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

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ABSTRACT

Background Wheezing is a symptom of potential respiratory disease and known to be associated with smoking. Electronic cigarette use ('vaping') has increased exponentially in recent years. This study examined the cross-sectional association of vaping with wheezing and related respiratory symptoms and compare this association with smokers and dual users.

Methods The Population Assessment of Tobacco and Health study wave 2 data collected from October 2014 to October 2015 with 28 171 adults were used. The cross-sectional association of vaping with self-reported wheezing and related respiratory symptoms relative to smokers and dual users of tobacco and electronic cigarettes were studied using multivariable logistic and cumulative logistic regression models with consideration of complex sampling design.

Results Among the 28 171 adult participants, 641 (1.2%) were current vapers who used e-cigarettes exclusively, 8525 (16.6%) were current exclusive smokers, 1106 (2.0%) were dual users and 17 899 (80.2%) were non-users. Compared with non-users, risks of wheezing and related respiratory symptoms were significantly increased in current vapers (adjusted OR (aOR)=1.67, 95% CI: 1.23 to 2.15). Current vapers had significantly lower risk in wheezing and related respiratory symptoms compared with current smokers (aOR=0.68, 95% CI: 0.53 to 0.87). No significant differences were found between dual users and current smokers in risk of wheezing and related respiratory symptoms (aOR=1.06, 95% CI: 0.91 to 1.24).

Conclusions Vaping was associated with increased risk of wheezing and related respiratory symptoms. Current vapers had lower risk in wheezing and related respiratory symptoms than current smokers or dual users but higher than non-users. Both dual use and smoking significantly increased the risk of wheezing and related respiratory symptoms.

INTRODUCTION

Cigarettes smoking is the leading cause of preventable death in the USA.[1] More than 480 000 annual deaths and 14 million comorbid conditions in 2009 were due to cigarettes use and secondhand exposure. Cigarettes smoking contributes to 8.7% of annual healthcare spending in the USA by 2010, amounting to $170 billion per year.[2] Smoking increases the risks of many types of cancers and numerous chronic diseases, such as stroke, heart disease, lung disease and osteoporosis.[3] Electronic cigarettes (e-cigarettes) gained popularity around the world during the past 10 years. Recent data from the National Center for Health Statistics indicated that 12.6% US adults have tried e-cigarettes, and 3.7% US adults currently use e-cigarettes.[4] E-cigarette is a device to heat and vaporise a liquid mixture that contains nicotine, propylene glycol, glycerin and flavourings to generate an aerosol inhaled by the users.[5] Chemical analysis of e-cigarettes aerosols identified respiratory irritants and toxicants, regular exposures to which are associated with impaired respiratory functioning.[6 7] Our recent study on effects of e-cigarettes flavouring chemicals on inflammatory and oxidative response using human monocytic cell lines showed biologically significant inflammatory response due to e-cigarette flavouring chemicals,[8 9] providing plausibility for the association. Previous studies have found that occupational inhalation of some common food-safe flavouring agents used in e-cigarettes could cause occupational asthma and asthmatic symptoms.[10] Furthermore, irreversible obstructive airway disease in healthy workers are caused by workplace inhalation exposure to flavouring agent diacetyl used in e-cigarettes.[10]

Whether complete or partial substitution of tobacco cigarettes with e-cigarettes (switching to vaping from smoking) leads to lower risk compared with continued smoking remains controversial.[11] Although e-cigarettes are marketed as a less harmful alternative for cigarette smoking, many concern remains on its relative toxicity and long-term health consequences. Investigating health risk in adult e-cigarette users is challenging since a significant proportion of vapers are also ex-smokers. Thus, it is critical to consider whether there is a prolonged effects of past smoking that contributes to the harm of e-cigarettes for current vapers who already quit smoking. Meanwhile, a majority of e-cigarette users also use conventional cigarettes,[12] but whether dual use of e-cigarettes and cigarettes is associated with added, maintained or reduced health risk remains unknown.[13]

Wheezing is a high-pitched lung sound due to narrowed or abnormal airways and is always associated with difficulty in breathing, which may be an indication of emphysema, gastro-oesophageal reflux disease, heart failure, lung cancer, sleep apnoea, and vocal cord dysfunction. Wheezing can be caused by inflammation and narrowing of the airway in any location from the throat to the lung. Asthma and chronic obstructive pulmonary disease are the most common causes of recurrent wheezing.[14] Several studies have focused on associations of e-cigarettes use with wheezing or whistling and reported mixed results.[7–9 12 15–23] One study on 2086 Southern California Children's Health Study adolescent participants found e-cigarettes use increased risks of chronic bronchitis symptoms in teens while no significant association of e-cigarettes use with wheeze were found in teens after adjusting for cigarettes use.[21] Another study on 533 participants aged 24+ from the Tobacco and Attitudes Beliefs Survey found e-cigarettes expenditures or use was associated with greater odds of wheezing and shortness of breath after controlling for cigarettes smoked per day.[12] Maternal e-cigarettes use is highly likely to increase the risk of childhood wheezing and subsequent asthma in offspring.[16] Significant associations between e-cigarettes use and asthma were reported in adolescents in Korea[20 24] and Hawaii,[22] although another study on 2086 adolescents did not find significant association between e-cigarettes use and wheezing.[21] A previous study on 481 e-cigarettes online forum adult users found e-cigarette users reported wheezing symptoms.[15] A recent crossover and placebo-controlled trial on 20 healthy volunteers and 10 asthmatic volunteers reported that a 1-hour acute vaping session of nicotine-free and flavour-free e-cigarette use failed to show significant impact on lung functions in either healthy or asthmatic subjects.[17] However, another study on 105 subjects did not find negative respiratory health outcomes after using e-cigarettes for 5 days.[19]

No study has investigated whether e-cigarette use alone is associated with wheezing in US adults and how this association might be different from cigarette use only and dual use, as well as the lingering effects of past smoking in current vapers who already quit smoking. Using the nationally representative Population Assessment of Tobacco and Health (PATH) study wave 2 data collected from October 2014 to October 2015 on 28 171 adults, we investigated the association of current vaping with wheezing and related respiratory symptoms in US adult population and compared the associations with current cigarette use and dual use.

METHODS

Study population

The PATH Study is a nationally representative, longitudinal cohort study of 45 971 adults and youth in the USA with the purpose of informing and monitoring the impact of Food and Drug Administration (FDA)'s regulatory actions to reduce tobacco-related death and disease.[3] The PATH study used a four-stage stratified area probability sample design with a two-phase design for sampling adults at the final stage. The PATH study questionnaires adapted many questions from existing well-established national surveys such as the Tobacco Use Supplement to the Current Population Survey, the National Epidemiological Survey on Alcohol and Related Conditions Survey, the National Health and Nutrition Examination Survey, the Global Appraisal of Individual Needs survey and the Patient Reported Outcomes Measurement Information System. The PATH study questionnaires were conducted using the Audio Computer-Assisted Self-Interviewing and Computer-Assisted Personal Interviewing. The PATH wave 2 data were collected from October 2014 to October 2015 including 28 362 adults and 12 172 youth.

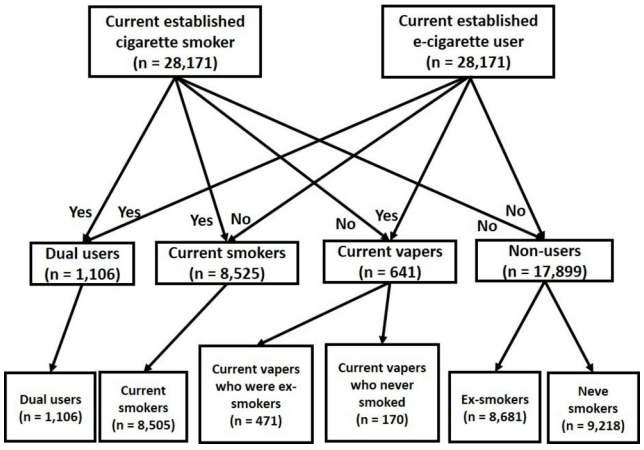

Figure 1 Diagram of deriving current vaping and smoking status variable.

Current vaping and smoking status

We created the current vaping and smoking status variable based on two derived variables in the cross-sectional PATH wave 2 data (figure 1). The first derived variable is the wave 2 adult current established cigarette smoker variable with 'yes' or 'no' values (established is defined as adult respondents who have smoked at least 100 cigarettes in their lifetime, and currently smoke every day or some days). The second derived variable is the wave 2 adult current established e-cigarette user variable with 'yes' or 'no' values (established is defined as adult respondents who have ever used an e-cigarette, have ever used fairly regularly, and currently use every day or some days). According to the 'yes' and 'no' values of the two derived variables, we created our own current vaping and smoking status variable with four categories: (1) dual users, (2) current smokers, (3) current vapers and (4) non-users. The dual users were defined as those adult respondents who had both 'yes' values in the current established cigarette smoker variable and the current established e-cigarette user variable. The current smokers were defined as adult respondents who had 'yes' value in the current established cigarette smoker variable and 'no' value in the current established e-cigarette user variable. The current vapers were defined as adult respondents who had 'no' value in the current established cigarette smoker variable and 'yes' value in the current established e-cigarette user variable. The non-users group was defined as adult respondents who has both 'no' values in the current established cigarette smoker variable and the current established e-cigarette user variable.

To explore whether there is a prolonged effect of ex-smoking that contributes to the association of vaping with wheezing and other related respiratory symptoms, we further separate the current vapers group into two subgroups: (1) vapers who were ex-smokers and (2) vapers who never smoked and now used e-cigarettes exclusively. Then, we created another current vaping and smoking status variable with six categories: (1) dual users, (2) current smokers, (3) current vapers who were ex-smokers, (4) current vapers who never smoked and now use e-cigarettes exclusively, (5) ex-smokers, (6) never smokers. The

cross-sectional PATH wave 2 data were downloaded from the National Addiction & HIV Data Archive Program website public user files (https://www.icpsr.umich.edu/icpsrweb/NAHDAP/studies/36231/datadocumentation).

Outcome variables and covariates

Self-reported health outcomes related to wheezing and whistling in the chest were examined. The following questions were used as outcome variables in the analysis: (1) ever had wheezing or whistling in chest at any time in past; (2) in past 12 months, wheezing or whistling in the chest; (3) in past 12 months, number of wheezing attacks; (4) in past 12 months, how often has sleep been disturbed due to wheezing; (5) in past 12 months, had speech been limited to only one or two words between breaths due to wheezing; (6) in past 12 months, chest has sounded wheezy during or after exercise; (7) in past 12 months, had a dry cough at night not associated with a cold or chest infection. All outcome variables are categorical variables with two or more levels. Covariates controlled for in the data analysis included age categories, sex, race/ethnicity, income level, bod mass index (BMI) categories, duration of e-cigarettes use, self-reported asthma, self-perception of physical health, self-perception of mental health and secondhand smoke exposure. Secondhand smoke exposure was measured through four questions including whether respondent lived with a regular smoker during childhood, whether currently lived with anyone who smokes cigarette, home rule on non-combustible tobacco product use and number of hours in close contact with smokers. All covariates were categorical variables except number of hours in close contact with smokers.

Statistical analysis

Weighted frequency distributions and the Rao-Scott modified likelihood ratio test were used to examine the association between covariates and established cigarette use status. Weighted regression analysis was used to examine the association of number of hours in close contact with smokers with established cigarette use status. Both univariable and multivariable weighted logistic regression models were used to examine the association of binary health outcomes with established cigarette use status. The covariates were adjusted in the multivariable weighted logistic regression models. For outcome variables with more than two categories, univariable and multivariable weighted cumulative logistic regression models were used to investigate both unadjusted and adjusted association of current vaping and smoking status with health outcomes. The same set of covariates were adjusted in the multivariable weighted cumulative logistic regression models. For exploratory analysis on the prolonged effect of ex-smoking, we fitted similar weighted logistic and cumulative logistic regression models with the same set of covariates adjusted.

The Fay's method, a variant of the balanced repeated replication method, was used to form replicate weights in variance estimation in all the PATH survey data analysis. ORs and their 95% CIs were used to quantify the association of current vaping and smoking status with wheezing and other related respiratory symptoms. Linear contrasts were used to obtain ORs and their 95% CIs for key comparisons. All analyses were conducted using the proc survey procedures in SAS V.9.4 (SAS Institute). All tests were two-sided with significance level set at 5%.

RESULTS

Current vaping and smoking status across demographic characteristics

Among the 28 362 adult participants, 28 171 adults indicated their current vaping and smoking status, with 1106 dual users (2.0%, 95% CI: 1.8% to 2.2%), 8525 current smokers (16.6%, 95% CI: 16.1% to 17.1%), 641 current vapers (1.2%, 95% CI: 1.1% to 1.4%) and 17 899 non-users (80.2%, 95% CI: 79.6% to 80.7%). Among 641 current vapers, 471 were ex-smokers (75.15%) and 170 (24.85%) were never smokers who now used e-cigarettes exclusively. According to the same question of quitting smoking, we also separated the non-users group into two subgroups: non-users who were ex-smokers and never smokers. There were 8681 adult respondents who were ex-smokers among 17 899 non-users (weighted percentage: 47.48%). The remaining 9218 adult respondents were never smokers (weighted percentage: 52.52%).

The majority of current vapers were aged 18–34 years (52.06%), while the majority of current smokers were aged 35–64 (56.63%) (table 1). Dual users were equally distributed between the 18–34 age group (47.91%) and the 35–64 age group (47.35%). Males were more likely to vape (58.52%) and smoke (54.81%) than females. Compared with non-Hispanics, Hispanics were less likely to vape and smoke. For race, the majority of vapers and smokers were white. High school graduates or those with some college (no degree) or associate degree were more likely to vape and smoke than people with other education levels. The prevalence of vaping and smoking varied across different income levels. Obese respondents (35.54%) were more likely to vape than overweight respondents (29.68%), while normal weight respondents were more likely to be current smokers (34.60%) or dual users (34.70%). Among all BMI categories, the underweight population was less likely to vape or smoke. Both current vapers and dual users tend to use e-cigarettes regular before age of 18 years. Adults who lived with a regular smoker during childhood were more likely to vape and smoke. Adults who allow non-combustible tobacco product use any time and anywhere in their home were more likely to be vapers or dual users. The asthma status was not significantly different among current vaping and smoking status. Both the self-perception of physical health and mental health were significantly different across current vaping and smoking status. Dual users had the highest number of contacts with smokers.

Association of wheezing and related respiratory symptoms with vaping and smoking

Both unadjusted and adjusted ORs from weighted logistic regression models and weighted cumulative logistic regression models were calculated to examine the association of wheezing and related respiratory symptoms with vaping and smoking (table 2). Compared with non-users, current vapers have almost doubled the unadjusted risk of wheezing and related respiratory symptoms. After adjusting the confounding variables listed in table 1, current vapers still have significantly increased risk of most wheezing and related respiratory symptoms compared with non-users (aORs ranged from 1.37 to 1.78 for significant aORs; $p<0.05$). Regarding the symptom that chest has sounded wheezy during or after exercise, current vapers has a significant unadjusted risk (OR=1.81, 95% CI: 1.41 to 2.31). While, after adjusting those confounding variables, the odds of chest sounded wheezy during or after exercise for vapers was not significantly different from non-users (aOR=1.20, 95% CI: 0.90 to 1.60). After adjusting for all the covariates, both current smokers and

Table 1 Characteristics of PATH wave 2 adult participants across current vaping and smoking status

	Current vaping and smoking status (% with 95% CI)				
	Current vapers	Current smokers	Dual users	Non-users	P value
Variables	(n=641)	(n=8525)	(n=1106)	(n=17 899)	
Age (years)					
18–34	52.06 (50.18 to 54.01)	34.88 (34.26 to 35.50)	47.91 (46.33 to 49.56)	28.47 (27.95 to 28.99)	<0.0001
35–64	41.78 (39.60 to 44.08)	56.63 (56.13 to 57.13)	47.35 (45.75 to 49.01)	49.69 (49.27 to 50.12)	
65+	6.16 (3.93 to 9.64)	8.49 (7.90 to 9.14)	4.73 (3.54 to 6.34)	21.84 (21.45 to 22.24)	
Sex					
Male	58.52 (56.87 to 60.21)	54.81 (54.40 to 55.22)	54.00 (52.58 to 55.46)	46.18 (45.81 to 46.56)	<0.0001
Female	41.48 (39.25 to 43.84)	45.19 (44.68 to 45.72)	46.00 (44.24 to 47.83)	53.82 (53.48 to 54.16)	
Ethnicity					
Hispanic	13.53 (11.34 to 16.14)	12.53 (11.90 to 13.18)	6.85 (5.44 to 8.63)	16.04 (15.67 to 16.43)	<0.0001
Non-Hispanic	86.47 (85.67 to 87.28)	87.47 (87.23 to 87.72)	93.15 (93.07 to 93.22)	83.96 (83.85 to 84.07)	
Race					
White alone	82.56 (81.00 to 84.14)	76.37 (75.82 to 76.93)	84.72 (84.39 to 85.05)	77.77 (77.50 to 78.05)	<0.0001
Black alone	7.71 (5.89 to 10.10)	15.97 (15.31 to 16.66)	5.69 (4.39 to 7.39)	11.87 (11.52 to 12.22)	
Others	9.73 (7.75 to 12.23)	7.65 (7.10 to 8.25)	9.59 (7.99 to 11.50)	10.36 (10.03 to 10.70)	
Education					
Less than high school	8.53 (6.64 to 10.95)	16.83 (16.19 to 17.51)	12.84 (11.10 to 14.86)	10.05 (9.61 to 10.51)	<0.0001
GED	6.98 (5.23 to 9.30)	11.34 (10.73 to 11.98)	11.34 (9.66 to 13.31)	3.73 (3.34 to 4.16)	
High school graduate	27.24 (24.42 to 30.38)	28.16 (27.52 to 28.82)	21.53 (19.27 to 24.06)	21.80 (21.26 to 22.36)	
Some college (no degree) or associates degree	45.66 (43.59 to 47.83)	32.19 (31.42 to 32.98)	41.53 (39.77 to 43.37)	31.63 (31.15 to 32.12)	
Bachelor's degree	8.31 (6.44 to 10.72)	8.76 (8.20 to 9.37)	9.25 (7.67 to 11.15)	20.44 (20.05 to 20.84)	
Advanced degree	3.28 (2.06 to 5.21)	2.71 (2.35 to 3.13)	3.50 (2.46 to 4.99)	12.35 (12.01 to 12.71)	
Income					
Less than $10 000	14.74 (12.46 to 17.43)	21.58 (20.90 to 22.29)	20.03 (18.03 to 22.25)	10.35 (9.75 to 10.98)	<0.0001
$10 000 to $24 999	19.85 (17.44 to 22.60)	27.71 (26.89 to 28.55)	25.27 (23.22 to 27.49)	17.97 (17.30 to 18.67)	
$25 000 to $49 999	25.95 (23.49 to 28.67)	24.35 (23.67 to 25.05)	22.95 (20.91 to 25.17)	22.42 (21.64 to 23.23)	
$50 000 to $99 999	25.31 (22.14 to 28.94)	19.14 (18.46 to 19.84)	22.15 (20.12 to 24.38)	27.76 (27.01 to 28.52)	
$100 000 or more	14.15 (11.44 to 17.48)	7.23 (6.68 to 7.82)	9.61 (7.95 to 11.61)	21.50 (20.62 to 22.42)	
BMI					
Underweight	2.42 (1.38 to 4.24)	2.95 (2.57 to 3.39)	2.17 (1.35 to 3.48)	1.94 (1.71 to 2.20)	<0.0001
Normal	32.36 (30.02 to 34.89)	34.60 (33.97 to 35.25)	34.70 (32.78 to 36.74)	31.73 (30.81 to 32.67)	
Overweight	29.68 (27.31 to 32.26)	32.63 (31.99 to 33.28)	30.80 (28.84 to 32.89)	34.12 (33.24 to 35.01)	
Obese	35.54 (33.23 to 37.98)	29.82 (29.17 to 30.49)	32.33 (30.39 to 34.40)	32.22 (31.36 to 33.09)	
Age when first used e-cigarette regularly					
<18	2.64 (1.56 to 4.47)	0.07 (0.03 to 0.20)	1.12 (0.57 to 2.20)	0.02 (0.01 to 0.05)	0.0007
18–24	1.19 (0.53 to 2.70)	0.03 (0.01 to 0.13)	0.52 (0.19 to 1.42)	0.01 (0.00 to 0.04)	
Lived with a regular smoker during childhood					
Yes	60.48 (58.77 to 62.24)	68.18 (67.47 to 68.90)	68.10 (66.77 to 69.46)	52.47 (51.69 to 53.25)	<0.0001
No	39.52 (37.29 to 41.88)	31.82 (31.18 to 32.47)	31.90 (30.02 to 33.90)	47.53 (46.52 to 48.55)	
Currently lived with anyone who smoke cigarette					
Yes	21.02 (18.66 to 23.69)	45.51 (44.74 to 46.28)	48.95 (47.33 to 50.61)	12.57 (12.03 to 13.14)	<0.0001
No	78.98 (78.09 to 79.87)	54.49 (54.07 to 54.91)	51.06 (49.50 to 52.67)	87.43 (86.91 to 87.94)	
Home rule on non-combustible tobacco product use					
It is not allowed anywhere or at any time inside my home	29.92 (27.54 to 32.52)	48.97 (48.38 to 49.56)	28.54 (26.61 to 30.61)	81.31 (80.80 to 81.81)	<0.0001
It is allowed in some places or at sometimes inside my home	22.08 (19.69 to 24.77)	20.29 (19.61 to 21.00)	20.85 (18.94 to 22.96)	10.71 (10.17 to 11.28)	
It is allowed anywhere and at any time inside my home	48.00 (45.73 to 50.36)	30.74 (29.85 to 31.66)	50.61 (49.05 to 52.21)	7.98 (7.53 to 8.45)	
Doctor, nurse or other health professional said you had asthma					
Yes	7.86 (6.04 to 10.23)	7.36 (6.82 to 7.94)	7.52 (6.05 to 9.33)	7.03 (6.53 to 7.56)	0.7899
No	92.14 (91.48 to 92.81)	92.64 (92.53 to 92.75)	92.48 (92.25 to 92.71)	92.97 (92.77 to 93.18)	

Continued

Table 1 Continued

Variables	Current vaping and smoking status (% with 95% CI)				P value
	Current vapers (n=641)	Current smokers (n=8525)	Dual users (n=1106)	Non-users (n=17 899)	
Self-perception of physical health					
Excellent	11.54 (9.46 to 14.09)	6.76 (6.24 to 7.33)	8.15 (6.65 to 9.97)	17.46 (16.69 to 18.27)	<0.0001
Very good	30.85 (28.31 to 33.62)	25.43 (24.77 to 26.11)	24.99 (23.08 to 27.05)	38.61 (37.84 to 39.40)	
Good	40.14 (37.59 to 42.87)	42.00 (41.37 to 42.65)	42.07 (40.36 to 43.86)	31.56 (30.88 to 32.26)	
Fair	14.16 (11.96,16.78)	20.49 (19.82 to 21.18)	19.12 (17.25 to 21.19)	10.44 (9.79 to 11.14)	
Poor	3.30 (2.08 to 5.24)	5.31 (4.83 to 5.84)	5.68 (4.38 to 7.35)	1.92 (1.65 to 2.22)	
Self-perception of mental health					
Excellent	17.97 (15.66 to 20.64)	15.27 (14.63 to 15.95)	15.46 (13.65 to 17.50)	25.17 (24.16 to 26.21)	<0.0001
Very good	28.73 (26.13 to 31.58)	27.99 (27.32 to 28.67)	25.15 (23.24 to 27.22)	38.46 (37.81 to 39.11)	
Good	32.09 (29.73 to 34.63)	32.80 (32.15 to 33.46)	32.09 (30.22 to 34.08)	25.57 (24.76 to 26.40)	
Fair	15.30 (13.06 to 17.93)	18.93 (18.26 to 19.61)	19.84 (17.96 to 21.92)	9.34 (8.74 to 9.98)	
Poor	5.91 (4.29 to 8.14)	5.01 (4.54 to 5.53)	7.46 (6.01 to 9.26)	1.46 (1.28 to 1.66)	
In past 7 days, number of hours in close contact with smokers					
Mean (95% CI)	6.83 (4.98 to 8.69)	16.33 (15.47 to 17.19)	20.43 (18.06 to 22.80)	2.28 (2.07 to 2.48)	<0.0001

BMI, body mass index; PATH, Population Assessment of Tobacco and Health study.

dual users had more than double the risk of wheezing and related respiratory symptoms compared with non-users (aORs ranged from 2.09 to 3.58; p<0.05). Compared with current smokers, current vapers had significantly reduced risk of wheezing and related respiratory symptoms (aORs ranged from 0.68 to 0.51; p<0.05), even after adjusting all the covariates. The risk of wheezing and related respiratory symptoms were not significantly different from dual users and current smokers.

Effect of past smoking on risk of wheezing and related respiratory symptoms associated with vaping and smoking

Table 3 summarises both unadjusted and adjusted ORs using never-smokers and ex-smokers as reference groups. Compared with never smokers, current vapers who were ex-smokers have doubled the risk of wheezing and had 1.5 times higher risk of related respiratory symptoms after adjusting all the covariates (aORs ranged from 1.50 to 2.28; p<0.05). However, no significant differences in wheezing and related respiratory symptoms was found when comparing current vapers who never smoked with never smokers. This is after controlling for same covariates as listed above. Current smokers has more than double or triple of the risk of wheezing and related respiratory symptoms compared with never smokers, even after adjusting for all the covariates in the model (all p<0.05). Compared with ex-smokers, current vapers who were ex-smokers had more than 50% increase in all wheezing and related respiratory symptoms except for chest has sounded wheezy during or after exercise and dry cough at night not associated with a cold or chest infection (p<0.05). Ex-smokers showed slightly significant increased risk of wheezing and related respiratory symptoms when compared with never smokers (p<0.05).

Elevated risks of wheezing and related symptoms were also observed for obesity and living with a regular smoker during childhood. Compared with adults with normal weight, obese adults had significantly elevated odds of wheezing and other related respiratory symptoms, after adjusting the effect of vaping and smoking and other confounding variables (aORs ranged from 1.22 to 1.63; p<0.05). Living with a regular smoker during childhood also increased the odds of wheezing and related respiratory symptoms after adjusting the effects of vaping and smoking and other covariates in the model (aORs ranged from 1.25 to 1.45; p<0.05).

DISCUSSION

Using the nationally representative large PATH wave 2 data from adult participants, we found a significant association of vaping with wheezing and related respiratory symptoms in adults, after adjustment for age, gender, race/ethnicity, income level, BMI categories, duration of e-cigarettes use, self-reported asthma, self-perception of physical health, self-perception of mental health and secondhand smoke exposure. These findings contribute evidence on the potential harms of vaping at the population level—vaping had elevated odds of reporting wheeze after adjustment for relevant covariates and potential confounders. At the same time, current vaping had lower (though still elevated) odds of wheezing relative to current smoking or dual use. This suggests a modicum of harm reduction on wheezing and related respiratory symptoms associated with vaping only which was a minority pattern of e-cigarettes use—dual use appeared to confer no reduction is relative risk. The results are informative regarding providing advice to patients about risks associated with vaping.

We also noticed that the risks of wheezing and related respiratory symptoms were significantly higher among current vapers who were ex-smokers than in ex-smokers who did not vape which also indicated potential harms of vaping in addition to prior smoking. Therefore, promoting complete cessation of both smoking and vaping will be beneficial to maximise the risk reduction of wheezing and other related respiratory symptoms. Importantly, we reported that ex-smokers who did not vape, although they already quit smoking, still have significantly elevated risk of wheezing and other related respiratory symptoms, compared with never smokers, suggesting long-term impact of prior smoking.

Though the sample size was small and likely did not allow sufficient statistical power to detect significance, there was a strong trend towards a risk for wheezing and related respiratory symptoms in current vapers who never smoked. This suggests a need for further research with a larger sample size. Recent studies have suggested that long-term inhalation of flavouring

Table 2 Unadjusted and adjusted ORs of wheezing and related respiratory symptoms associated with vaping and smoking

Wheezing and other related respiratory symptoms	Risk compared with non-users						Risk compared with smokers			
	Current vapers vs non-users		Current smokers vs non-users		Dual users vs non-users		Current vapers vs current smokers		Dual users vs current smokers	
	Unadjusted OR (95% CI)	Adjusted OR (95% CI)	Unadjusted OR (95% CI)	Adjusted OR (95% CI)	Unadjusted OR (95% CI)	Adjusted OR (95% CI)	Unadjusted OR (95% CI)	Adjusted OR (95% CI)	Unadjusted OR (95% CI)	Adjusted OR (95% CI)
Ever had wheezing or whistling in chest at any time in past	2.05 (1.69 to 2.49)	1.67 (1.23 to 2.15)	2.98 (2.78 to 3.19)	2.46 (2.21 to 2.73)	3.44 (3.01 to 3.94)	2.60 (2.18 to 3.11)	0.69 (0.56 to 0.84)	0.68 (0.53 to 0.87)	1.16 (1.01 to 1.32)	1.06 (0.91 to 1.24)
Wheezing or whistling in chest in past 12 months	2.00 (1.67 to 2.39)	1.68 (1.32 to 2.14)	3.22 (3.00 to 3.46)	2.75 (2.47 to 3.06)	3.69 (3.22 to 4.23)	2.83 (2.37 to 3.38)	0.62 (0.51 to 0.75)	0.61 (0.48 to 0.77)	1.14 (1.01 to 1.31)	1.03 (0.88 to 1.20)
Number of wheezing attacks more than 12 in past 12 months	1.88 (1.52 to 2.33)	1.67 (1.28 to 2.19)	3.74 (3.40 to 4.11)	3.28 (2.89 to 3.72)	4.13 (3.60 to 4.73)	3.35 (2.81 to 3.98)	0.50 (0.40 to 0.63)	0.51 (0.39 to 0.66)	1.10 (0.98 to 1.24)	1.02 (0.88 to 1.18)
One or more nights per week had sleep disturbed due to wheezing	1.88 (1.51 to 2.33)	1.70 (1.29 to 2.23)	3.71 (3.38 to 4.07)	3.23 (2.84 to 3.67)	4.01 (3.49 to 4.61)	3.42 (2.86 to 4.09)	0.51 (0.40 to 0.63)	0.52 (0.41 to 0.68)	1.08 (0.96 to 1.22)	1.06 (0.90 to 1.24)
Speech limited to only one or two words between breaths due to wheezing in past 12 months	1.92 (1.54 to 2.38)	1.78 (1.36 to 2.32)	3.76 (3.42 to 4.13)	3.30 (2.89 to 3.77)	4.24 (3.64 to 4.93)	3.58 (2.91 to 4.41)	0.51 (0.41 to 0.64)	0.54 (0.42 to 0.70)	1.13 (0.99 to 1.28)	1.08 (0.91 to 1.29)
Chest has sounded wheezy during or after exercise	1.81 (1.41 to 2.31)	1.20 (0.90 to 1.60)	2.95 (2.70 to 3.21)	2.09 (1.87 to 2.33)	3.71 (3.18 to 4.33)	2.32 (1.87 to 2.89)	0.61 (0.48 to 0.78)	0.58 (0.43 to 0.76)	1.26 (1.09 to 1.46)	1.11 (0.91 to 1.36)
Dry cough at night not associated with a cold or chest infection	1.60 (1.28 to 2.02)	1.37 (1.04 to 1.81)	3.22 (2.98 to 3.48)	2.31 (2.10 to 2.54)	3.51 (3.02 to 4.08)	2.63 (2.20 to 3.14)	0.50 (0.40 to 0.62)	0.59 (0.45 to 0.77)	1.09 (0.94 to 1.27)	1.14 (0.95 to 1.36)

The adjusted ORs controlled the effect of age categories, sex, race/ethnicity, income level, body mass index categories, duration of electronic-cigarette use, self-reported asthma, self-perception of physical health, self-perception of mental health and secondhand smoke exposure.

Table 3 Exploratory unadjusted and adjusted ORs of wheezing and related respiratory symptoms associated with vaping and smoking due to prolonged effect of past smoking

Wheezing and other related respiratory symptoms	Current vapers who were ex-smokers vs never-smokers		Current vapers who never smoked vs never-smokers		Current smokers vs never-smokers		Current vapers who were ex-smokers vs ex-smokers		Ex-smokers vs never-smokers	
	Unadjusted OR (95% CI)	Adjusted OR (95% CI)	Unadjusted OR (95% CI)	Adjusted OR (95% CI)	Unadjusted OR (95% CI)	Adjusted OR (95% CI)	Unadjusted OR (95% CI)	Adjusted OR (95% CI)	Unadjusted OR (95% CI)	Adjusted OR (95% CI)
Ever had wheezing or whistling in chest at any time in past	2.78 (2.25 to 3.43)	2.27 (1.71 to 3.01)	2.00 (1.29 to 3.08)	1.42 (0.75 to 2.70)	3.73 (3.37 to 4.12)	3.03 (2.63 to 3.50)	1.78 (1.46 to 2.18)	1.53 (1.18 to 1.97)	1.56 (1.41 to 1.72)	1.49 (1.31 to 1.70)
Wheezing or whistling in chest in past 12 months	2.67 (2.17 to 3.28)	2.21 (1.68 to 2.91)	1.96 (1.32 to 2.91)	1.49 (0.84 to 2.67)	4.00 (3.62 to 4.43)	3.33 (2.87 to 3.85)	1.74 (1.44 to 2.12)	1.54 (1.20 to 1.98)	1.53 (1.39 to 1.69)	1.43 (1.26 to 1.63)
Number of wheezing attacks more than 12 in past 12 months	2.42 (1.84 to 3.18)	2.21 (1.56 to 3.15)	1.77 (1.18 to 2.67)	1.38 (0.73 to 2.62)	4.47 (3.95 to 5.06)	3.95 (3.36 to 4.65)	1.70 (1.31 to 2.21)	1.57 (1.13 to 2.17)	1.42 (1.26 to 1.62)	1.41 (1.22 to 1.64)
One or more nights per week had sleep disturbed due to wheezing	2.37 (1.82 to 3.08)	2.19 (1.57 to 3.05)	1.84 (1.17 to 2.90)	1.52 (0.79 to 2.97)	4.43 (3.92 to 5.00)	3.87 (3.29 to 4.55)	1.67 (1.29 to 2.16)	1.56 (1.14 to 2.14)	1.42 (1.25 to 1.61)	1.40 (1.20 to 1.63)
Speech limited to only one or two words between breaths due to wheezing in past 12 months	2.43 (1.85 to 3.19)	2.28 (1.63 to 3.20)	1.88 (1.22 to 2.90)	1.64 (0.91 to 2.96)	4.50 (3.97 to 5.09)	3.96 (3.32 to 4.71)	1.71 (1.32 to 2.22)	1.63 (1.19 to 2.24)	1.42 (1.25 to 1.61)	1.40 (1.20 to 1.64)
Chest has sounded wheezy during or after exercise	2.10 (1.56 to 2.84)	1.50 (1.07 to 2.10)	1.80 (1.09 to 2.99)	0.85 (0.41 to 1.78)	3.30 (2.95 to 3.70)	2.32 (2.01 to 2.69)	1.67 (1.23 to 2.27)	1.22 (0.88 to 1.70)	1.26 (1.09 to 1.45)	1.23 (1.03 to 1.47)
Dry cough at night not associated with a cold or chest infection	1.72 (1.29 to 2.29)	1.54 (1.12 to 2.11)	2.10 (1.30 to 3.39)	1.59 (0.84 to 3.00)	3.63 (3.27 to 4.03)	2.61 (2.31 to 2.94)	1.35 (1.00 to 1.82)	1.22 (0.88 to 1.69)	1.28 (1.13 to 1.44)	1.26 (1.09 to 1.46)

The adjusted ORs controlled the effect of age categories, sex, race/ethnicity, income level, body mass index categories, duration of electronic-cigarette use, self-reported asthma, self-perception of physical health, self-perception of mental health and secondhand smoke exposure.

ingredients in e-cigarettes (such as benzaldehyde, a key ingredient in natural fruit flavours) may cause inflammation and irritation of the airways.[6 25 26]

Although we found the significant association of current vaping with wheezing and other related respiratory symptoms, especially for current vapers who were ex-smokers, we did not find significant association of chest sounded wheezy during or after exercise with current vaping. This might be due to the interactive effect of exercise and vaping. Exercise has been reported to reduce inflammation, which is the cause of wheezing, while vaping was reported to induce inflammations in the body.[8 18] However, we did find significantly elevated risk of wheeze during or after exercise when comparing current vapers who were ex-smokers with never smokers. Another study with 27 healthy smokers and 27 smokers with asthma also showed inflammatory effects due to vaping.[23] Recent studies suggest flavouring chemicals in some of e-cigarettes liquids was harmful to lung tissues through inflicting oxidative stress and pro-inflammatory responses.[27] Previous study had found significant association between obesity and incident asthma.[28] Thus, quitting smoking and vaping altogether as well as reducing body weight can both help alleviating wheezing and other related respiratory symptoms.

The strengths of current study include the nationally representative PATH study with large sample size which makes the results from this investigation robust. Meanwhile, many items in the questionnaires used in the PATH study are adapted from well-established existing national surveys with good internal consistency and reliability.

There are several limitations in this study. First, the PATH data are self-reported and may include recall bias. However, studies have found that self-reported chronic conditions had reasonable validity when compared with medical diagnoses.[29] Second, the analysis was based on the cross-sectional PATH wave 2 data and did not examine the longitudinal association of e-cigarettes use with wheezing and related symptoms which would be explored in future studies. These cross-sectional analyses do not provide evidence for the cause and effect relationship of vaping with wheezing and other related respiratory symptoms. Third, the analysis might miss potential important confounding variables due to lack of information in the PATH data such as the diet and physical activity information.

The FDA has recently finalised the rule of regulating all tobacco products including e-cigarettes.[30] E-cigarettes use is relatively new, thus very few studies have examined its effect on chronic health conditions. Our study provides evidence on hazards of e-cigarettes for FDA regulation purpose and underscores the importance of reducing e-cigarettes use for public health benefits.

What this paper adds

- E-cigarette users (vapers) had an increased risk of wheezing and related respiratory symptoms relative to non-users. Vaping only (no other tobacco use) was associated with reduced risk of wheezing and related respiratory symptoms compared with smoking or dual use. Dual use did not reduce the risk of wheezing and related respiratory symptoms compared with smoking.
- These findings indicate that vaping triggers wheezing and respiratory symptoms in susceptible population as shown by the data derived from a larger cohort of the Population Assessment of Tobacco and Health study wave 2.

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