JAMA Psychiatry | Original Investigation

Association of Comorbid Behavioral and Medical Conditions With Cannabis Use Disorder in Pregnancy

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IMPORTANCE Prenatal cannabis use continues to increase, yet studies of the demographic, psychiatric, and medical characteristics associated with cannabis use in pregnancy are limited by size and use of self-report, and often do not consider cannabis use disorder (CUD) or concomitant substance use disorders (SUDs). Understanding the factors associated with CUD in pregnancy is paramount for designing targeted interventions.

OBJECTIVE To examine the prevalence of co-occurring psychiatric and medical conditions of US pregnant individuals hospitalized with and without CUD by concomitant SUDs.

DESIGN, SETTING, AND PARTICIPANTS The study analyzed restricted hospital discharge data from the 2010 to 2018 Healthcare Cost and Utilization Project State Inpatient Databases in 35 states. Data were analyzed from January to August 2021. Weighted linear regressions tested whether the prevalence of psychiatric and medical conditions differed between individuals with and without a CUD diagnosis at hospitalization. Inpatient hospitalizations of pregnant patients aged 15 to 44 years with a CUD diagnosis were identified. Pregnant patients aged 15 to 44 years without a CUD diagnosis were identified for comparison. Patients were further stratified based on concomitant SUD patterns: (1) other SUDs, including at least 1 controlled substance; (2) other SUDs, excluding controlled substances; and (3) no other SUDs.

EXPOSURES CUD in pregnancy.

MAIN OUTCOMES AND MEASURES Prevalence of demographic characteristics, psychiatric disorders (eg, depression and anxiety), and medical conditions (eg, epilepsy and vomiting).

RESULTS The sample included 20 914 591 hospitalizations of individuals who were pregnant. The mean (SD) age was 28.24 (5.85) years. Of the total number of hospitalizations, 249 084 (1.19%) involved CUD and 20 665 507 (98.81%) did not. The proportion of prenatal hospitalizations involving CUD increased from 0.008 in 2010 to 0.02 in 2018. Analyses showed significant differences in the prevalence of almost every medical and psychiatric outcome examined between hospitalizations with and without CUD diagnoses, regardless of concomitant SUDs. Elevations were seen in depression (0.089; 95% CI, 0.083-0.095), anxiety (0.072; 95% CI, 0.066-0.076), and nausea (0.036; 95% CI, 0.033-0.040]) among individuals with CUD only at hospitalization compared with individuals with no SUDs at hospitalization.

CONCLUSIONS AND RELEVANCE Considerable growth was observed in the prevalence of CUD diagnoses among individuals hospitalized prenatally and in the prevalence of depression, anxiety, nausea, and other conditions in individuals with CUD at hospitalization. This study highlights the need for more screening, prevention, and treatment, particularly in populations with co-occurring CUD and psychiatric disorders. Research on the determinants and outcomes associated with CUD during pregnancy is needed to guide clinicians, policy makers, and patients in making informed decisions.

JAMA Psychiatry. doi:10.1001/jamapsychiatry.2021.3193
Published online November 3, 2021.

Supplemental content

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Prenatal cannabis use continues to increase despite potential adverse effects on pregnancy and offspring.[1] Cannabis is the most common illicit drug used during pregnancy, with an estimated 7.1% of pregnant people reporting past-month use in 2017.[2-4] Among pregnant people who reported past-month cannabis use, 60%, 40%, and 17% also reported past-month tobacco, alcohol, and other illicit drug use, respectively.[5] Individuals who use cannabis regularly may develop clinically significant impairment or distress as well as other general diagnostic features of a substance use disorder (SUD).[6,7] Cannabis use disorder (CUD) generally develops over an extended period and is commonly observed as the only SUD experienced by an individual; however, it also frequently occurs concurrently with other SUDs.[7,8] As US states move toward legalization and cannabis becomes increasingly available, a better understanding of the demographic, psychiatric, and medical characteristics associated with CUD in pregnancy will be paramount for guiding research and targeted public health interventions.

To date, studies are few and have important data limitations. Several studies documented increased prevalence of mood-related disorders in people reporting prenatal cannabis use.[9-12] For example, a recent study documented increased prevalence of anxiety, depression, and trauma in 11 681 patients who used cannabis prenatally.[13] However, most studies have been limited by relying on self-reported cannabis use and mood-related disorders, by examining cannabis use and not CUD, or by not considering concomitant SUDs. As the prevalence of polysubstance use among pregnant people who use cannabis is substantial,[5] it is critical to consider whether it may obfuscate factors specifically associated with CUD.

A smaller body of literature has begun elucidating medical conditions associated with cannabis use in pregnancy, documenting that managing nausea and vomiting during pregnancy is a common reason for use. Studies have mostly comprised small surveys examining cannabis use[14-16] (which, although important, are limited in determining prevalence); to our knowledge, larger studies have not considered concomitant SUDs.[17] Furthermore, studies have not examined the prevalence of chronic medical conditions, including pain disorders, epilepsy, multiple sclerosis, hepatitis C, and HIV/AIDS.[18]

This study leveraged the largest collection of all-payer US hospital discharge records to examine the prevalence of CUD at hospitalization among pregnant individuals and factors associated with presence of CUD. We examined individuals with and without CUD at hospitalization for differences in demographic characteristics and co-occurring psychiatric and medical conditions for which medical cannabis is often recommended. We implemented an inverse probability weighted regression adjustment approach using the propensity score to test whether the prevalence of such conditions was associated with CUD while controlling for sociodemographic characteristics. We stratified hospitalizations based on concomitant SUDs and compared hospitalizations of individuals with and without CUD within each stratum, accounting for group differences driven by co-occurring SUDs.

Key Points

Question What are the key demographic, psychiatric, and medical conditions associated with cannabis use disorder (CUD) in individuals who are hospitalized prenatally?

Findings In this cross-sectional study of 20 914 591 female individuals in 35 US states, the proportion of prenatal hospitalizations involving CUD increased substantially between 2010 and 2018. There was a higher prevalence of depression, anxiety, and nausea disorders in prenatal hospitalizations with CUD compared with those without CUD, regardless of concomitant substance use disorders.

Meaning The high prevalence of co-occurring mental health and medical disorders with CUD in prenatal hospitalizations highlights a critical need for treatment and support in this vulnerable population.

Methods

Procedures

We analyzed restricted hospital discharge data from the Healthcare Cost and Utilization Project (HCUP), a family of national and state health care databases developed through a federal-state-industry partnership sponsored by the Agency for Healthcare Research and Quality. HCUP includes the largest collection of hospital data in the US with all-payer encounter-level information. We relied on the 2010 to 2018 HCUP State Inpatient Databases (HCUP-SID). HCUP-SID contains a near census of hospital inpatient discharges in participating states and collects sociodemographic characteristics (race, ethnicity, age, sex, and expected payer), geographic (state and county), and clinician-reported *ICD-9* and *ICD-10* diagnostic and procedure codes (primary and secondary) associated with the discharge. Some states that do not participate in HCUP directly provide researchers with access to their inpatient records. We combined HCUP-SID with data from nonparticipating states (Louisiana, Delaware, Pennsylvania, and Tennessee) for a total of 35 states. As data were deidentified, this study was considered exempt from review by Weill Cornell Medicine's Institutional Review Board.

Participants

Hospitalizations of pregnant individuals aged 15 to 44 years (mean [SD] age, 28.24 [5.85] years) were identified using *ICD-9* and *ICD-10* diagnostic and procedure codes indicating pregnancy or childbirth (eMethods in the Supplement). Of all included individuals, 2 837 139 (14.31%) were Hispanic, 3 649 649 (18.41%) were non-Hispanic Black, 11 505 695 (58.05%) were non-Hispanic White, and 1 828 159 (9.22%) were of another non-Hispanic race (including individuals identified by HCUP or the state hospital discharge record as Asian or Pacific Islander, Native American, or other). Race and ethnicity data varied across states. We analyzed categories that could be better harmonized across states according to identification and reporting practices and included these data to elucidate the sociodemographic factors associated with CUD at hospitalization among

pregnant individuals. Most hospitalizations examined (92%) were for childbirth. The sample was stratified into mutually exclusive subgroups based on CUD and concomitant SUD diagnoses. Among 20 914 591 prenatal hospitalizations, a total of 249 084 hospitalizations involving CUD were stratified as follows: (1) 115 953 hospitalizations with CUD diagnosed but no other SUDs diagnosed (ie, CUD only diagnosed at hospitalization); (2) 48 939 hospitalizations with CUD and other SUDs diagnosed, including at least 1 other controlled substance; and (3) 84 192 hospitalizations with CUD and other SUDs diagnosed, excluding other controlled substances (ie, only alcohol or tobacco). Respective prenatal hospitalizations without a CUD diagnosis were stratified as follows: (4) 19 281 026 hospitalizations with no CUD diagnosed and no other SUDs diagnosed; (5) 278 958 hospitalizations with no CUD diagnosed but with other SUDs diagnosed, including at least 1 other controlled substance; and (6) 1 105 523 hospitalizations with no CUD diagnosed but with other SUDs diagnosed, excluding other controlled substances.

Statistical Analysis

We calculated the proportion of prenatal hospitalizations involving CUD overall and for subgroups with SUD diagnoses. To examine state-level patterns, we calculated the prevalence of CUD for each state using the 2 most recent data years (2017 and 2018). We then examined the prevalence of outcomes of interest by CUD and concomitant SUDs. Outcomes of interest included SUDs, demographic characteristics, and psychiatric and medical conditions authorized for medical cannabis use or associated with SUDs in previous studies.[18] Psychiatric conditions included specific disorders (eg, depression, anxiety, trauma, or attention-deficit/hyperactivity disorder) and a broader category (mood-related disorders). The mood-related disorders category was defined so as to capture broader *ICD* codes that have been previously used to identify mental health conditions in prenatal populations.[13,19-23] Medical conditions examined included epilepsy, multiple sclerosis, HIV/AIDS, hepatitis C, nausea, vomiting, and chronic pain. Outcomes were defined with codes established by the Centers for Medicare & Medicaid Services Chronic Conditions Data Warehouse and previous studies (eMethods in the Supplement).[13,24]

Weighted linear regressions[25-28] were used to examine differences in the prevalence of behavioral and medical outcomes between hospitalizations of individuals with and without CUD. These analyses tested whether any differences in prevalence (ie, mean treatment effect sizes) associated with CUD were statistically significant for each concomitant SUD subgroup, controlling for potential confounders. An inverse probability-weighted regression adjustment approach using propensity scores was used to reduce systematic differences between hospitalizations with and without CUD diagnoses.[26] A notable strength of inverse probability-weighted regression adjustment is its double-robust property, which offers protection against mismodeling.[29] We estimated propensity scores with a logistic model that regressed CUD status on sociodemographic, time, and geographic characteristics (age, age squared, expected payer, race, ethnicity, county of residence, and year-quarter) and generated weights for each individual. Each individual's weight was equal to the inverse of the probability of treatment. Robust sandwich standard errors[25] were estimated to account for sampling variability in the weights. All weighted linear regressions controlled for the same sociodemographic, time, and geographic characteristics used to estimate propensity scores. We reported mean treatment effect sizes, 95% CIs, and estimated prevalence in non-CUD groups. Mean treatment effect sizes capture the difference in the prevalence of a given outcome between the CUD and non-CUD group and can be interpreted as percentage point changes when multiplied by 100. Two-tailed *P* values were considered significant at < .05.

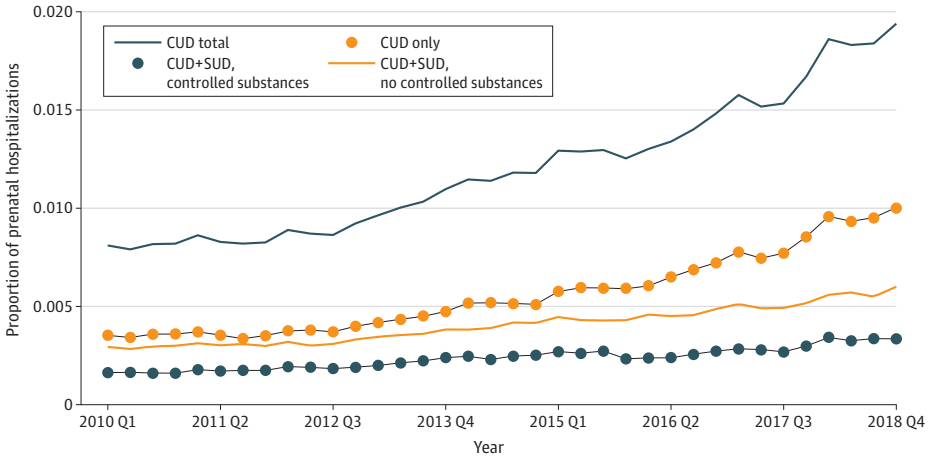
Results

The proportion of prenatal hospitalizations with any CUD diagnosis increased from 2010 to 2018 (0.008 to 0.02, respectively) (**Figure 1**). Although increases occurred across all CUD subgroups, hospitalizations with a CUD diagnosis only displayed the sharpest growth (from 0.003 in 2010 to 0.01 in 2018). Sensitivity analyses documented similar increases across prenatal hospitalizations of individuals with diagnosed depressive disorders or with any concomitant SUDs, suggesting increases in the proportion of hospitalizations with CUD diagnoses are not solely a by-product of increases in physician awareness of prenatal SUD (eFigure 1 in the Supplement) or an increase in the prevalence of disorders in pregnancy (eg, prenatal depression; eFigure 2 in the Supplement). Of the 35 states analyzed, Alaska, Oregon, New Mexico, Michigan, West Virginia, Vermont, and Maine had the highest prevalence of CUD diagnoses among prenatal hospitalizations (**Figure 2**).

Prevalence patterns of concomitant SUDs differed between hospitalizations of individuals with and without CUD (**Table 1**). Among individuals hospitalized with other SUDs, including controlled substances, those with CUD diagnoses showed higher rates of cocaine, amphetamine, tobacco, and alcohol use disorders, but lower rates of opioid use disorders compared with hospitalizations without CUD diagnoses. Among hospitalizations of individuals with other SUD diagnoses excluding controlled substances, alcohol use disorders were higher among hospitalizations of individuals with CUD diagnoses, but tobacco use disorders were slightly higher in hospitalizations of individuals without diagnosed CUD.

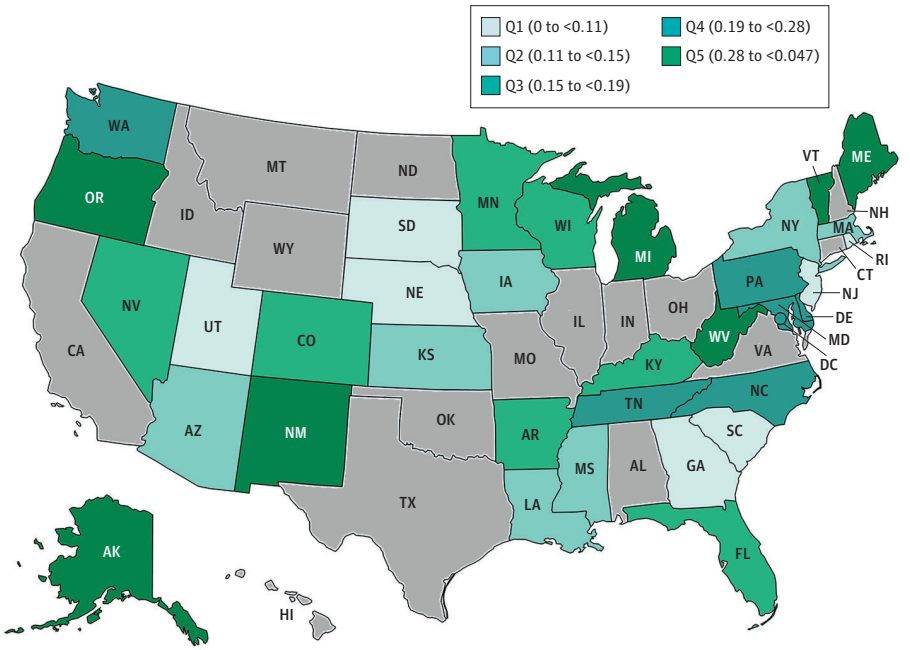
The prevalence of mood-related disorders was considerably higher for all CUD subgroups, regardless of concomitant SUDs. Compared with 928 132 of 19 281 026 individuals (5%) with neither SUDs nor CUD at hospitalization, mood-related disorders were present in 67 184 of 115 953 individuals (58%) with only CUD at hospitalization. Mood-related disorders were also higher in individuals with CUD and alcohol or tobacco disorders at hospitalization (54 709 of 84 192; 65%) compared with individuals with only alcohol or tobacco disorders at hospitalization (177 395 of 1 105 523; 16%). Similarly, higher rates of mood-related disorders were found in individuals with CUD and SUDs including other controlled substances, at hospitalization (32 472 of 48 939; 66%) than in individuals with SUDs

Figure 1. Cannabis Use Disorder (CUD) Among Prenatally Hospitalized Individuals, 2010-2018



CUD total indicates prenatally hospitalized individuals with any CUD; CUD only, prenatally hospitalized individuals with CUD and no other substance use disorder (SUD); CUD+SUD, controlled substances, prenatally hospitalized individuals with CUD and other SUDs including at least 1 controlled substance; CUD+SUD, no controlled substances, prenatally hospitalized individuals with CUD and other SUDs excluding any other controlled substance (alcohol and tobacco only); Q, quintile. Controlled substances include opioids, stimulants, hallucinogens, sedatives, hypnotics, and other drugs. Data are from the Healthcare Cost and Utilization Project State Inpatient Databases, 2010-2018.

Figure 2. Prevalence of Cannabis Use Disorder Among Prenatally Hospitalized Individuals by State, 2017-2018



Q indicates quintile. Figure shows the proportion of prenatally hospitalized individuals with a diagnosis of cannabis use disorder for each state included in analyses. Color shading denotes prevalence during 2017-2018, grouped by quintiles for easier interpretation. States not included in analyses are shaded in gray. Data are from the Healthcare Cost and Utilization Project State Inpatient Databases, 2010-2018.

including other controlled substances but without CUD at hospitalization (146 977 of 278 958; 53%). Similarly, individually examined, depression, anxiety, trauma, and attention-deficit/hyperactivity disorder were higher in all CUD subgroups, regardless of concomitant SUDs. Differences were most remarkable when comparing individuals with only CUD at hospitalization and individuals with neither SUDs nor CUD at hospitalization, where the prevalence of depression and anxiety disorders was more than 3 times higher in individuals with CUD only at hospitalization (depression, (11 953 of 115 953 [10%] vs 518 283 of 19 281 026 [3%]; anxiety, 10 044 of 115 953 [9%] vs 494 757 of 19 281 026 [3%]).

Most of the medical conditions examined were higher in individuals with CUD at hospitalization regardless of concomitant SUDs. The highest prevalence was detected for vomiting disorders, especially when comparing hospitalized individuals with neither SUDs nor CUD (196 016 of 19 281 026; 1%) and those with CUD only (5634 of 115 953; 5%). Multiple sclerosis

Table 1. Characteristics of Prenatally Hospitalized Patients by Cannabis Use Disorder (CUD), 2010-2018[a]

Characteristic	No. (%)						
	CUD (yes)			CUD (no)			
		With other SUDs			With other SUDs		
	No other SUDs (n = 115 953)	Including controlled substances[b] (n = 48 939)	Excluding controlled substances[b] (n = 84 192)	No SUDs (n = 19 281 026)	Including controlled substances[b] (n = 278 958)	Excluding controlled substances[b] (n = 1 105 523)	Total sample (N = 20 914 591)
SUDs							
Cannabis	115 953 (100)	48 939 (100)	84 192 (100)	0	0	0	249 084 (1.19)
Opioids	0	21 213 (43.35)	0	0	169 331 (60.70)	0	190 544 (0.91)
Cocaine	0	17 927 (36.63)	0	0	38 156 (13.68)	0	56 083 (0.27)
Amphetamine	0	13 936 (28.48)	0	0	36 931 (13.24)	0	50 867 (0.24)
Other drugs	0	8644 (17.66)	0	0	68 168 (24.44)	0	76 812 (0.37)
Tobacco	0	29 664 (60.61)	81 538 (96.85)	0	144 042 (51.64)	1 093 208 (98.89)	1 348 452 (6.45)
Alcohol	0	4411 (9.01)	5678 (6.74)	0	11 665 (4.18)	19 621 (1.77)	41 375 (0.20)
Mental health conditions							
Mood-related disorders	67 184 (57.94)	32 472 (66.35)	54 709 (64.98)	928 132 (4.81)	146 977 (52.69)	177 395 (16.05)	1 406 869 (6.73)
Depression	11 953 (10.31)	8532 (17.43)	11 087 (13.17)	518 283 (2.69)	42 104 (15.09)	89 525 (8.10)	681 484 (3.26)
Anxiety	10 044 (8.66)	7793 (15.92)	9330 (11.08)	494 757 (2.57)	40 809 (14.63)	80 037 (7.24)	642 770 (3.07)
Trauma	2869 (2.47)	2919 (5.96)	2826 (3.36)	56 280 (0.29)	10 755 (3.86)	12 614 (1.14)	88 263 (0.42)
ADHD	1674 (1.44)	1367 (2.79)	1761 (2.09)	49 101 (0.25)	5473 (1.96)	12 184 (1.10)	71 560 (0.34)
Physical health conditions							
Epilepsy	1600 (1.38)	1247 (2.55)	1467 (1.74)	85 033 (0.44)	6177 (2.21)	12 534 (1.13)	108 058 (0.52)
Multiple sclerosis	118 (0.10)	6 (0.14)	84 (0.1)	16 883 (0.09)	400 (0.14)	1372 (0.12)	18 926 (0.09)
Chronic pain	3065 (2.64)	2464 (5.03)	2597 (3.08)	217 700 (1.13)	16 704 (5.99)	27 666 (2.50)	270 196 (1.29)
Vomiting	5634 (4.86)	1481 (3.03)	2599 (3.09)	196 016 (1.02)	5187 (1.86)	12 709 (1.15)	223 626 (1.07)
Nausea	956 (0.82)	422 (0.86)	594 (0.71)	48 420 (0.25)	1926 (0.69)	3952 (0.36)	56 270 (0.27)
HIV/AIDS	516 (0.45)	513 (1.05)	382 (0.45)	24 136 (0.13)	1945 (0.70)	2366 (0.21)	29 858 (0.14)
Hepatitis C	779 (0.67)	5255 (10.74)	1546 (1.84)	27 710 (0.14)	45 355 (16.26)	16 902 (1.53)	97 547 (0.47)
Sociodemographic characteristics							
Age, y							
15-19	16 814 (14.51)	2604 (5.33)	8996 (10.69)	1 279 257 (6.64)	7829 (2.81)	85 303 (7.72)	1 400 803 (6.70)
20-24	46 522 (40.14)	13 915 (28.47)	30 869 (36.69)	4 144 833 (21.5)	65 407 (23.52)	348 910 (31.6)	4 650 456 (22.24)
25-29	32 088 (27.69)	16 834 (34.45)	25 032 (29.76)	5 544 449 (28.76)	99 834 (35.90)	339 660 (30.76)	6 057 897 (28.97)
30-34	14 677 (12.67)	10 450 (21.38)	13 298 (15.81)	5 223 168 (27.09)	70 073 (25.20)	215 332 (19.50)	5 546 998 (26.53)
35-44	5784 (4.99)	5067 (10.37)	5930 (7.05)	3 086 097 (16.01)	34 977 (12.58)	115 078 (10.42)	3 252 933 (15.56)
Race and ethnicity[c]							
Hispanic	10 676 (9.61)	3598 (7.70)	3961 (4.96)	2 755 922 (15.09)	18 243 (6.83)	44 739 (4.27)	2 837 139 (14.31)
Non-Hispanic							
Black	48 951 (44.04)	10 700 (22.89)	25 282 (31.67)	3 379 060 (18.50)	29 937 (11.21)	155 719 (14.85)	3 649 649 (18.41)
White	45 286 (40.74)	29 735 (63.62)	46 935 (58.8)	10 367 976 (56.76)	206 003 (77.14)	809 760 (77.22)	11 505 695 (58.05)
Other[d]	6237 (5.61)	2705 (5.79)	3639 (4.56)	1 764 310 (9.66)	12 862 (4.82)	38 406 (3.66)	1 828 159 (9.22)
Medicaid	89 443 (77.14)	38 432 (78.53)	67 315 (79.95)	7 975 189 (41.36)	215 071 (77.10)	779 891 (70.54)	9 165 341 (43.82)
Private insurance	19 907 (17.17)	5181 (10.59)	10 911 (12.96)	10 011 715 (51.93)	37 261 (13.36)	253 781 (22.96)	10 338 756 (49.43)
Other insurance	6606 (5.70)	5326 (10.88)	5966 (7.09)	1 294 150 (6.71)	26 627 (9.55)	71 852 (6.50)	1 410 527 (6.74)

Abbreviations: ADHD, attention-deficit/hyperactivity disorder; SUDs, substance use disorders.

[a] Data are from the Healthcare Cost and Utilization Project State Inpatient Databases, 2010-2018.

[b] Controlled substances include opioids, stimulants, hallucinogens, sedatives, hypnotics, and other drugs.

[c] Race and ethnicity data varied across states. We analyzed categories that could be better harmonized across states owing to states' identification and reporting practices and included these data to elucidate the sociodemographic factors associated with CUD at hospitalization among pregnant individuals.

[d] Other includes individuals identified by the Healthcare Cost and Utilization Project or the state hospital discharge record as Asian or Pacific Islander, Native American, or other. These categories were consolidated owing to differences in how categories were reported across states.

Table 2. Differences in the Prevalence of Behavioral and Medical Conditions Between Prenatally Hospitalized Individuals With and Without Cannabis Use Disorder by Concomitant Substance Use Disorder (SUD)[a]

	Other SUD								
	Including controlled substances[b]			Excluding controlled substances[b]			No other SUD		
Condition	MTE (95% CI)[c]	*P* value	Estimated prevalence[d]	MTE (95% CI)[c]	*P* value	Estimated prevalence[d]	MTE (95% CI)[c]	*P* value	Estimated prevalence[d]
Mental health conditions									
Mood-related disorders	0.151 (0.145 to 0.157)	<.001	0.528	0.551 (0.546 to 0.554)	<.001	0.160	0.631 (0.625 to 0.637)	<.001	0.048
Depression	0.035 (0.029 to 0.040)	<.001	0.151	0.052 (0.048 to 0.056)	<.001	0.080	0.089 (0.083 to 0.095)	<.001	0.027
Anxiety	0.025 (0.019 to 0.030)	<.001	0.146	0.043 (0.038 to 0.046)	<.001	0.071	0.072 (0.066 to 0.076)	<.001	0.026
Trauma	0.022 (0.019 to 0.026)	<.001	0.039	0.021 (0.019 to 0.023)	<.001	0.011	0.020 (0.018 to 0.023)	<.001	0.003
ADHD	0.008 (0.006 to 0.011)	<.001	0.019	0.008 (0.007 to 0.009)	<.001	0.011	0.011 (0.009 to 0.013)	<.001	0.003
Physical health conditions									
Epilepsy	0.003 (0.001 to 0.005)	.006	0.021	0.005 (0.003 to 0.006)	<.001	0.011	0.008 (0.006 to 0.010)	<.001	0.004
Multiple sclerosis	0.000 (−0.000 to 0.001)	.41	0.001	−0.000 (−0.000 to 0.000)	.29	0.001	0.000 (0.000 to 0.001)	.04	0.000
Pain	−0.010 (−0.013 to −0.007)	<.001	0.060	0.006 (0.003 to 0.008)	<.001	0.025	0.016 (0.014 to 0.019)	<.001	0.011
Vomiting	0.011 (0.009 to 0.014)	<.001	0.019	0.017 (0.014 to 0.018)	<.001	0.011	0.036 (0.033 to 0.040)	<.001	0.010
Nausea	0.002 (0.001 to 0.003)	.001	0.007	0.003 (0.002 to 0.004)	<.001	0.004	0.005 (0.004 to 0.007)	<.001	0.002
HIV/AIDS	0.001 (0.000 to 0.003)	.02	0.007	0.002 (0.001 to 0.002)	<.001	0.002	0.002 (0.001 to 0.003)	<.001	0.001
Hepatitis C	−0.026 (−0.032 to −0.021)	<.001	0.157	0.008 (0.006 to 0.009)	<.001	0.015	0.006 (0.005 to 0.007)	<.001	0.001

Abbreviations: ADHD, attention-deficit/hyperactivity disorder; MTE, mean treatment effect.

[a] Data are from the Healthcare Cost and Utilization Project State Inpatient Databases, 2010-2018. We drew a 50% sample of the overall population for computational efficiency.

[b] Controlled substances include opioids, stimulants, hallucinogens, sedatives, hypnotics, and other scheduled drugs.

[c] MTE is interpreted as a difference in prevalence between the CUD group compared with the non-CUD group. MTEs, 95% CIs, and estimated prevalence were generated with weighted linear regression models. An inverse probability–weighted regression adjustment approach using propensity scores was used to reduce systematic differences between prenatal hospitalizations with and without a CUD diagnosis.

[d] Indicates estimated prevalence in the comparison group.

was an exception, as prevalence was similar across groups with and without CUD. Further, although the prevalence of chronic pain and hepatitis C was elevated in hospitalized individuals with CUD with either no other SUDs or alcohol or tobacco disorders, both disorders were more prevalent in hospitalized individuals without CUD but with other SUDs including controlled substances. The demographic characteristics of prenatal patients varied across CUD subgroups. Compared with groups without CUD, groups with CUD had a higher proportion of younger patients (15 to 19 years and 20 to 24 years) and non-Hispanic Black patients. Hospitalized individuals with CUD were also more frequently expected to be covered by Medicaid and less frequently by private insurances, especially when comparing hospitalized individuals with CUD only to those with no CUD and no other SUDs.

Weighted linear regressions showed statistically significant differences in the prevalence of almost every medical and psychiatric outcome examined between hospitalized individuals with and without CUD, even when controlling for covariates (**Table 2**). In general, mean treatment effect sizes were largest when comparing hospitalized individuals with CUD only and those with no CUD and no other SUDs, followed by comparisons of hospitalized individuals with alcohol or tobacco disorders. That is, the prevalence of psychiatric and medical disorders was most similar across hospitalized individuals with and without CUD in the presence of other SUDs including controlled substances.

The most marked effect sizes were seen in mood-related disorders, depression, anxiety, and vomiting. The prevalence of depression was 0.089 (95% CI, 0.083-0.095) percentage points higher among individuals with CUD at prenatal hospitalization in the subgroup with no other SUDs. Compared with the prevalence in the comparison group (ie, no CUD and no other SUD), CUD was associated with a 329.6% (0.089/0.027) increase in prevalence of depression. When comparing hospitalized individuals with CUD and other SUDs, there was a 65% (0.052/0.080) increase in prevalence of depression in hospitalized individuals with CUD and other SUDs excluding controlled substances, and a 23% (0.035/0.151) increase in prevalence of depression in hospitalized individuals with CUD and other SUDs including controlled substances. The prevalence of anxiety also increased significantly in hospitalized individuals with CUD, showing a 277% (0.072/0.026) increase in the group with no other SUDs, 61% (0.043/0.071) in the group

with other SUDs excluding controlled substances, and 17% (0.025/0.146) in the group with other SUDs including controlled substances. Differences in the prevalence of vomiting disorders were most marked in hospitalized individuals with no other SUDs, where CUD was associated with a 360% (0.036/0.010) increase in prevalence.

Discussion

This study leveraged the largest collection of US hospital discharge records to examine CUD in pregnancy and characteristics associated with CUD in prenatally hospitalized individuals. Findings showed considerable increases in the prevalence of prenatal hospitalizations involving CUD and indicated that mood-related disorders and some medical disorders, particularly vomiting, were significantly more prevalent in individuals with CUD at hospitalization. Even when examining hospitalized individuals with comparable patterns of concomitant SUDs, hospitalized individuals with CUD still showed higher prevalence of these disorders, suggesting prevalence increases were not exclusively a function of increases in overall SUDs. Our findings highlight the dire need for more research on the mechanisms underlying associations between CUD and psychiatric and medical disorders.

Documented growth in CUD prevalence among prenatal hospitalizations is in line with previous studies finding increases in self-reported cannabis use during pregnancy.[2,9,30,31] Cannabis liberalization policies may be an important factor leading to increased cannabis use among existing users and growth in new users.[32-34,46] We found that among the 7 states with highest CUD prevalence, 5 (Alaska, Oregon, Michigan, Vermont, and Maine) had legalized recreational cannabis. Notably, many states adopting cannabis liberalization policies are silent regarding cannabis use during pregnancy.[35] Decreases in the perception of harmfulness, risk, and stigma associated with prenatal cannabis use may be another contributing factor. Studies have documented that some pregnant patients believe that safe levels of cannabis use during pregnancy exist.[5,36] One study suggests that up to 74% of people who use cannabis during pregnancy believe there to be no potential harm[14] and that many patients report thinking that cannabis is safer than other substances, including prescribed medications.[15]

Mental health disorders were elevated among hospitalized individuals with CUD, including depression and anxiety, even when considering concomitant SUDs. This is of concern, given prenatal distress can have ongoing effects on mother and child.[37] Our findings highlight a population in critical need of interventions, yet the association between CUD and psychiatric disorders requires elucidation. Psychiatric distress might be exacerbated by cannabis, prenatal populations in distress may use cannabis in attempts to assuage symptomatology,[17] or both. Addressing directionality will necessitate longitudinal studies with assessments that commence prior to the onset of psychiatric disorders and are able to rule out reverse causation.[38] Even then, other common factors (genetic or biological, social, or environmental) may be responsible for risk of both psychiatric illness and CUD.[39] Studies that control for polygenic risk for psychiatric illness or twin studies discordant for CUD and/or depression could address causality. At minimum, our propensity score methods mitigate bias from sociodemographic and geographic factors associated with CUD.

The study findings showed increased prevalence of a range of medical conditions in individuals with CUD at hospitalization, regardless of comorbid SUDs. Most notably, vomiting disorders were elevated in hospitalized individuals with CUD, particularly among those with only CUD. It is possible that cannabis has antiemetic properties that help alleviate nausea and vomiting, which are common conditions in pregnancy. In fact, in most states legalizing medical cannabis, cannabis can be recommended for nausea and vomiting.[47] As such, pregnant persons may be turning to cannabis to assuage these symptoms.[16,17,40] Alternatively, long-term CUD may result in cannabinoid hyperemesis syndrome.[41] Apart from multiple sclerosis, all other medical disorders examined in this study were overrepresented in the CUD groups, suggesting that CUD is not only associated with the conditions that typically arise in pregnancy (eg, nausea). Understanding the specific needs of pregnant persons with both preexisting medical disorders and with conditions that typically arise in pregnancy will be important for developing targeted interventions. Interventions offering alternatives (eg, medications for hyperemesis gravidarum) may be more suitable for one group and quantity-reduction strategies more appropriate for others.

In sum, our study suggests that CUD is on the rise among prenatally hospitalized individuals. One key contribution of the present study is identifying subgroups of pregnant people who might be at the highest need for support and treatment. Younger patients and patients receiving Medicaid were overrepresented in hospitalizations with CUD. Psychoeducation may be appropriate here, as young age and suboptimal access to medical care may translate into limited knowledge regarding alternatives. Our findings further suggest that practitioners should routinely screen for CUD among pregnant patients and those contemplating pregnancy and offer treatment and support. Screening is recommended by the American College of Obstetricians and Gynecologists, yet ethical considerations must be made, especially in states with mandatory reporting requirements.[42,43] Simultaneously, findings suggest detection of CUD in pregnancy should immediately trigger close monitoring of mental health and treatment. Until the outcomes of CUD in pregnancy are understood, practitioners should consider discussing treatment choices with patients, including nonpharmacological alternatives (eg, perinatal interpersonal therapy). However, designing and implementing interventions will continue to be limited by our lack of understanding of the determinants and outcomes of CUD in pregnancy. For example, identifying critical windows of exposure could be useful in guiding interventions, as it may be more feasible to work with patients around decreasing cannabis use in one trimester as opposed to the entire pregnancy.

Limitations

There are several limitations in this study. Because most hospitalizations examined were for childbirth, findings may not

generalize to patients earlier in pregnancy or those with home deliveries. We were also unable to examine when the CUD emerged, as our data were limited to the 1 hospital encounter analyzed. This information is vital to understanding transitions from cannabis use to misuse disorder. Data also included 35 US states, limiting generalizability to states not included, US territories, and other countries. Additionally, as with all medical record–based studies, error and bias in diagnosis is possible. Subthreshold use might be coded as disorder and vice versa. Clinicians may assess other disorders (psychiatric or medical) in the presence of SUDs, introducing bias to the estimates of groups with SUDs. Further, because we examined hospitalizations for all causes and not just SUDs or psychiatric disorders, physicians may have been less attentive to these problems in this general prenatal population and our results may underestimate the true scope of the issue. Moreover, increased awareness around CUD in pregnancy may contribute to growth in CUD diagnoses, as physicians may be more inclined to assess use and patients more inclined to report it. Studies are needed that directly examine how changes in physicians' awareness of CUD in pregnancy and other sources of bias, including racial and socioeconomic bias,[44] impact prevalence estimates.

Conclusions

To our knowledge, this study is the largest to date to examine the prevalence of cannabis use disorders and associated factors in prenatal hospitalizations. Careful consideration of concomitant SUDs allowed us to more directly examine factors specifically associated with CUD. By not considering SUD comorbidity, prior literature has been limited, providing little guidance to policy makers and clinicians, who have reported lacking sufficient knowledge about CUD in pregnancy.[45] Our study highlights the need for more treatment and support and research that empowers pregnant patients to make the best decisions for themselves and their offspring.

ARTICLE INFORMATION

Accepted for Publication: September 14, 2021.

Published Online: November 3, 2021. doi:10.1001/jamapsychiatry.2021.3193

Author Contributions: Dr Meinhofer had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.
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Statistical analysis: All authors.
Obtained funding: Meinhofer.
Administrative, technical, or material support: Meinhofer, Hinde, Lugo-Candelas.
Supervision: Meinhofer, Lugo-Candelas.

Conflict of Interest Disclosures: None reported.

Funding/Support: This work was supported by Gerber Foundation grant GF192350; Robert Wood Johnson Foundation grant RWJF77962; National Institute on Drug Abuse grants K01DA051777, P30DA040500, and R01DA054722; and National Institute of Mental Health grant K08MH117452.

Role of the Funder/Sponsor: The funders had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

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