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Supplement Article

User-Perceived Negative Respiratory Symptoms Associated with Electronic Cigarette Use

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Abstract

Introduction: Electronic cigarettes (ECIGs) expose users to an aerosol containing chemicals, which could affect the respiratory system negatively. This study examined negative respiratory symptoms associated with ECIG use.

Methods: In 2019, adult current ECIG users from 24 US states who reported experiencing negative respiratory symptoms from ECIG use (n = 49; 44.9% women; mean age = 35.2, SD = 11.5) completed an online survey and brainstormed statements that completed the prompt: "A specific negative effect or symptom related to my breathing, nose, mouth, throat, or lungs that I have experienced from vaping/using my e-cigarette is..." Participants sorted the final list of 56 statements into groups of similar content and rated statements on how true they were for them. Multidimensional scaling analysis identified thematic clusters.

Results: Eight ECIG use respiratory symptom clusters identified in analysis included Mucus and Congestion, Fatigue, Throat Symptoms, Breathing Problems, Mouth Symptoms, Chest Symptoms, Illness Symptoms, and Nose and Sinus Symptoms. Highly rated (ie, most common) symptoms included dry throat or mouth, fatigue during physical activity, coughing, shortness of breath, excessive phlegm, and bad taste in mouth. Mean cluster ratings did not differ based on lifetime cigarette smoking status (100 lifetime cigarettes smoked), but current cigarette smokers (ie, dual users) rated the Fatigue, Breathing Problems, Mucus and Congestion, and Nose and Sinus Symptoms clusters higher than noncurrent cigarette smokers.

Conclusions: Participant-identified respiratory symptoms perceived to be ECIG related, many similar to cigarette smoking symptoms. Future research should assess if these symptoms are associated with other negative health outcomes.

Implications: ECIG use exposes users to chemicals that may have negative health impacts on the respiratory system. Limited research has examined the broad range of negative respiratory symptoms associated with e-cigarette use. This study identified that ECIG–cigarette users perceive their ECIG use to be associated with negative respiratory symptoms. Many e-cigarette user-reported negative respiratory symptoms are similar to those associated with cigarette smoking, though

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Introduction

Electronic cigarettes (ECIGs) have become popular among youth^{1,2} and adults.³ ECIGs are devices that typically use a battery-powered heating element to aerosolize a liquid containing propylene glycol, vegetable glycerin, nicotine, and chemical flavorants.⁴ ECIG use exposes users to an aerosol, which often contains lower amounts and concentrations of many chemicals found in cigarette smoke such as tobacco-specific nitrosamines,^{5,6} resulting in reduced exposure to some chemicals.⁷ Many ECIG users report health benefits or low or reduced harm as reasons for ECIG use.^{8–12} However, in addition to propylene glycol, vegetable glycerin, and nicotine, research has demonstrated that ECIG-generated aerosol contains many other harmful toxicants including volatile organic compounds, aldehydes, and furfural, ^{13–17} which has spurred researchers to begin investigating the potential effects that ECIG use may have on health outcomes.

Research increasingly shows an association between ECIG use and negative respiratory symptoms and illnesses. ECIG use is associated with chronic bronchitic symptoms,¹⁸ asthma,^{19,20} and chronic obstructive pulmonary disorder,^{21–23} which are also known to be caused by cigarette smoking. However, focusing on these health outcomes may fail to account for effects that result from inhalation of chemicals that are specific to ECIG aerosol such as propylene glycol, vegetable glycerin, and chemical flavorants.²³ Indeed, preliminary research suggests that ECIG use may promote inflammatory response ²⁴ and may disrupt immune cells in the lungs.²⁵ Case studies also demonstrate that ECIG use may be associated with acute lung disease such as lipoid pneumonia.^{26–30} These studies suggest that ECIG use may result in some of the same health outcomes caused by cigarette smoking as well as distinct health outcomes when compared to cigarette smoking and highlight the need for continued research.

As research continues to examine possible causal mechanisms for ECIG-related negative health effects, there is a need for continued surveillance of indicators of negative health effects resulting from ECIG use. Describing a broad list of ECIG-related respiratory symptoms may be useful for developing screening tools that can be used by clinicians who treat tobacco users or identifying potential early indicators of negative health outcomes such lung disease. Much of the research examining negative health effects of ECIG use utilizes survey methods. Survey research has the strength of being able to provide prevalence and correlate estimates at the population level; however, other methods that allow for an iterative process for collecting open-ended responses may better capture more broadly behaviors and perceptions reported by ECIG users. Therefore, multiple surveillance methods are needed to identify ECIG-related negative respiratory symptoms. One method that can be used to identify, describe, and organize ECIG-related respiratory symptoms is concept mapping,³¹ a validated mixed-method participatory approach that combines the strengths of qualitative and quantitative methods.³² This approach yields similar results to an exploratory factor analysis with empirically identified latent constructs, but has the benefit of providing a visual representation of these constructs and does not require large sample sizes. This exploratory study used concept mapping to identify and describe negative respiratory symptoms reported by ECIG users.

Methods

Concept Mapping Procedure Overview

This study was approved by the East Carolina University and Medical Center Institutional Review Board and used concept mapping, an approach that uses participant tasks including brainstorming, sorting, and rating and quantitative analyses to generate thematic models that categorize and describe participant data. The result of this approach is a "concept map," which provides a visual representation of thematic clusters (ie, ECIG respiratory symptoms).

Participants

We recruited a convenience sample of current (past-30 day) adult ECIG users to participate in an online study by posting advertisements in 12 randomly selected Craigslist classified pages under the "et cetera" section. Craigslist markets were selected randomly from each of the four US census regions (eg, three states from the Northeast, Midwest, South, and West regions) to promote inclusion or participants from across the United States, capture potential regional trends, ensure that participants were not recruited from a single part of the United States, and increase generalizability of findings. Interested individuals followed a link in the advertisement to a screening questionnaire that included ECIG/tobacco use questions and the question, "Have you ever experienced any negative respiratory symptoms such as coughing; mouth, throat, or lung irritation; or some other illness while using or after using your electronic cigarette/vaping device that may have been caused by vaping?" Participants over the age of 18 were considered eligible for the current study if they reported past 30-day ECIG use and "yes" to the question regarding experiencing respiratory symptoms from "vaping." Eligible participants were sent an email that included a brief description of the study, including payment provided for completing each study task, as well as instructions for accessing the study website. Participants provided informed consent at the study website and then completed a brief survey and concept mapping tasks (brainstorming, sorting, and rating). Participants were asked to complete study tasks within one week of receiving their emailed instructions and study staff sent email reminders. To ensure valid responses for the survey and concept mapping tasks, participants each received a unique code that was required to be entered at the study website for participation and payment, and research staff reviewed and verified participant responses prior to providing payment. Additionally, research staff reviewed participant responses for the survey and sorting and rating activities (described below) to ensure responses were appropriate and participants had followed instructions. One participant completed the study and participant questions indicated that they were no longer a current ECIG user. Thus, this participant was removed from the analysis.

Measures

Prior to the concept mapping tasks, participants completed a brief survey at the study website which included ECIG use-related items including quantity and frequency of use, device and liquid characteristics, and dependence assessed using the E-Cigarette Dependence Scale.³³ Questions also examined other tobacco use and basic demographics including sex, age, race/ethnicity, and education.

Brainstorming

After the brief survey, participants (n = 45) completed the brainstorming task in which they were instructed to provide statements that completed the prompt: "A specific negative effect or symptom related to my breathing, nose, mouth, throat, or lungs that I have experienced from vaping/using my e-cigarette is ... " Although participants only needed to provide a single statement/symptom that completed the prompt in order to complete the brainstorming task, participants were encouraged to provide several responses that completed the prompt. Each statement was added to an ongoing list of statements. Importantly, this prompt emphasized that all identified respiratory symptoms should be perceived to be associated with ECIG use, not other products. Participants completed this task individually, however, multiple participants were able to access the study website at the same time. Statements generated were added to a running list and all previously generated statements were visible to subsequent participants. Participants were instructed to review previous responses to attempt to avoid duplicating previous content. This approach prevents interference resulting from having to wait one's turn to express an idea³⁴ and interactive brainstorming of this nature generates more ideas^{35,36} including more unique ideas.^{37,38} The purpose of this task was to generate all possible ECIG-related respiratory symptoms experienced ECIG users rather than only the most common or prevalent symptoms. The research team reviewed the statements as they were entered by participants with the aim to reach content saturation (ie, additional participants no longer provide unique statement content to the list). Participants generated 118 total statements describing respiratory-related symptoms from ECIG use and the research team determined that content saturation (ie, enrolling additional participants no longer yielded additional unique content) had been reached and closed the brainstorming task. Participants received a \$10 e-gift card for completing brainstorming.

Sorting

Some of the original statements included more than one idea (eg, "Nose stuffy and chest congestion, sick more often"). These statements were separated into statements that each only included a single idea creating a list for review (n = 138). Three researchers reviewed independently each of the brainstormed statements to identify duplicate content (eg, "coughing" and "sudden urge to cough") and content not related to the focus prompt (eg, "staring off into space") for removal. If two or three reviewers marked the statement either as redundant with other statements or as not relating to the focus prompt, that statement was removed. When more than one statement described the same idea, the statement that best described a single idea and contained fewer words was retained. The reviewers intentionally retained a broad range of symptoms that participants perceived may have been related to respiratory issues from ECIG use including symptoms beyond breathing or body parts in the respiratory system such as tiredness, nausea, headache, and others. Seventeen statements were identified as unrelated to the prompt and 65 were removed as duplicates/redundant content leaving 56 statements final after review and were uploaded to the study website.

We invited participants who completed brainstorming to participate in the sorting task. Additionally, participants who expressed interest in participating after the brainstorming task had been completed were also invited to participate in the sorting task. Individually, participants sorted the statements into groups of similar content by dragging statements into "piles." Piles were required to describe respiratory-symptom themes and not be organized by other criteria besides content similarly (ie, could not be "true/false," "agree/disagree," "I have/have not experienced," etc.). Research staff reviewed each participant's sorting task to confirm that instructions were followed providing additional assistance to participants upon request. Thirty-five participants attempted the sorting activity and 32 participants completed the sorting task following instructions including three participants who did not complete the brainstorming task. This number of participants is adequate for sorting: in most concept mapping studies, final model fit does not improve significantly beyond approximately 40 sorting participants.³² Participants received a \$25 e-gift card for completing the sorting task.

Rating

Immediately after the sorting task, participants rated each of the statements based on the following instructions: "Please rate the following statements, in the range indicated below based on the following prompt: I have experienced this negative respiratory symptom/effect from vaping/using my electronic cigarette." Response options ranged from 1 (Never) to 7 (Very Often). Study staff reviewed participant rating tasks to validate responses by ensuring that participant responses did not follow an obvious pattern. Thirty-nine participants attempted the rating activity and 38 completed it and received a \$10 e-gift card for completing rating.

Representation

Each participant's sorting data was used to create a 56×56 matrix of similarities. A "1" was entered in cells corresponding to statements that were sorted into the same pile. For example, if a participant put statements 2 and 25 into the same pile in the sorting task, a "1" would be entered into the corresponding cell in the matrix of similarities. All 32 participant matrices were aggregated to create a final matrix of similarities for all sorting data. Nonmetric multidimensional scaling analysis was used to create a "point map" where each statement was represented by a point in two-dimensional space. Using an algorithm,³⁹ each point was assigned a coordinate (x,y) so points that were close together on the map represented statements that were sorted together by more participants and points on the map that were farther apart represented statements that were sorted together by fewer participants. The stress value of the nonmetric multidimensional scaling representation was 0.23, within the range of values reported in other concept mapping studies,³² indicating good model fit, consistent sorting among participants, and congruence in the scaled data to the raw sorting data.

Analysis and Interpretation

Concept mapping software used an algorithm⁴⁰ to identify nonoverlapping cluster arrangements of statements that limited the distance of the points to the centroid of the identified clusters. Using a hierarchical cluster analysis, the research team explored models beginning with a two-cluster model. Subsequent models were built from this original two-cluster model by splitting one cluster into two clusters. This process was continued until a final model or "cluster map" (see Figure 1) was generated using interpretability (each cluster describes a single theme) and parsimony (fewer clusters preferred) as model fit indicators. The team reviewed models of up to

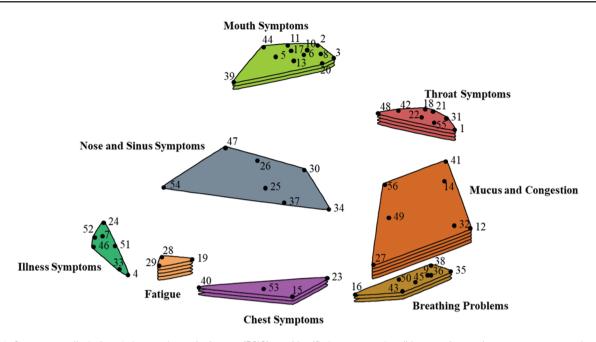


Figure 1. Concept map displaying 10 clusters electronic cigarette (ECIG) user-identified statements describing negative respiratory symptoms perceived to be related to ECIG use. Numbered points on the map that are closer to one another represent statements of more similar content, whereas points on the map that are further apart represent statements of less similar content. Greater number of layers in clusters indicate higher mean ratings of statements within each cluster based on the rating task. Mean ratings for clusters with one layer range from 2.80 to 3.01, two layers from 3.01 to 3.23, three layers from 3.23 to 3.45, four layers from 3.45 to 3.66, and five layers from 3.66 to 3.88.

nine clusters and determined that the eight-cluster model was the best fit. Mean cluster ratings, calculated by averaging all participant ratings of statements within each cluster, were compared between groups based on gender, frequency and duration of ECIG use, selfreported ECIG addiction, and use of other tobacco products.

Results

Participant Characteristics

Detailed sample characteristics are displayed in Table 1. In summary, approximately half (44.9%) were women, the majority were white (75.5%) and non-Hispanic (83.7%), and the mean age was 35.2 (SD = 11.5, range = 18-61). Over one third (38.8%) had completed a bachelor's degree or higher. Everyday ECIG use was reported by nearly 70% of the sample, with an average 24.3 (SD = 7.7) days of ECIG use in the past 30 days, and nearly three quarters (73.5%) had been using regularly for over a year. The most common ECIG device used was a pod mod (36.7%) followed by a rebuildable/mechanical or box mod (20.4%). Three quarters of the participants felt they were "addicted" to using ECIGs and mean E-Cigarette Dependence score was 2.2 (SD = 0.83), higher than reported among daily ECIG users previously.33 Around 15% of participants had smoked less than 100 cigarettes in their lifetime, and nearly 60% were current (past-30 day) cigarette smokers (M = 12.6 days in the past 30 days, SD = 12.7). Around two thirds reported smoking cigarettes less than 20 days in the past 30 days (range = 0-16 days). Among those who did report cigarette smoking in the past 30 days, 54.8% reported smoking five cigarettes or less on the days that they smoked.

Respiratory Symptoms Thematic Clusters

Eight thematic clusters were identified and are described below. Clusters are grouped based on similarity of the statements within each cluster as well as proximity to one another on the cluster map (Figure 1). A list of all clusters and statements as well as mean cluster and statement ratings are displayed in Table 2.

Fatigue, Illness Symptoms, and Chest Symptoms

Three clusters relating to general health issues that grouped together on the cluster map (and therefore indicated similarity of statement content) included the Fatigue, Illness Symptoms, and Chest Symptoms clusters. The Fatigue cluster had three statements and the highest mean cluster rating (M = 3.88, SD = 0.18). The symptoms in this cluster included experiencing fatigue or tiring quickly during physical activity, lowered stamina, and general "fatigue." Within this group, the Chest Symptoms cluster was the next highest rated cluster (M = 3.32, SD = 0.32) and included four statements. These statements described tightness in chest, difficulty of engaging in prolonged physical activity without losing one's breath, chest pain, and heart palpitations. The last cluster in this group of general health related clusters was the Illness Symptoms cluster which contained seven statements (M = 2.98, SD = 0.55). These statements included symptoms that affected many parts of the body including headache, dizziness, nausea/vomiting, and blurred vision. One statement also suggested some ECIG users felt they were sick more often as a result of ECIG use (Table 2).

Mucus and Congestion and Breathing Problems

Two clusters that were located close to one another on the cluster map related to symptoms in the chest, lungs, and other systems related to breathing. The first cluster was the Mucus and Congestion cluster which included seven statements (M = 3.70, SD = 0.23). In general, the statements in this cluster described congestion or excessive mucus in various parts of the respiratory system including the throat, nose, and chest as well as general congestion. One of the highest rated statements in this cluster indicated ECIG users frequently coughed up phlegm. Related to the Mucus and

| Table 1. | Sample Demographics and ECIG/Tobacco Use |
|----------|--|
| Charact | eristics |

| Characteristic | Ν | % |
|---|-----------------|------|
| Age (M, SD) | 35.2, 1.4 | |
| Sex | | |
| Female | 22 | 44.9 |
| Male | 27 | 55.1 |
| Transgender or other | 0 | 0 |
| Ethnicity Hispanic/Latino(a) | 8 | 16.3 |
| Race | 0 | 10.5 |
| American Indian/Alaskan Native | 2 | 4.1 |
| Asian | 1 | 2.0 |
| Native Hawaiian/Pacific Islander | 2 | 4.1 |
| Black/African American | 5 | 10.2 |
| White/European American | 37 | 75.5 |
| More than one race | 2 | 4.1 |
| Education | | |
| High school diploma or GED | 11 | 22.4 |
| Some college credit, but less than 1 year | 6 | 12.2 |
| 1 or more years of college, no degree | 7 | 14.3 |
| Associate's degree | 6 | 12.2 |
| Bachelor's degree | 14 | 28.6 |
| Higher than a bachelor's degree | 5 | 10.2 |
| Regular ECIG use history ^a | | |
| 0–3 mo | 3 | 6.1 |
| 4–6 mo | 3 | 6.1 |
| 7–12 mo | 7 | 14.3 |
| Between 1 and 2 y | 21 | 42.9 |
| More than 2 y | 15 | 30.6 |
| ECIG frequency | 0 | 160 |
| At least once per day | 8 | 16.3 |
| Every once in a while throughout the day | 9 | 18.4 |
| Fairly frequently throughout the day | 23 9 | 46.9 |
| Almost always throughout most of the day Days used ECIG in past-30 days (M, SD) | 9 24.7, 7.02 | 18.4 |
| Regular ECIG device | 24.7, 7.0. | 2 |
| Prefilled disposable/cig-alike | 9 | 18.4 |
| E-hookah | 1 | 2.0 |
| Vape pen/eGo style device | 8 | 16.3 |
| Rebuildable/mechanical mod or box mod | 10 | 20.4 |
| E-cigar | 3 | 6.1 |
| Pod mod such as JUUL | 18 | 36.7 |
| ECIG liquid nicotine concentration | | |
| 0–4 mg/mL | 11 | 22.3 |
| 5–10 mg/mL | 12 | 24.5 |
| 11–20 mg/mL | 10 | 20.4 |
| 21-30 mg/mL | 3 | 6.1 |
| 31-40 mg/mL | 2 | 4.0 |
| 50 mg/mL | 8 | 16.3 |
| Don't know | 3 | 6.1 |
| ECIG liquid flavor preference | | |
| Menthol or mint | 13 | 26.5 |
| Tobacco | 7 | 14.3 |
| Fruit | 13 | 26.5 |
| Other (including clove, spice, nut, alcoholic drink, coffee/tea, candy, or dessert) | 10 | 20.4 |
| I usually use multiple flavors | 6 | 12.2 |
| ECIG use after waking | 0 | 14.2 |
| After 60 min | 8 | 16.3 |
| | 8 18 | 36.7 |
| 31–60 min | | 50.7 |
| 31–60 min 6–30 min | 10 | 24.5 |

Table 1. Continued

| Characteristic | Ν | % |
|--|-------------------------|------|
| E-Cigarette Dependence Scale—Reach for ECIG ^b | | |
| Never | 1 | 2.0 |
| Rarely | 7 | 14.3 |
| Sometimes | 18 | 36.7 |
| Often | 14 | 28.6 |
| Almost always | 9 | 18.4 |
| E-Cigarette Dependence Scale-Vape more before n | ot allowed ^b | |
| Never | 2 | 4.1 |
| Rarely | 4 | 8.2 |
| Sometimes | 15 | 30.6 |
| Often | 16 | 32.7 |
| Almost always | 12 | 24.5 |
| E-Cigarette Dependence Scale—Drop everything to | buy ECIGs ^b | |
| Never | 6 | 12.2 |
| Rarely | 12 | 24.5 |
| Sometimes | 25 | 51.0 |
| Often | 6 | 12.2 |
| Almost always | 0 | 0 |
| E-Cigarette Dependence Scale—Craving gets intoler | able ^b | |
| Never | 5 | 10.2 |
| Rarely | 12 | 24.5 |
| Sometimes | 16 | 32.7 |
| Often | 8 | 16.3 |
| Almost always | 8 | 16.3 |
| Lifetime use of 100+ cigarettes | | |
| Yes | 42 | 85.7 |
| Days smoked cigarettes in past-30 days (M, SD) | | .7 |
| Current use of other tobacco products | | |
| Cigarettes | 32 | 65.3 |
| Cigar | 9 | 18.4 |
| Cigarillo or little cigar | 15 | 30.6 |
| Smokeless | 8 | 16.3 |
| Waterpipe | 15 | 30.6 |

Total *n* and percentages for sample characteristics are based on the 49 participants who completed the participant questions. ECIGs = electronic cigarettes. ^aRegular use was defined as using an ECIG some days or most days. ^bItems from the 4-item E-Cigarette Dependence Scale (Morean et al.³³) including "I find myself reaching for my e-cigarette without thinking about it," "I drop everything to go out and buy e-cigarettes or e-juice," "I vape more before going into a situation where vaping is not allowed," and "When I haven't been able to vape for a few hours, the craving gets intolerable."

Congestion cluster was the Breathing Problems cluster (M = 3.44, SD = 0.54). Although all relating to some type of breathing issues, the statements in this cluster described specific symptoms including coughing, shortness of breath, wheezing, and pain with taking deep breaths.

Mouth Symptoms, Nose and Sinus Symptoms, and Throat Symptoms

The final group of three clusters included statements describing various physical symptoms perceived to be ECIG use-related in the mouth, nose, and throat. The Mouth Symptoms cluster had the largest number of statements (n = 12; M = 3.36, SD = 0.71). Many of these statements related to taste including bad taste in mouth, deadened taste buds/sense of taste, bad breath, or metallic taste in mouth. Statements also described symptoms of itchy or dry mouth and tongue; sore tongue, throat, gums, or lips; and problems with

teeth. The Nose and Sinus Symptoms cluster had seven statements (M = 2.80, SD = 0.37). Symptoms described in this cluster included general "sinus issues," runny nose, and sneezing as well as more specific symptoms including burning or tingling sensation in nose and post-nasal drip that "tastes like e-liquid." Finally, the Throat Symptoms cluster had eight statements (M = 3.53, SD = 0.68). Some symptoms described in this cluster were similar to some from the Nose and Sinus Symptoms and Mouth Symptoms cluster with the main difference being the symptoms occurred in the throat. These symptoms included itchy, scratchy, or dry throat; sore throat; burned or tingling feeling in throat; and throat pain. One statement indicated some ECIG users experienced difficulty in swallowing that they perceived to be related to their ECIG use.

Cluster Comparisons

Men rated the Breathing Problems cluster higher (ie, experienced symptoms more frequently) compared with women (t = 3.36, p < 0.000.005). Although there were no differences in mean cluster ratings between participants who reported less than 100 lifetime cigarettes and those who had smoked 100 or more cigarettes in their lifetime, current cigarette smokers (ie, dual users) rated the Fatigue, Breathing Problems, Mucus and Congestion, and Nose and Sinus Symptoms clusters higher (eg, more frequent) than noncurrent cigarette smokers (ts = 2.16-3.97, ps < .05). The Mouth Symptoms, Mucus and Congestion, and Nose and Sinus Symptoms clusters were rated lower (eg, less frequent) among pod mod users relative to nonpod mod users (ts = 2.30-5.28, ps < .05). Those who reported using ECIGs regularly for less than 1 year had higher ratings for the Fatigue, Breathing Problems, and Mucus and Congestion clusters compared with those who had used ECIGs regularly for more than 1 year (ts = 3.20-5.15, ps < .01). Those who reported less frequent ECIG use (ie, using "at least once per day" or "every once in a while throughout the day") had higher ratings for the Fatigue and Mucus and Congestion clusters (t = 3.02-5.08, p < .02) relative to more frequent ECIG users (those who used "almost always throughout the day" or "fairly frequently throughout the day").

Discussion

This exploratory study examined ECIG user-reported negative respiratory symptoms perceived to be associated with ECIG use. Participants identified 56 unique respiratory-related symptoms that grouped into eight thematic clusters. Broadly, these symptoms indicated ECIG use may affect many parts of the body involved in the respiratory system including the mouth, nose, throat, and lungs as well as those indirectly related to the respiratory system. As a result, some ECIG users perceived their ECIG use may contribute to general illness symptoms, cardiovascular system problems, and fatigue. Many of these symptoms appeared similar to those experienced by cigarette smokers; however, some symptoms appeared to be unique to ECIG use, such as those related to a metallic taste in the mouth or postnasal drip that tastes like ECIG liquid. Furthermore, these symptoms are consistent with those identified previously using similar methods.⁴¹

We asked participants to identify the respiratory symptoms they perceived to be associated with their ECIG use. However, because only 15% of the sample had smoked less than 100 cigarettes in their lifetime and 60% of the participants were either every day or someday cigarette smokers, identifying the extent to which ECIG use (and not cigarette smoking) was associated with the respiratory symptoms described in the current study is limited. However, there were no significant differences in mean cluster ratings between participants based on 100 lifetime cigarette smoking status and current cigarette smokers (ie, dual users) only rated three clusters higher than noncurrent cigarette smokers suggesting that ECIG use likely contributed at least in part to some, if not most, of the symptoms identified in the current study. Future studies that include monitoring of the respiratory symptoms identified in the current study (and others that emerge) over time among exclusive ECIG users are needed to determine the extent to which ECIG use-related respiratory symptoms are similar to and unique from cigarette smoking-related respiratory symptoms. These studies will be informative for examining acute effects of ECIG use and long-term effects of ECIG use, including the latency period before ECIG-related symptoms may occur.

The lower ratings of clusters related to fatigue, congestion, and nose and sinus issues among noncurrent smokers suggest that although ECIG use appears to be associated with similar respiratory symptoms as cigarette smoking, switching completely from cigarettes to ECIGs may reduce some respiratory symptoms experienced by cigarette smokers. This is also supported by higher ratings for clusters related to fatigue, breathing problems, and nose and sinus symptoms among those who reported regular ECIG use for less than 1 y: many of these participants were also current cigarette smokers, whereas more of the long-term ECIG users were exclusive ECIG users. Similar findings have been reported previously in a randomized cigarette smoking cessation trial: cigarette smokers who switched completely to ECIGs reported reductions in coughing and phlegm as well as shortness of breath.⁴² Still, others report that ECIG use is associated with increased bronchitic symptoms including increased phlegm.¹⁸ These findings demonstrate the need for continued research on the health effects associated with ECIG use.

ECIG-related lung diseases that have involved the hospitalization of many ECIG users and several ECIG user deaths have been reported recently.43 Many of the symptoms reported by ECIG users in this study match the symptoms of individuals with pulmonary illness related to ECIG use.44 In an ongoing investigation of these ECIG-related severe lung diseases known as "e-cigarette, or vaping, product use-associated lung injury" (EVALI), the Centers for Disease Control stated liquids containing the chemical Vitamin E acetate found in some liquids containing tetrahydrocannabinol (THC) were "strongly linked" to this outbreak; however, "evidence is not sufficient to rule out the contribution of other chemicals of concern, including chemicals in either THC or non-THC products, in some of the reported EVALI cases."43 We did not ask participants to report if they used other substances in their ECIG devices, such as THC. However, our study was completed before EVALI cases associated with Vitamin E acetate containing ECIG liquids were widely used. Additionally, given recent data suggesting that ECIG use with liquids with and without nicotine (and also not containing THC compounds) may promote "poor response to infectious challenge"²⁵ and the statement describing ECIG users being sick more often from the current study, continued examination of the effects of inhaling chemicals produced from liquids common to most ECIG devices, such as propylene glycol and vegetable glycerin, are needed. Additionally, case reports involving in-depth medical exams of ECIG users that are hospitalized may be useful for identifying potential health concerns related to ECIG use, such as lipoid pneumonia.²⁶⁻³⁰

This study had several limitations. Because many ECIG users in the sample reported current or former cigarette smoking (as is the
 Table 2. ECIG User-Identified Clusters and Statements Describing

 ECIG-Related Negative Respiratory Symptoms

| | 2 00 |
|--|---|
| | 3.88 |
| 19. Get fatigued or tired quickly | 4.13 |
| during physical activity | |
| | 3.76 |
| 28. Fatigue | 3.74 |
| | 3.32 |
| | 3.66 |
| activity without losing breath | |
| 23. Tightness in chest | 3.63 |
| * | 3.05 |
| 40. Heart palpitations | 2.95 |
| | 2.98 |
| | 3.63 |
| | 3.42 |
| | 3.41 |
| | 3.03 |
| | 2.89 |
| | 2.66 |
| 24. Vomiting | 1.87 |
| | 3.70 |
| 22 F 11 / | 2.02 |
| | 3.92 |
| 0 0 1 1 0 | 3.84 |
| 2 | 3.82 |
| e e | 3.76 |
| 0 | 3.71 |
| | 3.68 |
| ° | 3.17 |
| | 3.44 |
| | 4.21 |
| | 4.05 |
| , . | 3.74 |
| | 3.61 |
| • | 3.26 |
| | 3.16 |
| | 3.05 |
| 16. Pain in back with deep breaths | 2.43 |
| 2 Delegation of | 3.36 |
| | 4.63 |
| - | 4.47 |
| , e | 4.37 3.55 |
| , | 5.55 |
| | 3.38 |
| | 3.16 |
| 0 | 3.08 |
| | 2.92 |
| | 2.72 |
| | 2.79 |
| | 2.63 |
| * ** * | 2.61 |
| 44. Toolii deeay | 2.80 |
| | 2.00 |
| 34 Sinus issues | 3.55 |
| | 3.03 |
| • | 2.87 |
| | 2.87 |
| · | 2./1 |
| c-iiquiu | |
| 54 Swollen lymph nodes | 2 5 5 |
| 54. Swollen lymph nodes37. Sneezy | 2.55 2.45 |
| | during physical activity 29. Lowered stamina 28. Fatigue 14. Incapable of prolonged physical activity without losing breath |

Table 2. Continued

| Cluster | Statement | Average rating |
|-----------------|-----------------------------------|----------------|
| Throat Symptoms | i | 3.53 |
| • * | 1. Throat feels itchy or scratchy | 4.58 |
| | 18. Dry throat | 4.21 |
| | 21. Throat feeling burned | 3.89 |
| | 31. Sore throat | 3.68 |
| | 55. Throat tingling | 3.39 |
| | 52. Throat pain after waking up | 3.37 |
| | 48. Hard time swallowing | 2.74 |
| | 22. White spots in throat | 2.37 |

Mean ratings are based on responses to the prompt "I have experienced this negative respiratory symptom/effect from vaping/using my electronic cigarette" using a 7-point scale from 1 (Never) to 7 (Very Often). ECIGs = electronic cigarettes.

case with the majority of adult ECIG users), the symptoms reported in the current study could be confounded by those caused by cigarette smoking. Future studies that examine biochemically verified exclusive ECIG users only may be better able to examine ECIG-specific respiratory symptoms and disentangle symptoms that may also be or only be associated with cigarette smoking. Similarly, because we did not ask about underlying health conditions, even though tobacco use may have played some role in these conditions and/or symptoms, the current study cannot be used to attribute specific symptoms to specific tobacco product. However, there is growing evidence that ECIG use is associated with respiratory symptoms in analyses of exclusive ECIG users or analyses that control for cigarette smoking18,45,46 suggesting ECIG use likely plays a causal role in respiratory symptoms and health effects. Although the sample size is adequate for concept mapping methods, participants indicated that they were from 22 states in the United States, and the online convenience sample of participants across the U.S. approach produces generalizable data,⁴⁷ prevalence estimates of the specific respiratory symptoms identified in this study and associations with participant characteristics (eg, demographic, in-depth tobacco use characteristics) were not possible. Future larger studies may be able to examine the percentages of ECIG users who report specific respiratory symptoms. Additionally, this study identified symptoms using retrospective assessment, future studies may also use real-time assessment of acute symptoms, such as studies using ecological momentary assessment methods, in addition to retrospective assessment that may be better suited to capture chronic symptoms. This study focused on self-reported respiratory symptoms among ECIG users. Therefore, future studies are needed to examine to what extent ECIG use is causal in the appearance of respiratory symptoms as well as if ECIG use is associated with asymptomatic health effects.

Long-term effects of ECIG use remain uncertain, but this study and others provide insight into the potential harms to the respiratory system that are associated with ECIG use. As ECIG products continue to evolve with regard to device characteristics from early devices that resembled cigarettes and delivered little nicotine to advanced second- and third-generation devices that operate at higher wattages to "pod mod" devices, such as JUUL, that use protonated nicotine/nicotine salts to those products that may be introduced to the market in the future, continued monitoring of ECIG-related health effects including symptoms reported by ECIG users is needed. These data will be critical for developing regulatory policies to prevent morbidity and mortality associated with tobacco use.

Supplementary Material

A Contributorship Form detailing each author's specific involvement with this content, as well as any supplementary data, are available online at https://academic.oup.com/ntr.

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Declaration of Interests

E.S. is named on a patent application for a smartphone app that determines electronic cigarette device and liquid characteristics.

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