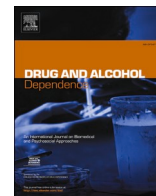




Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.



## Short communication

## Risk factors for COVID-19 among persons with substance use disorder (PWSUD) with hospital visits – United States, April 2020–December 2020<sup>☆</sup>

Amy R. Board<sup>a,b,c,\*</sup>, Sunkyung Kim<sup>a,d</sup>, Joohyun Park<sup>a,e</sup>, Lyna Schieber<sup>a,c</sup>, Gabrielle F. Miller<sup>a,f</sup>, Jamison Pike<sup>a,g</sup>, Laura J. Cremer<sup>a,c</sup>, Alice Asher<sup>a,h</sup>

<sup>a</sup> CDC COVID-19 Response, United States

<sup>b</sup> Epidemic Intelligence Service, Centers for Disease Control and Prevention, 4770 Buford Highway, Mailstop S106-8, Atlanta, GA 30341, United States

<sup>c</sup> Division of Overdose Prevention, National Center for Injury Prevention and Control, 4770 Buford Highway, Mailstop S106-8, Atlanta, GA 30341, United States

<sup>d</sup> Division of Foodborne, Waterborne, and Environmental Diseases, National Center for Emerging and Zoonotic Infectious Diseases, 1600 Clifton Rd., NE, Mailstop H24-10, Atlanta, GA 30333, United States

<sup>e</sup> Division of Diabetes Translation, National Center for Chronic Disease Prevention and Health Promotion, 4770 Buford Highway, Mailstop S107-3, Atlanta, GA 30341, United States

<sup>f</sup> Division of Injury Prevention, National Center for Injury Prevention and Control, 4770 Buford Highway, Mailstop S106-8, Atlanta, GA 30341, United States

<sup>g</sup> Immunization Services Division, National Center for Immunization and Respiratory Diseases, 1600 Clifton Rd., NE, Mailstop H24-4, Atlanta, GA 30333, United States

<sup>h</sup> Division of Viral Hepatitis, National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention, 12 Corp Sq Blvd, Mailstop US12-3, Atlanta, GA 30329, United States



## ARTICLE INFO

## Keywords:

COVID-19

Substance use disorder

Opioid

Cocaine

Alcohol use disorder

## ABSTRACT

**Introduction:** Sociodemographic factors and chronic conditions associated with coronavirus disease 2019 (COVID-19) among persons with substance use disorder (PWSUD) are not well understood. We identified risk factors associated with COVID-19 among PWSUD with hospital visits.

**Methods:** Using the Premier Healthcare Database Special COVID-19 Release, we conducted a case-control study using ICD-10-CM codes to identify PWSUD aged 12 years and older with hospital visits for any reason during April–December 2020. Multivariable logistic regression was used to calculate adjusted odds ratios (aOR) and 95% confidence intervals (CI) to identify factors associated with COVID-19 diagnosis among PWSUD (age, sex, race/ethnicity, U.S. Census Region, urban/rural classification, insurance payor type, comorbidities, and substance use disorder [SUD] type), and then stratified by SUD type.

**Results:** From April–December 2020, 18,298 (1.3%) of 1,429,154 persons with SUD in the database had a COVID-19 diagnosis. Among PWSUD, opioid use disorder (OUD; aOR = 1.24, 95% CI = 1.18–1.32), alcohol use disorder (AUD; aOR = 1.16, 95% CI = 1.11–1.22), cocaine or other stimulant use disorder (COUD; aOR = 1.28, 95% CI = 1.22–1.34), and multiple SUDs (aOR = 1.20, 95% CI = 1.15–1.26) were associated with higher odds of COVID-19, as were comorbidities such as chronic lower respiratory disease (aOR = 1.32, 95% CI = 1.26–1.37), chronic hepatitis (aOR = 1.45, 95% CI = 1.34–1.57), and diabetes (aOR = 1.78, 95% CI = 1.71–1.86).

**Conclusions:** Among a sample of PWSUD, OUD, AUD, COUD, multiple SUDs, and associated comorbidities were associated with COVID-19 diagnosis. Integration of COVID-related care, care of other comorbidities, and SUD treatment may benefit PWSUD. Future studies are needed to better understand COVID-19 prevention in this population and to reduce disparities among subpopulations at increased risk.

<sup>☆</sup> The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention/the Agency for Toxic Substances and Disease Registry.

\* Corresponding author. Present address: Division for Birth Defects and Infant Disorders, National Center on Birth Defects and Developmental Disabilities, Centers for Disease Control and Prevention, 4770 Buford Highway, MS-S106-3, Atlanta, GA 30341, United States.

E-mail addresses: [ocg3@cdc.gov](mailto:ocg3@cdc.gov) (A.R. Board), [wox0@cdc.gov](mailto:wox0@cdc.gov) (S. Kim), [ppw6@cdc.gov](mailto:ppw6@cdc.gov) (J. Park), [chn6@cdc.gov](mailto:chn6@cdc.gov) (L. Schieber), [ygm3@cdc.gov](mailto:ygm3@cdc.gov) (G.F. Miller), [kqv1@cdc.gov](mailto:kqv1@cdc.gov) (J. Pike), [qah6@cdc.gov](mailto:qah6@cdc.gov) (L.J. Cremer), [luq1@cdc.gov](mailto:luq1@cdc.gov) (A. Asher).

<https://doi.org/10.1016/j.drugalcdep.2022.109297>

Received 13 July 2021; Received in revised form 22 November 2021; Accepted 13 December 2021

Available online 11 January 2022

0376-8716/Published by Elsevier B.V.

## 1. Introduction

Persons with substance use disorder (PWSUD) face exposures and health challenges that may increase likelihood of infection with SARS-CoV-2, the virus that causes coronavirus disease 2019 (COVID-19). Substance dependence may lead to difficulty adhering to physical distancing measures due to seeking out drugs, using with others (Melamed et al., 2020; Vasylyeva et al., 2020) and exposure through congregate settings (Holloway et al., 2020). Some PWSUD may also experience suppressed immune response from opioid use (Schimmel and Manini, 2020) and higher likelihood of comorbidities that can lead to COVID-19 complications, such as human immunodeficiency virus (HIV), viral hepatitis, and impaired pulmonary functioning (Melamed et al., 2020; Vasylyeva et al., 2020).

Research on COVID-19 risk among PWSUD is limited. One U.S. study found that compared to persons without a substance use disorder (SUD), persons with a past-year SUD diagnosis had more than an 8-fold increased likelihood of COVID-19 (Wang et al., 2020). Odds of COVID-19 differed by SUD type, ranging from 5.3 (95% CI=4.4–6.4) for persons with cannabis use disorder (CAUD) to 10.2 (95% CI=9.1–11.5) for persons with opioid use disorder (OUD), compared to individuals without these diagnoses (Wang et al., 2020). Different SUD types may lead to differential COVID-19 exposures. Following the implementation of stay-at-home orders, persons may have transitioned from alcohol use in social settings to drinking alone (Boschuetz et al., 2020), while persons who use opioids are advised to never use alone in case of an overdose (Harm Reduction Coalition, 2020). PWSUD with COVID-19 have significantly worse clinical outcomes compared to individuals with COVID-19 without SUD, including increased risk for hospitalization and death (Allen et al., 2020; Baillargeon et al., 2021; Wang et al., 2020). To our knowledge, no study has yet examined whether specific subgroups of PWSUD are more likely to have a COVID-19 diagnosis, a key knowledge gap for successful public health strategies with this population. The objective of this study was to identify sociodemographic and clinical factors associated with increased risk for COVID-19 among PWSUD.

## 2. Material and methods

### 2.1. Study sample

We conducted a case-control study of PWSUD with COVID-19 compared to PWSUD without COVID-19 using the Premier Healthcare Database Special COVID-19 Release (PHD-SR, release date 02/02/2021), an electronic health record database representing over 800 U.S. facilities. The database includes all payor types and hospital and health systems in urban and rural areas. PHD-SR represents approximately 25% of U.S. inpatient admissions; outpatient visits associated with the hospital or healthcare system (e.g. emergency department [ED] visits) are also captured (Premier Applied Sciences®, 2020).

We identified all visits reported to the hospital or healthcare systems in PHD-SR from April to December 2020 among persons with diagnosed SUD aged 12 years and older. Diagnosis of SUD was based on International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM) F10-F19 codes (see Supplemental Table 1), excluding F17 codes for nicotine dependence. Any patient with an ICD-10-CM code for SUD in the health record between January 2019 and initial COVID-19 diagnosis (or end of the study period in the absence of a COVID-19 diagnosis) was classified as having SUD. The ICD-10-CM code U07.1 was used to identify a diagnosis of COVID-19 during patient discharge dates from April to December 2020 (Centers for Disease Control and Prevention, 2020). Due to limitations in PHD-SR outpatient data completeness, analyses were restricted to providers reporting patients treated in EDs and patients admitted to the hospital. This captured 94% of all providers in the PHD-SR (896 of 956 providers).

### 2.2. Statistical analysis

Multivariable logistic regression was conducted to calculate adjusted odds ratios (aOR) and 95% confidence intervals (CI) to identify factors associated with COVID-19 among PWSUD, including demographic variables and comorbidities (Supplemental Table 1). Comorbidities were chosen based on biological plausibility or evidence of increased risk for COVID-19 (Azar et al., 2020; Ferri et al., 2020; Olloquequi, 2020; Xu et al., 2020; Yang et al., 2020). All regression models were clustered using hospital identification numbers to account for possible correlation among patients' visits to the same hospital. Regression analysis was conducted for PWSUD overall and then separate regressions were run by SUD type – OUD, CAUD, alcohol use disorder (AUD), cocaine or other stimulant use disorder (COUD), and other SUD (e.g., sedative use disorder, inhalant use disorder, etc.; six models total). In the model with PWSUD overall, SUD types were also examined as covariates, as well as multiple (2+) SUDs. All analyses were performed using SAS (Version 9.4; SAS Institute, Cary, NC) and Stata (version 16.1; StataCorp, College Station, Texas). This activity was reviewed by CDC and was conducted consistent with applicable federal law and CDC policy<sup>1</sup>. This study was exempt from institutional review board approval because personal identifiers were not included in the data file, as defined under exemption 2 in 45 CFR 46.101 (<https://www.hhs.gov/ohrp/regulations-and-policy/regulations/45-cfr-46/index.html>).

## 3. Results

Of 1,429,154 persons with diagnosed SUD, 18,298 (1.3%) had a COVID-19 diagnosis during the study period (Table 1). The majority of PWSUD with COVID-19 were male (67.4%), aged 45 and older (60.2%), and sought care at urban facilities (89.7%). The distributions of age, sex, race/ethnicity, insurance payor type, hospital region, and hospital urban/rural classification among PWSUD with COVID-19 were significantly different from those without COVID-19.

Among PWSUD, persons aged 65 and older had significantly increased odds of COVID-19 (aOR=2.05, 95% CI=1.69–2.48) compared to people aged 12–17 (Table 2). Overall, males with SUD had increased odds of COVID-19 compared to females (aOR = 1.28, 95% CI = 1.23–1.33). Non-Hispanic Black persons (aOR = 1.44, 95% CI = 1.34–1.56), non-Hispanic persons categorized as 'other, non-Hispanic'<sup>2</sup> (aOR = 1.98, 95% CI = 1.76–2.24), and Hispanic persons (aOR = 2.44, 95% CI = 2.14–2.78) had higher odds of COVID-19 compared to non-Hispanic White persons. Having chronic lower respiratory disease (aOR = 1.32, 95% CI = 1.26–1.37), chronic hepatitis (aOR = 1.45, 95% CI = 1.34–1.57), or diabetes (aOR = 1.78, 95% CI = 1.71–1.86) were associated with higher odds of COVID-19.

Persons with OUD (aOR = 1.24, 95% CI = 1.18–1.32), AUD (aOR = 1.16, 95% CI = 1.11–1.22), COUD (aOR = 1.28, 95% CI = 1.22–1.34), and multiple SUDs (aOR = 1.20, 95% CI = 1.15–1.26) had increased odds of COVID-19 compared to persons with other SUD types (Table 2 and Supplemental Table 2). Among persons with AUD, all age groups 25 years and older had higher odds of COVID-19 than those aged 12–17 years (Table 2). Only age 65 years and older was associated with higher odds of COVID-19 among persons with COUD (aOR = 1.60, 95% CI = 1.04–2.46) and CAUD (aOR = 1.36, 95% CI = 1.08–1.72). Among Hispanic persons with AUD, odds of COVID-19 were 2.78 times that of non-Hispanic White persons with AUD (95% CI = 2.42–3.20). Males with AUD also had higher likelihood of COVID-19 compared to females with AUD (aOR = 1.44, 95% CI = 1.37–1.52). Higher odds of COVID-19 were

<sup>1</sup> See e.g., 45 C.F.R. part 46, 21 C.F.R. part 56; 42 U.S.C. §241(d); 5 U.S.C. §552a; 44 U.S.C. §3501 et seq.

<sup>2</sup> 'Other, non-Hispanic' includes persons who reported their race/ethnicity as non-Hispanic American Indian/Alaskan Native, Asian or Pacific Islander, mixed race, or other race

**Table 1**  
Comparisons of characteristics among persons with substance use disorder (SUD) with and without COVID-19 diagnosis—April 2020–December 2020.<sup>1</sup>

	Any SUD <sup>2</sup> (N = 1,429,154)		P-value <sup>4</sup>
	COVID-19 <sup>3</sup> n = 18,298 (1.3%)	No COVID-19 n = 1,410,856 (98.7%)	
<b>Age group in Years</b>			<b>&lt; .001</b>
12–17	219 (1.2%)	25,452 (1.8%)	
18–24	1,373 (7.5%)	144,836 (10.3%)	
25–34	2,765 (15.1%)	296,351 (21.0%)	
35–44	2,937 (16.1%)	266,826 (18.9%)	
45–54	3,267 (17.9%)	239,756 (17.0%)	
55–64	3,946 (21.6%)	259,606 (18.4%)	
65+	3,791 (20.7%)	178,029 (12.6%)	
<b>Sex</b>			<b>&lt; .001</b>
Male	12,332 (67.4%)	843,899 (59.8%)	
Female	5,959 (32.6%)	565,934 (40.1%)	
Unknown	7 (0.0%)	1,023 (0.1%)	
<b>Race/ethnicity</b>			<b>&lt; .001</b>
White, non-Hispanic	9,075 (49.6%)	885,447 (62.8%)	
Black, non-Hispanic	4,023 (22.0%)	274,822 (19.5%)	
Hispanic	2,929 (16.0%)	127,690 (9.1%)	
Other, non-Hispanic <sup>5</sup>	1,878 (10.3%)	97,726 (6.9%)	
Unknown	393 (2.1%)	25,171 (1.8%)	
<b>Insurance Payor type</b>			<b>&lt; .001</b>
Medicare	5,280 (28.9%)	310,551 (22.0%)	
Medicaid	6,767 (37.0%)	561,903 (39.8%)	
Private	3,308 (18.1%)	275,019 (19.5%)	
Self-Pay	1,628 (8.9%)	189,527 (13.4%)	
Other	1,315 (7.2%)	73,856 (5.2%)	
<b>Hospital Urban/Rural Classification</b>			<b>&lt; .001</b>
Urban	16,417 (89.7%)	1,190,503 (84.4%)	
Rural	1,881 (10.3%)	220,353 (15.6%)	
<b>Hospital US Census Region</b>			<b>&lt; .001</b>
Midwest	4,494 (24.6%)	349,132 (24.7%)	
Northeast	3,217 (17.6%)	210,638 (14.9%)	
South	7,415 (40.5%)	590,746 (41.9%)	
West	3,172 (17.3%)	260,340 (18.5%)	
<b>Multiple Substance Use Disorders (2 or more)<sup>2</sup></b>			<b>&lt; .001</b>
Yes	4,205 (23.0%)	285,434 (20.2%)	
No	14,093 (77.0%)	1,125,422 (79.8%)	
<b>Comorbidities<sup>6</sup></b>			
Chronic lower respiratory disease	4,798 (26.2%)	261,681 (18.5%)	<b>&lt; .001</b>
Chronic hepatitis	812 (4.4%)	33,331 (2.4%)	<b>&lt; .001</b>
Diabetes	4,768 (26.1%)	187,765 (13.3%)	<b>&lt; .001</b>
Other potentially immunocompromising conditions <sup>7</sup>	665 (3.6%)	37,695 (2.7%)	<b>&lt; .001</b>

Note: Bold typeface denotes statistical significance.

<sup>1</sup>Among patients with hospital visits between April and December 2020 in the Premier Healthcare Dataset Special COVID-19 Release and a substance use disorder visit between January 2019 and COVID-19 diagnosis date or end of study period.

<sup>2</sup>Patients with an F11-F19 ICD-10-CM code between January 2019 and COVID-19 diagnosis date or end of study period (excluding F17 codes for nicotine dependence), classified into the following categories: any SUD, opioid use disorder (OUD), alcohol use disorder (AUD), cannabis use disorder (CAUD), cocaine or other stimulant use disorder (COUD), and other SUD (see Supplemental Table 1 for a listing of all ICD-10-CM codes for SUD types).

<sup>3</sup>Defined using the ICD-10-CM code U07.1.

<sup>4</sup>Calculated using chi-square test.

<sup>5</sup>Includes all races other than Black or White, including non-Hispanic American Indian/Alaskan Native, Asian or/Pacific Islander, mixed race, or other race.

<sup>6</sup>Defined using ICD-10-CM codes for each of the conditions listed here; see Supplemental Table 1.

<sup>7</sup>Including HIV/AIDS, Primary or secondary immunologic disorder, rheumatologic disorders, and cancers.

observed for certain comorbidities and SUD type (e.g., chronic lower respiratory disease among persons with OUD: aOR = 1.39, 95% CI = 1.27–1.51; chronic hepatitis among persons with CAUD: aOR = 1.89, 95% CI = 1.64–2.18).

#### 4. Discussion

Understanding risk factors for COVID-19 among PWSUD can allow public health officials to focus efforts for mitigating transmission in this population. This study found specific subpopulations of PWSUD with greater odds of COVID-19, including males, older adults, Hispanic persons, non-Hispanic Black persons, and non-Hispanic persons of other races, as well as persons with chronic lower respiratory diseases, chronic hepatitis, and diabetes. Additionally, persons with OUD, AUD, COUD, and multiple SUDs had greater odds of COVID-19 compared to persons with other SUD types. This aligns with previous research that found increased odds of COVID-19 among persons with a recent diagnosis of AUD, COUD, CAUD, and OUD, and among African American persons with a recent diagnosis of SUD (Wang et al., 2020). COVID-related racial and ethnic disparities are pronounced and can be traced to longstanding systemic inequities (Webb Hooper et al., 2020). Structural inequities have also contributed to disparities in access to SUD treatment and overdose (Banks et al., 2021; National Academies of Sciences, 2021), amplifying risk for PWSUD who belong to racial and ethnic minority groups. This study also found the likelihood of being diagnosed with COVID-19 varied by type of SUD. This may be due to differences in drug seeking or use, leading to unique opportunities for exposure. It could also reflect a different spectrum of underlying conditions that might confer increased vulnerability.

Although this study exclusively examined likelihood of COVID-19 among PWSUD, findings should be considered in tandem with existing evidence on risk for the general population. Nearly one-third of PWSUD have a chronic health condition, and one-fifth reported living in poverty (Walker and Druss, 2017). The prevalence of chronic conditions is higher among PWSUD compared to people without SUD (Bahorik et al., 2017); combined with the disproportionate risks of SARS-CoV-2 infections that PWSUD face due to socioeconomic and drug use conditions (Holloway et al., 2020; Melamed et al., 2020; Vasylyeva et al., 2020), this population demonstrates a heightened vulnerability to COVID-19. Furthermore, PWSUD who have been vaccinated against COVID-19 have a greater risk of breakthrough infections, owing largely to increased prevalence of chronic comorbidities and adverse socioeconomic factors (Wang et al., 2021).

These findings provide valuable insights to enhance education, outreach, and testing strategies for PWSUD. A recent survey found that 41% of U.S. adults reported mental or behavioral health concerns associated with the COVID-19 pandemic, with 13% reporting initiating

**Table 2**Adjusted odds of being diagnosed with COVID-19 by substance use disorder (SUD) type<sup>1</sup> – April 2020–December 2020.<sup>2</sup>

	Any SUD <sup>3</sup> , n = 1,402,590	Opioid, n = 269,967	Cocaine or other stimulants, n = 303,567	Cannabis, n = 432,374	Alcohol use disorder, n = 635,886	Other substance, n = 240,576
<b>Age group, years (ref=12–17)</b>						
18–24	1.06 (0.89,1.27)	0.53 (0.26,1.08)	0.87 (0.57,1.32)	1.08 (0.88,1.33)	1.23 (0.90,1.68)	1.23 (0.83,1.81)
25–34	1.01 (0.85,1.20)	0.52 (0.27,1.01)	0.98 (0.66,1.47)	1.04 (0.85,1.27)	<b>1.39</b> <b>(1.03,1.87)</b>	1.19 (0.80,1.76)
35–44	1.11 (0.93,1.33)	0.58 (0.29,1.15)	1.04 (0.69,1.57)	1.02 (0.83,1.25)	<b>1.72</b> <b>(1.28,2.32)</b>	1.49 (1.00,2.20)
45–54	<b>1.25</b> <b>(1.05,1.50)</b>	0.70 (0.36,1.37)	1.19 (0.79,1.80)	1.05 (0.85,1.30)	<b>1.84</b> <b>(1.36,2.47)</b>	1.47 (0.99,2.18)
55–64	<b>1.33</b> <b>(1.11,1.60)</b>	0.80 (0.41,1.58)	1.24 (0.82,1.87)	1.13 (0.92,1.39)	<b>1.85</b> <b>(1.37,2.49)</b>	1.67 (1.12,2.49)
65+	<b>2.05</b> <b>(1.69,2.48)</b>	1.20 (0.60,2.39)	<b>1.60</b> <b>(1.04,2.46)</b>	<b>1.36</b> <b>(1.08,1.72)</b>	<b>2.61</b> <b>(1.92,3.55)</b>	<b>2.45</b> <b>(1.61,3.73)</b>
<b>Sex (ref=Female)</b>						
Male	<b>1.28</b> <b>(1.23,1.33)</b>	<b>1.19</b> <b>(1.11,1.27)</b>	<b>1.23</b> <b>(1.15,1.31)</b>	<b>1.32</b> <b>(1.24,1.41)</b>	<b>1.44</b> <b>(1.37,1.52)</b>	<b>1.29</b> <b>(1.20,1.40)</b>
<b>Race/ethnicity (ref=White, non-Hispanic)</b>						
Black, non-Hispanic	<b>1.44</b> <b>(1.34,1.56)</b>	<b>1.50</b> <b>(1.34,1.66)</b>	<b>1.28</b> <b>(1.16,1.41)</b>	<b>1.58</b> <b>(1.40,1.78)</b>	<b>1.35</b> <b>(1.23,1.48)</b>	<b>1.36</b> <b>(1.22,1.53)</b>
Hispanic	<b>2.44</b> <b>(2.14,2.78)</b>	<b>1.53</b> <b>(1.24,1.89)</b>	<b>2.10</b> <b>(1.83,2.40)</b>	<b>2.27</b> <b>(1.98,2.60)</b>	<b>2.78</b> <b>(2.42,3.20)</b>	<b>2.02</b> <b>(1.72,2.37)</b>
Other, non-Hispanic <sup>4</sup>	<b>1.98</b> <b>(1.76,2.24)</b>	<b>1.61</b> <b>(1.33,1.94)</b>	<b>1.76</b> <b>(1.51,2.04)</b>	<b>1.84</b> <b>(1.58,2.13)</b>	<b>2.26</b> <b>(1.95,2.62)</b>	<b>1.65</b> <b>(1.34,2.02)</b>
<b>Urban/rural status of hospital (ref=Rural)</b>						
Urban	<b>1.44</b> <b>(1.25,1.67)</b>	<b>1.38</b> <b>(1.12,1.71)</b>	<b>1.55</b> <b>(1.28,1.89)</b>	<b>1.51</b> <b>(1.27,1.81)</b>	<b>1.34</b> <b>(1.13,1.58)</b>	<b>1.44</b> <b>(1.18,1.76)</b>
<b>U.S. Census Division (ref=Northeast)</b>						
Midwest	1.03 (0.87,1.23)	0.84 (0.68,1.04)	1.13 (0.91,1.41)	1.08 (0.87,1.34)	1.09 (0.91,1.30)	1.05 (0.84,1.31)
South	0.95 (0.81,1.13)	0.88 (0.73,1.08)	0.92 (0.75,1.13)	1.01 (0.80,1.26)	0.91 (0.77,1.07)	0.85 (0.70,1.04)
West	0.85 (0.69,1.05)	<b>0.71</b> <b>(0.55,0.92)</b>	1.03 (0.82,1.29)	1.00 (0.80,1.26)	0.80 (0.64,1.01)	0.93 (0.73,1.19)
<b>Insurance Payor Type (ref=Private)</b>						
Medicaid	<b>0.86</b> <b>(0.81,0.91)</b>	0.98 (0.86,1.11)	0.94 (0.81,1.08)	<b>0.82</b> <b>(0.72,0.92)</b>	0.96 (0.88,1.04)	0.89 (0.76,1.04)
Medicare	<b>0.90</b> <b>(0.85,0.96)</b>	0.96 (0.84,1.09)	1.07 (0.94,1.21)	0.92 (0.84,1.00)	1.06 (0.99,1.15)	0.95 (0.84,1.08)
Self-Pay	<b>0.67</b> <b>(0.60,0.74)</b>	0.81 (0.66,1.00)	<b>0.82</b> <b>(0.69,0.96)</b>	<b>0.69</b> <b>(0.60,0.79)</b>	<b>0.73</b> <b>(0.64,0.83)</b>	<b>0.69</b> <b>(0.56,0.84)</b>
Other	<b>1.29</b> <b>(1.14,1.45)</b>	<b>1.26</b> <b>(1.01,1.57)</b>	<b>1.70</b> <b>(1.40,2.06)</b>	<b>1.28</b> <b>(1.09,1.51)</b>	<b>1.35</b> <b>(1.18,1.54)</b>	<b>1.43</b> <b>(1.15,1.78)</b>
<b>Comorbidities<sup>1</sup></b>						
Chronic lower respiratory diseases	<b>1.32</b> <b>(1.26,1.37)</b>	<b>1.39</b> <b>(1.27,1.51)</b>	<b>1.25</b> <b>(1.16,1.35)</b>	<b>1.36</b> <b>(1.27,1.46)</b>	<b>1.29</b> <b>(1.22,1.36)</b>	<b>1.33</b> <b>(1.22,1.46)</b>
Chronic hepatitis	<b>1.45</b> <b>(1.34,1.57)</b>	<b>1.47</b> <b>(1.31,1.64)</b>	<b>1.61</b> <b>(1.45,1.80)</b>	<b>1.89</b> <b>(1.64,2.18)</b>	<b>1.60</b> <b>(1.44,1.78)</b>	<b>1.56</b> <b>(1.34,1.81)</b>
Diabetes	<b>1.78</b> <b>(1.71,1.86)</b>	<b>1.82</b> <b>(1.70,1.96)</b>	<b>1.65</b> <b>(1.53,1.78)</b>	<b>1.55</b> <b>(1.43,1.68)</b>	<b>1.80</b> <b>(1.70,1.90)</b>	<b>1.89</b> <b>(1.72,2.07)</b>
Other potentially immunocompromising conditions <sup>5</sup>	1.01 (0.93,1.10)	1.12 (0.98,1.28)	<b>1.36</b> <b>(1.19,1.56)</b>	1.08 (0.89,1.30)	1.07 (0.95,1.20)	<b>1.34</b> <b>(1.12,1.61)</b>
<b>SUD type<sup>3</sup></b>						
Opioid (ref: no Opioid)	<b>1.24</b> <b>(1.18,1.32)</b>	–	–	–	–	–
Cocaine or other stimulants (ref: no Cocaine)	<b>1.28</b> <b>(1.22,1.34)</b>	–	–	–	–	–
Cannabis (ref: no Cannabis)	0.97 (0.92,1.02)	–	–	–	–	–
Alcohol (ref: no Alcohol)	<b>1.16</b> <b>(1.11,1.22)</b>	–	–	–	–	–
Other SUD (ref: either Opioid or cocaine or cannabis or alcohol)	1.02 (0.97,1.08)	–	–	–	–	–

Note: Bold typeface denotes statistical significance.

<sup>1</sup>People can have multiple types of substance use disorders or comorbidities. See Supplemental Table 1 for a full list of comorbidities and ICD-10-CM codes used to identify them.

<sup>2</sup>Among patients with hospital visits documented in the Premier Healthcare Dataset Special COVID-19 Release between April and December 2020 and a substance use disorder visit between January 2019 and COVID-19 diagnosis date or end of study period; results presented in the table as adjusted odds ratio (95% confidence interval).

<sup>3</sup>Patients with an F11-F19 ICD-10-CM code between January 2019 and COVID-19 diagnosis date or end of study period (excluding F17 codes for nicotine dependence), classified into the following categories: any SUD, opioid use disorder (OUD), alcohol use disorder (AUD), cannabis use disorder (CAUD), cocaine or other stimulant use

disorder (COUD), and other SUD (see [Supplemental Table 1](#) for a listing of all ICD-10-CM codes for SUD types). Reference groups for each specific type of SUD was the presence of any other type of SUD (for example, the reference group for OUD is any other SUD except for OUD, including AUD, CAUD, COUD, and other SUD).

<sup>4</sup>Includes all races other than Black or White, including non-Hispanic American Indian/Alaskan Native, Asian or/Pacific Islander, mixed race, or other race.

<sup>5</sup>Including HIV/AIDS, Primary or secondary immunologic disorder, rheumatologic disorders, and cancers.

or increasing substance use (Czeisler et al., 2020). Stress and social isolation caused by the pandemic might lead to increases in SUD, adding urgency to the need to tailor COVID-19 prevention and vaccination strategies for this population, and the inclusion of COVID-19 risks in substance use interventions.

This study has several limitations. First, SUD was likely under-reported by only relying on ICD-10-CM codes recorded since January 2019. We also did not capture patients who received a SUD diagnosis after their initial COVID-19 visit; it is unknown whether these patients might have had SUD prior to their COVID-19 diagnosis. Additionally, ICD-10-CM codes for SUD may not indicate current drug use, and PWSUD who had a hospital visit for an unrelated concern may not have had an ICD-10-CM code for SUD included in their visit record. Outpatient visit representativeness is limited in PHD-SR, which only captures visits from outpatient facilities associated with a hospital or healthcare system (Premier Applied Sciences®). Further, we only included facilities that reported both ED and inpatient visits. For these two reasons, in addition to the fact that COVID-19 was defined using ICD-10-CM codes rather than SARS-CoV-2 test results, our study might have been more likely to include those with a more severe form of COVID-19, those with other severe conditions, and those with SUD-attributable ED and inpatient visits, all of which could bias our estimates. Additionally, large sample sizes may have driven statistical significance for some comparisons; results for variables in which the absolute difference in prevalence was small should be interpreted with caution. Finally, facility geographic indicators were used as a proxy for patient residence; however, this might not reflect a patient's U.S. region of residence or urban/rural classification in all cases.

## 5. Conclusions

Identifying which PWSUD are at increased risk for COVID-19 can inform public health action, specifically: ensuring PWSUD are integrated into COVID-19 vaccine implementation efforts through partnerships with substance use treatment and recovery programs and syringe services programs; leveraging these same partnerships to disseminate COVID-19 prevention resources; and tailoring COVID-19 prevention strategies and messages to incorporate substance use prevention and harm reduction efforts. For example, persons who use opioids are advised to never use alone in case of an overdose (Harm Reduction Coalition, 2020); to help reduce the risk of COVID-19, persons who use drugs or alcohol with others and are not fully vaccinated should practice good hand hygiene, wear masks, and maintain six feet apart as much as possible (Centers for Disease Control and Prevention, 2021). In addition, expanding access to naloxone and other harm reduction services is critical to reducing the risk of overdose (Centers for Disease Control and Prevention, 2018). PWSUD with associated comorbidities are at increased risk for COVID-19, especially those with OUD, COUD, and AUD; efforts to integrate COVID-related care, care of other comorbidities, and SUD treatment may benefit PWSUD and improve overall health outcomes. Future studies are needed to understand the impact of COVID-19 prevention in this population and to reduce disparities among subpopulations with greater risk, including PWSUD from racial and ethnic minority groups.

## Role of funding source

Nothing declared. This analysis did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

## CRedit authorship contribution statement

All authors have approved the final article. Amy Board conceptualized the study and drafted the manuscript. Sunkyung Kim and Joohyun Park conducted the analysis with oversight from Gabrielle Miller and Jamison Pike. Lyna Schieber provided guidance on the methodology and statistical analyses. Laura Cremer and Alice Asher provided subject matter input. All authors reviewed and edited the content of the manuscript.

## Acknowledgements

The authors would like to acknowledge Joshua Schier, Kristie Clarke, Heather Scobie, Daisy Christensen, and Erin Parker for their contributions to this study.

## Conflicts of interest

None. The authors have no conflicts of interest to declare.

## Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at [doi:10.1016/j.drugalcdep.2022.109297](https://doi.org/10.1016/j.drugalcdep.2022.109297).

## References

- Allen, B., Shahawy, El, Rogers, O., Hochman, E.S., Khan, S., Krawczyk, N, M.R., 2020. Association of substance use disorders and drug overdose with adverse COVID-19 outcomes in New York City: January-October 2020. *J. Public Health fdaa241*.
- Azar, W.S., Njeim, R., Fares, A.H., Azar, N.S., Azar, S.T., El Sayed, M., Eid, A.A., 2020. COVID-19 and diabetes mellitus: how one pandemic worsens the other. *Rev. Endocr. Metab. Disord.* 21 (4), 451–463.
- Bahorik, A.L., Satre, D.D., Kline-Simon, A.H., Weisner, C.M., Campbell, C.I., 2017. Alcohol, Cannabis, and Opioid Use Disorders, and Disease Burden in an Integrated Health Care System. *J. Addict. Med.* 11 (1), 3–9.
- Baillargeon, J., Polychronopoulou, E., Kuo, Y.F., Raji, M.A., 2021. The impact of substance use disorder on COVID-19 outcomes. *Psychiatr. Serv.* 72 (5), 578–581.
- Banks, D.E., Carpenter, R.W., Wood, C.A., Winograd, R.P., 2021. Commentary on Furr-Holden et al.: As opioid overdose deaths accelerate among Black Americans, COVID-19 widens inequities—a critical need to invest in community-based approaches. *Addiction* 116 (3), 686–687.
- Boschuetz, N., Cheng, S., Mei, L., Loy, V.M., 2020. Changes in alcohol use patterns in the United States during COVID-19 pandemic. *WmJ* 119 (3), 171–176.
- Centers for Disease Control and Prevention, 2020. New ICD-10-CM code for the 2019 Novel Coronavirus (COVID-19), April 1. (<https://www.cdc.gov/nchs/data/icd/Announcement-New-ICD-code-for-coronavirus-3-18-2020.pdf>). (Accessed March 27, 2021).
- Centers for Disease Control and Prevention, 2018. Evidence-Based Strategies for Preventing Opioid Overdose: What's Working in the United States. National Center for Injury Prevention and Control, Centers for Disease Control and Prevention. U.S. Department of Health and Human Services.
- Centers for Disease Control and Prevention, 2021. COVID-19 Questions and Answers: For People Who Use Drugs or Have Substance Use Disorder. (<https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/other-at-risk-populations/people-who-use-drugs/QA.html>). (Accessed 27 March 2021).
- Czeisler, M., Lane, R.I., Petrosky, E., Wiley, J.F., Christensen, A., Njai, R., Weaver, M.D., Robbins, R., Facer-Childs, E.R., Barger, L.K., Czeisler, C.A., Howard, M.E., Rajaratnam, S.M.W., 2020. Mental Health, Substance Use, and Suicidal Ideation During the COVID-19 Pandemic - United States, June 24-30, 2020. *MMWR Morb. Mortal. Wkly. Rep.* 69 (32), 1049–1057.
- Ferri, C., Giuggioli, D., Raimondo, V., L'Andolina, M., Tavoni, A., Cecchetti, R., Guiducci, S., Ursini, F., Caminiti, M., Varcasia, G., Gigliotti, P., Pellegrini, R., Olivo, D., Colaci, M., Murdaca, G., Brittelli, R., Mariano, G.P., Spinella, A., Bellando-Randone, S., Aiello, V., Bilia, S., Giannini, D., Ferrari, T., Caminiti, R., Brusi, V., Meliconi, R., Fallahi, P., Antonelli, A., 2020. COVID-19 and rheumatic autoimmune systemic diseases: report of a large Italian patients series. *Clin. Rheuma* 39 (11), 3195–3204.
- Harm Reduction Coalition, 2020. Overdose risks and prevention. (<https://harmreduction.org/issues/overdose-prevention/overview/overdose-basics/opioid-od-risks-prevent-ion/>) (Accessed 18 March 2021).

- I.W. Holloway A.C. Spaulding A. Miyashita Ochoa L.A. Randall A.R. King COVID-19 vulnerability among people who use drugs: recommendations for global public health programmes and policies. The HBOU Study. P.M. Frew. Team J. Int. AIDS Soc. 23 (7) 2020 e25551.
- Melamed, O.C., Hauck, T.S., Buckley, L., Selby, P., Mulsant, B.H., 2020. COVID-19 and persons with substance use disorders: Inequities and mitigation strategies. *Subst. Abus.* 41 (3), 286–291.
- National Academies of Sciences, E., Medicine, Health, Medicine, D., Board on Health Care, S., Forum on Mental, H., Substance Use, D., 2021. The National Academies Collection: Reports funded by National Institutes of Health, in: Graig, L., Friedman, K. (Eds.), *Mental Health and Substance Use Disorders in the Era of COVID-19: The Impact of the Pandemic on Communities of Color: Proceedings of a Workshop—in Brief*. National Academies Press (US), Washington (DC).
- Oloquequi, J., 2020. COVID-19 Susceptibility in chronic obstructive pulmonary disease. *Eur. J. Clin. Investig.* 50 (10), e13382.
- Premier Applied Sciences®, 2020. Premier Healthcare Database (COVID-19) white paper: Data that Informs and Performs, April 10. (<https://learn.premierinc.com/white-papers/premierhealthcaredatabase-whitepaper>) (Accessed 27 March 2021).
- Schimmel, J., Manini, A.F., 2020. Opioid use disorder and COVID-19: biological plausibility for worsened outcomes. *Subst. Use Misuse* 55 (11), 1900–1901.
- Vasylyeva, T.I., Smyrnov, P., Strathdee, S., Friedman, S.R., 2020. Challenges posed by COVID-19 to people who inject drugs and lessons from other outbreaks. *J. Int. AIDS Soc.* 23 (7), e25583.
- Walker, E.R., Druss, B.G., 2017. Cumulative burden of comorbid mental disorders, substance use disorders, chronic medical conditions, and poverty on health among adults in the U.S.A. *Psychol. Health Med.* 22 (6), 727–735.
- Wang, L., Wang, Q., Davis, P.B., Volkow, N.D., Xu, R., 2021. Increased risk for COVID-19 breakthrough infection in fully vaccinated patients with substance use disorders in the United States between December 2020 and August 2021. *World Psychiatry*.
- Wang, Q.Q., Kaelber, D.C., Xu, R., Volkow, N.D., 2020. COVID-19 risk and outcomes in patients with substance use disorders: analyses from electronic health records in the United States. *Mol. Psychiatry* 1–10.
- Webb Hooper, M., Nápoles, A.M., Pérez-Stable, E.J., 2020. COVID-19 and racial/ethnic disparities. *JAMA* 323 (24), 2466–2467.
- Xu, Y., Liu, H., Hu, K., Wang, M., 2020. Clinical Management of Lung Cancer Patients during the Outbreak of 2019 Novel Coronavirus Disease (COVID-19). *Zhongguo fei ai za zhi = Chin. J. lung Cancer* 23 (3), 136–141.
- Yang, J.M., Koh, H.Y., Moon, S.Y., Yoo, I.K., Ha, E.K., You, S., Kim, S.Y., Yon, D.K., Lee, S.W., 2020. Allergic disorders and susceptibility to and severity of COVID-19: a nationwide cohort study. *J. Allergy Clin. Immunol.* 146 (4), 790–798.