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Concurrent use of e-cigarettes and cannabis and associated COVID-19 symptoms, testing, and diagnosis among student e-cigarette users at four U. S. Universities

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ABSTRACT

Introduction: This investigation assessed whether current (past 30-day) electronic cigarette (e-cigarette) and cannabis use was associated with coronavirus disease 2019 (COVID-19) symptomatology, testing, and diagnosis among college student e-cigarette users.

Methods: Participants were 18–26-year-old college student e-cigarette users attending four geographically diverse, large U.S. public universities during October-December 2020 (N = 800). Multivariable logistic regression models explored associations between exclusive e-cigarette use and concurrent e-cigarette and cannabis use and COVID-19 symptoms, testing, and diagnosis. Models controlled for demographics, university site, and current use of combustible cigarettes, cigars, and smokeless tobacco.

Results: Over half of student e-cigarette users (52.0%) concurrently used cannabis. Compared to exclusive e-cigarette users, concurrent e-cigarette and cannabis users were 3.53 times more likely (95%CI = 1.96–6.36) to report COVID-19 symptoms, after adjusting for the covariates. Compared to infrequent exclusive e-cigarette users, infrequent concurrent users (AOR = 4.72, 95%CI = 1.31–17.00), intermediate concurrent users (AOR = 5.10, 95%CI = 1.37–18.97), and frequent concurrent users (AOR = 7.44, 95%CI = 2.06–26.84) were at increased odds of reporting COVID-19 symptoms. Compared to exclusive e-cigarette users, concurrent e-cigarette and cannabis users were 1.85 times more likely (95%CI = 1.15–2.98) to report a COVID-19 diagnosis. Intermediate concurrent users (AOR = 2.88, 95%CI = 1.13–7.35) and frequent concurrent users (AOR = 3.22, 95%CI = 1.32–7.87) were at increased odds of reporting a COVID-19 diagnosis, compared to infrequent exclusive e-cigarette users.

Conclusions: Concurrent use of e-cigarettes and cannabis may be an underlying risk factor of COVID-19 symptomatology and diagnosis, with more pronounced odds found among intermediate and frequent users. Results highlight the need to educate students about the impacts of e-cigarette and cannabis use on respiratory, immune, and overall health.

1. Introduction

Transmission of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the virus responsible for causing coronavirus disease 2019 (COVID-19), has led to unprecedented morbidity and mortality across the U.S. (Dong et al., 2020). Risk factors for COVID-19-related

Abbreviations: e-cigarettes, electronic cigarettes; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; COVID-19, coronavirus disease 2019; LGBTQ, lesbian, gay, bisexual, transgender, and questioning; AOR, adjusted odds ratio; CI, confidence interval; Ref, reference category.

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severe illness resulting in possible hospitalization include: active or former smoking status and/or having pre-existing comorbidities or an immunocompromised status (Centers for Disease Control and Prevention, 2021). Combustible and non-combustible tobacco users are vulnerable to clinical morbidities, including impaired pulmonary function and respiratory illnesses (National Academies of Sciences, Engineering, and Medicine, 2018; U.S. Department of Health and Human Services, 2014). Research suggests combustible smoking or vaping cannabis is associated with respiratory-related symptoms and disease (National Academies of Sciences, Engineering, and Medicine, 2017). Additionally, vaping nicotine, flavorings, and/or tetrahydrocannabinol (THC) products may place individuals at increased risk for COVID-19-related symptomatology and illness due to impairment of normal pulmonary defenses to inhaled viral pathogens (Keith and Bhatnagar, 2021; Madison et al., 2019; Kaur et al., 2020; Volkow, 2020). Smoking, and possibly e-cigarette use, can upregulate the angiotensin-converting enzyme-2 (ACE2) receptor, which is the receptor for SARS-CoV-2 (Brake et al., 2020). However, human research studies are lacking on concurrent e-cigarette and cannabis use and COVID-19-related health outcomes.

Research has linked respiratory symptoms or disease with adult current e-cigarette use (Bhatta and Glantz, 2020), current cannabis combustible smoking and vaping (Braymiller et al., 2020), and lifetime e-cigarette and cannabis use (Xie and Li, 2020). College student e-cigarette use and cannabis smoking and vaping reached historical highs between 2017 and 2019 (Schulenberg et al., 2020). Currently, 22% and 14% of students report past 30-day nicotine and cannabis vaping, respectively (Schulenberg et al., 2020). Over one-in-four (26%) students report current cannabis use including other routes of administration (e.g., combustible smoking), with 1-in-17 (6%) reporting daily cannabis use. While current dual use of e-cigarettes and combustible cigarettes has been associated with increased risk of COVID-19 symptoms and diagnosis among 13–24-year-olds (Gaiha et al., 2020), less is known about COVID-19-related risks associated with concurrent e-cigarette and cannabis use. Given the high prevalence of e-cigarette and cannabis use among college students (Schulenberg et al., 2020), research is needed to assess the associations between concurrent use and COVID-19-related outcomes.

This investigation assessed whether current e-cigarette and cannabis use was associated with COVID-19 symptomatology, testing, and diagnosis among college student current e-cigarette users. We hypothesized concurrent users of e-cigarettes and cannabis would be at increased odds of experiencing COVID-19 symptoms and having a prior positive COVID-19 diagnosis compared with exclusive e-cigarette users. Additionally, we assessed whether frequency of e-cigarette and cannabis use was associated with COVID-19 symptoms, testing, and diagnosis. We hypothesized that when compared to infrequent exclusive e-cigarette users, intermediate or daily exclusive e-cigarette users as well as infrequent, intermediate, and frequent concurrent e-cigarette and cannabis users would be at increased odds of reporting COVID-19 symptoms and diagnosis. Based on COVID-19 random selection testing policies at each university during the study period, we posited there would be no difference in COVID-19 testing between the exclusive e-cigarette and concurrent use groups.

2. Materials and methods

2.1. Participants and procedures

Data are from a cross-sectional, online survey conducted October-December 2020. Participants were college students (N = 800) ages 18–26 years from four geographically diverse, large U.S. public universities (two southwestern, two midwestern) who reported current e-cigarette use. Institutional review boards (IRBs) at each university independently vetted and approved all study procedures by November 2020; data collection occurred after respective IRB approval. Students at each university had the option to complete their coursework online, in-person, or a hybrid model. Students residing in university housing/residences were allowed to remain on each of the respective campuses during the data collection period. COVID-19 testing programs at each of the four respective campuses were similar and required randomly selected students to undergo testing.

Eligible participants were recruited by disseminating emails via campus-wide listservs and undergraduate and graduate course listservs. Participant recruitment strategically took place at least over one month into the fall semester due to the study's aim of capturing past 30-day behavior during the academic year. Solicitations sought students between the ages of 18–26 who "vape or use e-cigarettes" and were currently on campus. The recruitment email included a website link to a survey hosted on Qualtrics (Qualtrics, 2021), and stated the estimated completion time was 10 minutes. Potential participants were provided with a research information sheet which they needed to acknowledge prior to proceeding to the survey. The information sheet reinforced the recruitment email's information (e.g., anonymous nature of the survey; ability to refuse to answer any questions and cease participation at any time without penalty).

Response rates were not available due to recruitment strategies employed. However, sample size calculations using a 95% confidence interval (95%CI), 100,000-population size, and a conservative 50–50 split considering the population is relatively varied (Salant and Dillman, 1994), assert a minimum of 383 completed surveys were needed to have sufficient power for statistical analysis.

2.2. Measures

2.2.1. Current e-cigarette and cannabis use

The following statement was provided prior to any questions: "The next several questions ask about electronic vapor products, such as JUUL, Vuse, MarkTen, and blu. Electronic vapor products include e-cigarettes, vapes, vape pens, e-cigars, e-hookahs, hookah pens, and mods." To assess e-cigarette use, students were asked, "During the past 30 days, on how many days did you use an electronic vapor product?" (range = 0–30).

To assess cannabis use, students were asked, "During the past 30 days, how many times did you use marijuana?" Response options were: 0, 1–2, 3–9, 10–19, 20–39, and 40 or more times. We classified the sample of current e-cigarette users based on their current cannabis use response as: exclusive e-cigarette users (0 times) and concurrent e-cigarette and cannabis users ($\geq$ 1 time).

To assess frequency of use patterns, we combined responses from the item on how many times students used cannabis with the item on how many days students used e-cigarettes in the past 30 days (range = 1–30). For exclusive e-cigarette use frequency, we adopted previously employed criteria: infrequent use defined as 1–5 days; intermediate use defined as 6–29 days; and daily use defined as all 30 days (Amato et al., 2016). To assess concurrent use frequency, we assessed the distribution and quartiles of cannabis use, which yielded a six-group variable to classify students as: infrequent exclusive e-cigarette users (1–5 days); intermediate exclusive e-cigarette users (6–29 days); daily exclusive e-cigarette users (all 30 days); infrequent concurrent e-cigarette and cannabis users (1–2 times); intermediate concurrent users (3–9 times); and frequent concurrent users ($\geq$ 10 times).

2.2.2. COVID-19 outcomes

A multiple response question asked about COVID-19-related symptoms, based on the Centers for Disease Control and Prevention's symptoms list (Centers for Disease Control and Prevention, 2021),"Are you currently experiencing any COVID-19 symptoms?" Options included: "no symptoms," "cough," "fever or chills," "shortness of breath or difficulty breathing," "fatigue," "muscle or body aches," "headache," "new loss of taste or smell," "nasal congestion or runny nose," "sore throat," "nausea or vomiting," "diarrhea," and other (please specify)." We

assessed COVID-19 symptoms dichotomously as no (no symptoms) versus yes (≥ 1 of the 12 symptoms).

A yes/no question asked students, "Have you been tested for COVID-19?" If students responded "yes," a follow-up yes/no question asked, "Have you been diagnosed with COVID-19?" If students responded "yes" to having received a confirmatory COVID-19 diagnosis, two follow-up questions asked, "How long did it take you to recover from COVID-19? (in days)" (range = 0 to ≥ 30 days); and "Were you hospitalized because of COVID-19?" (yes/no).

2.2.3. Covariates

Student demographic information included: age, sex, race/ethnicity, and sexual orientation. Other student characteristics included university site (Texas, Arkansas, Indiana, Ohio), current fraternity/sorority membership, and current residence. Other tobacco product use characteristics were assessed including current: combustible cigarette smoking via "During the past 30 days, on how many days did you smoke cigarettes?;" cigar smoking via "During the past 30 days, on how many days did you smoke cigars, cigarillos, or little cigars?;" and smokeless tobacco use via "During the past 30 days, on how many days did you use chewing tobacco, snuff, dip, snus, or dissolvable tobacco products, such as Copenhagen, Grizzly, Skoal, or Camel Snus? (Do not count any electronic vapor products.)." Students who answered ≥ 1 day were considered current users of combustible cigarettes, cigars, and smokeless tobacco. It was important to take into consideration these student characteristics as covariates since demographics, current residence (e.g., crowding), and combustible cigarette smoking are potential risk factors for COVID-19 infection (Centers for Disease Control and Prevention, 2021).

2.3. Statistical analysis

We calculated descriptive statistics for all variables of interest. To assess potential differences in current e-cigarette and cannabis use based on covariates, we performed a series of chi-square tests for the categorical covariates (e.g., sex) and an independent *t* test for the continuous covariate (i.e., age). Then, a series of multivariable logistic regression models were fitted to explore the associations between exclusive e-cigarette use and concurrent e-cigarette and cannabis use and COVID-19 symptoms, testing, and diagnosis. All models controlled for demographics, university site, fraternity/sorority membership, residence, combustible cigarette smoking, cigar smoking, and smokeless tobacco use. To assess frequency of e-cigarette and cannabis use, we built three similar logistic regression models adjusting for the covariates. We present adjusted odds ratios (AORs) and 95%CIs. Missing data were removed prior to analyses, and all analyses were two-tailed with statistical significance set at $p < 0.05$ and performed using Stata SE version 16 (StataCorp., 2019).

3. Results

Among the 800 student e-cigarette users, average age was 20.51 (SD = 1.82) years and 48.4% were female (Table 1). The majority of students were non-Hispanic White (61.6%), followed by Hispanic (15.4%), non-Hispanic Other/Multiracial (14.6%), and non-Hispanic Black (8.4%). Over one-in-five (21.0%) self-identified as LGBTQ. Over one-in-four (26.1%) were a current member of a fraternity/sorority, and the majority lived in off-campus housing (56.9%). Concerning other current tobacco product use, 43.3% reported combustible cigarette smoking, 27.8% reported cigar smoking, and 23.4% reported smokeless tobacco use.

Less than half of the sample (48.0%; $n = 384$) were exclusive e-cigarette users, with slightly more (52.0%; $n = 416$) being concurrent e-cigarette and cannabis users. Regarding frequency of use, 12.3% ($n = 98$) were infrequent exclusive e-cigarette users, 22.6% ($n = 181$) were intermediate exclusive e-cigarette users, 13.1% ($n = 105$) were daily

Table 1
Descriptive Characteristics of College Student E-Cigarette Users According to Current Use of E-Cigarettes and Cannabis.

		Current Use of E-Cigarettes and Cannabis		
	Overall (N = 800)	Exclusive E-Cigarette Users (*n* = 384)	Concurrent E-Cigarette and Cannabis Users (*n* = 416)	*p*-value
Student Characteristics	*n* (%)[a]	*n* (%)[a]	*n* (%)[a]	
Age, *M* (SD)	20.51 (1.82)	20.42 (1.70)	20.59 (1.93)	0.180
Sex				0.051
Male	413 (51.6)	212 (55.2)	201 (48.3)	
Female	387 (48.4)	172 (44.8)	215 (51.7)	
Race/Ethnicity				0.145
Non-Hispanic White	493 (61.6)	230 (59.9)	263 (63.2)	
Non-Hispanic Black	67 (8.4)	27 (7.0)	40 (9.6)	
Non-Hispanic Other/ Multiracial[b]	117 (14.6)	66 (17.2)	51 (12.3)	
Hispanic	123 (15.4)	61 (15.9)	62 (14.9)	
Sexual Orientation				< 0.001
Heterosexual	632 (79.0)	342 (89.1)	290 (69.7)	
LGBTQ	168 (21.0)	42 (10.9)	126 (30.3)	
University Site				< 0.001
University in Texas	345 (43.1)	208 (54.2)	137 (32.9)	
University in Arkansas	203 (25.4)	95 (24.7)	108 (26.0)	
University in Indiana	197 (24.6)	58 (15.1)	139 (33.4)	
University in Ohio	55 (6.9)	23 (6.0)	32 (7.7)	
Fraternity/Sorority Membership				0.001
No	591 (73.9)	304 (79.2)	287 (69.0)	
Yes	209 (26.1)	80 (20.8)	129 (31.0)	
Current Residence				< 0.001
Off-campus housing	455 (56.9)	222 (57.8)	233 (56.0)	
Campus residence hall	214 (26.7)	121 (31.5)	93 (22.4)	
Other university housing	72 (9.0)	20 (5.2)	52 (12.5)	
Parent's home	59 (7.4)	21 (5.5)	38 (9.1)	
Current Combustible Cigarette Smoking				< 0.001
No	454 (56.7)	262 (68.2)	192 (46.1)	
Yes	346 (43.3)	122 (31.8)	224 (53.9)	
Current Cigar Smoking[c]				< 0.001
No	578 (72.2)	306 (79.7)	272 (65.4)	
Yes	222 (27.8)	78 (20.3)	144 (34.6)	
Current Smokeless Tobacco Use				< 0.001
No	613 (76.6)	327 (85.2)	286 (68.7)	
Yes	187 (23.4)	57 (14.8)	130 (31.3)	

Abbreviations: e-cigarette use, electronic cigarette use; LGBTQ, lesbian, gay, bisexual, transgender, and questioning.

[a] Percent refers to column percent, unless otherwise noted.

[b] Non-Hispanic Other/Multiracial category includes Asian or Pacific Islander, American Indian, Alaska Native, or Native Hawaiian, Biracial, and Multiracial.

[c] Cigars include traditional cigars, cigarillos, and little cigars.

exclusive e-cigarette users, 16.0% ($n = 128$) were infrequent concurrent e-cigarette and cannabis users, 14.6% ($n = 117$) were intermediate concurrent users, and 21.4% ($n = 171$) were frequent concurrent users.

3.1. Student characteristics and current e-cigarette and cannabis use

Chi-square test results indicated student sexual orientation, university site, fraternity/sorority membership, residence, combustible cigarette smoking, cigar smoking, and smokeless tobacco use differed based on e-cigarette and cannabis use (see Table 1). Those with higher percentages of being concurrent e-cigarette and cannabis users were LGBTQ, at universities in Indiana and Ohio, were fraternity/sorority members, lived in university housing, smoked combustible cigarettes, smoked cigars, and used smokeless tobacco products.

3.2. Current e-cigarette and cannabis use and COVID-19 symptoms

Overall, 14.3% ($n = 114$) of student e-cigarette users reported experiencing at least one COVID-19 symptom (range = 1–8) at survey completion; 5.1% ($n = 41$) had nasal congestion/runny nose, 5.1% ($n = 41$) had cough, 4.1% ($n = 33$) had fatigue, 4.1% ($n = 33$) had sore throat, 3.8% ($n = 30$) had shortness of breath/difficulty breathing, 3.1% ($n = 25$) had fever/chills, 2.5% ($n = 20$) had new loss of taste/smell, 2.4% ($n = 19$) had nausea/vomiting, 1.5% ($n = 12$) had headache, 1.1% ($n = 9$) had diarrhea, and 0.8% ($n = 6$) had muscle/body aches. Higher rates of COVID-19 symptoms were reported among concurrent e-cigarette and cannabis users (22.6%) (Table 2). Compared to exclusive e-cigarette users, concurrent users were 3.53 times more likely (95%CI = 1.96–6.36) to report COVID-19 symptoms, after adjusting for the covariates. Significant covariates were noted and student age showed a positive association with COVID-19 symptoms. Students who also currently used smokeless tobacco were at increased odds of reporting COVID-19 symptoms (see Table 2).

Concerning frequency of use, when compared to infrequent exclusive e-cigarette users, results indicated infrequent concurrent e-cigarette and cannabis users (AOR = 4.72, 95%CI = 1.31–17.00), intermediate concurrent users (AOR = 5.10, 95%CI = 1.37–18.97), and frequent concurrent users (AOR = 7.44, 95%CI = 2.06–26.84) were at increased odds of reporting COVID-19 symptoms (Table 3).

3.3. Current e-cigarette and cannabis use and COVID-19 testing and diagnosis

A total of 85.5% ($n = 684$) of student e-cigarette users were tested for COVID-19, with 16.8% ($n = 115$) reporting a COVID-19 diagnosis. Of

Table 2
Associations of Current Use of E-Cigarettes and Cannabis with COVID-19 Symptoms, Testing, and Diagnosis among College Student E-Cigarette Users.

	COVID-19 Symptoms			COVID-19 Test			COVID-19 Diagnosis		
Student Characteristic	***n* (%)**	**AOR[a]**	**95% CI**	***n* (%)**	**AOR[a]**	**95% CI**	***n* (%)**	**AOR[a]**	**95% CI**
Current E-Cigarette and Cannabis Use									
Exclusive e-cigarette use	20 (5.2)	Ref	Ref	317 (82.6)	Ref	Ref	38 (12.0)	Ref	Ref
Concurrent e-cigarette and cannabis use	94 (22.6)	**3.53*****	**1.96–6.36**	367 (88.2)	1.23	0.79–1.93	77 (21.0)	**1.85***	**1.15–2.98**
Age	–	**1.25****	**1.09–1.42**	–	0.92	0.80–1.05	–	0.97	0.84–1.12
Sex									
Male	65 (15.7)	Ref	Ref	355 (86.0)	Ref	Ref	69 (19.4)	Ref	Ref
Female	49 (12.7)	1.56	0.92–2.65	329 (85.0)	1.18	0.75–1.86	46 (14.0)	**0.55***	**0.35–0.87**
Race/Ethnicity									
Non-Hispanic White	63 (12.8)	Ref	Ref	425 (86.2)	Ref	Ref	85 (20.0)	Ref	Ref
Non-Hispanic Black	22 (32.8)	1.15	0.54–2.45	63 (94.0)	1.29	0.41–4.07	4 (6.4)	0.34	0.11–1.05
Non-Hispanic Other/Multiracial	15 (12.8)	1.58	0.77–3.24	92 (78.6)	0.73	0.41–1.28	10 (10.9)	**0.40***	**0.19–0.84**
Hispanic	14 (11.4)	0.94	0.43–2.04	104 (84.6)	1.26	0.69–2.29	16 (15.4)	0.77	0.41–1.44
Sexual Orientation									
Heterosexual	65 (10.3)	Ref	Ref	539 (85.3)	Ref	Ref	91 (16.9)	Ref	Ref
LGBTQ	49 (29.2)	1.28	0.74–2.23	145 (86.3)	0.76	0.44–1.31	24 (16.6)	1.05	0.61–1.82
University Site									
University in Texas	21 (6.1)	Ref	Ref	261 (75.7)	Ref	Ref	42 (16.1)	Ref	Ref
University in Arkansas	70 (34.5)	1.90	0.71–5.06	194 (95.6)	**8.52*****	**3.04–23.84**	20 (10.3)	**0.23****	**0.09–0.59**
University in Indiana	15 (7.6)	1.03	0.49–2.18	187 (94.9)	**5.72*****	**2.79–11.75**	40 (21.4)	1.06	0.61–1.84
University in Ohio	8 (14.6)	2.28	0.87–5.96	42 (76.4)	1.00	0.48–2.05	13 (31.0)	1.62	0.72–3.62
Fraternity/Sorority Membership									
No	62 (10.5)	Ref	Ref	497 (84.1)	Ref	Ref	76 (15.3)	Ref	Ref
Yes	52 (24.9)	0.99	0.57–1.71	187 (89.5)	1.06	0.62–1.84	39 (20.9)	**1.68***	**1.03–2.73**
Current Residence									
Off campus housing	36 (7.9)	Ref	Ref	374 (82.2)	Ref	Ref	65 (17.4)	Ref	Ref
Campus residence hall	41 (19.2)	1.27	0.63–2.59	199 (93.0)	1.16	0.58–2.33	30 (15.1)	1.44	0.78–2.65
Other university housing	25 (34.7)	2.14	0.98–4.66	66 (91.7)	1.56	0.62–3.95	14 (21.2)	1.18	0.57–2.43
Parent's home	12 (20.3)	0.87	0.35–2.16	45 (76.3)	**0.42***	**0.20–0.89**	6 (13.3)	1.07	0.39–2.94
Current Combustible Cigarette Smoking									
No	27 (6.0)	Ref	Ref	379 (83.5)	Ref	Ref	57 (15.0)	Ref	Ref
Yes	87 (25.1)	1.29	0.68–2.46	305 (88.2)	0.86	0.52–1.42	58 (19.0)	1.22	0.74–2.01
Current Cigar Smoking									
No	40 (6.9)	Ref	Ref	483 (83.6)	Ref	Ref	77 (15.9)	Ref	Ref
Yes	74 (33.3)	1.32	0.64–2.69	201 (90.5)	1.60	0.85–3.02	38 (18.9)	1.66	0.91–3.03
Current Smokeless Tobacco Use									
No	40 (6.5)	Ref	Ref	515 (84.0)	Ref	Ref	87 (16.9)	Ref	Ref
Yes	74 (39.6)	**2.81***	**1.17–6.72**	169 (90.4)	0.69	0.32–1.50	28 (16.6)	1.10	0.51–2.38

Abbreviations: e-cigarette, electronic cigarette; coronavirus disease 2019, COVID-19; AOR, adjusted odds ratio; CI, confidence interval; Ref, reference category.

[a] Multivariable logistic regression model includes current e-cigarette and cannabis use and the covariates.

***$p < 0.001$, **$p < 0.01$, *$p < 0.05$.

Table 3
Associations of Frequency of E-Cigarette and Cannabis Use with COVID-19 Symptoms, Testing, and Diagnosis among College Student E-Cigarette Users.

	COVID-19 Symptoms			COVID-19 Test			COVID-19 Diagnosis		
	n (%)	AOR[a]	95% CI	*n* (%)	AOR[a]	95% CI	*n* (%)	AOR[a]	95% CI
Frequency of Current E-Cigarette and Cannabis Use									
Infrequent exclusive e-cigarette use (1–5 days)	3 (3.1)	Ref	Ref	74 (75.5)	Ref	Ref	8 (10.8)	Ref	Ref
Intermediate exclusive e-cigarette use (6–29 days)	13 (7.2)	1.79	0.47–6.79	155 (85.6)	1.05	0.54–2.04	18 (11.6)	1.61	0.63–4.10
Daily exclusive e-cigarette use (30 days)	4 (3.8)	1.79	0.38–8.48	88 (83.8)	1.39	0.67–2.91	12 (13.6)	1.34	0.49–3.66
Infrequent concurrent e-cigarette and cannabis use (1–2 times)	24 (18.8)	**4.72***	**1.31–17.00**	115 (89.8)	1.98	0.91–4.29	17 (14.8)	1.67	0.65–4.29
Intermediate concurrent e-cigarette and cannabis use (3–9 times)	29 (24.8)	**5.10***	**1.37–18.97**	105 (89.7)	1.36	0.60–3.08	23 (21.9)	**2.88***	**1.13–7.35**
Frequent concurrent e-cigarette and cannabis use (≥ 10 times)	41 (24.0)	**7.44****	**2.06–26.84**	147 (86.0)	1.02	0.51–2.05	37 (25.2)	**3.22***	**1.32–7.87**

Abbreviations: e-cigarette, electronic cigarette; coronavirus disease 2019, COVID-19; AOR, adjusted odds ratio; CI, confidence interval; Ref, reference category.
[a] Logistic regression adjusting for age, sex, race/ethnicity, sexual orientation, university site, fraternity/sorority membership, current residence, current combustible cigarette smoking, current cigar smoking, and current smokeless tobacco use. $^{**}p < 0.01$, $^{*}p < 0.05$.

those with a prior COVID-19 diagnosis, the mean number of days to recover was 9.55 (SD = 6.95; range = 0 to ≥ 30 days) and 15.7% (n = 18) were hospitalized due to COVID-19. No differences were found between the two current user groups and COVID-19 testing (see Table 2). Multivariable results indicated two university sites, the universities in Arkansas and Indiana, had increased odds of being tested for COVID-19 compared to the university in Texas, and e-cigarette users who currently lived in their parent's home had reduced odds relative to those living in off-campus housing. No differences were found between frequency of current use groups and COVID-19 testing (see Table 3).

Compared to exclusive e-cigarette users, concurrent e-cigarette and cannabis users were 1.85 times more likely (95%CI = 1.15–2.98) to have a prior positive COVID-19 diagnosis, after adjusting for the covariates (see Table 2). Significant covariates were noted, and those with reduced odds to have a COVID-19 diagnosis were students who were female, non-Hispanic Other/Multiracial, and attended the university in Arkansas compared to students who were male, non-Hispanic White, and attended the university in Texas, respectively. Those at increased odds of reporting a COVID-19 diagnosis were fraternity/sorority members (see Table 2).

Concerning frequency of use, intermediate concurrent e-cigarette and cannabis users (AOR = 2.88, 95%CI = 1.13–7.35) and frequent concurrent users (AOR = 3.22, 95%CI = 1.32–7.87) were at increased odds of reporting a COVID-19 diagnosis than infrequent exclusive e-cigarette users (see Table 3).

4. Discussion

This study provides evidence college student e-cigarette users who concurrently use cannabis in the past 30-days are at greater likelihood of experiencing COVID-19 symptoms and having a positive COVID-19 diagnosis, compared with exclusive e-cigarette users. Confirming our hypothesis, frequency of concurrent e-cigarette and cannabis use was associated with increased odds of COVID-19 symptoms and diagnosis, with more pronounced odds observed as frequency of use groups increased, independent of student demographics and current use of combustible cigarettes, cigars, and smokeless tobacco. Thus, there appears to be a dose-related relationship, such that as use increased so too did the risk of experiencing COVID-19 symptoms and receiving a positive diagnosis. Specifically, for COVID-19 symptoms, effect size estimates were 3.5-fold among concurrent e-cigarette and cannabis users at any frequency of use, and these estimates ranged from nearly 5-fold to 7.5-fold among infrequent, intermediate, and frequent concurrent users. Similar findings were indicated for COVID-19 diagnosis, with odds of nearly two times for concurrent users at any frequency of use, and approximately a 3-fold increase among both intermediate and frequent concurrent users.

There are several potential explanations of why concurrent e-cigarette and cannabis users, especially those with more frequent use patterns, were at higher risk of experiencing COVID-19 symptoms when compared with exclusive e-cigarette users. First, combustible cannabis and tobacco smoke contain similar carcinogenic and other harmful chemical toxins, but cannabis topography results in higher tar and gas per-puff exposures than that of combustible tobacco smoke (Tashkin and Roth, 2019). This can lead to acute respiratory health symptoms (e.g., cough), and potentially airway inflammation and infection especially among heavy or long-term cannabis users (Ghasemiesfe et al., 2018; Yayan and Rasche, 2016; Martinasek et al., 2016; Gates et al., 2014). Second, e-liquids of nicotine- and THC-containing vaping products vary in constituents and are a potential source of inhaled toxic metal exposure (Zhao et al., 2020), and there are over 400 brands that provide diverse products (Hsu et al., 2018). THC-containing e-liquids may be distinct from nicotine-containing e-liquids and can lead to higher respiratory illness likely due to varying inhaled chemical constituents (Traboulsi et al., 2020). For example, it is important to note e-cigarette, or vaping, product use-associated lung injury (EVALI) was linked to illicit THC-containing vaping products and vitamin E acetate in nearly all (94%) of cases, with median EVALI case patient age of 23 years and the majority being male (69%) (Blount et al., 2020). For these and other reasons, the Centers for Disease Control and Prevention recommends individuals not use THC-containing vaping products due to the potential of tampering with e-liquids (Krishnasamy et al., 2020). While law enforcement seized vaping products containing vitamin E acetate intended for the illicit market (Taylor et al., 2019), the clinical manifestations and symptoms of EVALI and COVID-19 and other respiratory illness overlap (Medicine, 2020). Further research is needed to assess the associations of e-cigarette and cannabis use with COVID-19 outcomes based on use patterns including cannabis inhalation route, and device type and ingredients among vapers.

Current smokeless tobacco use increased student e-cigarette users' odds by nearly 3-fold for reporting COVID-19 symptoms, which aligns with previous research documenting increased risk of respiratory symptoms from smokeless tobacco use (Gudnadóttir et al., 2017). Combustible cigarette smoking and cigar smoking were not significant covariates of COVID-19 symptoms, despite prior research linking dual e-cigarette and combustible cigarette use with increased self-reported respiratory symptoms compared to exclusive e-cigarette use (Li et al., 2020). Additionally, no differences were found based on current combustible cigarette, cigar, or smokeless tobacco use and COVID-19 diagnosis. Prior research indicates all forms of tobacco use may increase COVID-19 infection susceptibility via the ACE2 receptor (Brake et al., 2020) and the furin enzyme found in oral mucosa (Gaunkar et al., 2020), and has been recognized as a risk factor for severe COVID-19 manifestations (Gupta et al., 2021). Future research using objective

measures is warranted to better understand the complex associations between tobacco product type and COVID-19-related outcomes.

As posited, no differences were detected between current use groups and COVID-19 testing, likely based on similar random testing policies at each university during the data collection period. Concerning our findings on COVID-19 diagnosis, the active ingredients of THC and nicotine and toxic substances vary among cannabis and e-cigarette products, respectively, and cannabis chemicals are metabolized slower in the body, placing cannabis users at increased risk of COVID-19 infection (Borgonhi et al., 2021). Interestingly, this study found those who were male and White had the highest percentages of having a COVID-19 diagnosis. Notably, the literature indicates the highest prevalence of EVALI cases are among those who are male and White (Krishnasamy et al., 2020). Although this diagnosis was not assessed in this study, future work should examine the associations of e-cigarette and cannabis use and COVID-19 diagnoses and other specific diagnoses such as EVALI or pneumonia. Other explanations for higher odds of concurrent users having a COVID-19 diagnosis are behavior-related, including tendencies of sharing devices with others and hand-to-lip contact while using these products (World Health Organization. Coronavirus disease (COVID-19), 2021), which also increases COVID-19 risk via contact and fomite transmission (World Health Organization, 2021). About 1-in-2 young adult lifetime e-cigarette users report sharing devices with others (McKelvey and Halpern-Felsher, 2020), which may explain this study's finding that fraternity/sorority members had a higher likelihood of reporting a COVID-19 diagnosis. Moreover, e-cigarette use may ultimately increase risk-taking behaviors during young adulthood, including but not limited to concurrent cannabis use (Lanza et al., 2020; Temple et al., 2017). Research indicates dual e-cigarette and combustible cigarette use is associated with poor compliance with COVID-19-related social distancing behaviors (Chen and Kyriakos, 2021). Thus, it is highly likely e-cigarette users who engage in concurrent use of cannabis did not engage in recommended preventive health behaviors (e.g., physical distancing).

While this study has several strengths, limitations should be noted. First, while students were enrolled at four geographically diverse universities across the U.S., our cross-sectional sample is not nationally representative and therefore our results are not generalizable to all U.S. student e-cigarette users. Longitudinal research is needed to assess causal associations between e-cigarette and cannabis use patterns with COVID-19-related outcomes. In a similar vein, we were unable to objectively measure COVID-19 symptoms, testing, and diagnosis. For example, the survey language specifically asked whether students were currently experiencing any COVID-19 symptoms from the Centers for Disease Control and Prevention's COVID-19 symptoms list (Centers for Disease Control and Prevention, 2021); but since some of the symptoms were nonspecific to COVID-19, students may have reported a symptom (e.g., headache) while not having COVID-19 concerns. Additionally, since our student sample included those who currently used e-cigarettes, we were unable to compare exclusive e-cigarette use versus non-use nor exclusive cannabis use. We assessed self-reported e-cigarette use frequency in number of days and cannabis use frequency in number of times used in the past 30 days and used categorical cutpoints to minimize the potential for recall bias. We used standard national survey question language (e.g., Monitoring the Future) to collect data on past 30-day cannabis use frequency based on number of times (SAMHSA's Center for the Application of Prevention Technologies, 2017). Thus, we did not collect cannabis use frequency in number of days, and suggest this as a measure to be used in further research. Additionally, we did not collect information on cannabis use route (e.g., vaping). Future research should consider the use of biomarkers (e.g., cotinine the major metabolite of nicotine (Benowitz et al., 2009), and THC carboxylic acid the major metabolite of delta-9-tetrahydrocannabinol (Huestis, 2007)) and patient medical records to cross-validate self-reported responses. Additionally, studies should take into consideration overall preventive health behaviors (e.g., hand hygiene) and statewide and local policies (e.g., business operation policies to reduce risk for customers (Centers for Disease Control and Prevention, 2021) that may reduce infectious disease risk.

Due to our recruitment methods (e.g., campus-wide listservs), we could not calculate response rates, which resulted in varying participation rates that may have biased the sample. All four university campuses remained "open" during data collection. While we did not collect course engagement data (i.e., in person, online, or hybrid), future research should account for frequency of in-person class participation, which may have increased COVID-19 exposure and susceptibility. We did not have access to information on COVID-19 random testing rates at each university. COVID-19 testing rates may have varied at each campus based on test availability and accessibility on and off campuses (e.g., during primary care visits).

5. Conclusions

Compared to exclusive e-cigarette use, we assert concurrent use of e-cigarettes and cannabis may be an underlying risk factor of COVID-19 symptomatology and diagnosis. We report a potential dose–response relationship between frequency of use and COVID-19 outcomes, with concurrent users with intermediate or frequent use patterns having more pronounced odds of reporting COVID-19 symptoms and diagnosis. Results highlight the need to educate students about the impacts of e-cigarette and cannabis use on respiratory, immune, and overall health. University-based substance use and COVID-19 prevention initiatives are urgently needed to reduce e-cigarette and cannabis use among students that may increase their risk for COVID-19-related outcomes. Longitudinal research is needed to provide insights into the temporal associations and the underlying mechanistic and clinical outcome differences between e-cigarette and cannabis use and frequency of use and risk of COVID-19 symptomatology and diagnosis over time.

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7. Contributors

ALM conceptualized and designed the study, conducted the statistical analysis, and wrote the first draft of the manuscript. AMR conceptualized and designed the study, and revised the manuscript for critically important intellectual content. EMMG conceptualized and designed the study, and wrote the first draft of the manuscript. AEB conceptualized and designed the study, and revised the manuscript for critically important intellectual content. MY conceptualized and designed the study, and revised the manuscript for critically important intellectual content. HCL conceptualized and designed the study, interpreted the data, and revised the manuscript for critically important intellectual content. All authors contributed to and have approved the final manuscript.

CRediT authorship contribution statement

Ashley L. Merianos: Conceptualization, Methodology, Formal analysis, Investigation, Writing – original draft, Funding acquisition. **Alex M. Russell:** Conceptualization, Methodology, Investigation,

Writing – review & editing. **E. Melinda Mahabee-Gittens:** Conceptualization, Writing – original draft, Funding acquisition. **Adam E. Barry:** Conceptualization, Methodology, Investigation, Writing – review & editing. **Meng Yang:** Conceptualization, Methodology, Writing – review & editing. **Hsien-Chang Lin:** Conceptualization, Methodology, Investigation, Writing – review & editing.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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