CLINICAL RESEARCH STUDY

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# The Impact of Marijuana Use on Glucose, Insulin, and Insulin Resistance among US Adults

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## ABSTRACT

**BACKGROUND:** There are limited data regarding the relationship between cannabinoids and metabolic processes. Epidemiologic studies have found lower prevalence rates of obesity and diabetes mellitus in marijuana users compared with people who have never used marijuana, suggesting a relationship between cannabinoids and peripheral metabolic processes. To date, no study has investigated the relationship between marijuana use and fasting insulin, glucose, and insulin resistance.

**METHODS:** We included 4657 adult men and women from the National Health and Nutrition Examination Survey from 2005 to 2010. Marijuana use was assessed by self-report in a private room. Fasting insulin and glucose were measured via blood samples after a 9-hour fast, and homeostasis model assessment of insulin resistance (HOMA-IR) was calculated to evaluate insulin resistance. Associations were estimated using multiple linear regression, accounting for survey design and adjusting for potential confounders.

**RESULTS:** Of the participants in our study sample, 579 were current marijuana users and 1975 were past users. In multivariable adjusted models, current marijuana use was associated with 16% lower fasting insulin levels (95% confidence interval [CI], −26, −6) and 17% lower HOMA-IR (95% CI, −27, −6). We found significant associations between marijuana use and smaller waist circumferences. Among current users, we found no significant dose-response.

**CONCLUSIONS:** We found that marijuana use was associated with lower levels of fasting insulin and HOMA-IR, and smaller waist circumference.

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**KEYWORDS:** Glucose; Insulin; Insulin resistance; Marijuana use

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Marijuana is the most commonly used illicit drug in the United States, and use is increasing. The 2010 National Survey on Drug Use and Health reported that between 2007 and 2010, the prevalence of marijuana use among persons aged 12 years and older increased from 5.8% to 6.9%, meaning there are an estimated 17.4 million current users of marijuana. Approximately 4.6 million of these users smoked marijuana daily or almost daily.[1] With the recent legalization of recreational marijuana in 2 states and the legalization of medical marijuana in 19 states and the District of Columbia, physicians will increasingly encounter marijuana use among their patient populations.[2] Marijuana use is associated with an acute increase in caloric intake,[3] and people who smoke marijuana have higher average caloric intake levels than nonusers.[4,5]

Despite these associations with increased caloric intake, marijuana use has been associated with lower body mass index (BMI)[4] and a lower prevalence of obesity[6] and diabetes mellitus.[7] The mechanisms underlying this paradox have not been determined, and the impact of regular marijuana use on insulin resistance and cardiometabolic risk factors remains unknown. In this study of 4657 participants in the National Health and Nutrition Examination Survey (NHANES) from 2005 to 2010, we examined the associations between habitual marijuana use and measures of fasting glucose and insulin levels, insulin resistance, and components of the metabolic syndrome.

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## MATERIALS AND METHODS

### Study Population

The NHANES is a cross-sectional, continuous survey administered annually by the National Center for Health Statistics;[8] data are released in 2-year increments. The survey uses a complex, multistage probability sampling design to select a nationally representative sample of individuals in the US population, and uses interview, physical examination, and laboratory components to assess health and nutritional status. From 2005 to 2010, 11,335 persons aged 20 to 59 years completed the questionnaire on illicit drug use, including 4657 participants who also were asked to provide a fasting blood sample.

**CLINICAL SIGNIFICANCE**

- Marijuana use is increasingly common, and use of medical marijuana is now legal in 19 states and the District of Colombia.
- Despite its associations with increased appetite and caloric intake, marijuana use also is associated with lower body mass index and prevalence of diabetes.
- In a nationally representative survey population, we found current use of marijuana to be associated with lower levels of fasting insulin, lower insulin resistance (homeostasis model assessment of insulin resistance), and smaller waist circumference.

### Assessment of Marijuana Use

Participants completed the drug use questionnaire in a private room, using the Audio Computer Assisted Self Interview system. They were asked:

- "Have you ever, even once, smoked marijuana or hashish?" (yes, no, refused, don't know);
- "How long has it been since you last used marijuana or hashish?" (answers were given as number of days, weeks, months, or years); and
- "During the past 30 days, on how many days did you use marijuana or hashish?"

Responses to these questions were used to classify participants as never users (never smoked marijuana, n = 2103); past users (smoked marijuana at least once but not in the past 30 days, n = 1975); and current users (smoked marijuana at least once in the prior 30 days, n = 579).

### Outcomes

**Insulin, Glucose, Homeostatic Model Assessment Insulin Resistance Score, High-Density Lipoprotein Cholesterol, Hemoglobin A1c, and Triglycerides.** Participants provided blood samples in the morning after a 9-hour fast. The homeostasis model assessment of insulin resistance (HOMA-IR), a measure of insulin resistance, was calculated as fasting serum insulin (μU/mL) × fasting plasma glucose (mg/dL)/405.

From 2005 to 2006, high-density lipoprotein cholesterol (HDL-C) testing was performed at Johns Hopkins University, using the Hitachi 717 and Hitachi 912 (Roche Diagnostics, Indianapolis, Ind). In this cycle, values were corrected because of bias from quality controls (Solomon Park Research Laboratories, Kirkland, Wash), using the following formula: corrected HDL-C = [(Solomon Park assigned HDL-C value) × (participant HDL-C)]/(quality control HDL-C value associated with participant sample)]. From 2007 to 2010, HDL-C testing was performed at the University of Minnesota, using the Roche Modular P chemistry analyzer (Roche Diagnostics).

From 2005 to 2006, hemoglobin A1c measurements were performed on the A1c 2.2 Plus Glycohemoglobin Analyzer (Tosoh Medics, Inc, South San Francisco, Calif). From 2007 to 2010, measurements were performed on the A1c G7 HPLC Glycohemoglobin Analyzer (Tosoh Medics, Inc). The hemoglobin A1c data from 2007 to 2010 exhibited higher values compared with the 1999 to 2006 data. No relationship to laboratory method, survey design, or population changes could be determined for this shift; therefore, no adjustments were made to these values.

**Blood Pressure, Body Mass Index, and Waist Circumference.** All measurements were collected during the physical examination in mobile examination centers, according to standard NHANES protocol.[9] Blood pressure estimates were calculated by averaging 3 blood pressure readings. BMI was calculated as weight in kilograms divided by the square of height in meters.

### Characterization of Sociodemographics and Health Habits

Participants reported age, sex, race/ethnicity, education level, income, marital status, tobacco use, physical activity level, and alcohol use. Race/ethnicity was classified as Hispanic, non-Hispanic white, non-Hispanic black, or other. We classified education level as less than high school, high school or equivalent, or some college. Income was categorized as less than $20,000, $20,000 to $44,999, $45,000 to $74,999, and greater than or equal to $75,000. Participants were classified into 3 groups of tobacco cigarette exposure: current user of tobacco cigarettes, past user of tobacco cigarettes, and lifetime nonsmoker (defined as <100 cigarettes in lifetime). Physical activity was classified as active, defined as report of any regular moderate or vigorous physical activity, or inactive, defined as report of no regular moderate or vigorous physical activity. Alcohol use was classified as nondrinkers, less than or equal to 1 drink per week, 1 to 14 drinks per week, or more than 14 drinks per week.