

# An Urgent Call for Studies That Address the Cardiovascular Consequences of Legalization of Marijuana

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## Abstract

In about a decade, half of the United States has legalized marijuana for recreational use. The drug has been associated with acute myocardial infarction, acute stroke, congestive heart failure, and various cardiac arrhythmias. Data have shown that legalization of the drug led to an increase of its use as well as an increase in tetra hydro cannabinoid positive tests in patients admitted to emergency departments. In Colorado, one of the earlier states to implement legalization, there was an increase in traffic accidents, suicide rates, and even total mortality. However, there is a paucity of data on the effect of marijuana legalization on various cardiovascular events. It is prudent to have well-designed studies with enough power to provide consumers and health care providers the information they need to decide whether the risks of marijuana, especially on the cardiovascular front, are worth the “high” or potential benefits that have been described for other medical conditions.

**Keywords:** Marijuana; Legalization; Cardiovascular events

## Introduction

Marijuana is an old drug. The first documentation of its use was during the time of the ancient Chinese emperors and the civilization of the Egyptian pharaohs [1]. Of particular interest are the discussions about the medicinal values and the healing powers of the drug [2]. The first state in the United States (USA) to legalize marijuana in 1996 was California, for its potential medicinal value. Now, over 25 years later, 38 other states in the USA have legalized marijuana for medical use,

and 24 states have legalized it for recreational use, without substantial studies looking at the safety of the drug. It is true that marijuana has an established clinical benefit such as improvements in neuropathic pain, beneficial effects in patients with multiple sclerosis, epilepsy, improving appetite and reducing nausea and vomiting related to chemotherapeutic agents for cancer, as well as others [3]. It also may have increased risk in some patients. Therefore, it is prudent to establish a clear understanding of the risk/benefit ratio.

## Background

As early as 1972, it was described that marijuana smoking led to acceleration of pulse rate and changes in regional blood flow, as well as electrocardiographic abnormalities [4]. Our own interest in this drug started in 2003. We reported a 34-year-old man who used marijuana daily for years. He presented to us with syncope and sustained ventricular tachycardia. Workup showed normal coronary arteries with the no-reflow phenomenon and inducible ventricular tachycardia. After stopping the marijuana use, repeat angiography showed normal coronary flow, and on repeat electrophysiologic testing, ventricular tachycardia was no longer inducible [5].

We, and others, reported strong signals for increased cardiac events temporarily related to marijuana use [6-8]. Despite this, and with a lack of safety studies, the tide of legalizing marijuana for recreational use increased to now a total of 24 states. With an increase in the number of states that have legalized marijuana and the increase in availability of the drug in general, combined with the widespread belief that its use is generally safe, there has been an increase in marijuana use. Using the nationwide inpatient sample database, there were 819,175 hospitalizations of acute myocardial infarction between 2007 to 2018 [9]. The sample studied was in younger patients (18 - 49 years of age). Of these patients, 28% admitted to cannabis use. There was also an increase in the incidence of myocardial infarction among young adults who used cannabis from 2.36% in 2007 to 6.55% in the year 2018. The incidence was higher in males as well as in African Americans. In another study, Shah et al studied marijuana users in the behavioral risk factor surveillance system for the years 2016 - 2018 [10]. Marijuana use was associated with a 2.3% increase in the incidence of both coronary artery disease and myocardial infarction. Phillips et al studied cannabis users in 275 patients and compared them with matched non-user controls in the state of Hawaii [11]. Cannabis users had

Manuscript submitted March 20, 2024, accepted April 25, 2024  
Published online April 15, 2024

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doi: <https://doi.org/10.14740/cr1641>

a statistically significant increase in health care admissions to both inpatient and outpatient services, as well as an increase in the incidence of myocardial infarction and other cardiovascular events. Other epidemiologic studies have shown an increase in the incidence of acute ischemic strokes [12] and cardiac arrhythmias [13] in cannabis users. The drug was also an independent predictor of congestive heart failure in the National Inpatient Sample that included a database of patients ages 18 - 55 years [14]. A recent study confirmed this finding [14]. Dhillon et al [15] studied 7,780 young women with congestive heart failure; 5.5% were cannabis users. Cannabis users reported a higher prevalence of ventricular tachycardia and paroxysmal atrial fibrillation. However, in another study there was no clear increase in the incidence of emergency department visits with acute myocardial infarction in the states that legalized marijuana [3]. With other studies showing an increase in cardiovascular events, including myocardial infarction and stroke, is there any epidemiologic evidence that it may result in increased mortality?

Sun et al studied 86,453 person-years of observations of adults aged 20 - 59 years old from 2005 to 2014 [16]. In this study, cannabis use was significantly associated with 2-3% increased mortality, particularly in the younger age group. The same pattern was noted in the older age group, with an increase in cardiovascular mortality in both men and women [17]. Thus, many studies have indicated an increase in cardiovascular events, and some indicated an increase in mortality, in people who use marijuana. An important question is, did legalization of marijuana in any states cause an increase in cardiovascular events and/or mortality?

## Review

### Effect of marijuana legalization

With marijuana as the most commonly abused drug, and with its known complications, it is expected that legalization of marijuana may increase such complications [18]. One clear effect of marijuana legalizations is the increase in traffic accidents, similar to the increase in accidents when people drive under the influence of alcohol. In the report of the Rocky Mountain High Intensity Drug Trafficking Areas (RMHIDTA) program [19], the legalization of marijuana led to an increase in the number of drivers who tested positive for marijuana. That was also associated with an increase in Colorado traffic deaths by 29%. The increase was also progressive with the number of years of legalization. Traffic deaths included drivers, passengers, even bicyclists. In the same published report, there was a progressive increase in the number of suicides per year with a positive toxicologic test for marijuana. In a detailed review by Farrelly et al, there was a clear relation between marijuana legalization and an increase in traffic accidents [20].

Another clear effect of marijuana legalization was an increase of marijuana positive blood or urine testing in most states that legalized marijuana [21]. A relationship, however, between marijuana positive testing and the presenting emer-

gency department clinical event was not studied in this report.

To determine whether marijuana legalization in the state of Colorado affected the incidence of cardiovascular events, Jeffers et al [22] utilized the State Inpatient Database (SID) in Colorado to examine the incidence of all causes of hospitalizations. They reviewed hospitalizations for acute cardiovascular events between the years 2008 through 2015. There was no increase in cardiovascular hospital admissions during this period. The study was presented in abstract form, but to the best of our knowledge, it has not yet appeared as a full-length paper in a peer-reviewed manuscript. A scientific statement published by the American Heart Association extensively reviewed the effects of marijuana on the cardiovascular system [3]. A few papers show an increase in the use of marijuana in patients presenting to emergency departments following legalization [23]. Tolan et al [23] reported the incidence of immunoassay for tetra hydro cannabinoid in the state of Massachusetts for patients admitted to emergency departments. They examined the effect of marijuana legalization on the incidence of cannabis users admitted to emergency departments. There was an increase of 7% with positive immunoassay test following legalization (2012 - 2019.) The legalization of marijuana resulted in an increase in both children and adults being seen in emergency departments with cannabis use. The main reason for the presentation was either trauma from accidents or various mental and physical complaints following the drug use [24, 25]. With the increase in signals for cardiovascular events following marijuana use, there is a paucity of data about the effect of legalization on cardiovascular events. With the active lobbying for cannabis legalization, policy makers must be aware of this potential problem [17].

## Conclusions

There is a compelling need to have a well-designed study, with enough power, to give our society a clear answer to this question. There is an urgent need for organizations such as the National Institutes of Health (NIH) and other federal and state agencies to fund definitive studies that answer the question of whether legalization of marijuana has increased major adverse cardiovascular events in states that have legalized the substance for medical use, recreational use, or both. There is also an urgent need to educate the public consumer as well as the health care provider about the potential cardiovascular adverse events that may be associated with marijuana use.

## Acknowledgments

The authors acknowledge the assistance of Marie Fleisner in preparing this manuscript for submission.

## Financial Disclosure

None to declare.

## Conflict of Interest

None to declare.

## Informed Consent

Not applicable.

## Author Contributions

Both authors contributed equally to this manuscript. Shereif Rezkalla performed the initial literature search and wrote the initial draft. Robert Kloner critically reviewed the paper and provided additional references. Both authors approve the final manuscript and its submission.

## Data Availability

The authors declare that data supporting the findings of this study are available within the article.

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