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ORIGINAL ARTICLE

Retrospective Study

Contemporary nationwide trends in major adverse cardiovascular events in young cannabis users without concomitant tobacco, alcohol, cocaine use

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Abstract

BACKGROUND

Cannabis use has increased among young individuals in recent years. Although dependent cannabis use disorder (CUD) has been associated with various cardiac events, its effects on young adults without concurrent substance use remain understudied.

AIM

To examine trends in hospitalizations for major adverse cardiac and cerebrovascular events (MACCE) in this cohort.

METHODS
We used the National Inpatient Sample (2016-2019) to identify hospitalized young individuals (18-44 years), excluding those with concurrent substance usage (tobacco, alcohol, and cocaine). They were divided into CUD+ and CUD-. Using International Classification of Diseases-10 codes, we examined the trends in MACCE hospitalizations, including all-cause mortality (ACM), acute myocardial infarction (AMI), cardiac arrest (CA), and acute ischemic stroke (AIS).

RESULTS
Of 27.4 million hospitalizations among young adults without concurrent substance abuse, 4.2% (1.1 million) had co-existent CUD. In CUD+ group, hospitalization rates for MACCE (1.71% *vs* 1.35%), AMI (0.86% *vs* 0.54%), CA (0.27% *vs* 0.24%), and AIS (0.49% *vs* 0.35%) were higher than in CUD- group ($P < 0.001$). However, rate of ACM hospitalizations was lower in CUD+ group (0.30% *vs* 0.44%). From 2016 to 2019, CUD+ group experienced a relative rise of 5% in MACCE and 20% in AMI hospitalizations, compared to 22% and 36% increases in CUD- group ($P < 0.05$). The CUD+ group had a 13% relative decrease in ACM hospitalizations, compared to a 10% relative rise in CUD- group ($P < 0.05$). However, when adjusted for confounders, MACCE odds among CUD+ cohort remain comparable between 2016 and 2019.

CONCLUSION
The CUD+ group had higher rates of MACCE, but the rising trends were more apparent in the CUD- group over time. Interestingly, the CUD+ group had lower ACM rates than the CUD- group.

Key Words: Cannabis; Major adverse cardiac and cerebrovascular events; Myocardial infarction; Cardiac arrest; Stroke; All-cause mortality; Young adults; Trends

Core Tip: Higher rates of major adverse cardiac and cerebrovascular events were observed in young adults with cannabis use disorder (CUD), while noting a relative decrease in all-cause mortality hospitalizations compared to those without CUD.

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INTRODUCTION

Cannabis is the most widely used recreational substance, both in the United States and globally[1]. In 2022, 61.9 million people aged 12 years or older used marijuana in the past year regardless of the mode. It was highest among young adults aged 18 years to 25 years (38.2%), followed by adults aged 26 years or older (20.6%), and adolescents aged 12 years to 17 years (11.5%)[2]. As of November 2023, 40 states, along with the District of Columbia, have legalized marijuana for medical purposes, and 24 states, along with the District of Columbia, have legalized its recreational use[3]. Delta 9 tetrahydrocannabinol (THC) and cannabidiol are the two principal psychoactive components of cannabis. THC interacts with the body's endocannabinoid system *via* the cannabinoid receptors, which have a broad distribution throughout the body[4]. The possible clinical cardiovascular consequences of cannabis usage have drawn attention. Emerging research suggests that while cannabis use is often associated with relaxation and stress relief, its impact on cardiovascular health is complex and multifaceted. For instance, studies have indicated that acute cannabis consumption can lead to an increase in heart rate and blood pressure, potentially elevating the risk of cardiovascular events, especially in individuals with preexisting conditions such as hypertension or coronary artery disease[5]. There is evidence that the hemodynamic effects of cannabis may raise myocardial oxygen demand while reducing its supply, similar to smoking cigarettes[6]. Although the data is presently conflicting, there have been reports that cannabis usage is linked to adverse cardiovascular outcomes, including an increased risk of myocardial infarction and stroke, particularly in young people[7]. However, much of this evidence is confounded by other substance use, complicating our understanding of the direct impact of cannabis on cardiovascular health. In our study, we aimed to address this gap by examining contemporary trends in major adverse cardiac and cerebrovascular events (MACCE) in young hospitalized adults with dependent cannabis use or cannabis use disorder (CUD), while excluding concomitant tobacco, alcohol, or cocaine use disorders. By reducing the confounding effects of these concurrent substance abuse, we sought to better understand the impact of CUD using a modern-day nationwide cohort.

MATERIALS AND METHODS

The National Inpatient Sample is a large United States all-payer inpatient healthcare dataset containing discharge data from 20% of United States hospitals in 48 states. It includes more than 7 million discharges every year, which equals about 35 million weighted nationwide discharges from 2016-2019, with one primary and up to 39 secondary discharge diagnoses. Weighing is determined by the total number of discharges from all acute care hospitals in the United States divided by the number of discharges included in the 20% sample, which makes it nationally representative. This national data is deidentified; therefore, the institutional review board approval was not mandatory.

We identified hospitalized young adults aged 18 years to 44 years with no substance abuse disorders like tobacco, alcohol, or cocaine using the International Classification of Diseases (ICD)-10 codes F17.210, F10.2 and F14.2. We then divided this population into two groups. *i.e.*, those who have dependent CUD and those who don't have CUD using ICD-10 codes F12.20 and F12.10. CUD is defined as a problematic pattern of cannabis use that results in clinically significant impairment or distress that manifests by at least two of the DSM-5 criteria occurring within a 12-month period. The criteria include using more than intended, unsuccessful attempts to cut down, cravings, neglect of major responsibilities, physical impairment, and withdrawal symptoms, among others. The dependent CUD contains three critical elements, which are preoccupation with the acquisition of cannabis, compulsive use, and relapse to or recurrent use of cannabis.

The outcomes of the study were to determine the rates of hospitalizations for MACCE, which included events such as all-cause mortality (ACM), acute myocardial infarction (AMI), cardiac arrest (CA), and acute ischemic stroke (AIS) in this population using ICD-10 codes (I21.9, I46.9, I63). In addition to this, we aimed to analyze the trends in hospitalizations for MACCE, ACM, AMI, CA and AIS between 2016-2019 in these two cohorts. Categorical and continuous data between cohorts were assessed using Pearson's χ^2 test and Kruskal Wallis test, respectively. Whereas trends for hospitalizations between 2016 and 2019 were assessed by a linear-by-linear association test using discharge weights in SPSS v25 (IBM Corp., Armonk, NY, United States). We also performed a multivariable regression analysis for the association between CUD and MACCE along with ACM, AMI, CA, AIS. The factors adjusted for regression analysis are age, payer type, race, median household income, acquired immune deficiency syndrome, depression, chronic pulmonary disease, obesity, diabetes, hypertension, hyperlipidemia, peripheral vascular disease, cancer, prior stroke, and prior myocardial infarction. We considered a two-tailed *P* value of less than 0.05 as statistical significance.

RESULTS

From 2016 to 2019, we identified a total of 27.47 million United States nationwide hospitalizations among young patients (18-44 years) after excluding cases with a concurrent history of alcohol, tobacco, and cocaine use. Of which, 4.2% (1.1 million) patients had CUD (Figure 1). The median age at admission was consistently 28 years across the four years in CUD+ cohort, with interquartile ranges of 23 years to 44 years ($P < 0.001$) (Table 1). There was a statistically significant shift in the sex distribution among hospitalized individuals in CUD+ cohort, with male patients decreasing from 58.3% in 2016 to 55.5% in 2019 and female patients increasing correspondingly from 41.7% to 44.5%, resulting in an overall percentage of 56.8% for males and 43.2% for females ($P < 0.001$) (Table 1). Racially, White patients made up a slight majority each year, averaging 54.0% over the period, followed by Black patients and Hispanic patients, with the proportions of each group remaining relatively stable ($P <0.001$).

Socioeconomic data indicated significant disparities based on the median household income quartile for the patient's ZIP code, with the largest group falling within the 0-25th percentile each year ($P < 0.001$). In terms of healthcare coverage, a majority were covered by Medicaid, with little change year over year, averaging 51.2% (Table 1). Hospital location and teaching status also showed significant changes over time; the proportion of patients in urban teaching hospitals increased from 67.9% in 2016 to 75.9% in 2019 ($P < 0.001$), while rural and urban non-teaching hospitals saw a decrease from 24% to 16.3% (Table 1). Geographically, the South and Midwest regions were the most common hospital locations for these patients, with the South increasing from 34.3% in 2016 to 36.0% in 2019 in CUD+ cohort. Regarding comorbidities, there were statistically significant increases in hypertension (15.7% to 16.3%), diabetes (7.4% to 8.2%), hyperlipidemia (4.5% to 5.1%), and obesity (9% to 10.6%) over the four-year period ($P < 0.001$ for all) (Table 1). However, no significant change was observed in the incidence of prior myocardial infarction ($P = 0.187$) or cancer ($P = 0.147$). Notably, there was a significant but slight increase in the prevalence of prior stroke or transient ischemic attack (TIA) from 0.9% in 2016 to 1.0% in 2018 ($P = 0.004$) (Table 1).

The comparison of baseline characteristics and comorbidities between the CUD+ and CUD- cohorts is presented in Supplementary Table 1. Individuals in the CUD+ cohort were younger compared to those in the CUD- cohort, with a median age at admission of 28 years *vs* 31 years, respectively. Moreover, the CUD+ cohort had a higher proportion of males compared to the CUD- cohort (56.8% *vs* 21.6%), along with a higher representation of Black individuals (30.9% *vs* 19.5%) and individuals belonging to the lower income quartile (40% *vs* 30.6%) (Supplementary Table 1). In terms of comorbidities, the CUD+ cohort exhibited lower rates of diabetes (7.9% *vs* 9.5%), obesity (9.8% *vs* 14.3%), and hypothyroidism (2.4% *vs* 4.5%) compared to the CUD- cohort. Conversely, the rates of hypertension (16% *vs* 12.6%), hyperlipidemia (4.8% *vs* 4.3%), prior myocardial infarction (0.8% *vs* 0.5%), and depression (13.6% *vs* 7.1%) were higher in the CUD+ cohort compared to the CUD- cohort (Supplementary Table 1).

The frequency of admissions for MACCE (1.71% *vs* 1.35%), AMI (0.86% *vs* 0.54%), CA (0.27% *vs* 0.24%), and AIS (0.49% *vs* 0.35%) was higher in CUD+ group as compared to CUD- group ($P < 0.001$) (Figure 2). Interestingly, the frequency of ACM hospitalizations (0.30% *vs* 0.44%) was lower in CUD+ group compared to the CUD- group (Figure 2). From 2016 to 2019, the trends in hospitalizations for MACCE showed a greater relative increase among CUD- group (1.23% to 1.5%;

Table 1 Baseline characteristics of young adults hospitalized with cannabis use disorder in absence of concomitant tobacco/cocaine/alcohol use disorder (2016-2019)

		2016	2017	2018	2019	Overall	*P* value
Age at admission, median (interquartile range)		28 (23, 44)	28 (23, 44)	28 (23, 44)	28 (23, 44)	28 (23, 44)	< 0.001
Sex	Male	58.3	57.2	56.2	55.5	56.8	< 0.001
	Female	41.7	42.8	43.8	44.5	43.2	
Race	White	55.1	53.8	53.6	53.6	54.0	< 0.001
	Black	30.8	31.1	30.9	30.8	30.9	
	Hispanic	11.8	12.7	13.1	13.2	12.7	
	Asian/PI	1.1	1.3	1.3	1.3	1.3	
	Native American	1.2	1.0	1.1	1.1	1.1	
Median household income national quartile for patient ZIP code	0-25th	40.3	39.8	39.6	40.2	40.0	< 0.001
	26th-50th	25.1	26.5	27.1	25.6	26.1	
	51th-75th	20.9	20.2	20.1	20.9	20.5	
	76th-100th	13.7	13.5	13.2	13.3	13.4	
Payer type	Medicare	9.4	9.0	8.9	8.4	8.9	< 0.001
	Medicaid	50.6	51.9	51.6	50.6	51.2	
	Private	26.0	25.5	25.2	25.8	25.6	
	Self-pay	13.0	12.7	13.4	14.1	13.3	
	No charge	1.0	1.0	0.9	1.0	1.0	
Hospital location and teaching status	Rural	8.1	8.0	7.8	7.7	7.9	< 0.001
	Urban nonteaching	24.0	20.6	18.7	16.3	19.8	
	Urban teaching	67.9	71.5	73.5	75.9	72.3	
Hospital region	Northeast	18.6	18.7	18.6	17.6	18.4	< 0.001
	Midwest	25.1	25.4	24.6	24.6	24.9	
	South	34.3	33.4	34.3	36.0	34.5	
	West	22.1	22.5	22.5	21.8	22.2	
Comorbidities							
Hypertension		15.7	15.9	16.2	16.3	16.0	< 0.001
Diabetes		7.4	8.0	7.9	8.2	7.9	< 0.001
Hyperlipidemia		4.5	4.7	4.8	5.1	4.8	< 0.001
Obesity		9.0	9.7	10.0	10.6	9.8	< 0.001
Peripheral vascular disease		0.7	0.7	0.7	0.8	0.7	< 0.001
Prior MI		0.8	0.8	0.8	0.8	0.8	0.187
Prio stroke/transient ischemic attack		0.9	0.9	1.0	0.9	0.9	0.004
Chronic pulmonary disease		12.7	13.1	12.8	12.9	12.9	< 0.001
Hypothyroidism		2.4	2.3	2.3	2.5	2.4	0.001
Other thyroid disorders		0.6	0.7	0.7	0.8	0.7	< 0.001
Valvular heart disease		0.3	0.3	0.3	0.3	0.3	0.054
Cancer		1.0	1.0	1.0	1.0	1.0	0.147

$P < 0.05$ indicate statistical significance. MI: Myocardial infarction.

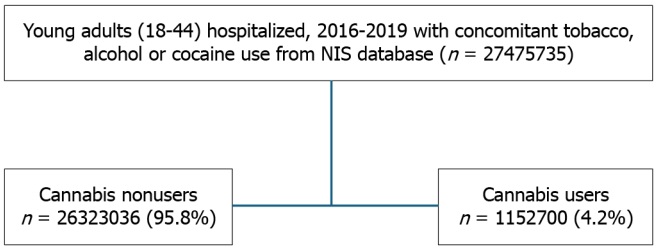

Figure 1 Flowchart showing the inclusion data for the analysis.

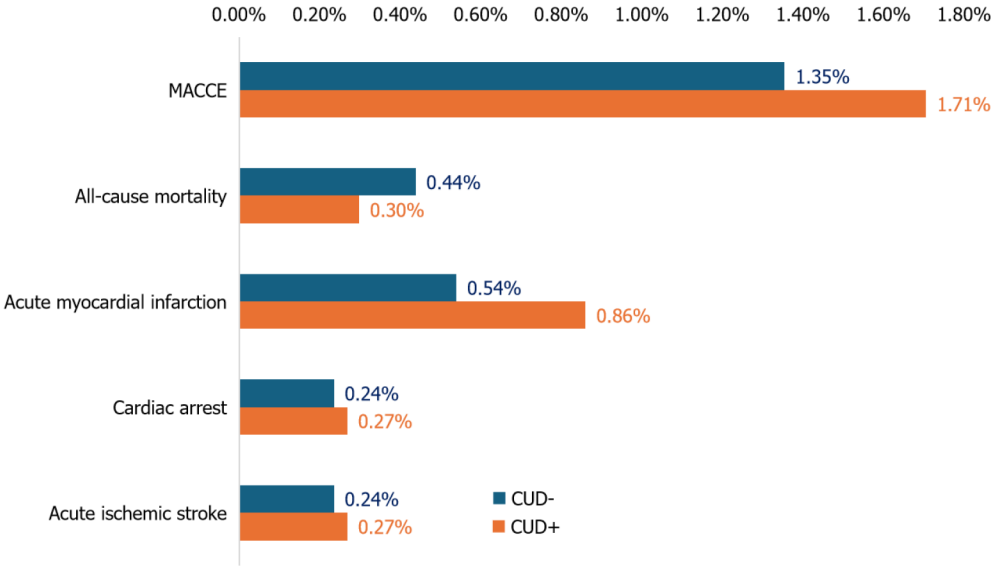

Figure 2 Frequency of major adverse cardiac and cerebrovascular events in young (18-44 years) cannabis users (1152700) *vs* non-users (26323036). Pearson's χ^2 test and Kruskal Wallis test are used to analyze the categorical and continuous variables. CUD: Cannabis use disorder; MACCE: Major adverse cardiac and cerebrovascular events.

22% relative increase, $P < 0.001$) as compared to CUD+ group (1.67% to 1.75%; 4.7% relative increase, $P = 0.018$) (Figure 3). The trends in AMI hospitalizations showed a significant relative increase among the CUD- group (0.47% to 0.64%; 36% relative increase, $P < 0.001$) as compared to CUD+ group (0.79% to 0.95%; 20% relative increase, $P < 0.001$). Surprisingly, trends in ACM showed a relative increase among the CUD- group (0.42% to 0.46%; 10% relative increase, $P < 0.001$), while the CUD+ group showed a relative decrease in ACM hospitalizations (0.32% to 0.28%; 13% relative decrease, $P = 0.043$) (Figure 3). However, trends in CA and AIS hospitalizations did not show a significant change in CUD+ group from 2016 to 2019, while the CUD- group exhibited a 11% (0.22% to 0.25%, $P < 0.001$) and 13% (0.3% to 0.4%, $P < 0.001$) relative increase in CA and AIS respectively. An age-specific analysis was conducted by stratifying the population into narrower age groups (18-24, 25-29, 30-34, 35-44), revealing a progressive increase in rates of MACCE, ACM, AMI, CA, and AIS with advancing age (Supplementary Figure 1). However, the trends in MACCE across the four-year period from 2016 to 2019 did not display significant variations across all age groups (Supplementary Figure 2).

A multivariable regression analysis did not show a significant association between cannabis use and MACCE in this population [odds ratio (OR): 1.00, 95%CI: 0.96-1.03, $P = 0.818$] (Table 2). Similarly, there was no significant association observed for ACM (OR: 0.98, 95%CI: 0.91-1.06, $P = 0.623$), AMI (OR: 1.04, 95%CI: 1.00-1.09, $P = 0.077$), CA (OR: 0.96, 95%CI: 0.88-1.03, $P = 0.252$), and AIS (OR: 0.97, 95%CI: 0.92-1.03, $P = 0.332$) (Table 2).

DISCUSSION

In recent years, recreational cannabis use among young adults has significantly increased with changing legal policies and its widespread availability. As we see this rise in cannabis consumption, there is a need to pay attention to its impact on health, particularly cardiovascular health. In this study, we examined the rates and trends of MACCE in young hospitalized adults with CUD in the absence of concomitant tobacco, alcohol, or cocaine use from 2016 to 2019. We observed that rates of MACCE (1.71% *vs* 1.35%) were higher in cannabis users than non-users. The trends in MACCE hospitalizations among cannabis users had a 5% relative increase from 2016-2019, which is consistent with a previous study that reported increasing trends in MACCE among CUD+ during 2010-2014[8]. It is imperative to consider the neurobiological underpinnings that may predispose this population to both increased health risks and the sustenance of CUD. The

Table 2 Multivariable analysis of major adverse cardiac and cerebrovascular events-related admissions in young adults with dependent cannabis use in the absence of concomitant tobacco, alcohol, or cocaine use disorder with calendar year 2016-2019

In hospital outcomes	Odds ratio	Lower 95%CI	Upper 95%CI	*P* value
Major adverse cardiac and cerebrovascular events	1	0.96	1.03	0.818
All-cause mortality	0.98	0.91	1.06	0.623
Acute myocardial infarction	1.04	1	1.09	0.077
Cerebral vascular	0.96	0.88	1.03	0.252
Acute ischemic stroke	0.97	0.92	1.03	0.332

Multivariable analysis was adjusted for factors like age, payer type, race, median household income, acquired immune deficiency syndrome, depression, chronic pulmonary disease, obesity, diabetes mellitus, hypertension, hepatolenticular degeneration, peripheral vascular disease, cancer, prior stroke/transient ischemic attack, prior myocardial infarction. $P < 0.05$ considered significant.

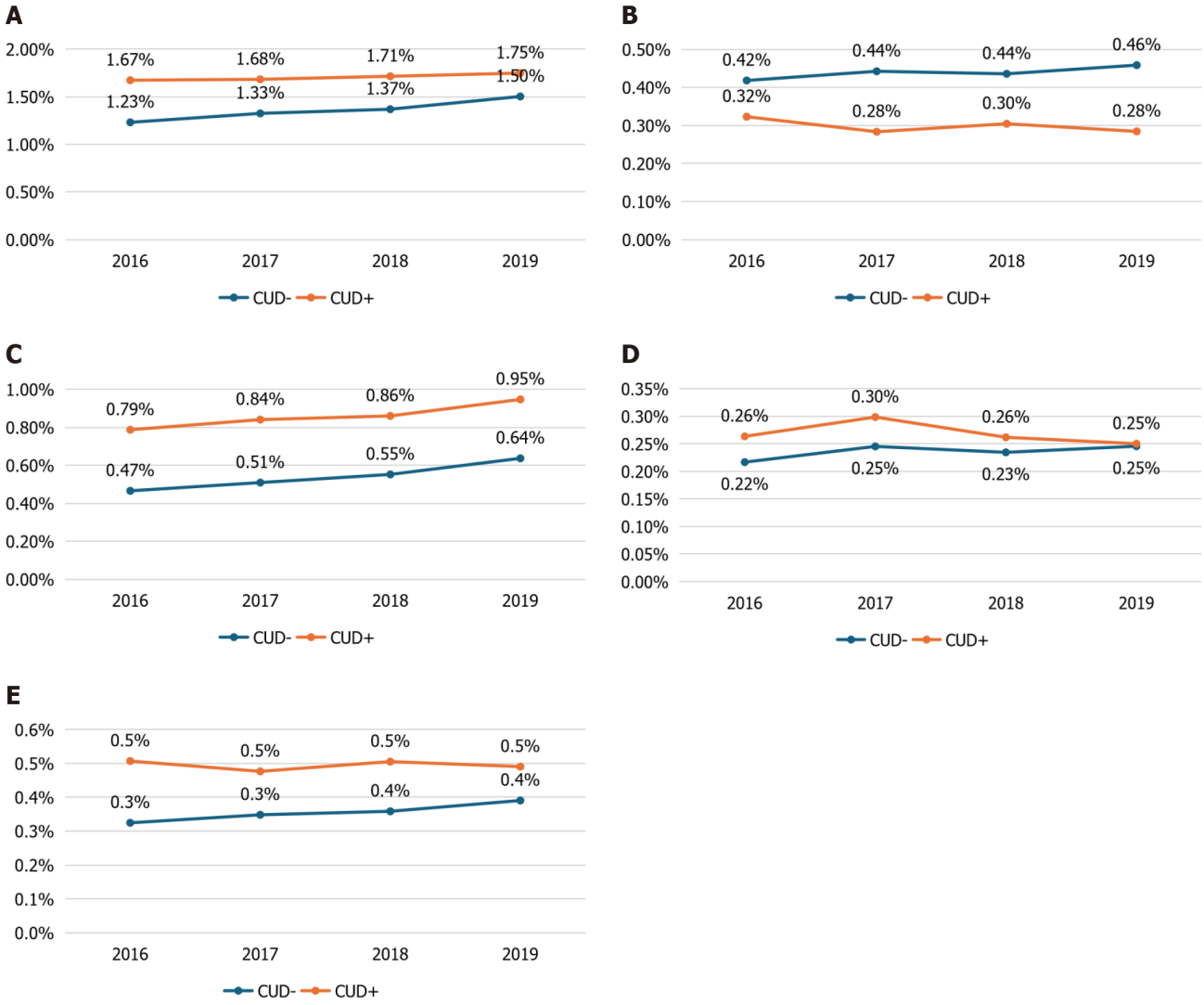

Figure 3 Trends in hospitalizations for major cardiovascular and cerebrovascular events among cannabis users vs. non-users of age 18-44 years, excluding cases with concomitant substance abuse (Alcohol, tobacco, and cocaine) from 2016-2019. A: Trends in hospitalizations for major adverse cardiac and cerebrovascular events; B: Trends in hospitalizations for all-cause mortality; C: Trends in hospitalizations for acute myocardial infarction; D: Trends in hospitalizations for cardiac arrest; E: Trends in hospitalizations for stroke. CUD: Cannabis use disorder.

process of myelination in the brain, wherein a protective layer forms around axons to expedite nerve impulse transmission, is critical for neural efficiency and functionality. Notably, young brains, particularly those under 25 years of age, have not yet achieved complete myelination, rendering them more susceptible to the influences of external substances. This developmental stage is crucial because neurons that are simultaneously active tend to forge stronger connections, adhering to the principle that "cells that fire together wire together"[9]. This mechanism is thought to underlie the formation of addiction pathways; hence, repeated cannabis use during this formative period can result in myelination patterns that inadvertently promote and sustain cannabis addiction. This neurobiological perspective provides a plausible explanation for the observed phenomenon that individuals initiating cannabis use before the age of 18 years are significantly more likely to develop a CUD compared to those who start in adulthood. Understanding these mechanisms is essential for interpreting the trends observed in our research.

Cannabinoid-1 receptors are mainly located in the cardiovascular system, the central nervous system, and peripheral vasculature, play a critical role in mediating the cardiovascular effects of THC[10]. Acute exposure to THC leads to a dose-dependent rise in blood pressure and heart rate, a reaction to which cannabis users may quickly develop tolerance, often resulting in the consumption of higher doses more frequently. Such increased usage has been linked to a higher incidence of cardiac arrhythmias and myocardial infarction[10]. Additionally, long-term THC use is associated with a more frequent occurrence of angina, potentially due to lowered angina thresholds and compromised autonomic nervous system functioning. This includes reduced efficiency in sympathetic and parasympathetic nervous system signaling, increased levels of serum aldosterone, and both central and peripheral vasoconstriction, culminating in hypertension[10]. Low to moderate doses lead to increased heart rate and blood pressure due to increased sympathetic activity. In contrast, high doses or chronic use cause decreased heart rate and blood pressure by increasing parasympathetic activity[11]. In our study, the prevalence of AMI was higher (0.86% *vs* 0.54%) among cannabis users as compared to non-users, and the trends in AMI hospitalizations among cannabis users had increased by 22% from 2016 to 2019. These findings align with previous studies that indicate cannabis use is associated with an increased prevalence of AMI, particularly among younger age groups[12]. Furthermore, AMI-related hospitalizations have seen a rise in cannabis users, even after accounting for confounding factors such as tobacco, alcohol, and other stimulant drug abuse[13]. It leads to dose-dependent changes in heart rate and blood pressure in most individuals. Moreover, CUD leads to higher levels of carboxyhemoglobin, which reduces the blood's ability to carry oxygen[14]. It also promotes platelet aggregation and activates factor VII, which can potentially contribute to blood clot formation. These changes may trigger an AMI by increasing the myocardial oxygen demand while decreasing its supply[14].

Another finding is that the prevalence of AIS was higher in cannabis users than non-users. Many recent studies also reported that cannabis use is associated with a higher prevalence of stroke even after adjusting for confounding factors like tobacco smoking[15]. Heavy cannabis users in the general community also have a higher rate of AIS, particularly among the young, with nearly three times the odds compared to non-users[16]. A prospective study by Wolff *et al*[17] revealed that cannabis use was associated with multifocal intracranial angiopathy leading to ischemic stroke in young individuals. Possible mechanisms for cannabis-induced stroke were abnormal blood flow regulation through sympathetic activity inhibition, symptomatic cerebral vasospasm, and embolism from cardiac arrhythmias[18]. In the central nervous system, THC has been observed to enhance cerebral vasculature tone and elevate central blood pressure, subsequently leading to a reduction in cerebrovascular blood flow. This diminished flow is linked to a heightened risk of cerebral vascular accidents (CVA) and TIAs, indicating a relationship between TIAs and a reversible impact of cannabis on cerebrovascular health, potentially due to temporary vasospasm and/or increased central blood pressure reducing cerebral circulation[10]. Additionally, it has been proposed that cannabis usage could elevate CVA risk in individuals predisposed to cardiovascular disease, regardless of secondary prevention with the use of anti-platelet drugs[10].

We also found that the rates of cerebral vascular (CA)-related admissions were marginally higher among cannabis users than non-users. There were reported cases of CA after cannabis use[19,20] and a few reported cases associated with synthetic cannabinoid use[21,22]. Cannabis might cause an increase in parasympathetic tone and activity, causing a sudden asystolic arrest, which may lead to sudden cardiac death[23]. The other plausible mechanistic links could be due to several interconnected mechanisms. Cannabis use may induce a sympathetic predominance, contributing to arrhythmias and blood pressure variability, thereby exerting additional strain on the cardiovascular system, especially in individuals with pre-existing cardiac conditions. Additionally, it may also trigger myocardial infarction by causing either significant coronary vasospasm or endothelial dysfunction. These factors, alone or in combination, can result in a higher risk of CA among CUD patients.

An interesting finding of this study is that cannabis users had lower rates of ACM (0.30% *vs* 0.44%) compared to non-users. Additionally, there was a decreasing trend in admissions for ACM among cannabis users from 2016 to 2019. Mixed results were reported on this association in the previous studies. Some have reported that cannabis use was associated with lower rates of ACM[24,25], while a few have reported that ACM was higher among young cannabis users hospitalized for AMI[8]. This can be partly attributed to the fact that cannabis users are often younger, male, and African American, with a reduced incidence of cardiovascular risk factors[26]. They have lower total cholesterol, reduced lipid accumulation, weight loss, and improved glycemic control[27]. The physiological effects of cannabinoids have been associated with metabolic processes, as evidenced by a lower prevalence of obesity and diabetes mellitus among marijuana users. Specifically, there is a correlation between cannabis use and lower waist circumference, and body mass index[28,29]. These findings imply that cannabis' anti-inflammatory properties might help reduce the risk factors linked to cardiovascular diseases. Additionally, medical cannabis has shown promise in reducing opioid usage for chronic pain management, resulting in improved quality of life and potentially contributing to lower mortality rates associated with opioid overdose[30]. These factors appear to influence cannabis beneficial association with ACM.

Although our study observed higher rates of MACCE, AMI, CA, and AIS among young adults with CUD, the multivariable analysis revealed no significant association between CUD and these outcomes. This indicates that the observed differences in rates between CUD+ cohorts and CUD- cohorts may be attributed to confounding factors such as age, socioeconomic status, or comorbidities. After adjusting for these confounders, cannabis by itself did not emerge as a significant risk factor for MACCE-related admissions.

Treatment for CUD primarily focuses on psychosocial interventions, with cognitive-behavioral therapy (CBT) and motivational enhancement therapy (MET) standing out for their evidence-based efficacy[31]. CBT, recommended as the first-line treatment, targets the identification and management of thoughts, behaviors, and triggers related to substance use, and has been shown to significantly reduce cannabis use among patients. Similarly, MET emphasizes building motivation for treatment and abstinence, showing comparable effectiveness to CBT. Brief interventions may be beneficial, particularly for adolescents and young adults identified outside healthcare settings, involving one to two short sessions of motivational enhancement techniques, though their long-term efficacy remains uncertain[31]. For those seeking treatment, psychosocial approaches are preferred over medication due to stronger evidence of success, with treatments doubling the likelihood of abstinence at follow-up compared to no treatment, although long-term abstinence rates are generally low. Monitoring treatment progress is critical, with weekly checks initially recommended, adjusting based on patient stability and progress. If initial responses to CBT or MET are insufficient, combining these therapies or incorporating contingency management, which uses incentives to promote abstinence, may enhance outcomes[31].

This study has a few limitations. First, the study design is observational, which means causality cannot be established. Despite efforts to exclude concomitant substance abuse and adjusting cardiovascular risk factors in multivariable regression analysis, it is challenging to determine if the higher rates of MACCE in the CUD+ group could still be influenced by other residual confounding factors as with any retrospective study. Second, the study lacks detailed information on the extent and frequency of cannabis use among the participants. This limits the ability to explore potential dose-response relationships and fully understand the impact of different patterns of cannabis consumption on MACCE. Third, the study analyzes trends over a limited timeframe (2016-2019). Long-term data and follow-up would provide a more comprehensive understanding of the relationship between cannabis use and MACCE. Literature reporting CA after cannabis use was limited to case reports/series and warrant more prospective studies to compare the independent association of CUD with CA in absence of other concomitant substance abuse. Lastly, we could not take into account the impact of medication history, other laboratory parameters, and follow-up data while performing this study, and this limitation warrants more longitudinal prospective studies. Despite these limitations, it is essential to underscore the significance of this study as it examines the trends of MACCE among hospitalized young adults within the CUD group compared to their non-CUD counterparts, distinctly in the absence of other simultaneous substance abuse. The focus on young adults is particularly pertinent, given their susceptibility to developing addictive behaviors, which could adversely impact cardiovascular and metabolic health over the long term. This foundational work not only fills a critical gap in the literature but also sets the stage for future research, guiding healthcare strategies aimed at mitigating the cardiovascular risks associated with cannabis use among young adults.

Future directions

Moving forward, the findings from this study emphasize the need for informed policy-making, especially given the increasing recreational use of cannabis among young adults. There's a pressing demand to integrate these insights into legislative discussions, ensuring safer recreational practices. Healthcare systems should allocate resources towards targeted interventions, like early screening for high-risk young adults with polysubstance abuse histories. Public awareness campaigns can further enlighten both professionals and the public about the cardiovascular risks tied to cannabis use, especially when combined with other substances. Tailored preventative care like comprehensive risk assessments and lifestyle counseling for identified high-risk groups, coupled with longitudinal studies, can provide deeper insights into the long-term effects of cannabis on cardiovascular health.

CONCLUSION

Our study revealed higher rates and growing trends in hospitalizations for MACCE, including AMI, CA, and stroke, from 2016-2019 among young adults with CUD in the absence of concurrent substance abuse. Interestingly, hospitalized cannabis users had lower rates and showed a decreasing trend for ACM during this study period. However, our multivariable analysis did not find a significant association between cannabis use and these outcomes after adjusting for confounding factors. This suggests that the observed differences in rates between CUD+ cohorts and CUD- cohorts may be influenced by factors such as age, socioeconomic status, or comorbidities rather than cannabis use alone. However, it is crucial to recognize that cannabis may still pose cardiovascular health risks through other pathways, such as its potential to increase sympathetic activity and alter hemodynamic parameters. Therefore, comprehensive risk assessment and tailored interventions are warranted for individuals with CUD to mitigate potential cardiovascular risks effectively. These findings call for long-term and comprehensive studies to explore dose-response relationships, the impact of different cannabis products, and their interaction with other risk factors. Furthermore, our findings highlight the importance of continued research to unravel the complex interplay between cannabis use and cardiovascular health outcomes in this population. By understanding these dynamics, healthcare professionals can better address the evolving landscape of cannabis use and its implications for public health and clinical practice.

FOOTNOTES

Author contributions: Desai R was responsible for conceptualization, methodology, software, formal analysis, resources, data curation, and project administration; Gurram P, Mohammad AS, Salian RB, Lingamsetty SSP, Guntuku S, Medarametla RVSK, Muslehuddin Z, Ghantasala P, and Jahan P were responsible for writing, original draft; Desai R, Gurram P, Mohammad AS, and Ghantasala P were responsible for writing, original draft, writing, review, editing, and visualization; all authors contributed to the article and approved the submitted version.

Institutional review board statement: This manuscript is exempt from Institutional Review Board Approval Form or Document since National Inpatient Sample database was used to draw specific patient samples. The National (Nationwide) Inpatient Sample (NIS) is part of a family of databases and software tools developed for the Healthcare Cost and Utilization Project (HCUP). The NIS is the largest publicly available all-payer inpatient healthcare database designed to produce U.S. regional and national estimates of inpatient utilization, access, cost, quality, and outcomes. Unweighted, it contains data from around 7 million hospital stays each year. Weighted, it estimates around 35 million hospitalizations nationally. Developed through a Federal-State-Industry partnership sponsored by the Agency for Healthcare Research and Quality (AHRQ), HCUP data inform decision making at the national, State, and community levels.

Informed consent statement: Consent from patient was not needed as the data used has unidentified information.

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