CLINICAL RESEARCH STUDY

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Metabolic Syndrome Among Marijuana Users in the United States: An Analysis of National Health and Nutrition Examination Survey Data

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ABSTRACT

BACKGROUND: Research on the health effects of marijuana use in light of its increased medical use and the current obesity epidemic is needed. Our objective was to explore the relationship between marijuana use and metabolic syndrome across stages of adulthood.

METHODS: An analysis of 20- to 59-year-olds (n = 8478) who completed the 2005-2010 National Health and Nutrition Examination Surveys was conducted. Marijuana use was categorized as: never used, past use (used previously but not within the last 30 days), and current use (≥1 day in the last 30 days). Metabolic syndrome was defined as ≥3 of the following: elevated fasting glucose, high triglycerides, low high-density-lipoprotein cholesterol, elevated systolic/diastolic blood pressure, and increased waist circumference. An age-stratified analysis was conducted to examine the relationship between marijuana use and metabolic syndrome among emerging adults (20-30 years), adults (31-44 years), and middle-aged adults (45-59 years).

RESULTS: Fourteen percent (13.8%) of current marijuana users and 17.5% of past marijuana users presented with metabolic syndrome, compared with 19.5% of never users ($P = .0003$ and $P = .03$, respectively). Current marijuana users had lower odds of presenting with metabolic syndrome than never users (adjusted odds ratio [AOR] 0.69; 95% confidence interval [CI], 0.47-1.00; $P = .05$). Among emerging adults, current marijuana users were 54% less likely than never users to present with metabolic syndrome. Current (AOR 0.49; 95% CI, 0.25-0.97) and past (AOR 0.61; 95% CI, 0.40-0.91) middle-aged adult marijuana users were less likely to have metabolic syndrome than never users.

CONCLUSIONS: Current marijuana use is associated with lower odds of metabolic syndrome across emerging and middle-aged US adults. Future studies should examine the biological pathways of this relationship.

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KEYWORDS: Cardiovascular diseases; Marijuana; Metabolic syndrome; NHANES

Marijuana is the most commonly used drug in the US.[1] In 2013, 19.1% of emerging adults (18-25 years old) reported current marijuana use, a rate considerably higher than what is reported for youth (7.1%) and adults (>25 years) (5.6%) combined. An overwhelming majority (80.6%) of current illicit drug users reported the use of marijuana.[1] Recent legalization of recreational and medical use across the US makes it unlikely that the prevalence and frequency of marijuana use will decline in the near future.

Despite record high support (58%) for legalizing marijuana use in the US,[2] there is a gap in clinical research

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literature of its use.[3] Health risks of marijuana use are a growing concern due to the increasing levels of the main psychoactive ingredient of marijuana, tetrahydrocannabinol, which has increased over the past two decades.[4,5] The impact of increased tetrahydrocannabinol levels on cardiometabolic health is poorly understood; yet, concurrently, the nation is facing epidemic levels of obesity, diabetes, and cardiovascular disease.[6]

Metabolic syndrome, a significant risk factor for type 2 diabetes and cardiovascular disease,[7-14] is defined as the presence of a cluster of ≥3 of the following risk factors: elevated waist circumference, systolic or diastolic blood pressure (or both), triglycerides, fasting glucose, and low high-density lipoprotein (HDL) cholesterol. Some studies have reported an association between marijuana use and individual metabolic syndrome factors, while others have found no relationship.[15-17] This association has been understudied,[17] across stages of adulthood in particular. The objective of this study was to evaluate the relationship between marijuana use and metabolic syndrome in a US population-based sample. Given the differences in the prevalence of marijuana use and obesity by age, the secondary objective was to assess these relationships by stages of adulthood.

CLINICAL SIGNIFICANCE

- Current and past marijuana users have lower odds of presenting with metabolic syndrome than those with no history of marijuana use, depending on the age group.
- There was a lower prevalence of metabolic syndrome among current and past marijuana users when compared with never users.
- Individual metabolic syndrome component mean estimates varied across use categories but were generally lower among marijuana users compared with never users, with the exception of blood pressure.

METHODS

Study Population

An analysis of 20- to 59-year-olds (N = 8478) from combined 2005-2010 National Health and Nutrition Examination Survey (NHANES) cycles were included to increase statistical reliability.[18] The age group was determined based on respondents for key variables used in the study. NHANES is a continuous survey administered by the Centers for Disease Control and Prevention's National Center for Health Statistics that uses a stratified, multistage probability sampling design. In-home questionnaire, laboratory, and physical examination data were collected.[18] Participants provided informed consent, and protocols were approved by the National Center for Health Statistics' Institutional Review Board.

Participants were excluded from the study sample if they did not complete the drug questionnaire (n = 1509), reported current use of heroin, cocaine, or methamphetamines along with marijuana use (n = 234), reported current use of insulin (n = 220) or blood sugar-lowering medication (n = 453), or self-reported or tested positive for pregnancy via urine test (n = 450).

Marijuana Use

Marijuana use was defined using the following questions: 1) "Have you ever, even once, used marijuana or hashish?" (yes, no, refused, don't know); 2) "How long has it been since you last used marijuana or hashish?" (number of days, weeks, months, years, refused, don't know); and 3) "During the past 30 days, on how many days did you use marijuana or hashish?" (number of days 1 to 30 reported).[19] Degree of use was then categorized using the Addiction Severity Index 5th Edition[20] as a guide into the following categories: past marijuana users (lifetime use at least once, but not in last 30 days), current marijuana users (≥1 day in the last 30 days). The reference group was defined as participants who reported no lifetime marijuana use (never users). Audio Computer-Assisted Self-Interview (ACASI) software was used to administer the drug use questionnaire.[19] Validity of responses were verified by ACASI software programming that alerted participants of potential errors and checks for valid responses.[19]

Metabolic Syndrome

The primary outcome was metabolic syndrome, a cluster of ≥3 of the following risk factors: waist circumference, systolic/diastolic blood pressure, HDL cholesterol, triglycerides, and fasting glucose.[9] Protocol, standardization, and reliability of data collection information and procedures are described elsewhere.[21-23] Standardized[9] abnormal/elevated cut-off values were as follows: 1) waist circumference ≥102 cm (40 in) for men, waist circumference ≥88 cm (35 in) for women; 2) systolic blood pressure ≥130 mm Hg, or diastolic blood pressure ≥85 mm Hg (or the report of current hypertensive medication use); 3) HDL cholesterol ≤40 mg/dL for men, ≤50 mg/dL for women; 4) triglycerides ≥150 mg/dL; and 5) fasting glucose ≥100 mg/dL.

Covariates

Sex, age, race/ethnicity, poverty-to-income ratio, and cigarette use were considered covariates a priori. NHANES captured sex as male/female, age in years, and race/ethnicity as Non-Hispanic White, Non-Hispanic Black, Mexican American, Other Hispanic, and Other (which includes Asian Americans, Multi-Race, etc.). Mexican American and Other Hispanic categories were combined to create a "Hispanic" classification for analyses. Poverty-to-income ratio was calculated by dividing family income by the poverty

guidelines to create an index variable used to classify socioeconomic status.[24] Current cigarette use was defined using the following question: "Do you now smoke cigarettes?" (every day, some days, not at all).[25]

Statistical Analysis

The sample was analyzed using survey design methods in SAS version 9.3 (SAS Institute, Inc., Cary, NC). Subsample weights, clusters, and strata were taken into account in accordance with analytical guidelines for combining survey cycles.[18] Survey frequencies and chi-squared tests were used to compare descriptive characteristics as well as prevalence of each metabolic syndrome component within marijuana use categories. Mean values of each metabolic syndrome component were obtained and compared between degree of marijuana use categories using least squares means comparisons within the survey regression procedure. A P-value of $\leq .05$ was considered statistically significant.

Logistic regression models were fit with metabolic syndrome as a binary outcome (Y $\geq$3 abnormal factors; N $\leq$3 abnormal factors). Age, sex, race/ethnicity, poverty-to-income ratio, and cigarette use were included in the model. Given that we combined survey cycles over a 6-year period, we adjusted for time (expressed as the year of the survey cycle) in the model. Adjusted odds ratios (AOR) were reported with corresponding 95% confidence intervals and P-values with an alpha set to .05.

The sub-analysis stratifying by age was conducted by creating 3 categories: emerging adults (20- to 30-year-olds), adults (31- to 44-year-olds), and middle-aged adults (45- to 59-year-olds). The majority of items asked in the NHANES drug use questionnaire were limited to adults aged 20-59 years. Age categories were created using cut-offs in previous reports on prevalence of overweight and obesity in the US from NHANES data as a guide.[26]

RESULTS

Sample Characteristics

Demographic characteristics of the sample are described in Table 1. The majority were Non-Hispanic White, completed some college or were a college graduate, and were current cigarette smokers. Stratified by degree of marijuana use, males represented the majority of past and current marijuana users. The majority of current and past marijuana users reported cigarette use in the last 30 days.

Figure 1 illustrates the prevalence of marijuana use by age group. Among the overall sample, 60% reported using marijuana at some point in their lifetime. Twenty percent of emerging adults reported marijuana use within the last 30 days, and 43.0% reported use but not within the last 30 days. About 11.0% of adults reported current use of marijuana, and almost half (47.8%) reported past use. The majority (53.2%) of middle-aged adults were past users of marijuana.

Mean Individual Metabolic Syndrome Risk Factors by Marijuana Use Categories

Waist Circumference. Females presented with an elevated mean waist circumference in all marijuana use categories, while males had no abnormal mean values (Table 2). Waist circumference was significantly lower among males who reported current marijuana use (93.8 cm, $P < .0001$) when compared with never users (100.7 cm).

Blood Pressure. Current marijuana users had higher systolic blood pressure (119.4 mm Hg) than never users (117.7 mm Hg, $P = .01$). Past marijuana users had a significantly higher diastolic blood pressure (72.0 mm Hg) than never users (71.0 mm Hg, $P = .03$). There were no differences between current marijuana users and never users in regard to mean diastolic blood pressure values.

HDL Cholesterol. Among the overall sample of males, past (47.0 mg/dL, $P = .01$) and current (51.1 mg/dL, $P < .0001$) marijuana users had a significantly higher mean HDL cholesterol than never users (45.4 mg/dL).

Mean HDL cholesterol was significantly higher among female past marijuana users (59.4 mg/dL) when compared with never users (57.2 mg/dL, $P = .02$). There were no significant differences in HDL cholesterol values among female current marijuana users when compared with never users.

Triglycerides. There were no differences in mean values for triglycerides between either past or current marijuana users when compared with never users. All categories were below the abnormal cut-off value of 150 mg/dL.

Fasting Glucose. Mean fasting glucose levels were significantly lower among current marijuana users (97.3 mg/dL) when compared with never users (99.6 mg/dL, $P = .02$). Past marijuana users also had lower fasting glucose levels (98.4 mg/dL) than never users (99.6 mg/dL, $P = .03$).

Prevalence of Abnormal Metabolic Syndrome Risk Factors by Marijuana Use Categories

The prevalence of metabolic syndrome and its individual components by marijuana use categories is illustrated in Figure 2. About fourteen percent (13.8%) of current and 17.5% of past marijuana users presented with metabolic syndrome, compared with 19.5% of never users ($P = .0003$ and $P = .03$, respectively).

Among male current marijuana users, the prevalence of elevated waist circumference (25.5%) was significantly lower than never users (42.0%, $P < .0001$). The prevalence of abnormal HDL cholesterol values were also lower among male past (34.7%, $P = .03$) and current (25.1%, $P < .0001$) marijuana users when compared with male never users (39.7%). There were no significant differences in the prevalence of abnormal metabolic syndrome or HDL cholesterol among females.

Table 1 Characteristics of Overall Sample by Marijuana Use Category, National Health and Nutrition Examination Surveys, 2005-2010

	Overall N = 8478			Never* n = 3847	Past† n = 3623	Current‡ n = 1008
Characteristic	n	Weighted n	%	n (%)	n (%)	n (%)
Sex						
Male	4257	67,262,455	50.6	1677 (44.1)	1931 (52.5)	649 (65.5)
Female	4221	65,578,892	49.6	2170 (55.9)	1692 (47.5)	359 (34.5)
Age category						
20-30 years old	2430	36,530,493	27.5	994 (25.7)	951 (24.2)	485 (47.2)
31-44 years old	3101	46,750,542	35.2	1471 (36.6)	1304 (34.8)	326 (32.1)
45-59 years old	2947	49,560,312	37.3	1382 (37.7)	1368 (41.0)	197 (20.7)
Ethnicity						
Non-Hispanic White	3934	91,744,152	69.1	1292 (56.8)	2111 (78.7)	531 (71.4)
Non-Hispanic Black	1672	14,735,666	11.1	681 (11.5)	703 (9.4)	288 (16.7)
Hispanic	2475	18,482,739	13.9	1627 (22.1)	699 (8.5)	149 (7.9)
Other	397	7,878,790	5.9	247 (9.6)	110 (3.4)	40 (4.0)
Education level						
Less than 9^{th} grade	683	5,574,501	4.2	534 (7.6)	123 (2.0)	26 (1.8)
9^{th}-11^{th} grade	1322	15,059,161	11.3	591 (10.8)	520 (10.3)	211 (17.3)
High School diploma/GED	2001	30,953,510	23.3	831 (21.7)	885 (23.6)	285 (27.8)
Some college or AA degree	2601	43,081,063	32.5	1032 (29.8)	1216 (33.7)	353 (36.5)
College graduate or above	1863	38,040,395	28.7	853 (30.1)	877 (30.4)	133 (16.6)
Current cigarette use						
No	1475	25,902,697	43.4	400 (46.2)	928 (48.7)	147 (23.4)
Yes	2271	33,781,200	56.6	507 (53.8)	1175 (51.3)	589 (76.6)

*Defined as participants with no report of lifetime marijuana use, even once.
†Defined as participants who used marijuana before in lifetime but not in the last 30 days.
‡Defined as participants who used marijuana at least once in the last 30 days.

There were no significant differences in the prevalence of elevated systolic or diastolic blood pressure with the exception of one category. Past marijuana users had a higher prevalence of elevated diastolic blood pressure (10.6%) then never users (8.8%, $P = .01$). There were no significant differences in the prevalence of elevated triglycerides by marijuana use category. Current marijuana users had a lower prevalence of elevated fasting glucose (15.4%) than never users (18.7%, $P = .04$).

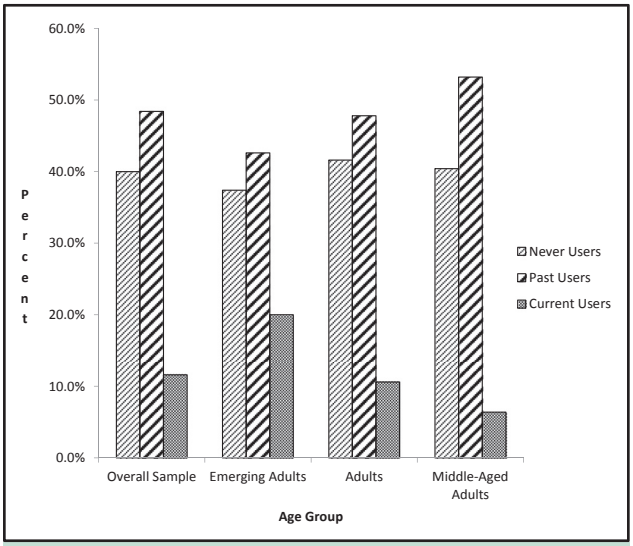

Figure 1 Prevalence of marijuana use by age group; National Health and Nutrition Examination Surveys, 2005-2010.

Odds of Metabolic Syndrome by Marijuana Use Categories

The adjusted odds of presenting with metabolic syndrome are detailed in **Table 3**. There were no significant relationships between metabolic syndrome and marijuana use among past marijuana users (AOR 0.76; 95% CI, 0.57-1.02) in the overall sample. The relationship was marginally significant among current marijuana users (AOR 0.69; 95% CI, 0.47-1.00). Age was significant in the relationship between both past and current marijuana use and metabolic syndrome in the overall sample (past marijuana users: AOR 1.04; 95% CI, 1.03-1.05; current marijuana users: AOR 1.04; 95% CI, 1.03-1.06). Poverty-to-income ratio was also significant in the relationship between marijuana use and metabolic syndrome (past marijuana users: AOR 0.89; 95% CI, 0.82-0.96; current marijuana users: AOR 0.86; 95% CI, 0.78-0.95). Sex, race/ethnicity, cigarette use, and survey cycle year were not found to be related to the relationship between metabolic syndrome and marijuana use (data not shown).

Because age was significant in the relationship between metabolic syndrome and marijuana use in the overall sample, a sub-analysis was conducted by age groups created using

Table 2 Estimates of Mean Metabolic Syndrome Component Values by Marijuana Use Category among Overall Sample, National Health and Nutrition Examination Surveys, 2005-2010

	Marijuana Use Category				
Metabolic Syndrome Component	Never Used* (Reference) n = 3847 Mean (SE)	Past Use† n = 3623 Mean (SE)	*P*-Value	Current Use‡ n = 1008 Mean (SE)	*P*-Value
Waist circumference, cm§					
Males	100.7 (0.55)	100.5 (0.48)	.75	**93.8 (0.75)**	**<.0001**
Females	93.4 (0.48)	92.7 (0.57)	.26	91.9 (1.10)	.17
Systolic blood pressure, mm Hg	117.7 (0.40)	118.1 (0.29)	.36	**119.4 (0.48)**	**.01**
Diastolic blood pressure, mm Hg	71.0 (0.41)	**72.0 (0.33)**	**.03**	70.3 (0.40)	.18
HDL cholesterol, mg/dL§					
Males	45.4 (0.37)	**47.0 (0.40)**	**.01**	**51.1 (0.84)**	**<.0001**
Females	57.2 (0.47)	**59.4 (0.68)**	**.02**	57.7 (0.90)	.60
Triglycerides, mg/dL	127.7 (2.95)	132.8 (2.76)	.25	126.4 (4.1)	.81
Fasting glucose, mg/dL	99.6 (0.51)	**98.4 (0.38)**	**.03**	**97.3 (0.78)**	.02

Bold values were significant, $P < .05$.
*Defined as participants with no report of lifetime marijuana use, even once.
†Defined as participants who used marijuana before in lifetime but not in the last 30 days.
‡Defined as participants who used marijuana at least once in the last 30 days.
§Sex-specific standardized cut-off values.

past age cut-offs as a reference.[26] Emerging adult current marijuana users had lower odds of metabolic syndrome than never users (AOR 0.46; 95% CI, 0.24-0.89). Among adults, there were no significant relationships between marijuana use and metabolic syndrome. Middle-aged adult current marijuana users had half the odds of presenting with metabolic syndrome when compared with never users (AOR 0.49; 95% CI, 0.25-0.97). Middle-aged past marijuana users had lower odds of metabolic syndrome than never users (AOR 0.61; 95% CI, 0.40-0.91) (**Table 3**).

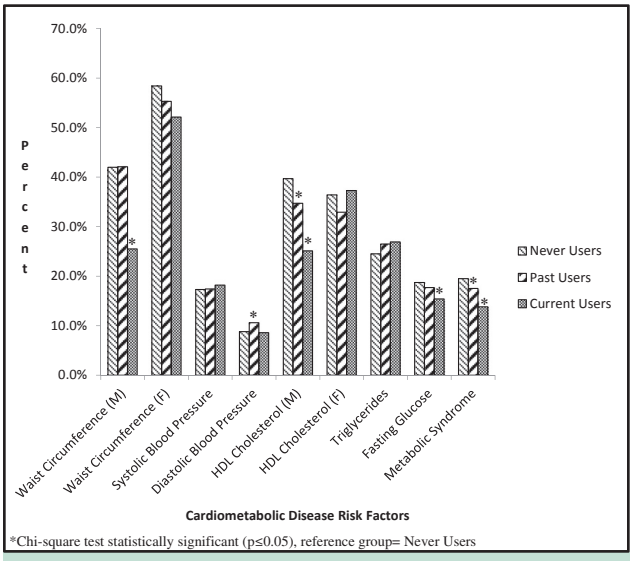

Figure 2 Prevalence of metabolic syndrome components by marijuana use categories among overall sample; National Health and Nutrition Examination Surveys, 2005-2010. *Chi-squared test statistically significant ($P \leq .05$), reference group = Never Users.

DISCUSSION

This is the first study to examine relationships of marijuana use with the metabolic syndrome and its individual components at the population level across stages of adulthood. Findings suggest that the relationship between marijuana use and metabolic syndrome is negative but varies across adulthood. Results also showed that the prevalence of individual components of the metabolic syndrome varied by

Table 3 Adjusted* Odds of Metabolic Syndrome by Marijuana Use Category by Age Group, National Health and Nutrition Examination Surveys, 2005-2010

	Reference Group = Never Used Marijuana
	Metabolic Syndrome AOR (95% CI)
Overall sample	
Past use	0.76 (0.57-1.02)
Current use	0.69 (0.47-1.00)
Emerging adults	
Past use	0.62 (0.30-1.27)
Current use	**0.46 (0.24-0.89)**
Adults	
Past use	1.14 (0.81-1.61)
Current use	1.05 (0.70-1.56)
Middle-aged adults	
Past use	**0.61 (0.40-0.91)**
Current use	**0.49 (0.25-0.97)**

AOR = adjusted odds ratio; CI = confidence interval.
Bold values were significant, $P < .05$.
*Adjusted for age, sex, race/ethnicity, poverty-to-income ratio, cigarette smoking, survey cycle year.

marijuana use category. These findings have important implications for the nation as marijuana use becomes more accepted and we simultaneously face multiple epidemics of obesity, cardiovascular disease, and diabetes.

Marijuana Use and Metabolic Syndrome

The prevalence of current marijuana use among our sample is similar to what has been reported.[1] In the current study, 20.0% of emerging adults were current marijuana users, compared with 10.6% of adults and 6.4% of middle-aged adults. Using the Adult Treatment Panel III's definition of the metabolic syndrome,[12] others have estimated that approximately 22% of the US adult population (24% after age adjustment) has metabolic syndrome.[27] Our findings show that 13.8% of US adults between the ages of 20 and 59 years who reported the current use of marijuana have metabolic syndrome. Emerging adult current marijuana users had the lowest prevalence of metabolic syndrome (6.4%) compared with adults (19.4%) and middle-aged adults (22.0%), suggesting that prevalence may increase as participants' age increases and chronic disease (eg, type 2 diabetes or cardiovascular disease) emerges.

Marijuana Use and Metabolic Syndrome Risk Factors

Our results for individual metabolic syndrome risk factors are generally consistent with previously reported studies, but direct comparisons between our analyses and others are difficult due to the methodological differences between studies (ie, sex-specific HDL cholesterol/waist circumference levels were used in current study). Similar to other studies,[15] results showed lower mean waist circumference and fasting glucose values among male and female current marijuana users vs never users. Marijuana contains cannabinoids, appetite-stimulating compounds that attach to receptors in the brain and other parts of the body, suggesting that increased use may result in increased caloric intake and poor cardiometabolic health outcomes, including elevated waist circumference.[28] However, our results as well as others are counterintuitive to this.[28]

The majority of the literature that presents physical health effects of marijuana describes cardiovascular implications. Several report increased heart rate, cardiac output, and blood pressure after marijuana use and advise patients with high risk of cardiovascular disease to refrain from using marijuana.[29-31] Similarly, our findings show that among the overall sample, current marijuana users have a high prevalence of elevated systolic blood pressure compared with never users. The relationship remained when examined among emerging adults, adults, and middle-aged adults. Potential physiological pathways may be via the smoke inhalation of marijuana, which has been shown to increase blood pressure and risk of stroke shortly after use. Proposed mechanisms for marijuana-associated cerebral infarction include vasospasm and arrhythmia. For example, one study demonstrated an odds ratio for acute ischemic stroke with marijuana use of 1.76 (95% CI, 1.15-2.71), even when controlling for other risk factors.[32]

Similar HDL cholesterol levels among both male and female current and nonusers have been reported by others.[15,16] In the current study, males who were current marijuana users in the overall sample, as well as within each stage of adulthood, had a higher mean HDL cholesterol level than never users. Abnormal HDL cholesterol levels are sex-specific, and a low value reflects a risk for metabolic syndrome; therefore, based on the mean estimates of HDL cholesterol in the current study, marijuana use has a positive effect on the levels among males. Female current marijuana users did not present with significant differences in HDL cholesterol; however, female past marijuana users presented with increased HDL cholesterol levels when compared with females who never used marijuana in the overall sample.

Study Strengths and Limitations

Some study limitations should be noted. First, a causal relationship cannot be determined due to the cross-sectional NHANES design. Second, marijuana use information was self-reported; however, marijuana and cigarette use data were captured via ACASI, which increased privacy to reduce bias. The current study did not include diet or physical fitness. Future studies should consider the role nutrition and physical activity has on the association between marijuana use and metabolic syndrome. Furthermore, participants with diabetes were excluded, which likely impacted the overall prevalence of metabolic syndrome in this sample.

Despite the limitations, there were several study strengths. Standardized cut-off metabolic syndrome values were used to increase generalizability and to allow for comparisons with other samples and populations. Population-based epidemiologic studies rarely include significant numbers of participants categorized as current drug users or with drug use disorders; yet, response rates for the 3 NHANES cycles used for the current study averaged to about 77% for the interview (20- to 59-year-olds) to 75% for the examination (20- to 59-year-olds).[33] Furthermore, we increased the sample size by merging 3 cycles of NHANES data, thereby increasing the statistical stability of our study.[18]

Strengths of the current study also include the fact that cigarette use was accounted for in the regression model. Cigarette smoking is a known risk factor for cardiovascular disease[34] and has also been shown to be used in conjunction with marijuana use.[1] The interaction between cigarette smoking and marijuana use in the relationship with metabolic syndrome was examined and was not found to have significant results either in the overall sample, nor among any of the stages of adulthood. Furthermore, serum cotinine and self-reported current use of cigarettes was found to be highly correlated ($r = 0.82$, $P < .0001$), which justified the use of self-report data for comparisons in the current study.

CONCLUSION

Current and past marijuana use were both associated with lower prevalence of metabolic syndrome and most of its components. Current marijuana use is associated with lower odds of metabolic syndrome among US emerging adults and middle-aged adults. Past marijuana use is also associated with lower odds of metabolic syndrome among middle-aged adults. The current study contributes cross-sectional evidence to inform future prospective studies to examine the biological pathways of this association.

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