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Emerging Issues for our Nation's Health: The Intersection of Marijuana Use and Cardiometabolic Disease Risk

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Abstract

Current marijuana use rates are the highest in the past decade and not likely to decrease given the legalization of marijuana for medicinal and/or recreational use. Concurrently, the nation is facing epidemic levels of obesity, cardiovascular disease and diabetes but little is known about the intersecting relationships of marijuana use and cardiometabolic health. The objective of this study was to explore emerging issues in context to the intersection of cardiometabolic risk and marijuana use. This topic has potential important implications for our nation's health as we relax our approach to marijuana but continue to have unacceptable rates of cardiometabolic illnesses.

Keywords

Cannabis; Marijuana; Cardiometabolic Risk; Obesity; Diabetes

INTRODUCTION

Marijuana (cannabis) use rates in the United States is reportedly the highest seen in the past decade^{1, 2} and the prevalence is not likely to decrease given the legalization of marijuana use for both medicinal and recreational use in various states^{3–5}. In 2012, current marijuana use was reported in 8 percent of the US population (18.9 million) and by 79% of current illicit drug users. These figures represent a 5 million user increase in just the past 5 years^{2, 6}. The

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World Health Organization lists cannabis as the most widely cultivated and abused illicit drug in the world indicating that its use is not unique to the United States⁷.

Concurrent with the increasing use of marijuana are the current unrelenting epidemics of cardiovascular disease, diabetes, and obesity^{2, 8}. One third of our nation's adult population currently lives with at least one type of cardiovascular disease⁹, 80 million have pre-diabetes, and 26 million have diabetes¹⁰. The World Health Organization estimates that about 82% of the United States population will be overweight (Body Mass Index ≥ 25 kg/m²) by the year 2015¹¹. Modifiable risk factors for both cardiovascular disease and type 2 diabetes, often referred to cardiometabolic disease when occurring simultaneously, include low high-density lipoprotein cholesterol levels, elevated low-density lipoprotein cholesterol, triglycerides, highly sensitive c-reactive protein, and waist circumference, dyslipidemia, insulin resistance, hypertension, and obesity^{12–15, 16}.

The relationship between marijuana use and these current cardiometabolic health challenges in the US population have been broached but not determined. Diabetic patients who reported use of alcohol, illicit drugs, or a combination of both have been found to have an earlier onset of type 2 diabetes mellitus compared to nonusers of alcohol/illicit drugs¹⁶. A study published in 2012¹⁷ found decreased prevalence of diabetes in 20-to-59 year-old current marijuana users; however, the study analyzed National Health and Nutrition Examination Survey III (1988–1994) data before the increased prevalence of current marijuana use shown in recent findings^{1, 2}.

Due to a combination of the striking increase in marijuana use and the rising prevalence of diabetes and cardiovascular disease in the United States over the past decade, our objective was to identify emerging issues of cardiometabolic risk surrounding marijuana use within literature published during this same time period.

Marijuana Use in United States

Cannabis is the most widely used illicit drug in the United States^{18–20}. This may be partially attributed to the general perception that it is the least harmful when compared to other illicit drugs such as cocaine and heroin^{21, 22}. However, the long term effects of marijuana and the trajectory of its use over the lifespan as a gateway into “hard” or illicit drug use later in life is unclear²¹. According to the National Institute of Drug Abuse's Monitoring the Future survey, marijuana use and accessibility among youth is the highest reported in the last decade; yet, perceived risk of marijuana use is at the lowest¹⁸. According to the 2012 National Survey on Drug Use and Health, emerging adults (aged 18-to-25-years) reported the highest current use of marijuana. Adults over 26 years of age reported marijuana use as most frequently used drug compared to other illicit drugs. In older adults aged 50+ years, the highest increase in reported current marijuana use was among 55-to-59-year-olds. The proportion of current use has tripled in the past decade in this age group². These trends present evidence of a growing prevalence of marijuana use and need to study long term effects since its use is not likely to stop in the near future.

Cardiometabolic Risk in United States

Cardiometabolic risk factors include a number of cardiovascular and metabolic abnormalities that can ultimately lead to overt cardiovascular disease and diabetes^{23–25}. These risk factors include low high-density lipoprotein cholesterol level, elevated low-density lipoprotein cholesterol, highly sensitive c-reactive protein, waist circumference, total cholesterol, body mass index (BMI), systolic and diastolic blood pressure, triglycerides, fasting glucose and insulin levels, and tobacco smoking^{12–15}. Independently, the risk factors pose a set of negative health related outcomes, but when presented in a cluster, the outcomes become more severe. Moreover, those with the metabolic syndrome, a clustering of several of these factors (elevated systolic and/or diastolic blood pressure, fasting glucose, lipids and central adiposity)¹³ have a significantly increased risk of stroke, coronary heart disease, and myocardial infarction^{23, 26, 27}. The International Diabetes Federation^{12, 28}, National Cholesterol Education Program Adult Treatment Panel III²⁹, and World Health Organization¹⁴ have created criteria to define adults with the metabolic syndrome (Table 1); yet a consensus has not been made regarding exact cutoff values of risks that define metabolic syndrome in adolescents.

Comparison of the National Health and Nutrition Examination Survey III (1988–1994) versus 1999–2006 showed that approximately 34% of the United States adult population currently has the metabolic syndrome, which represents a 22.6% increase in roughly one decade. Even more alarming was the finding that the largest increase in prevalence was among 20-to-39-year-olds in both males and females³⁰. Other studies have reported that those with the metabolic syndrome have a 78% increased risk for cardiovascular disease events and death versus those without the syndrome^{27, 31}. Not surprisingly, several studies have reported that the presence of the metabolic syndrome is a strong predictor of both type 2 diabetes and cardiovascular disease^{28,32}.

Cardiometabolic Risk among Marijuana Users

Evidence suggests increased marijuana use and increased cardiometabolic risk independently; however, little research has been published identifying prevalence or trends of metabolic syndrome or cardiometabolic risk among previous or current marijuana users in the United States.^{32, 33} Physical inactivity and high-carbohydrate diets have been found to lead to an increased risk for the metabolic syndrome^{15, 34}. Studies dating back to the late 1970's have reported that marijuana use increases appetite and food intake^{35–38} with a significant increase in total calories and snack food intake high in carbohydrates^{36, 39, 40}. Though the reported increase in caloric intake has been documented, a consensus has not been reached regarding the effects on cardiometabolic risk factors.

Obesity—The majority of published findings regarding cardiometabolic health-related consequences of marijuana use have been centered upon exploring associations between obesity as measured by BMI. The association between marijuana use and BMI is not clear. For example, no significant association was found in a study by Rodondi et al. (2006)³⁸, but an increase in BMI among those who report marijuana use was found by others^{41, 42}. The most common finding among the limited published data indicates lower BMI among current marijuana users^{40, 43–46}. Since excess weight has been described increased cardiometabolic

risk factors such as hypertension, insulin resistance, type 2 diabetes, and dyslipidemia⁴⁷, the weight status of marijuana users is of health significance.

While some studies reported lower BMI in current users, others such as Huang et al. (2013) suggest there may be a dose-response relationship⁴². Huang et al. (2013) conducted a study among adolescents and found that those with an increasing pattern of marijuana use were at a greater risk of becoming obese in young adulthood compared to non-marijuana users. Infrequent users were at a lower risk of obesity than non-users. They concluded that the risk of obesity increases with a consistent marijuana use pattern over time⁴². Despite studies published on association, evidence of a causal relationship between marijuana use and obesity is limited. .

Studies of the association between marijuana use and waist circumference are limited. Rodondi et al. (2006)³⁸ reported a higher waist circumference among marijuana users than in nonusers in unadjusted analyses. Such association disappeared in analyses adjusted for age, gender, race, study center, tobacco use, amount of alcohol per day, other illicit drug use (cocaine, crack, heroin, amphetamine), daily physical activity, physical fitness, education, income levels, BMI, and baseline level of waist circumference³⁸. Penner et al. (2013)⁴⁸ reported lower waist circumference among current marijuana users compared to those who never reported use; however, the study did not use gender-specific waist circumference values. This may be a limitation since abnormal waist circumference cut-off values that define cardiometabolic risk differ between males and females.^{12, 13}

Glucose and Insulin—Associations between habitual marijuana use and insulin resistance, fasting glucose and insulin were evaluated in a recent analysis of 2005–2010 National Health and Nutrition Examination Survey data⁴⁸. The study reported decreased fasting insulin and glucose, BMI, and the homeostasis model assessment of insulin resistance (HOMA-IR, a method used to quantify insulin resistance and beta-cell function) in current marijuana users compared to lifetime nonusers. In an analysis of the National Health and Nutrition Examination Survey III data (1988–1994), current marijuana users aged 20-to-59 years had lower prevalence of diabetes compared to noncurrent marijuana users¹⁷.

Cardiovascular Implications—The majority of studies that discuss the physical health effects of marijuana describe cardiovascular implications. Several reported increased heart rate, cardiac output, and blood pressure after marijuana use^{41, 49–55}; and have advised that patients with high risk to cardiovascular disease should refrain from using marijuana^{49, 51}. An almost 5-fold increased risk for myocardial infarction within the hour after marijuana use was reported by Mittleman and colleagues. However, they also found the risk to decrease after the initial hour post-use⁴¹. Similar to the conflicting reports of marijuana use and obesity, evidence regarding the effect of marijuana use on systolic blood pressure is unclear. A significant increase in systolic blood pressure has been reported; yet, other studies report a non-significant increase among current marijuana users compared to non-current users^{38, 48}.

Other Cardiometabolic Risk Factors—There have been limited reports on potential associations between marijuana use and elevated cholesterol levels. Studies have reported

similar high density lipoprotein cholesterol levels among current and non marijuana users^{38, 48} and a significant increased total cholesterol level among current users compared to nonusers³⁸. Identical findings were reported with respect to increased but insignificant triglyceride levels among current marijuana users compared to nonusers after multiple covariates were adjusted in the model^{38, 48}.

DISCUSSION

A review of the literature suggests that studies are needed to explore possible relationships between marijuana use and cardiometabolic risk in the United States population. Studies have described lower BMI among current marijuana users compared to non-users; however, it has been reported that accumulation of fat in the visceral depot has been identified as a more reliable predictor of cardiovascular disease than BMI^{56, 57} suggesting that studies should look beyond the calculation of BMI as the sole indicator of cardiometabolic risk. Furthermore, most studies that reported association between marijuana use and BMI were cross-sectional in nature which limits the ability to determine a temporal relationship.

Although published literature did not find a significant association between current marijuana use and obesity or glucose/insulin levels, it is important to incorporate short-term and lifetime risk factors when assessing cardiometabolic disease risk⁵⁸. While lower BMI or glycemic control were found among current marijuana users, higher BMI and other cardiometabolic risk factors such as insulin, glucose, HOMA-IR, triglycerides, and waist circumference were found in past users^{38, 48}. Furthermore, the dose-response difference between categories of marijuana use seems to result in varied cardiometabolic risk levels.⁴²

Limitations

One of the common limitations of past studies includes the measurement of marijuana use. The self-report nature of marijuana use may likely be underreported and lead to information bias. Another limitation of past studies includes the lack of a uniform definition of cut-off values for cardiometabolic risk factors¹⁵. Depending on which source investigators use (International Diabetes Federation, National Cholesterol Education Program, or World Health Organization), cardiometabolic risk and/or Metabolic Syndrome risk may differ across studies which can further contribute to conflicting results.

CONCLUSION

Emerging issues surrounding the intersection of marijuana use and cardiometabolic risk are unclear but their study is timely given the current prevalence of cardiometabolic disease and increasing marijuana use for recreational and medicinal purposes in the United States. Further attention should be given to the relationship between varied doses of marijuana use (current, past, sporadic use) and individual cardiometabolic risk factors as well as the metabolic syndrome. Further, longitudinal studies are needed to determine temporal relationships between marijuana use and cardiometabolic risk outcomes. These types of analyses could provide important information to health care professionals who provide medical care to those at high risk for cardiometabolic disease.

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Table 1

Comparison of Definitions for Clinical Diagnosis of the Metabolic Syndrome

Clinical Measure	International Diabetes Federation ²⁸	National Cholesterol Education Program/Adult Treatment Panel-III ²⁹	World Health Organization ¹⁴
Abdominal Obesity	Waist Circumference Men: 94 cm (in) Women: 80 cm (in)	Waist Circumference Men: >102 cm (>40 in) Women: >88 cm (>35 in)	Body Mass Index $\geq 30\text{kg/m}^2$ and/or waist:hip ratio >0.9 in men, >0.85 in women
Triglycerides	150 mg/dL	150 mg/dL	150 mg/dL
High-Density Lipoprotein Cholesterol	Men: <40 mg/dL Women: <50 mg/dL Or specific treatment for lipid abnormality	Men: < 40 mg/dL Women: <50 mg/dL	<0.9 mmol/L in men or <1.0 mmol/L in women
Blood Pressure	130 mmHg systolic 85 mmHg diastolic or treatment of previously diagnosed hypertension	130 mmHg systolic 85 mmHg diastolic or antihypertensive medication	140 mmHg systolic 90 mmHg diastolic and/or antihypertensive medication
Fasting Glucose	100 mg/dL or previously diagnosed type 2 diabetes	110 mg/dL	Type 2 diabetes, impaired fasting glucose, or impaired glucose tolerance