ELSEVIER

Contents lists available at ScienceDirect

### Addictive Behaviors Reports

journal homepage: www.elsevier.com/locate/abrep



# Cigarette smoking status and COVID-19 hospitalization in the context of cannabis use: An electronic health record cohort study in northern California

Dian Gu<sup>a,b</sup>, Patrick Ha<sup>c,d</sup>, Jesse T. Kaye<sup>e,f</sup>, Michael C. Fiore<sup>e,f</sup>, Janice Y. Tsoh<sup>a,d,g,\*</sup>

- <sup>a</sup> The Center for Tobacco Control Research and Education, University of California, San Francisco, CA, United States
- <sup>b</sup> Division of General Internal Medicine, San Francisco General Hospital, University of California, San Francisco, CA, United States
- <sup>c</sup> Department of Otolaryngology Head and Neck Surgery, School of Medicine, University of California, San Francisco, CA, United States
- <sup>d</sup> UCSF Helen Diller Family Comprehensive Cancer Center, San Francisco, CA, United States
- e Center for Tobacco Research and Intervention, University of Wisconsin School of Medicine and Public Health, Madison, WI, United States
- f Carbone Cancer Center, University of Wisconsin School of Medicine and Public Health, Madison, WI, United States
- g Department of Psychiatry and Behavioral Sciences, School of Medicine, University of California, San Francisco, CA, United States

#### ARTICLE INFO

## Keywords: Cigarette smoking Cannabis use COVID-19 hospitalization

#### ABSTRACT

*Background:* Research investigating the association between cigarette smoking and COVID-19 outcomes has yielded mixed results, often overlooking cannabis use. This study examined the association between cigarette smoking and COVID-19 hospitalization with consideration of cannabis use.

*Methods*: We used electronic health record data from adult patients with COVID-19 (2/1/2020 to 2/3/2022) at a northern California academic medical center. The outcome was COVID-19 hospitalization. We conducted three multivariable logistic models to examine the relationship between cigarette smoking and hospitalization. Model 1 included cigarette smoking status and other covariates; Model 2 added cannabis use status to Model 1; Model 3 added interaction term of cigarette and cannabis use to Model 2, followed by a post-hoc analysis.

Results: Of the 14,440 patients, 8.5 % had COVID-19 hospitalization, 4.9 % and 24.1 % currently and formerly smoked cigarettes, respectively; 7.2 % currently used cannabis, 62.8 % had unknown cannabis use status. Both current and former cigarettes smoking were associated with hospitalization (Models 1–2). In Model 3, the cigarette-cannabis interaction was significant. Former cigarette smoking had higher odds for hospitalization (adjusted odds ratio [AOR] = 1.36; 95 % confidence interval [CI] 1.09-1.70) only among people who did not currently use cannabis. Current cigarette smoking yielded higher odds of hospitalization (AOR = 1.47; 95 % CI 1.02-2.12) among people whose cannabis use was unknown. Cigarette smoking status was not associated with hospitalization among people who currently used cannabis.

Conclusions: Cigarette smoking's associations with COVID-19 hospitalization varied by cannabis use. Future research should include both cigarette and cannabis use in understanding risk factors for COVID-19 outcomes.

#### 1. Introduction

The existing literature on the association between cigarette smoking status and COVID-19 severe outcomes have yielded inconsistent findings based on studies conducted such as United States (US), Canada, China and United Kingdom (UK) (Farsalinos et al., 2021; Griffith et al., 2024; Piasecki et al., 2023; Razjouyan et al., 2022; Reddy et al., 2021; Simons, Shahab, Brown, & Perski, 2021; Umnuaypornlert, Kanchanasurakit,

Lucero-Prisno, & Saokaew, 2021; Williamson et al., 2020; Young-Wolff, Slama, Alexeeff, et al., 2023; Young-Wolff, Slama, Sakoda, et al., 2023). Current cigarette smoking, compared to never smoking, is demonstrated to be linked to an increased risk of severe illness from COVID-19 (Piasecki et al., 2023; Reddy et al., 2021; Simons et al., 2021; Williamson et al., 2020; Young-Wolff, Slama, Alexeeff, et al., 2023; Young-Wolff, Slama, Sakoda, et al., 2023). However, the evidence pertaining to the relationship between current smoking, compared with never

E-mail address: janice.tsoh@ucsf.edu (J.Y. Tsoh).

https://doi.org/10.1016/j.abrep.2024.100565

Received 4 April 2024; Received in revised form 19 September 2024; Accepted 24 September 2024 Available online 26 September 2024

2352-8532/© 2024 The Authors. Published by Elsevier Ltd. This is an open access article under the CC BY-NC license (http://creativecommons.org/licenses/by-nc/4.0/).

<sup>\*</sup> Corresponding author at: Department of Psychiatry and Behavioral Sciences, University of California, San Francisco, 675 18<sup>th</sup> Street, San Francisco, CA 94143, United States.

smoking, and severity of COVID-19 outcomes (e.g., COVID-19 hospitalization, mortality, intensive care unit [ICU] admission) has been inconclusive (Farsalinos et al., 2021; Griffith et al., 2024; Razjouyan et al., 2022; Umnuaypornlert et al., 2021; Young-Wolff, Slama, Alexeeff, et al., 2023; Young-Wolff, Slama, Sakoda, et al., 2023). For example, a study conducted among 1,885,826 participants in California indicated that current smoking (vs. never smoking) was associated with lower odds of COVID-19 hospitalization (Young-Wolff et al., 2023). Another study conducted among 10,216 COVID-19 patients in Texas found that people who currently smoked were less likely to be hospitalized for COVID-19 compared with people who never smoked (Puebla Neira et al., 2021). On the contrary, a UK study with 421,469 participants showed that people who currently smoked had higher risks of hospitalization compared to people who never smoked (Clift et al., 2022). Additionally, a study conducted among 5,698 COVID-19 patients in Michigan found that there was no significant difference in risk of hospitalization between people who currently and never smoked (Gu et al., 2020).

Although cigarette use in the US has been trending downward during the past decades (Cornelius et al., 2023), cannabis use has had a significant rise (Hasin & Walsh, 2021). When smoked, cannabis can irritate the lungs and increase the risk of respiratory infections (Howden & Naughton, 2011; Tashkin, 2013). Thus, people who use cannabis may be a vulnerable group for severe COVID-19 outcomes. The research on the association between cannabis use and COVID-19 severe outcomes was limited and the findings were mixed both within and outside the US (Huang, Xu, & Na, 2022; Shover et al., 2022). For example, a study of 1,831 hospitalized COVID-19 patients in California showed that cannabis consumption is associated with lower COVID-19 severity, including decreased need for ICU admission or mechanical ventilation (Shover et al., 2022). Nevertheless, a UK study with 1,925 COVID-19 patients demonstrated that people who regularly use cannabis had worse COVID-19-related survival (Huang et al., 2022). A recent US study showed that cannabis use is an independent risk factor for COVID-19 hospitalizations and ICU admissions (Griffith et al., 2024).

Cigarette and cannabis use commonly co-occur in western countries (Gravely et al., 2022). According to International Tobacco Control Four Country Survey, the rate of regular co-use of cigarettes and cannabis in 2020 was 24.4 % in the US (Gravely et al., 2022). Global data indicate the negative health consequences associated with co-use are worse than those associated with use of cigarettes or cannabis alone (Correa, Myers, Tully, & Doran, 2020; Meier & Hatsukami, 2016; Tan et al., 2009). Previous studies found that people co-using cigarettes and cannabis could have higher levels of toxicant exposure (Meier & Hatsukami, 2016). In addition, people who co-used had higher risk of respiratory symptoms than those who used only one substance (Correa et al., 2020; Tan et al., 2009). It is possible that co-use has different responses for COVID-19 infection compared to smoking cigarettes alone. Yet, the association among cigarette smoking status, cannabis use and COVID-19 severe outcomes has been underexplored. Although the recent US study (Griffith et al., 2024) showed that cannabis use and smoking status are independent risk factors for COVID-19 hospitalizations, this study did not examine how the effect of cigarette smoking on COVID-19 hospitalization differs by cannabis status.

To fill the literature gap, this study examined the association between cigarette smoking status and COVID-19 hospitalization, in the context of cannabis use. Findings will provide insights in understanding mixed associations found between current or former cigarette smoking and COVID-19 hospitalization with considering cannabis use, which will have important implications for future prevention and control in public health emergency of respiratory diseases.

#### 2. Methods

#### 2.1. Study design and data source

This study is part of the CEC-UW (ClinicalTrials.gov: NCT04506528), a retrospective cohort study supported by the National Cancer Institute, (D'Angelo et al., 2019) which involves 21 health care systems in the US providing selected electronic health records (EHR) from their COVID-19 patients. We analyzed EHR data from the University of California San Francisco (UCSF) Health System, which contributed to the CEC-UW cohort, included patients' preferred language and added the California Healthy Place Index based on patients' residential postal zip code. This study utilized EHR data extracted between 2/1/2020 and 2/3/2022 from California adult patients aged 18 or older with a positive COVID-19 PCR test who had valid smoking status on the first positive COVID-19 test date during the study period. Each patient's first positive COVID-19 test date was set as the index date.

#### 2.2. Outcome measures

The outcome was COVID-19 hospitalization, defined as (1) hospitalized within 14 days of the index date (+/- 7 days centered at the admission date) and/or having an ICD-10 (International Classification of Diseases 10th Revision) COVID-19 diagnosis (U07.1 or J12.82) during the hospitalization and within 90 days (Ellingson et al., 2023) of the index date and (2) hospitalized for COVID-19 for at least 24 h, or having died within 24 h of admission or been transferred to the ICU within 24 h of admission.

#### 2.3. Cigarette smoking and cannabis use status

Patients' cigarette smoking and cannabis use status, as documented in their encounters on the index date, was self-reported. Cigarette smoking status was classified as currently, formerly or never smoked cigarettes. In this EHR, cannabis use was recorded under the term "marijuana", a major type of cannabis, and categorized as "current use", "not current use", or "unknown" when cannabis use was not assessed or reported.

#### 2.4. Other covariates

Other covariates comprised of sociodemographic factors, comorbidity burden, neighborhood socioeconomic condition, and health behavior. Sociodemographics were measured on the index date and included race/ethnicity (non-Hispanic White [NHW], Hispanic, non-Hispanic Black [NHB], non-Hispanic Asian [NHA] and non-Hispanic other [NHA]), preferred language (English, Spanish, Chinese, other), age (18–34, 35–49, 50–64,  $\geq$ 65), sex (female, male), health insurance (commercial, public, other).

Comorbidity burden was assessed by the Charlson Comorbidity Index (CCI) score (0, 1,  $\geq$ 2) (Quan et al., 2005). It is a weighted comorbidity score synthesizing comorbid diagnoses for the one year within the index date.

Neighborhood socioeconomic condition was determined by the California Healthy Place Index (HPI) quartile. It was the division of California HPI version 3.0 score. California HPI 3.0 is the latest version of HPI with a score (from 0 to 1) based on community-level conditions associated with health (California Healthy Place Index, 2022). We used the patients' zip codes on the index date to link the HPI 3.0 score file to obtain the HPI scores aggregated to zip code tabulation areas. Areas with lower HPI scores have fewer opportunities for residents to lead healthy lives.

Health behavior was vaccination status (full, partial and no). Fully vaccinated was defined as two weeks after their second dose in a two-dose primary series, such as the Pfizer or Moderna vaccines, or two weeks after a single-dose vaccine, such as the Johnson & Johnson

vaccine. Partial vaccinated was the status between not vaccinated and fully vaccinated. We also included time periods in reference to vaccines availability (index date on or before 12/31/2020, between 1/1 and 3/31/2021, 4/1/2021 or after).

#### 2.5. Final study sample

There were 20,755 adult patients with COVID-19, residing in California and having valid smoking status on the index date during the study period. After excluding those with incomplete information for the all the variables except race/ethnicity and cannabis use, 20,158 patients remained in the cohort. The overall missingness for the variables, except for cannabis use and race/ethnicity, was low (2.9 %). Therefore, we kept an "unknown" category for cannabis use and race/ethnicity. To ensure all the patients can be traced back to 90 days prior to the end of the study for the COVID-19 hospitalization outcome, the patients whose index date was less than 90 days prior to the study end time and had no COVID-19 hospitalizations indicated were excluded from the analyses. The final study sample contained 14,440 adult COVID-19 patients (Fig. 1).

#### 2.6. Statistical analyses

We first tabulated descriptive statistics to summarize all the variables. Second, we used bivariate chi-squared tests to determine if there were significant differences in the proportion of patients hospitalized for COVID-19 across cigarette and cannabis use status. Third, to examine how the association between cigarette smoking and COVID hospitalization is influenced by cannabis use, we implemented a series of three multivariable logistic regression models. Model 1 was designed to establish the association between cigarette smoking and COVID-19 hospitalization, so it only included smoking status and other covariates. Model 2 was designed to examine whether the inclusion of cannabis use status changed any associations and to determine if cigarette and cannabis use are independent risk factors. Therefore, it built on Model 1 by adding cannabis use status. Model 3 included both smoking status and cannabis status, covariates, and the interaction term between cigarette smoking and cannabis use status. Then, post-hoc analyses were conducted to estimate the association between cigarette smoking and COVID-19 hospitalization by each cannabis use status category while adjusting for all other variables. We also conducted a supplementary

analysis to gain some understanding of the factors associated with unknown versus know cannabis use status, controlling for cigarette smoking status and all other covariates in a logistic regression model. All analyses were performed using SAS V.9.4 (SAS Institute, Cary, North Carolina, USA). Significance was defined by  $P \leq 0.05$ .

#### 3. Results

Table 1 shows the sample characteristics. Patients in the final sample were distributed equally across the age groups. There were more women (56.8%) than men (43.2%), and the largest racial and ethnic group was non-Hispanic White (42.0%). English speakers dominated (90.4%), followed by Spanish speakers (5.9%). Also, most patients were covered by public insurance (49.1%), and 3,782 patients lived in the areas with the lowest California HPI quartile. The majority had zero CCI score (70.8%). Half had an index date on or before 12/31/2020, and 78.8% were not vaccinated by the index date. Fig. 2 shows that all cigarette smoking groups had high levels of unknown cannabis use status, with people who never smoked cigarettes having the highest portion of unknown cannabis use status (64.9%).

Fig. 3 shows the proportion of patients with COVID-19 hospitalizations by cigarette smoking status and cannabis use status. Among the 14,440 patients, 1,222 (8.5 %) were hospitalized with COVID-19. Significant differences in proportion of hospitalized patients were found with respect to both smoking status and cannabis use status. The proportion of COVID-19 hospitalization was highest (12.1 %) among people who currently smoked cigarettes or people who currently used cannabis (11.2 %).

Table 2 displays the results from Models 1 and 2. Both people who currently and formerly smoked cigarettes were more likely to be hospitalized (vs. people who never smoked), in unadjusted models and adjusted for cannabis use status. The overall interaction term between cigarette smoking and cannabis use statuses were statistically significant in Model 3 (Type III p=0.0033; data not shown). The supplement Figure 1 plots the interaction term. Table 3 presents the post-hoc stratified analyses of Model 3. Among people who currently used cannabis, neither current nor former cigarette smoking was significantly associated with COVID-19 hospitalization. Among people who currently did not use cannabis, people who formerly smoked cigarettes were more likely to be admitted for COVID-19 (adjusted odds ration [AOR] = 1.36; 95 % confidence interval [CI] 1.09–1.70). Among people with unknown

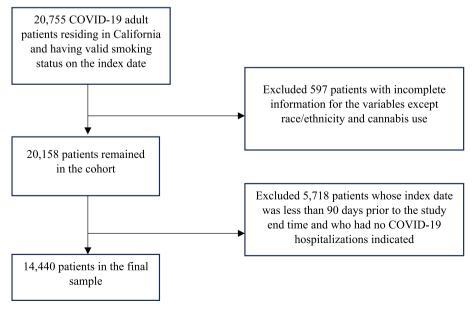


Fig. 1. Selection of the final study sample.

**Table 1**Sample Characteristics.

	Entire Sample( $N = 14,440$ )
Cigarette smoking status	N (%)
Current	711 (4.9 %)
Former	3,478 (24.1 %)
Never	10,251 (71.0 %)
Cannabis use status	
Current	1,044 (7.2 %)
Not current	4,329 (30.0 %)
Unknown	9,067 (62.8 %)
Age	2 497 (24 1 04)
18–34 35–49	3,487 (24.1 %) 3,422 (23.7 %)
50–64	3,771 (26.1 %)
65+	3,760 (26.0 %)
Sex	
Female	8,202 (56.8 %)
Male	6,238 (43.2 %)
n militir	
Race/Ethnicity	6.060.640.6.20
Non-Hispanic White	6,063 (42.0 %)
Hispanic	3,086 (21.4 %)
Non-Hispanic Black	1,270 (8.8 %)
Non-Hispanic Asian	2,121 (14.7 %)
Non-Hispanic Other	882 (6.1 %)
Unknown	1,018 (7.0 %)
Language	
English	13,050 (90.4 %)
Spanish	850 (5.9 %)
Chinese	158 (1.1 %)
Other	382 (2.6 %)
Health Insurance	
Commercial	5,723 (39.6 %)
Public	7,093 (49.1 %)
Other	1 624 (11.2 %)
Charlson Comorbidity Index	
0	10,219 (70.8 %)
1	1,402 (9.7 %)
	2,819 (19.5 %)
California Healthy Index quartile	0.700 (0( 0.0)
Lowest quartile	3,782 (26.2 %)
Second quartile	3,438 (23.8 %)
Third quartile	3,776 (26.1 %)
Highest quartile	3,444 (23.9 %)
Time periods when COVID-19 was first diagnosed	
On or before 12/31/2020	7,244 (50.2 %)
1/1 2021—3/31/2021	2,869 (20.5 %)
1/1 2021—3/31/2021 4/1/2021 or after	4,227 (29.3 %)
COVID-19 Vaccination status at the index date	
Not vaccinated/ None	11,376 (78.8 %)
Partial	431 (3.0 %)
Full	2,633 (18.2 %)

cannabis use status, those who currently smoked cigarettes were more likely to be hospitalized (AOR = 1.47; 95 % CI 1.02-2.12).

Supplementary Table 1 shows that patient demographics (being male, having unknown race/ethnicity, speaking Spanish, and having other types of insurance), living in areas with the lowest California HPI quartile, being infected early in the pandemic, and being unvaccinated were associated with higher odds of having unknown EHR-documented

cannabis use status.

#### 4. Discussion

To the best of our knowledge, our study is among the first examining the association between cigarette smoking and COVID-19 hospitalization in the context of cannabis use. The association varies depending on cannabis use. Our findings contribute to the broader scientific understanding of the interplay between behavioral risk factors and severe COVID-19 outcomes, which can inform future efforts in tobacco control, public health messaging and clinical practice.

Our multivariate results revealed that both current and former cigarettes smoking were associated with hospitalization for COVID-19 irrespective of cannabis use status. This corroborates previous findings regarding the positive association between former cigarette smoking and COVID-19 hospitalization (Griffith et al., 2024; Piasecki et al., 2023; Simons et al., 2021; Young-Wolff, Slama, Alexeeff, et al., 2023; Young-Wolff, Slama, Sakoda, et al., 2023). While previous research findings have been inconsistent (Farsalinos et al., 2021; Griffith et al., 2024; Razjouyan et al., 2022; Umnuaypornlert et al., 2021; Young-Wolff, Slama, Alexeeff, et al., 2023; Young-Wolff, Slama, Sakoda, et al., 2023), our study provides evidence supporting a positive association between current smoking and COVID-19 hospitalization. This is plausible, as cigarette smoking leads to a variety of negative consequences such as suppressing the function of innate immune cells and decreasing clearance of inflammatory cells and debris from the lungs, which reduces the immune system's effectiveness (Usman et al., 2021). This immune suppression can contribute to the disease severity in COVID-19 patients and thereby raising the likelihood of hospitalization. In comparison to previous studies (Farsalinos et al., 2021; Griffith et al., 2024; Razjouyan et al., 2022; Umnuaypornlert et al., 2021; Young-Wolff, Slama, Alexeeff, et al., 2023; Young-Wolff, Slama, Sakoda, et al., 2023), our study controlled for a more robust set of covariates – sociodemographics (e.g., language), comorbidity burden (CCI), health behavior (COVID-19 vaccine status), and neighborhood socioeconomic condition (California HPI). This broader control could decrease the bias in the model estimates.

Patients with unknown cannabis use status in this cohort were less likely to have COVID-19 hospitalization compared to those who currently used cannabis, which is difficult to explain. Although we included a comorbidity burden measurement (CCI) in the multivariable models, this index could not comprehensively reflect patients' health status. It is possible that people who currently used cannabis were sicker due to some immunological factors for which we cannot control in the models, so they are more likely to be hospitalized. Future investigation is warranted to elucidate the strong association between unknown cannabis status in the EHR and severe COVID-19 outcomes.

When stratifying by cannabis use status, the co-use of cigarettes and cannabis was not found to be associated with hospitalization. The small sample size of people who used both substances might have limited statistical power to detect a significant association. Well-designed studies with larger sample sizes are warranted. Moreover, people who currently smoked cigarettes (vs. people who never smoked) were more likely to be admitted when their cannabis use status was unknown. Posthoc analyses showed that the associations between cigarette smoking status and COVID-19 hospitalization were different depending on cannabis use status. These findings might provide insight into some of the discrepancies observed in the literature concerning the associations between cigarette smoking and COVID-19 outcomes. Further investigation is needed to examine the underlying mechanism.

Our study has several limitations. First, the smoking status and cannabis use status were self-reported, which could potentially result in classification errors. Self-reported measurements of smoking status generally have high sensitivity and specificity compared to biochemical validation (Patrick et al., 1994). Hence, the misclassification rate of smoking status should be low. Although there have been a few studies

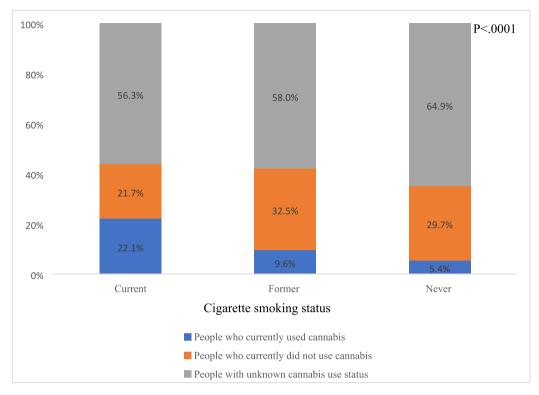


Fig. 2. Cannabis use status composition by cigarette smoking status.

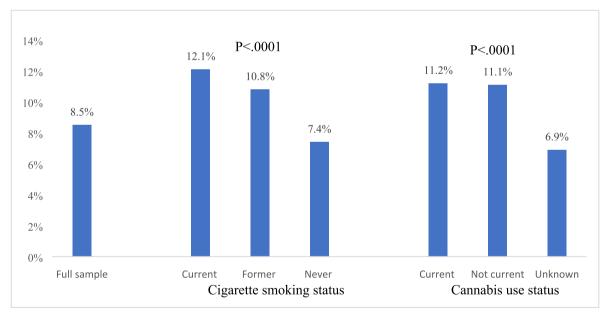


Fig. 3. Proportion of patients with COVID-19 hospitalization by cigarette smoking status and cannabis use status.

reporting high validity of self-reported cannabis use for biochemical testing (Salottolo et al., 2022; Skelton, Donahue, & Benjamin-Neelon, 2022), this area remains under-researched. Second, a large proportion of patients did not have cannabis use documented, which could bias our result interpretation. Of note, all the correlates that differed between unknown and known cannabis use status based on the supplementary analysis, were already included in our analyses of COVID hospitalization. Exploring the deeper reasons for unknown cannabis status in the EHR is beyond the scope of our study and warrants further investigation. The lack of EHR documentation may reflect a deficiency in health system support for, and prioritization of assessing and documenting

cannabis use. Such large extent of missing data hampers both clinical care and the understanding of cannabis use's relationship with health outcomes. Our study underscores the urgent need for integrating comprehensive cannabis use assessment and documentation into EHRs. Building in prompts within the EHR (Sajdeya, Goodin, & Tighe, 2021) could be considered to enhance the documentation. Third, the EHR limitation — our study did not distinguish between different types of cannabis consumption (e.g., smoking, vaping), which might have different effects on patients' respiratory health (Tashkin, 2015). Lastly, our study only examined one severe COVID-19 outcome — hospitalization. Continued research on other COVID-19 outcomes, such as

**Table 2**Multivariable logistic regression of COVID-19 hospitalization.

	Model 1(Before adjusting for cannabis use)	Model 2(Adjusted for cannabis use)
Smoking status	AOR (95 % CI)	AOR (95 % CI)
Current	1.47 (1.14–1.89) *	1.38 (1.07-1.79) *
Former	1.21 (1.05–1.39) **	1.18 (1.03–1.37) *
Never	REF	
Cannabis use status		
Not current	_	0.86 (0.68–1.09)
Unknown	_	0.60 (0.48-0.75) ***
Current	REF	
Age		
35–49	1.03 (0.84–1.26)	1.02 (0.83–1.26)
50–64	1.18 (0.98–1.44) 1.47 (1.21–1.8) **	1.20 (0.98–1.45)
65+ 18–34	REF	1.51 (1.23–1.85) ***
Corr		
Sex Male	1.33 (1.17–1.51) ***	1.35 (1.19–1.53) ***
Female	REF	1.00 (1.17-1.00)
Race/Ethnicity		
Race/Ethnicity Hispanic	1.52 (1.25–1.86) ***	1.51 (1.24–1.85) ***
Non-Hispanic Black	1.87 (1.51–2.31) ***	1.81 (1.46–2.24) ***
Non-Hispanic Asian	1.74 (1.43–2.13) ***	1.73 (1.42–2.11) ***
Non-Hispanic Other	1.39 (1.06–1.81) *	1.36 (1.04-1.77) *
Unknown	0.73 (0.52–1.02)	0.76 (0.54–1.07)
Non-Hispanic White	REF	
Language		
Spanish	1.91 (1.50–2.42) ***	2.03 (1.60–2.59) ***
Chinese	3.83 (2.60–5.64) ***	3.91 (2.66–5.76) ***
Other English	3.31 (2.55–4.31) *** REF	3.28 (2.52–4.27) ***
** 1.1 *		
Health Insurance	1 06 (1 66 0 00) ***	100(1(0,000)
Public	1.96 (1.66–2.30) ***	1.90 (1.62–2.24) ***
Other Commercial	0.73 (0.54–1.00) REF	0.75 (0.55–1.03)
Charlson Comorbidity 1	Index 1.24 (1.01–1.52) *	1 14 (0 93_1 40)
ı ≥2	1.62 (1.41–1.87) ***	1.14 (0.93–1.40) 1.51 (1.30–1.74) ***
0	REF	1.31 (1.30–1.74)
California Healthy Inc	dex quartile	
Lowest quartile	1.85 (1.51–2.26) ***	1.89 (1.55-2.31) ***
Second quartile	1.44 (1.17–1.77) **	1.45 (1.18–1.78) **
Third quartile	1.24 (1.01–1.53) *	1.24 (1.01–1.53) *
Highest quartile	REF	
Time periods		
On or before 12/31/ 2020	0.38 (0.32–0.45) ***	0.34 (0.28–0.40) ***
1/13/31/2021	0.37 (0.30-0.45) ***	0.34 (0.28-0.41) ***
4/1/2021 or after	REF	
Vaccination status		
No	1.73 (1.41-2.11) ***	1.83 (1.50-2.25) ***
Partial	0.69 (0.43–1.12)	0.75 (0.46–1.21)
Full	REF	

Note: \*p < 0.05; \*\* p < 0.01; \*\*\* p < 0.001.

mortality or long-COVID is needed.

#### 5. Conclusion

This study revealed that the associations between cigarette smoking

**Table 3**Post-hoc analyses of Model 3.

$\label{lem:covid-status} \mbox{Adjusted association between smoking status and COVID-19 hospitalization by cannabis status}$			
Among people who currently used cannabis ( $n = 1,044$ )			
Cigarette smoking status	AOR (95 % CI)		
Current	1.45 (0.82–2.56)		
Former	0.67 (0.40–1.12)		
Never	REF		
Among people who curren	tly did not use cannabis ( $n = 4,329$ )		
Cigarette smoking status	AOR (95 % CI)		
Current	0.84 (0.47–1.50)		
Former	1.36 (1.09–1.70) **		
Never	REF		
Among people with unkno	own cannabis use status (n = $9,067$ )		
Cigarette smoking status	AOR (95 % CI)		
Current	1.47 (1.02–2.12) *		
Former	1.18 (0.96–1.45)		
Never	REF		

Note: The analyses adjusted for age, sex race/ethnicity, language, health insurance, Charlson Comorbidity score, California Health Index quartile, time periods when COVID-19 was first diagnosed, and COVID-19 vaccination status at the index date.

\*p < 0.05; \*\* p < 0.01; \*\*\* p < 0.001.

status and COVID-19 hospitalization varied depending on the status of cannabis use, including whether cannabis use was documented in EHR. The mixed associations between cigarette smoking and COVID-19 outcomes reported in the prior literature might be due to the lack of consideration of cannabis use status. Further investigations are needed to unravel the underlying mechanism among cigarette smoking, cannabis use, and COVID-19 severe outcomes. With the continued increase in cannabis use, our findings suggest the importance of screening both tobacco use and cannabis use, particularly among patients tested positive for COVID-19. Future investigations of risk factors for COVID-19 outcomes should consider both cigarette and cannabis use.

#### 6. Role of funding source

This work was supported by the National Cancer Institute (CRDF Award 66590; T32CA113710) and the National Institute on Drug Abuse (T32DA007250). The funders had no role in the study design, collection, analysis or interpretation of the data, writing the manuscript, or the decision to submit the paper for publication.

#### 7. Contributors

JT designed the study, acquired data, led manuscript preparation and revised the manuscript. DG led data management and analyses, wrote the original draft, and reviewed and revised the manuscript. PH, JTK, and MCF reviewed and revised the manuscript.

#### CRediT authorship contribution statement

**Dian Gu:** Writing – review & editing, Writing – original draft, Methodology, Formal analysis. **Patrick Ha:** Writing – review & editing. **Jesse T. Kaye:** Writing – review & editing. **Michael C. Fiore:** Writing – review & editing. **Janice Y. Tsoh:** Writing – review & editing, Supervision, Methodology, Conceptualization.

#### 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.

#### Data availability

The data that has been used is confidential.

#### Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.abrep.2024.100565.

#### References

- California Healthy Place Index(2022). HPI 3.0 Technical Report.Available from https://www.healthyplacesindex.org/learning-center. Accessed 1/11 2024.Accessed 7/1/2024.
- Clift, A. K., von Ende, A., Tan, P. S., Sallis, H. M., Lindson, N., Coupland, C. A. C., & Hopewell, J. C. (2022). Smoking and COVID-19 outcomes: An observational and Mendelian randomisation study using the UK Biobank cohort. *Thorax*, 77(1), 65–73.
- Cornelius, M. E., Loretan, C. G., Jamal, A., Davis Lynn, B. C., Mayer, M., Alcantara, I. C., & Neff, L. (2023). Tobacco product use among adults - United States, 2021. MMWR. Morbidity and Mortality Weekly Report, 72(18), 475–483.
- Correa, J. B., Myers, M. G., Tully, L. K., & Doran, N. (2020). Co-occurring use of cannabis and tobacco and the presence of acute respiratory symptoms among young adult light and intermittent smokers. Substance Use & Misuse, 55(13), 2129–2137.
- D'Angelo, H., Rolland, B., Adsit, R., Baker, T. B., Rosenblum, M., Pauk, D., & Fiore, M. C. (2019). Tobacco treatment program implementation at NCI cancer centers: Progress of the NCI cancer moonshot-funded cancer center cessation initiativetobacco treatment program implementation at cancer centers. Cancer Prevention Research, 12 (11), 735–740.
- Ellingson, K. D., Hollister, J., Porter, C. J., Khan, S. M., Feldstein, L. R., Naleway, A. L., & Fowlkes, A. L. (2023). Risk factors for reinfection with SARS-CoV-2 omicron variant among previously infected frontline workers. *Emerging Infectious Diseases*, 29(3), 599–604.
- Farsalinos, K., Bagos, P. G., Giannouchos, T., Niaura, R., Barbouni, A., & Poulas, K. (2021). Smoking prevalence among hospitalized COVID-19 patients and its association with disease severity and mortality: An expanded re-analysis of a recent publication. Harm Reduction Journal, 18(1), 1–9.
- Gravely, S., Driezen, P., McClure, E. A., Hammond, D., Cummings, K. M., Chan, G., & Fong, G. T. (2022). Differences between adults who smoke cigarettes daily and do and do not co-use cannabis: Findings from the 2020 ITC four country smoking and vaping survey. Addictive Behaviors, 135, Article 107434.
- Griffith, N. B., Baker, T. B., Heiden, B. T., Smock, N., Pham, G., Chen, J., & Chen, L.-S. (2024). Cannabis, tobacco use, and COVID-19 outcomes. *JAMA Network Open*, 7(6), e2417977–e.
- Gu, T., Mack, J. A., Salvatore, M., Prabhu Sankar, S., Valley, T. S., Singh, K., & Mukherjee, B. (2020). Characteristics associated with racial/ethnic disparities in COVID-19 outcomes in an academic health care system. *JAMA Network Open*, 3(10), e2025197.
- Hasin, D., & Walsh, C. (2021). Trends over time in adult cannabis use: A review of recent findings. Current Opinion in Psychology, 38, 80–85.
- Howden, M. L., & Naughton, M. T. (2011). Pulmonary effects of marijuana inhalation. Expert Review of Respiratory Medicine, 5(1), 87–92.
- Huang, D., Xu, R., & Na, R. (2022). Cannabis use is associated with lower COVID-19 susceptibility but poorer survival. Frontiers in Public Health, 10, Article 829715.
- Meier, E., & Hatsukami, D. K. (2016). A review of the additive health risk of cannabis and tobacco co-use. Drug and Alcohol dependence, 166, 6–12.
- Patrick, D. L., Cheadle, A., Thompson, D. C., Diehr, P., Koepsell, T., & Kinne, S. (1994). The validity of self-reported smoking: A review and meta-analysis. *American Journal of Public Health*, 84(7), 1086–1093.

- Piasecki, T. M., Smith, S. S., Baker, T. B., Slutske, W. S., Adsit, R. T., Bolt, D. M., & Fiore, M. C. (2023). Smoking status, nicotine medication, vaccination, and COVID-19 hospital outcomes: Findings from the COVID EHR Cohort at the University of Wisconsin (CEC-UW) Study. Nicotine & Tobacco Research, 25(6), 1184–1193.
- Puebla Neira, D., Watts, A., Seashore, J., Polychronopoulou, E., Kuo, Y. F., & Sharma, G. (2021). Smoking and risk of COVID-19 hospitalization. *Respiratory Medicine*, 182, Article 106414.
- Quan, H., Sundararajan, V., Halfon, P., Fong, A., Burnand, B., Luthi, J. C., & Ghali, W. A. (2005). Coding algorithms for defining comorbidities in ICD-9-CM and ICD-10 administrative data. *Medical Care*, 43(11), 1130–1139.
- Razjouyan, J., Helmer, D. A., Lynch, K. E., Hanania, N. A., Klotman, P. E., Sharakhaneh, A., & Amos, C. I. (2022). Smoking status and factors associated with COVID-19 In-hospital mortality among US veterans. *Nicotine & Tobacco Research*, 24 (5), 785–793.
- Reddy, R. K., Charles, W. N., Sklavounos, A., Dutt, A., Seed, P. T., & Khajuria, A. (2021). The effect of smoking on COVID-19 severity: A systematic review and meta-analysis. *Journal of Medical Virology*, 93(2), 1045–1056.
- Sajdeya, R., Goodin, A. J., & Tighe, P. J. (2021). Cannabis use assessment and documentation in healthcare: Priorities for closing the gap. *Preventive Medicine*, 153, Article 106798
- Salottolo, K., McGuire, E., Madayag, R., Tanner, A. H., 2nd, Carrick, M. M., & Bar-Or, D. (2022). Validity between self-report and biochemical testing of cannabis and drugs among patients with traumatic injury: Brief report. *Journal of Cannabis Research*, 4 (1), 29.
- Shover, C. M., Yan, P., Jackson, N. J., Buhr, R. G., Fulcher, J. A., Tashkin, D. P., & Barjaktarevic, I. (2022). Cannabis consumption is associated with lower COVID-19 severity among hospitalized patients: A retrospective cohort analysis. *Journal of Cannabis Research*, 4(1), 46.
- Simons, D., Shahab, L., Brown, J., & Perski, O. (2021). The association of smoking status with SARS-CoV-2 infection, hospitalization and mortality from COVID-19: A living rapid evidence review with Bayesian meta-analyses (version 7). Addiction, 116(6), 1319–1368.
- Skelton, K. R., Donahue, E., & Benjamin-Neelon, S. E. (2022). Validity of self-report measures of cannabis use compared to biological samples among women of reproductive age: A scoping review. BMC Pregnancy and Childbirth, 22(1), 344.
- Tan, W. C., Lo, C., Jong, A., Xing, L., Fitzgerald, M. J., Vollmer, W. M., & Sin, D. D. (2009). Marijuana and chronic obstructive lung disease: A population-based study. CMAJ: Canadian Medical Association Journal, 180(8), 814–820.
- Tashkin, D. P. (2013). Effects of marijuana smoking on the lung. *Annals of the American Thoracic Society*, 10(3), 239–247.
- Tashkin, D. P. (2015). How beneficial is vaping cannabis to respiratory health compared to smoking? Addiction, 110(11), 1706–1707.
- Umnuaypornlert, A., Kanchanasurakit, S., Lucero-Prisno, D. E. I., & Saokaew, S. (2021).
  Smoking and risk of negative outcomes among COVID-19 patients: A systematic review and meta-analysis. Tobacco Induced Diseases, 19, 09.
- Usman, M. S., Siddiqi, T. J., Khan, M. S., Patel, U. K., Shahid, I., Ahmed, J., & Michos, E. D. (2021). Is there a smoker's paradox in COVID-19? BMJ Evidence-Based Medicine, 26(6), 279–284.
- Williamson, E. J., Walker, A. J., Bhaskaran, K., Bacon, S., Bates, C., Morton, C. E., & Goldacre, B. (2020). Factors associated with COVID-19-related death using OpenSAFELY. *Nature*, 584(7821), 430–436.
- Young-Wolff, K. C., Slama, N., Alexeeff, S. E., Sakoda, L. C., Fogelberg, R., Myers, L. C., & Prochaska, J. J. (2023). Tobacco smoking and risk of SARS-CoV-2 infection and disease severity among adults in an integrated healthcare system in California. Nicotine & Tobacco Research, 25(2), 211–220.
- Young-Wolff, K. C., Slama, N., Sakoda, L. C., Prochaska, J. J., Fogelberg, R., & Alexeeff, S. E. (2023). Current tobacco smoking and risk of SARS-CoV-2 infection and hospitalization: Evaluating the role of socio-demographic factors and comorbidities. *Preventive Medicine*, 172, Article 107523.