including never users, ex-smokers, and current smokers). Many e-cigarette users were former smokers.<sup>31</sup> Some studies showed significant changes in DNA methylation in the nasal epithelia of ex-smokers,<sup>32</sup> suggesting the long-lasting effects of smoking. However, many studies that examined the association of vaping with susceptibility to COPD did not distinguish current vapers who were ex-smokers from current vapers who never smoked, as well as ex-smokers from never users,<sup>17,33</sup> which made it difficult to draw conclusions about the association between vaping and susceptibility to COPD. In this study, we further grouped current vapers into two groups, current vapers who were ex-smokers and current vapers who never smoked. In addition, we grouped current nonsmokers into ex-smokers and never users to exclude the long-term health effects of past smoking. With these additional groupings, we showed that current vapers who never smoked had significantly higher aORs for self-reported COPD diagnosis than never users, which demonstrate that vaping is associated with self-reported COPD diagnosis in never-smokers. Furthermore, compared to ex-smokers, current vapers who were ex-smokers showed significantly higher aORs, suggesting the significant association of vaping with self-reported COPD diagnosis in ex-smokers. In addition, compared to current smokers, dual users had a slightly higher association with self-reported COPD diagnosis as indicated by aORs. Altogether, our results indicated that vaping is significantly associated with self-reported COPD diagnosis.

Tobacco smoking has many health consequences, including cancer, heart diseases, and respiratory diseases. Smoking cessation is critical to reduce health risks. Vaping has been associated with complete switching from cigarettes to e-cigarettes or dual use of both traditional cigarettes and e-cigarettes.<sup>34</sup> In this study, we showed that compared to current smokers, dual users had higher association with self-reported COPD diagnosis, while current vapers who were ex-smokers had a slightly lower association with self-reported COPD diagnosis. These data are consistent with previous findings that dual use did not reduce carcinogen and toxin exposure compared to smoking but vaping did.<sup>35</sup> Another explanation could be that dual users might be more addicted to smoking or heavy smokers, which might account for higher association with self-reported COPD diagnosis relative to smokers or vapers.

E-cigarettes contain hundreds of chemicals while cigarettes contain thousands of constituents,<sup>36–38</sup> and thus, e-cigarette use is considered potentially less harmful than smoking, though not safe.<sup>39,40</sup> Several studies showed that e-cigarette use had substantially reduced risk in tobacco-related carcinogens and toxins compared to smoking.<sup>35,41</sup> Our studies showed that current vapers who were ex-smokers or never smoked had significantly lower associations with self-reported COPD diagnosis compared to current smokers, as indicated by small aORs, which is consistent with previous findings that switching from smoking to e-cigarette use attenuated

respiratory infections.<sup>42–45</sup> However, another possible explanation for the reduced association with self-reported COPD diagnosis in vapers compared to smokers could be that the duration of vaping may be not as long as smoking, as e-cigarettes have been on the market for a much shorter period of time. Therefore, the long-term association of vaping with self-reported COPD diagnosis may not yet have emerged. Together, extra caution should be taken in interpreting these results especially considering unknown long-lasting health effects of vaping, and current results could underestimate the association of vaping with self-reported COPD diagnosis. Another possibility is that we could overestimate the association of vaping with self-reported COPD diagnosis due to some unmeasured confounding variables.

Although our data showed that without considering long-term health effects of vaping, vaping has a lower association with self-reported COPD diagnosis relative to smoking, it still significantly increased the association with self-reported COPD diagnosis compared to never users. Compared to never users, current vapers who never smoked had a lower unadjusted OR (OR = 0.71; 95% CI = 0.53 to 0.96) but higher aOR (aOR = 1.47; 95% CI = 1.01 to 2.12) for self-reported COPD diagnosis. By examining the contribution of each covariate in the model, we identified that the age contributed the most to this flip in the association, which suggests that the age is an important covariate in the association of vaping with self-reported COPD diagnosis. Our further subgroup age analysis showed that the association of vaping with self-reported COPD diagnosis was the strongest among older adults. Compared to young adults with age 18–34, the aORs for self-reported COPD diagnosis among vapers or smokers were higher among adults with age 35–64, which is consistent with the general notion that the onset for COPD is around 40 years old. Older adults with age over 65 had the highest aORs for self-reported COPD diagnosis among vapers or smokers. Compared to never users, although aORs for self-reported COPD diagnosis increased with age, this was not statistically significant for current vapers who never smoked. However, this may well be due to the small sample sizes in the older age groups for current vapers who never smoked, as the relationship between age and self-reported COPD diagnosis in this category of vapers was significant when these two older age groups were combined to provide greater power for analyses. This independent association of vaping alone with self-reported COPD diagnosis raises potential health concerns.

While our studies confirmed the long-term association of past smoking with self-reported COPD diagnosis as indicated by significantly higher aOR of ex-smokers compared to never users, our data also showed that ex-smokers had a significantly lower aOR than current smokers, demonstrating that quitting smoking can significantly reduce the association with self-reported COPD diagnosis.

The current study focused on vaping and self-reported COPD diagnosis and did not examine asthma. As the two most common respiratory diseases, asthma and COPD have both similarities and differences.<sup>46</sup> While the onset for COPD is around 40 years old, asthma may begin at earlier ages.<sup>47</sup> Therefore, they should be studied separately.<sup>25</sup> Considering that participants in the BRFSS survey were over 18 years old, we restricted our focus to COPD.

Due to the cross-sectional characteristics of the BRFSS survey data, we could not test the causal relationship between vaping and self-reported COPD diagnosis. The association of vaping with self-reported COPD diagnosis could have two different explanations. One is that patients who had respiratory disorder (such as COPD) began vaping to alleviate the respiratory symptoms. This explanation

might be true for dual users. However, it is not reasonable for participants who never smoked to start vaping due to respiratory disorder. Another explanation is that vaping might contribute to the development of respiratory disorder. Since the BFRSS data do not provide such information about the duration of self-reported COPD diagnosis and vaping, we could not support either explanation in this study.

In this study, COPD was not measured directly. The recommended diagnosing guideline for COPD is below 0.70 for the ratio of the forced expiratory volume in the first second to the forced vital capacity (FEV1:FVC).<sup>48</sup> However, since the BRFSS data do not provide the measurement of FEV1:FVC, we could not measure COPD directly. Instead, self-reported COPD diagnosis was used as the outcome variable, which is another limitation of this study. Although one previous study showed that the long-term e-cigarette use without any smoking history did not show an association with any health concerns including respiratory symptoms,<sup>49</sup> the results were not conclusive since it was only 3.5-year study with only nine young subjects (average 27–28 years old). Therefore, we need longitudinal data on a large sample of vapers who never smoked to determine the causal effect of vaping on COPD.

We classified participants into six groups based on their smoking and vaping status. Since the BRFSS data do not provide any information about the duration and amount of e-cigarette use, we could not determine whether the exposure to e-cigarettes was sufficient for the development of COPD. In addition, there might be other covariates relevant to the association of vaping with self-reported COPD diagnosis, such as the duration and frequency of smoking, and some nontobacco-related factors (such as air quality), which could not be included in our models due to their unavailability in the BRFSS data.

Similar to all survey data, BRFSS data are self-reported and subject to recall error. Another limitation is that the health effects of secondhand smoking as well as the long-term health effects of vaping could not be evaluated due to the limitation of BRFSS data. With the increasing prevalence of vaping in middle school and high-school students, it is critical to investigate the association of vaping with self-reported COPD diagnosis during adolescence.

In summary, the current study demonstrated a significant association between vaping and self-reported COPD diagnosis. Though somewhat less than the association with smoking, this relation with self-reported COPD diagnosis was present even among vapers who never smoked, suggesting an independent risk for vaping. Taken with prior findings from basic studies of respiratory effects of e-cigarette components<sup>8,10,15</sup> and human studies<sup>21–24</sup> demonstrating associations of vaping with respiratory symptoms, the current findings regarding the significant association between vaping and self-reported COPD diagnosis in adults raise concerns about respiratory risks associated with vaping.

## Supplementary Material

Supplementary data are available at *Nicotine and Tobacco Research* online.

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## Declaration of Interests

None declared.

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ZX and DL conceived and designed the study. ZX analyzed the data. ZX, DJO, IR, and DL assisted with the interpretation of analyses and wrote and edited the manuscript. 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 Food and Drug Administration.

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