AJPM FOCUS

INCLUSIVITY IN PEOPLE, METHODS, AND OUTCOMES

RESEARCH ARTICLE

Inductive Characterization of ENDS-Associated Adverse Events Among California Young Adults



Joshua S. Yang, PhD, MPH, Pauline Lim¹, Kristen Ojeda¹, Raphael E. Cuomo, PhD, ² Vidya Purushothaman, MPH, Tim Mackey, PhD, MAS^{3,4}

Introduction: Previous studies have identified numerous adverse events experienced with the use of ENDS or E-cigarettes. However, much remains unknown about adverse event frequency, duration, and response experienced by users. The purpose of this study was to inductively characterize ENDS-attributed adverse events among young adults.

Methods: Sixteen focus groups were held with 114 young adults (aged 18–29 years) who have reported lifetime ENDS use in April 2021. Discussion topics included current and previous tobacco, nicotine, and cannabis use; specific symptoms and frequency and duration of and response to symptoms of ENDS-attributed adverse events; and the impact of other conditions such as COVID-19 on ENDS use. Data were inductively analyzed using a team-based approach.

Results: More than 40 ENDS-attributed adverse events were reported in focus groups among approximately three quarters of all study participants, with headache, coughing, lightheadedness, nausea, dry or sore throat, and dizziness the most common. In general, adverse events were transient, with most resolving in a few hours, although some tended to last for longer. The frequency of adverse events varied most between every time ENDS were used and when someone vaped excessively. Finally, behavioral responses varied by adverse events, with difficulty in breathing, chest pain, and lung discomfort more likely to result in quitting permanently.

Conclusions: Overall, the results of this study show that not only do adverse events vary greatly, but they also vary across multiple dimensions of user experience.

AJPM Focus 2022;1(2):100040. © 2022 The Author(s). Published by Elsevier Inc. on behalf of The American Journal of Preventive Medicine Board of Governors. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

INTRODUCTION

Electronic nicotine delivery systems (ENDS) or E-cigarettes have become the leading form of tobacco use among youth and young adults.^{1,2} In 2019, a total of 10.5% of middle school and 27.5% of high school students reported using E-cigarettes, the highest of any tobacco product³ and the highest since 2011, when 0.6% of middle school and 1.5% of high school students used E-cigarettes. In 2021, among young adults aged 18-24 years, E-cigarettes were the most commonly used tobacco product (9.4%), the highest among all age groups.² Increasing

From the ¹Department of Public Health, College of Health and Human Development, California State University, Fullerton, Fullerton, California; ²Department of Anesthesiology, School of Medicine, University of California, San Diego, San Diego, California; ³San Diego Supercomputer Center, University of California, San Diego, San Diego, California; and ⁴Global Health Program, University of California, San Diego, San Diego, Califor-

Address correspondence to: Joshua S. Yang, PhD, MPH, Department of Public Health, California State University, 800 North State College Boulevard, KHS 161A, Fullerton CA 92834. E-mail: jsyang@fullerton.edu.

2773-0654/\$36.00

https://doi.org/10.1016/j.focus.2022.100040

ENDS use places youth and young adults at risk for harm from nicotine exposure⁴ and a greater likelihood of cigarette smoking.⁵

In addition to their relationship with nicotine and combustible tobacco use, ENDS use has direct adverse physiologic effects, triggering potentially harmful cardiovascular^{6,7} and pulmonary response, impaired respiratory function,^{8,9} and immune and developmental effects. 10 The National Academies of Sciences, Engineering, and Medicine concluded that potentially toxic substances are emitted from most ENDS, although ENDS are likely less hazardous than combustible cigarettes and emit lower levels of toxic substances than those found in cigarette smoke. 11 In the summer of 2019, an outbreak of lung injury associated with ENDS drew public attention to the potential harms of their use. Although the cause of what would be termed E-cigarette or vaping product use-associated lung injury (EVALI) was attributed primarily to vitamin E acetate in cannabis vaping products, ¹² reports of defective ENDS¹³ and having 14% of all those hospitalized for EVALI reporting exclusive use of ENDS¹⁴ raised concern over the safety of ENDS.

In a study of U.S. adults examining adverse symptoms of ENDS use, more than half of all ever E-cigarette users attributed one or more adverse symptoms to ENDS use. Cough, dry or irritated mouth or throat, and dizziness or lightheadedness were the most commonly reported symptoms, with younger adults more likely to report symptoms than older adults. Other symptoms include headache/migraine, chest pain, abdominal pain, blurry vision, and fatigue. In addition, the Center for Tobacco Products in the U.S. Food and Drug Administration (FDA), which has the responsibility for reviewing voluntary communications regarding adverse events (AEs), reported that more than half of their tobacco-related AE reports have been for ENDS and include serious AEs.

Although evidence suggests that a wide range of ENDS-attributed AEs are experienced by a large proportion of ENDS users, much remains unknown about their relative frequency and duration, how users respond to AEs, or their long-term health effects. Without clear scientific evidence of the nature and effects of ENDS, information about constituents and potential benefits and harms are varied. Studies suggest that harm perception of E-cigarettes is lower than for conventional cigarettes among youth and young adults, although overall harm perceptions of ENDS are increasing among the general U.S. adult population. ^{17–19} Thus, evidence on ENDSattributed AEs and the impact of ENDS on health will be an important part of ongoing, long-term efforts to understand the harms of ENDS use, clearly communicate harm messages, and support the FDA's efforts at appropriate regulatory oversight of ENDS. Hence, the

purpose of this study was to gain insights into young adult ENDS use by inductively characterizing ENDS-attributed AEs.

METHODS

Study Sample

In March and April 2021, a market research firm recruited and screened individuals to participate in online focus group discussions on ENDS-attributed AEs from a proprietary list of more than 250,000 individuals on a panel of potential participants. In addition to initial contact with individuals on its panel, the market research firm recruited individuals through referral. Study inclusion criteria were as follows: (1) aged 18–29 years, (2) used an ENDS in the past 3 years, and (3) resident of California. Potential participants were assigned to one of 16 focus groups stratified on 3 criteria: (1) having ever experienced an ENDS-attributed AE, (2) current (past 30-day) or former (past 3 years but not past 30-day) ENDS user, and (3) ENDS use pattern (ENDS only, ENDS and cigarette dual use, ENDS and alternative tobacco product dual use, and ENDS and cannabis product dual use).

Measures

An empirical phenomenologic approach, which focuses on lived experiences of a phenomenon while bracketing previous understanding, was adopted for the broader project from which this analysis is derived.²⁰ More specifically, this study was designed to describe how ENDS users perceived and experienced AEs that they attributed to ENDS use. Before online focus group discussions, participants completed an online consent form and survey, which covered demographic characteristics, tobacco use patterns, and tobacco-related social media use. Age and individual and household income were collected as open-ended variables, with sex, sexual orientation, race/ethnicity, educational attainment, and employment status recorded as categorical variables with response options as listed in Table 1. Tobacco use patterns were obtained through questions asking about lifetime, past 3-year, and past 30-day use of cigarettes; cigars, little cigars, or cigarillos; electronic cigarettes; noncombusted cigarettes (heated tobacco product, heat-not-burn product, IQOS); chewing tobacco, moist snuff, snus, or similar products; water pipes (e.g., hookah, shisha, narghile, and argileh); bidis; kreteks; dissolvable tobacco products; and spliffs. Questions related to social media use asked: whether participants use social media (yes/no); what social media channels they use from a list of 9 social media platforms; and what type of tobacco-related material they post on social media (tobaccorelated news [e.g., events, news reports]; tobacco-related behavior [e.g., smoking, vaping]; tobacco marketing [e.g., new products, price discounts]; communicate with others about tobacco [e.g., opinions, reviews, post questions or answers]; interact with or follow tobacco-related influencers, celebrities, personalities; other; do not post about tobacco on social media). Participants were also asked to identify whether they experienced any of the 28 AEs from a list derived from the literature on the online questionnaire. Past 30-day cannabis use was determined from screener questions. A total of 192 individuals consented to participate in the study, with 157 assigned to focus groups. Completion of informed consent forms and online questionnaires was confirmed before online focus groups were conducted.

Table 1. Sample Description

Characteristics	N=114, %
Age	24.1 years
Sex	
Male	45.6
Female	51.8
Other	2.6
Sexual orientation	
Bisexual	10.5
Gay	1.8
Lesbian	2.6
Heterosexual	80.7
Decline	4.4
Race/ethnicity	
White	39.5
Black	8.8
AA-NHPI	16.7
Latino	17.5
MENA	5.3
2 or more	12.3
Highest level of education completed	
HS diploma	17.5
Some college	16.7
Associate's	13.9
Vocational	3.5
Bachelor's	38.6
Graduate	4.4
Student status	
Yes	43.0
No	56.3
Employment status	
Not working, not looking	13.2%
Not working, looking	22.8
Part-time	28.1
Full-time	34.2
Marital status	
Married	4.4
Living with partner	17.5
Separated	1.8
Never married	76.3
Number of tobacco products used in lifetime	
1	11.4
2	14.9
3	19.3
4	21.1
5	18.4
6	10.5
7+	3.6
Past 30-day tobacco use	
Yes	69.3
No	30.7
	(continued)

Table 1. Sample Description (continued)

Characteristics	N=114, %
Past 30-day E-cigarette use	
Yes	50.9
No	49.1
Current E-cigarette and THC dual user	14.0
Past 3 years, not current E-cigarette and THC dual user	30.7

AA-NHPIN, Asian American-Native Hawaiian Pacific Islander; MENA, Middle Eastern or North African; HS, high school; THC, tetrahydrocannabinol.

Online focus groups facilitated by the first author were held in April 2021 with a total of 114 participants, all of whom completed the online questionnaire. Focus group discussions included current and previous tobacco, nicotine, and cannabis use (What kinds of nicotine vape products do you currently or have you ever used? Can you tell me more about when and how you use them? Can you also tell me about use of any other combustible tobacco product you currently or have ever used, like cigarettes, cigars, hookah, or IQOS [heat-not-burn] products? What about smokeless products, like chewing tobacco, lozenges, or heat-not-burn products? What about THC products that are inhaled, like vaping THC or dabbing?), ENDS-attributed AEs (Can you tell me about any adverse symptoms you've experienced with nicotine vaping or have heard of other people experiencing? Please tell me more about when you [or another person] experienced the symptoms; What did you [or another person do in response to experiencing these symptoms?), EVALI knowledge and experiences (In 2019, there were reports of an outbreak of lung injury from vaping. The condition was eventually called E-cigarette, or vaping, product use-associated lung injury, or EVALI. Can you tell me when you first heard about these cases? What did you first hear about it? How did your understanding of what was happening change over time? How did you feel about vaping when you heard about EVALI?), and COVID-19 and ENDS and other product use (What have you heard about vaping or other tobacco use and their relationship to COVID-19? Where do you get your information about vaping and its relationship to COVID-19? How has the COVID-19 outbreak affected your attitude toward vaping or combustible tobacco use?). Focus groups were video and audio recorded. On average, there were 7.1 individuals in each group (range: 4-9), and the average duration of discussions was 90 minutes (range: 55-118 minutes). On completion of the focus group, a \$150 incentive was issued to each participant. The study protocol was approved by the IRB at California State University, Fullerton.

Data Analysis

Focus group recordings were professionally transcribed, reviewed for accuracy, and analyzed using ATLAS.ti 9. The codebook for the analysis was developed using a team-based approach.²¹ The first author developed an initial coding scheme on the basis of the focus group discussion protocol, informal focus group notes, and a close reading of 2 transcripts. Research assistants coded a subset of transcripts using the coding scheme and added new codes as needed. The analysis team met to review and finalize the coding scheme.

Two research assistants both coded the same transcript until an intercoder agreement of Krippendorff's α =0.883 was reached on

Table 2. Reported AEs

Inductive AE	Survey percentage ^a	Focus group mentions
Headache	52.6	35
Coughing	50	22
Lightheadedness	1.8 (cough up blood) 57.9	22
Nausea	43.0	22
Dry/sore throat	34.2	21
Dizziness	38.6	17
Difficulty breathing	33.3 (shortness of breath) 16.7 (wheezing)	14
Throat pain	28.1	13
Chest pain	18.4 (chest tightness)	12
Head rush		8
Phlegm	5.3 (extra sputum)	7
Itchy/scratchy throat		6
Sluggishness		6
Stomach pain		5
Dry mouth		4
Insomnia	14.0 (sleep disturbance)	4
Hair loss		4
Lung discomfort		4
Cotton mouth		3
Panicky		3
Raspy voice	9.6 (harsh voice quality)	3
Anxiety		2
Dehydration		2
Heart palpitation		2
Heart rate increase	17.5	2
Not motivated		2
Spins		2
Vomiting	11.4	2
Adrenaline rush		1
Blisters in mouth and tongue		1
Changes in voice		1
Fatigue	23.7	1
Heartburn	4.4	1
	4.4 (change or loss of taste)	1
Loss of appetite	4.4 (change of loss of taste)	1
Mood swings		1
Night sweats		1
Restlessness		1
Snoring		1
Vertigo		1
Weakness		1
Weight loss	6.1	1
-	7.0	0
Dry eyes	5.3	0
Sweat	5.3	0
Dry skin	5.3	
Constipation		0
Heartburn	4.4	0
Chills	3.5	0
Fever	2.6	0
		(continued

Table 2. Reported AEs (continued)

Inductive AE	Survey percentage ^a	Focus group mentions
Itching skin	2.6	0
Total		263

 $^{^{\}rm a}\!\text{AE}$ name as listed in the survey in parenthesis if differs from the term used in focus groups.

AE, adverse event.

the first coding, after which the remaining transcripts were coded by 1 research assistant.²² Every unique instance of a participant discussing an AE was extracted from the data and organized into a table that included verbatim text on specific symptom and AE frequency, duration, and response. Inductively derived response categories were created by the first author for AE duration, frequency, and response (see Appendix, available online) and applied to the data, then reviewed for appropriateness by the third author. Differences in interpretation and application were resolved using a consensus approach. Focus group transcripts were recoded in ATLAS.ti using categories from Table 1. Through an iterative analysis of data memos, qualitative cross-tabulations of subcodes, and analysis of focus group texts, patterns in frequency, duration, and response for each AE were developed. In addition, an analytical data set was generated with focus group participants as cases and each reported AE as a binary variable. For AEs where n>5, a correlation matrix of Spearman correlation coefficients was computed to identify distinct broader symptomologies vis a vis unique clusters of multiple symptoms.

RESULTS

The study included 114 participants with an average age of 24.1 years; 45.6% were female (Table 1). Among the participants, 39.5% identified as White; 17.5% identified as Latino; 16.7% identified as Asian American, Native Hawaiian, or Pacific Islander; 8.8% identified as Black; 5.3% identified as Middle Eastern or North African; and 12.3% identified as of 2 or more racial/ethnic categories. Most participants tried between 3 and 5 tobacco products in their lifetime, and 85 participants (74.6%) reported ever experiencing at least 1 AE.

The average numbers of lifetime AEs from survey responses were 5.03 AEs, and 45.5% of respondents reported experiencing between 4 and 8 AEs. A total of 42 AEs were mentioned by study participants in focus groups (Table 2), with 24 inductively identified AEs not included on the online questionnaire; 8 AEs reported on the online questionnaire were not brought up by participants in focus groups. The most commonly mentioned AEs in the focus groups (20 or more mentions) were headache, coughing, lightheadedness, nausea, and dry or sore throat. Dizziness, difficulty in breathing, throat pain, and chest pain were mentioned by 12–17 participants. Although the ordering differed, the 6 most

Table 3. Pairwise Spearman Correlation Coefficients Between Self-Reported Adverse Events in Focus Group Cohort

AE	Chest pain	Cough	Dizziness	Dry/ sore throat	Headrush	Headache	Itchy/ scratchy throat	Lightheadedness	Nausea	Phlegm	Difficulty in breathing
Coughing	-0.045										
Dizziness	-0.007	-0.111									
Dry/sore throat	-0.051	0.004	-0.122								
Headrush	-0.083	-0.065	0.086	0.126							
Headache	0.085	-0.119	0.11	0.091	-0.132						
Itchy/scratchy throat	0.103	0.172	-0.128	0.375	-0.083	0.181					
Lightheadedness	-0.045	-0.046	0.252	0.132	0.136	0.055	-0.045				
Nausea	-0.045	-0.046	0.034	-0.189	0.036	0.055	-0.045	0.019			
Phlegm	-0.083	-0.166	0.086	0.225	0.066	0.047	0.252	0.136	-0.166		
Difficulty in breathing	0.138	0.073	-0.111	-0.243	-0.008	0.028	0.011	-0.082	-0.005	-0.127	
Sluggishness	0.103	-0.153	-0.007	0.375	0.085	0.277	-0.076	0.064	-0.045	0.085	-0.117

Note: Boldface indicates statistical significance (p<0.05).

AE, adverse event

commonly reported AEs were the same in focus groups as in the survey.

Among the AEs reported at least 5 times in focus groups, some were experienced together. Positive correlations were between dry/sore throat and itchy/scratchy throat (p<0.001), dry/sore throat and sluggishness (p<0.001), headache and sluggishness (p=0.010), dizziness and lightheadedness (p<0.001), itchy/scratchy throat and phlegm (p=0.020), and dry/sore throat and phlegm (p=0.039), which were AE combinations that were significantly correlated (Table 3). A negative correlation was observed between dry/sore throat and difficulty breathing (p=0.025). Therefore, the following 5 AEs clustered with at least one other AE: itchy/scratchy throat, phlegm, sluggishness, dry/sore throat, and headache. Although lightheadedness and dizziness were correlated, neither of these AEs exhibited a statistically significant correlation with an AE in the 5-symptom cluster.

More than half of all AEs discussed in focus groups lasted for 3 hours or less, and nearly three quarters were resolved within 24 hours. For example, most respondents who had chest pain reported that it lasted for <30 minutes (Table 4), with 1 person reporting pain lasting for 1-3 hours and 1 person reporting that "the next day I just felt. . . chest pain for a couple days." Coughing, dizziness, and lightheadedness were also reported to generally last for <30 minutes, with only a few participants reporting lightheadedness lasting for >1 and up to 12 hours. Nausea was also reported to generally last for 30 minutes or less, although a larger proportion of participants reported that it lasted for up to 3 hours compared with chest pain, coughing, dizziness, and lightheadedness. Other AEs tended to last longer. For example, dry and sore throat, throat pain, phlegm, and sluggishness were reported to last for more than 12 hours to >1 day by half of those mentioning a duration.

Headaches had the greatest variability in reported duration among the most frequently reported symptoms. There were similar numbers of respondents reporting headaches lasting for <30 minutes, 1–3 hours, 3–12 hours, 12–24 hours, and >24 hours.

The frequency of AEs varied greatly for most symptoms. Among the most frequently cited AEs, participants described the frequency of AEs as occurring either always or every time or depending on usage, which was most often periods when participants were vaping more. The split between always or every time and depending on usage was particularly true for coughing, dizziness, dry or sore throat, headache, lightheadedness, and nausea, with no distinction observed among current and former ENDS users. Among the most frequently cited AEs, shortness of breath and throat pain were discussed more commonly as happening always or every time, and no differences appeared between those who were current or former ENDS users.

Participants' responses to experiencing an AE were highly variable (Table 5), although the most common responses across all AEs were to either quit successfully or do nothing. Temporarily stopping until symptoms pass, switching to other tobacco products, drinking water, and switching to tetrahydrocannabinol products were other less common but notable responses to AEs. Relatively high proportions of participants who experienced difficulty in breathing or chest pain reported quitting permanently in response to AEs, with lower proportions of participants who reported experiencing lung discomfort or nausea permanently quitting or cutting back. Temporarily cutting back was a more common response to coughing, dry or sore throat or mouth, and headache.

Participants also reported switching to other tobacco or nicotine products in response to a wide range of AEs.

Table 4. Example Quotes for Thematic Findings

Thematic area	Adverse event	Example quote
Adverse event duration	Chest pain	"Not too long, probably just like a minute or so"
	Nausea	"The nausea probably only really lasts, like 20 minutes" "Just feel sick to my stomach it's at least an hour"
	Headaches	"A headache that would last maybe about 20—30 minutes" "I would get these headaches for like an hour or a few hours" "For my headaches it takes at least 6 hours" "I had a headache for a day" "Headache lasted for about 2 days"
Adverse event frequency	Coughing (always or every time or depends on usage)	"I would just cough I would have the same result every time" "Too much use, it's either a headache or coughing a lot"
	Dizziness (always or every time or depends on usage)	"I realized I would get these headaches and dizziness from them every time I would [vape]" "Dizziness, just if I had took too many hits"
	Dry or sore throat (always or every time or depends on usage) Lightheadedness (always or every time or depends on usage)	"A sore throat, that'll be every time" "If I [vape] too much, I would get like a sore throat" "Each time I did it, I felt [lightheaded]" "I would be like smoking a lot and I would get lightheaded"
	Nausea (always or every time or depends on usage)	"I haven't had an experience where I don't just feel sick to my stomach" "Just super nauseous if I smoked a lot"
	Shortness of breath (always or every time)	"Shortness of breath was like every time"
	Throat pain (always or every time)	"Always a sore throat, always like a pain in my throat"
Response to adverse event	Difficulty in breathing (quit)	"I also feel a shortness of breath so it just makes me want to stop doing that because I did not like it"
	Chest pain (quit)	"A pain in my chest like a poke, almost a stabbing kind of pain and then since I stopped the JUUL, it's never been there again"
	Lung discomfort (quit)	"I noticed my lungs would hurt sometimes and that made me quit because I realized it was more of a long-term impact"
	Nausea (quit)	"To smoke something that then caused [nausea], it was like, uh, maybe no"
	Coughing (cut back)	"When I am vaping more often, then I notice I'm coughing or having a harder time breathing, I tone it down and vape less"
	Dry or sore throat or mouth/ headache (cut back)	"I would get like a sore throat, sometimes I would get headaches, too [my girlfriend and I] are just like, 'let's take a break' then we kind of just get back to it"
	Dizziness (switch products)	"Dizzy, lightheaded I don't trust these vapes at all anymore so I went back to smoking cigarettes"
	Headache (switch products)	"The e-cigarette pens I would have, like, a headache, throat pain, and that's why I leaned more onto my (cannabis) pen more"

Specifically, participants switched to cannabis products in response to weakness, throat pain, raspy voice, nausea, lightheadedness, headache, or dry or sore throat, with a larger proportion of those experiencing dizziness or headache.

DISCUSSION

This study sought to inductively characterize ENDSattributed AEs from the experiences of young adult ENDS users. More than 40 ENDS-attributed AEs were reported among approximately three quarters of all study participants, with headache, coughing, lightheadedness, nausea, dry or sore throat, and dizziness being the most common. In general, AEs were transient, with most resolving in a few hours, although some tended to last for longer. The frequency of AEs varied most between every time ENDS were used and when someone vaped excessively. Finally, behavioral responses varied by AE, with difficulty in breathing, chest pain, and lung discomfort more likely to result in quitting permanently. In contrast, coughing, dry or sore throat or mouth, and headache were dealt with by temporarily cutting back,

Table 5. Behavioral Responses to Most Commonly Reported Adverse Events

Adverse event	Behavioral responses
Chest pain	Quit permanently Cut back permanently Quit for a period then start again Cut back temporarily
Coughing	Quit permanently Cut back permanently Temporarily cut back Switch to other tobacco products Drink water Do nothing
Dizziness	Quit for a period then start again Temporarily stop until symptom passes Switch to other tobacco product Drink water Sit or lay down Do not inhale smoke Do nothing
Dry or sore throat	Quit for a period then start again Cut back permanently Temporarily stop until symptoms pass Temporarily cut back Consider quitting or cutting back Switch to THC product Switch to other product types (e.g., coffee) Do nothing
Stomach pain	Quit permanently Quit for a period then start again Temporarily stop until symptoms pass Switch to other tobacco products Do nothing
Headache	Quit permanently Quit for a period then start again Temporarily stop until symptom passes Temporarily cut back Switch to THC products Switch to other tobacco products Drink water Do not inhale smoke Take medication Do nothing
Lightheadedness	Temporarily stop until symptoms pass Temporarily cut back Switch to THC products Switch to other tobacco products Wait out symptom Drink water Do not inhale smoke Do nothing
Nausea	Quit permanently Quit for a period then start again Temporarily stop until symptom passes Consider quitting or cutting back Switch to THC products Eat something Do not inhale smoke Take medication Do nothing
Phlegm	Quit permanently Unsuccessfully attempt to quit or cut back Temporarily quit or cut back Switch to other tobacco product Spit or clear throat Do nothing
	(continued)

Table 5. Behavioral Responses to Most Commonly Reported Adverse Events (continued)

Adverse event	Behavioral responses
Difficulty in breathing	Quit successfully
	Temporarily stop until symptom passes
	Temporarily cut back
	Do nothing
Throat pain	Quit for a period then start again
	Unsuccessfully attempt to quit or cut back
	Switch to THC products
	Switch to other tobacco products
	Drink water
	Do not inhale smoke
	Do nothing

THC, tetrahydrocannabinol.

and switching products was more commonly reported with dizziness and headache. Overall, the results of this study show that not only do AEs vary greatly, but they also vary across multiple dimensions of user experience.

The results of this study confirm previously identified ENDS-attributed AEs and point to additional AEs. The variations reported in AE duration and frequency may be reflective of an evolving ENDS product landscape where youth and young adults are particularly susceptible to marketing and initiation and may also reflect the use of other tobacco and nontobacco substances or multiple product use or administration. Different behavioral responses are likely a result of inadequate information and advice on how users should respond when experiencing an AE. In this context, the inductive categories developed in this study for AEs experienced and AE duration, frequency, and response provide a basis for advancing efforts to better measure and characterize ENDS-attributed AEs using multiple data sources such as future survey instruments and surveillance of ENDSattributed AEs. A closer examination of AEs that are specific to ENDS compared with those specific to other tobacco, substance use, or multiple product use is also needed.

It is important to note that new tobacco products, including ENDS, must receive market authorization from the FDA to be legally marketed in the U.S. through an extensive premarket review process. Once authorized, postmarket surveillance of AEs is critical to fully understanding the risk and safety profile of new and emerging ENDS. Currently, most AE data are derived from voluntary reporting through the FDA Tobacco Product Adverse Event Reporting webpage. However, public data from the FDA show that in 2021, only 94 voluntary reports of tobacco product health and safety problems were submitted, of which 62 were related to ENDS. The relatively low volume of formal AE reporting compared with the high proportion of respondents reporting AE experiences may underlie a challenge with

underreporting as suggested by this and other studies. 15,25 Hence, more proactive efforts to assess ENDS-related AEs should be developed to more fully assess the risks associated with these products and their potential impact on the short- and long-term health of young adults.

The findings from this study can also inform future efforts to reduce ENDS use. As this study suggests, some AEs prompt ENDS users to make attempts at quitting ENDS. Public information campaigns and cessation programs should leverage these experiences to guide ENDS users from contemplation of or attempt at quitting or cutting back to successful cessation of ENDS. This is especially important with the proliferation of tobacco products on the market as well as the growth and expanding legalization of cannabis products that may serve as alternatives to ENDS. This will require additional research to enhance the understanding of how AEs may vary by ENDS use status, including the frequency and volume of use and product mix. Enhancing the appeal of quitting tobacco and cannabis products altogether instead of switching among products will be an important element of future tobacco control and cessation efforts.

Limitations

This study has limitations. First, the convenience sample of participants limits the generalizability or representativeness of the study findings to other young adults, and the use of a commercial incentive rate may have biased the sample, such as crowding out individuals who may have participated in the study for other or lower incentives. Second, the small sample size prevented deeper exploration of less commonly reported AEs or the relationship between AEs and other variables. There may also be additional AEs not captured in this study. In addition, questionnaires and focus group discussions were focused on AE experiences over a number of years, which may have introduced recall bias. This study was limited to ENDS-attributed AEs and was unable to distinguish whether AEs attributed to ENDS may have been a result of co-use or coadministration of other products. With greater diversity of tobacco products and within the ENDS product market, future studies should expand the scope of AEs to other tobacco products and delineate by specific product types or brands within the ENDS market for more targeted regulatory impact.

CONCLUSIONS

ENDS-attributed AEs are highly variable in their symptoms, duration, and frequency. The widespread

experience of AEs among ENDS users and their varying health impacts suggest a need for more novel surveil-lance approaches and the incorporation of these results into regulatory considerations in evaluating ENDS products both before and after market. In addition, AEs prompt some ENDS users to consider or attempt quitting or cutting back their use. Although some users successfully quit on their own, tobacco control efforts should leverage the experiences of user AEs to actively support cessation efforts.

ACKNOWLEDGMENTS

The study protocol was approved by the IRB at California State University, Fullerton (HSR 19-20-565).

The opinions and conclusions herein are those of the author and do not necessarily represent those of The Regents of the University of California or any of its programs.

This project was partially supported by funds provided by The Regents of the University of California, Tobacco-Related Diseases Research Program, grant number T31|P1928.

Declarations of interest: none.

CREDIT AUTHOR STATEMENT

Joshua S. Yang: Conceptualization, Formal analysis, Investigation, Methodology, Supervision, Writing—original draft, Writing—review and editing. Pauline Lim: Data curation, Formal analysis. Kristen Ojeda: Data curation, Formal analysis. Raphael E. Cuomo: Data curation, Formal analysis, Writing—original draft. Vidya Purushothaman: Data curation, Formal analysis. Tim Mackey: Conceptualization, Funding acquisition, Writing—review and editing.

SUPPLEMENTARY MATERIALS

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.focus.2022.100040.

REFERENCES

- 1. Wang TW, Gentzke A, Sharapova S, Cullen KA, Ambrose BK, Jamal A. Tobacco product use among middle and high school students —United States, 2011-2017. MMWR Morb Mortal Wkly Rep. 2018;67 (22):629–633. https://doi.org/10.15585/mmwr.mm6722a3.
- Cornelius ME, Loretan CG, Wang TW, Jamal A, Homa DM. Tobacco product use among adults—United States, 2020. MMWR Morb Mortal Wkly Rep. 2022;71(11):397–405. https://doi.org/10.15585/mmwr.mm7111a1.
- Wang TW, Gentzke AS, Creamer MR, et al. Tobacco product use and associated factors among middle and high school students—United States, 2019. MMWR Surveill Summ. 2019;68(12):1–22. https://doi. org/10.15585/mmwr.ss6812a1.
- Siqueira LM, Committee on Substance Use and Prevention. Nicotine and tobacco as substances of abuse in children and adolescents. *Pediatrics*. 2017;139(1):e20163436. https://doi.org/10.1542/peds.2016-3436.
- Soneji S, Barrington-Trimis JL, Wills TA, et al. Association between initial
 use of e-cigarettes and subsequent cigarette smoking among adolescents
 and young adults: a systematic review and meta-analysis [published correction appears in *JAMA Pediatr.* 2018;172(1):92–93] [published

- correction appears in *JAMA Pediatr.* 2018;172(1):98] [published correction appears in *JAMA Pediatr.* 2020;174(5):509]. *JAMA Pediatr.* 2017;171 (8):788–797. https://doi.org/10.1001/jamapediatrics.2017.1488.
- Macdonald A, Middlekauff HR. Electronic cigarettes and cardiovascular health: what do we know so far? Vasc Health Risk Manag. 2019;15:159–174. https://doi.org/10.2147/VHRM.S175970.
- Qasim H, Karim ZA, Rivera JO, Khasawneh FT, Alshbool FZ. Impact of electronic cigarettes on the cardiovascular system. *J Am Heart Assoc.* 2017;6(9):e006353. https://doi.org/10.1161/JAHA.117.006353.
- Chun LF, Moazed F, Calfee CS, Matthay MA, Gotts JE. Pulmonary toxicity of e-cigarettes. Am J Physiol Lung Cell Mol Physiol. 2017;313 (2):L193–L206. https://doi.org/10.1152/ajplung.00071.2017.
- Soule EK, Bode KM, Desrosiers AC, Guy M, Breland A, Fagan P. User-perceived negative respiratory symptoms associated with electronic cigarette use. *Nicotine Tob Res.* 2020;22(suppl 1):S45–S53. https://doi.org/10.1093/ntr/ntaa179.
- Overbeek DL, Kass AP, Chiel LE, Boyer EW, Casey AMH. A review of toxic effects of electronic cigarettes/vaping in adolescents and young adults. Crit Rev Toxicol. 2020;50(6):531–538. https://doi.org/10.1080/ 10408444.2020.1794443.
- National Academies of Sciences, Engineering, and Medicine. Public Health Consequences of E-Cigarettes. Washington, DC: The National Academies Press; 2018. https://nap.nationalacademies.org/catalog/24952/ public-health-consequences-of-e-cigarettes. Accessed August 30, 2022.
- Blount BC, Karwowski MP, Shields PG, et al. Vitamin E acetate in bronchoalveolar-lavage fluid associated with EVALI. N Engl J Med. 2020;382(8):697–705. https://doi.org/10.1056/NEJMoa1916433.
- Seitz CM, Kabir Z. Burn injuries caused by e-cigarette explosions: a systematic review of published cases. Tob Prev Cessat. 2018;4:32. https://doi.org/10.18332/tpc/94664.
- Krishnasamy VP, Hallowell BD, Ko JY, et al. Update: characteristics of a nationwide outbreak of e-cigarette, or vaping, product use-associated lung injury—United States, August 2019-January 2020. MMWR Morb Mortal Wkly Rep. 2020;69(3):90–94. https://doi.org/10.15585/ mmwr.mm6903e2.

- King JL, Reboussin BA, Wiseman KD, et al. Adverse symptoms users attribute to e-cigarettes: results from a national survey of US adults. *Drug Alcohol Depend*. 2019;196:9–13. https://doi.org/10.1016/j.dru-galcdep.2018.11.030.
- Chen IL. FDA summary of adverse events on electronic cigarettes. Nicotine Tob Res. 2013;15(2):615–616. https://doi.org/10.1093/ntr/nts145.
- Parker MA, Villanti AC, Quisenberry AJ, et al. Tobacco product harm perceptions and new use. *Pediatrics*. 2018;142(6):e20181505. https://doi.org/10.1542/peds.2018-1505.
- Huang J, Feng B, Weaver SR, Pechacek TF, Slovic P, Eriksen MP. Changing perceptions of harm of e-cigarette vs cigarette use among adults in 2 US national surveys from 2012 to 2017. *JAMA Netw Open.* 2019;2(3): e191047. https://doi.org/10.1001/jamanetworkopen.2019.1047.
- Wagoner KG, Cornacchione J, Wiseman KD, Teal R, Moracco KE, Sutfin EL. E-cigarettes, hookah pens and vapes: adolescent and young adult perceptions of electronic nicotine delivery systems. *Nicotine Tob* Res. 2016;18(10):2006–2012. https://doi.org/10.1093/ntr/ntw095.
- Christensen M. The empirical-phenomenological research framework: reflecting on its use. *J Nurs Educ Pract*. 2017;7(12):81. https://doi.org/ 10.5430/jnep.v7n12p81.
- MacQueen KM, McLellan E, Kay K, Milstein B. Codebook development for team-based qualitative analysis. *Cult Anthropol.* 1998;10 (2):31–36. https://doi.org/10.1177/1525822X980100020301.
- 22. Friese S. *Qualitative Data Analysis With Atlas.Ti.* Thousands Oak, CA: Sage Publications Ltd, 2019.
- Safety reporting portal. U.S. Food and Drug Administration. https:// www.safetyreporting.hhs.gov. Accessed September 2, 2022.
- Tobacco product problem reports. U.S. Food and Drug Administration. https://www.fda.gov/tobacco-products/tobacco-science-research/tobacco-product-problem-reports. Updated August 1, 2022. Accessed September 2, 2022
- King JL, Reboussin BA, Merten JW, Wiseman KD, Wagoner KG, Sutfin EL. Negative health symptoms reported by youth e-cigarette users: results from a national survey of US youth. *Addict Behav*. 2020;104:106315. https://doi.org/10.1016/j.addbeh.2020.106315.