HHS Public Access

Author manuscript

Andrology. Author manuscript; available in PMC 2018 July 01.

Published in final edited form as:

Andrology. 2017 July ; 5(4): 732–738. doi:10.1111/andr.12358.

Marijuana use and serum testosterone concentrations among U.S. males

Jake E. Thistle[1], **Barry I. Graubard**[1], **Megan Braunlin**[1], **Hubert Vesper**[2], **Britton Trabert**[1], **Michael B. Cook**[1], and **Katherine A. McGlynn**[1]

[1]Division of Cancer Epidemiology and Genetics, National Cancer Institute, NIH, Bethesda, MD

[2]National Center for Environmental Health, Centers for Disease Control and Prevention, Atlanta, GA

Abstract

Background—Marijuana has been reported to have several effects on the male reproductive system. Marijuana has previously been linked to reduced adult testosterone, however, a study in Denmark reported increased testosterone concentrations among marijuana users. This study was performed to estimate the effect of marijuana use on testosterone in U.S. males.

Methods—Data on serum testosterone, marijuana use and covariates for 1577 men from the 2011–2012 U.S. National Health and Nutrition Examination Survey (NHANES) were analyzed. Information on marijuana use was collected by a self-administered computer-assisted questionnaire. Serum testosterone was determined using isotope dilution liquid chromatography tandem mass spectrometry. The effects of marijuana use on serum testosterone concentrations were examined by frequency, duration, and recency of use. Adjusted means and 95% confidence intervals (CI) of serum testosterone across levels of marijuana use were estimated using multiple linear regression weighted by the survey weights.

Results—The majority (66.2%) of the weighted study population reported ever using marijuana with 26.6% reporting current marijuana use. There was no difference in serum testosterone between ever users (adjusted mean = 3.69 ng/mL, 95% CI: 3.46, 3.93) and never users (adjusted mean = 3.70 ng/mL, 95% CI: 3.45, 3.98) upon multivariable analysis. However, serum testosterone was inversely associated with time since last regular use of marijuana (*p-value for trend* = 0.02). When restricted to men aged 18 – 29 years, this relationship strengthened (*p-value for trend* < 0.01) and serum testosterone was also inversely associated with time since last use (*p-value for trend* < 0.01), indicating that recency of use, and not duration or frequency, had the strongest relationship with testosterone levels.

Conflict of Interest

The authors declare no conflicts of interest or financial disclosures.

Author Contributions

JET analyzed and interpreted the data, assisted in study design, and drafted the manuscript. BIG assisted in data analysis and interpretation and study design. MB acquired the data and assisted in data analysis and interpretation. HV performed the laboratory analyses and assisted in data interpretation. BT assisted in data interpretation and study design. MBC assist in data interpretation and study design. KAM designed the study, assisted in data interpretation, assisted in drafting the manuscript, and oversaw the study. All authors critically reviewed and approved the final manuscript.

Discussion—Serum testosterone concentrations were higher in men with more recent marijuana use. Studies are needed to determine the extent to which circulating testosterone concentrations mediate the relationship of marijuana use to male reproductive outcomes.

Introduction

Marijuana is the most widely used illicit drug in the U.S. with an estimated 22.2 million current users (CBHSQ, 2015). Among men, the prevalence of past-year marijuana use has nearly doubled in recent years (Hasin et al., 2015). Several studies have demonstrated negative effects of marijuana use on male reproductive health, particularly decreased semen quality (Battista et al., 2008; du Plessis et al., 2015; Fronczak et al., 2012; Rossato et al., 2008). Further, marijuana use has been reported to increase the risk of testicular germ cell tumors (TGCT) (Daling et al., 2009; Lacson et al., 2012; Trabert et al., 2011), in particular, nonseminomatous TGCT. The incidence of TGCT, the most common malignancy in U.S. men aged 15 to 44 years, has been rising since the mid-20th century (Ghazarian et al., 2015) but to date, few established risk factors have been identified (McGlynn & Cook, 2009).

Marijuana may be related to reproductive health due to changes in circulating hormones, through tetrahydrocannabinol (THC), the principal active component of marijuana, which binds to cannabinoid system receptors (du Plessis et al., 2015). THC has been shown to have a pronounced regulatory effect on the hypothalamic-pituitary-gonadal axis (Hillard, 2015). As marijuana laws undergo reform, with the prevalence of marijuana use expected to rise further (Cerda et al., 2012), the potential effects of marijuana on male reproductive health requires further elucidation.

Testosterone is the principal steroid hormone of adult males with a central role in male reproductive development and has important behavioral manifestations. It has been hypothesized that TGCT, and other conditions comprising the Testicular Dysgenesis Syndrome (Skakkebaek et al., 2001), may originate from low testosterone in the fetal environment (Juul et al., 2014), and environmental factors that alter testosterone production may contribute to increasing incidence of TGCT (Sharpe & Skakkebaek, 2008). The role of androgen disruption after the fetal period, however, has not been evaluated.

Prior studies of marijuana use and serum testosterone levels have produced inconsistent findings. While an early study (Kolodny et al., 1974) reported that testosterone levels were lower among marijuana users, most subsequent studies reported no difference in testosterone levels between users and non-users (Barnett et al., 1983; Block et al., 1991; Coggins et al., 1976; Cushman, 1975; Mendelson et al., 1978; Mendelson et al., 1974; Schaefer et al., 1975). Recently, however, a large cohort study of young, healthy men in Denmark reported increased testosterone concentrations among marijuana users (Gundersen et al., 2015). Thus, we sought to examine the association of marijuana use and serum testosterone concentration in a large population-based sample of U.S. men.

Materials and Methods

Study Population

To examine the marijuana-testosterone relationship with sufficient control for demographics and lifestyle factors, we used data from the 2011–2012 National Health and Nutrition Examination Survey (NHANES). NHANES is a cross-sectional survey administered by the National Center for Health Statistics (NCHS) of the Centers for Disease Control and Prevention (CDC) that collects information from a nationally representative sample of non-institutionalized civilians. In Mobile Examination Centers (MECs), NHANES participants complete a self-administered computer-assisted interview, are physically examined, and provide serum specimens. Testosterone concentrations were quantified in serum specimens collected in the 2011–2012 NHANES cycle. Testosterone concentrations were linked to data from the interviews and physical examinations to identify information on marijuana usage as well as potential covariates. A total of 2376 men had their testosterone concentration determined and were administered the drug questionnaire. Men were excluded if they did not answer information on marijuana usage (n = 676) or if serum testosterone concentrations could not be determined (n = 119). Further, we excluded men with a self-reported generic prescription of testosterone (n = 4). The analytic population consisted of 1577 men.

Data Collection

Marijuana Use—Information on marijuana use was collected by questionnaire (Supplementary Materials and Methods) using a self-administered computer-assisted system. For analysis, marijuana use was categorized in terms of frequency, duration, and recency using questionnaire data.

Serum Testosterone Concentrations—Serum specimens were processed, stored, and shipped to the Division of Environmental Health Laboratory Sciences at CDC for central assay. Testosterone concentrations were determined using isotope dilution liquid chromatography tandem mass spectrometry methods traceable to the National Institute for Standards and Technology's (NIST) reference material (Botelho et al., 2013).

Covariates—Potential covariates considered were age at examination, body mass index (BMI), physical activity per week (hours), race / ethnicity, serum cotinine, cigarette smoking status, diabetes status, fasting length (hours), and time of blood draw. Age was self-reported as a continuous variable. Race/ethnicity was self-reported as mutually-exclusive categories: non-Hispanic white (NH white), non-Hispanic black (NH black), non-Hispanic Asian (NH Asian), Mexican American, other Hispanic, and other. BMI was determined from the measured weight and height and categorized into the following WHO groups: < 25.0 m/kg^2, 25.0 – < 30.0 m/kg^2, and ≥ 30 m/kg^2. Physical activity per week was the number of hours per week of self-reported vigorous work activity (activity that causes large increases in breathing or heart rate for 10 minutes continuously), moderate work activity (activity that causes small increases in breathing or heart rate), walking or bicycle for travel, vigorous recreational activity, and moderate recreational activity, and categorized into the following groups: < 1 hour, 1 – < 5 hours, 5 – < 10 hours, 10 – < 20, and ≥ 20 hours. Cigarette smoking status was categorized into current, former and never based on the following

questions in men aged 20 or older: 1) “Have you smoked at least 100 cigarettes in your entire life?” (yes, no, refused, don’t know), and 2) “Do you now smoke cigarettes?” (every day, some days, not at all, refused, don’t know), and on the following question in men aged 18 and 19: 1) “About how many cigarettes have you smoked in your entire life?” (I have never smoked, not even a puff, 1 or more puffs but never a whole cigarette, 1 cigarette, 2 to 5 cigarettes, 6 to 15 cigarettes, 16 to 25 cigarettes, 26 to 99 cigarettes 100 or more cigarettes, refused, don’t know) and 2) “On how many of the past 30 days did you smoke a cigarette?”. Current smokers were smokers who reported more than 100 cigarettes in their lifetime as well as smoking “every day” or “some days” or more than 1 cigarette in the last 30 days. Former smokers were defined as those who smoked more than 100 cigarettes in their lifetime and did not currently smoke. Serum cotinine, a biomarker of exposure to tobacco smoke, was determined by isotope dilution liquid chromatography tandem mass spectrometry. Cotinine was categorized into the following groups: < 1 ng/mL, 1 – < 10.0 ng/mL, and ≥ 10 ng/mL. Diabetes status was self-reported with those reporting borderline status considered negative. Fasting length was the self-reported time since the participant last ate food and categorized into the following groups: < 1 hour, 1 – < 3 hours, 3 – < 6 hours, 6 – < 12 hours, and ≥ 12 hours. The time of blood draw was the session in which the participant was examined (morning, afternoon, evening).

Statistical Analysis

All analyses were performed in SAS 9.3 (SAS Institute Inc., Cary, NC) using survey procedures to account for the sampling design of NHANES. The frequency and proportion of covariates were calculated within categories of marijuana use. Median and weighted mean serum testosterone concentrations were calculated within all categories of marijuana use and within all categories of covariates. Multiple linear regression, weighted by the survey weights, was used to conduct unadjusted and adjusted analyses of serum testosterone concentrations across levels of marijuana use with adjustment for *a priori* selected covariates, age at examination, BMI, physical activity per week, race / ethnicity, cigarette smoking status, diabetes status, fasting length, and time of blood draw. Least squares means were used to estimate adjusted means and 95% confidence interval (CI)s. Prior to all regression analyses, serum testosterone values were log-transformed to account for a skewed distribution. The exponential function was applied to estimates of log transformed testosterone values from regression analyses to obtain means and 95% CIs in ng/mL. Tests for trend were constructed for ordinal categorizations of marijuana use with 3 or more categories, using the median value or mid-value (for categories with a range of values) in each level of marijuana use as a continuous covariate. Two-sided p-values from Wald F-tests were reported. To investigate the role of androgen disruption in age groups corresponding to periods of increased risk to seminomatous and nonseminomatous TGCT, all analyses were repeated stratified by age (18 – 29 years, and ≥ 30 years). In addition, we performed a sensitivity analysis to examine the effect of cigarette use on the association between marijuana use and testosterone concentration. The following variables were included in the model: 1) Serum cotinine (categorical and continuous), 2) time since last cigarette use, 3) time since last regular cigarette use, and 4) cigarette use frequency in last month. We also performed analyses stratified by time of blood draw to assess the influence of diurnal

variation in testosterone. All analyses were repeated using SAS-callable SUDAAN to obtain predictive margins and 95% CIs.

Results

Weighted mean and median values of serum testosterone by demographic characteristics are shown in Table 1. Serum testosterone concentrations decreased with increasing age, increasing BMI, decreasing physical activity per week, and later time of day of blood collection. Testosterone concentrations were higher among current smokers, non-diabetics and NH black men.

Frequency and weighted proportion of demographic characteristics of the participants are shown by marijuana use status in Table 2. Ever users of marijuana were more likely to be aged 50 years or older, NH white, and current/former cigarette smokers. Never users were more likely to be physically active for < 1 hour per week. Ever users and never users did not differ by BMI or time of blood draw.

Table 3 shows the weighted associations between marijuana use and testosterone levels. The majority of participants (66.2%) reported being ever users of marijuana. Among ever users, 26.6% reported current use and 50.2% reported ever using regularly. Ever users had an unadjusted mean serum testosterone of 3.84 ng/mL (95% CI: 3.66, 4.02) and never users had an unadjusted mean of 3.70 ng/mL (95% CI: 3.51, 3.91). Serum testosterone was slightly higher among current marijuana users (mean = 4.27 ng/mL, 95% CI: 4.03, 4.53) and among those who ever used marijuana regularly (mean = 4.03 ng/mL, 95% CI: 3.87, 4.21), compared to never users.

In the adjusted model, there was no difference in serum testosterone between ever users (adjusted mean = 3.69 ng/mL, 95% CI: 3.46, 3.98) and never users (adjusted mean = 3.70 ng/mL, 95% CI: 3.45, 3.98). Slightly higher serum testosterone concentrations persisted in current users (adjusted mean = 3.96 ng/mL, 95% CI: 3.55, 4.42) and ever regular users (adjusted mean = 3.90 ng/mL, 95% CI: 3.56, 4.29) after adjustment, but 95% CIs of mean estimates overlapped widely with those of never users. In a dose-response analysis, serum testosterone increased with decreasing time since regular use of marijuana (*p-value for trend* = 0.02). There was no dose-response relationship between serum testosterone and time since last use, frequency during regular use, number of joints / pipes smoked per day during regular use, and years of regular use. All estimates were similar when obtaining predictive margins (results not shown).

Table 4 shows the weighted associations between marijuana use and testosterone levels, stratified by age group. Among men aged 18 – 29 years, the adjusted analysis found that serum testosterone levels among ever users were lower than among never users (adjusted mean = 4.03 ng/mL, 95% CI: 3.26, 4.97 vs. adjusted mean = 4.35 ng/mL, 95% CI: 3.40, 5.58). Among ever users, levels in current users were higher than past users (adjusted mean = 4.15 ng/mL, 95% CI: 3.77, 4.58 vs. adjusted mean = 3.86 ng/mL, 95% CI: 3.51, 4.25) and levels among ever regular users were higher than never regular users (adjusted mean = 4.12, 95% CI: 3.68, 4.61 vs. adjusted mean = 3.81, 95% CI: 3.27, 4.44) but neither current users

or ever regular users had higher levels than never users. When restricted to men aged 18 – 29 years, the inverse relationship to time since last regular use strengthened (*p-value for trend* < 0.01) and serum testosterone was also inversely associated with time since last use (*p-value for trend* < 0.01). Among men aged ≥ 30 years, there was a slight increase in ever users relative to never users (adjusted mean = 3.51 ng/mL, 95% CI: 3.25, 3.77 vs. adjusted mean = 3.41 ng/mL, 95% CI: 3.12, 3.73). Among current users (adjusted mean = 3.81 ng/mL, 95% CI: 3.32, 4.39), and ever regular users (adjusted mean = 3.71 ng/mL, 95% CI: 3.33, 4.13), testosterone levels were slightly higher, but 95% CIs overlapped with never users. The dose-response relationship between testosterone level and time since last regular was weaker in this age group (*p-value for trend* = 0.10).

Finally, as marijuana use tends to be associated with cigarette use, and cigarette use is known to affect testosterone levels, we performed a sensitivity analysis to control for possible confounding. The analysis resulted in no meaningful change in the relationship of marijuana and serum testosterone in any of the models (results not shown). In addition, there was no meaningful difference for analyses stratified by time of blood draw.

Discussion

In this population-based study of U.S., men, there was no difference in serum testosterone levels among ever users of marijuana compared to never users. We observed, however, a dose-response relationship between increasing serum testosterone and decreasing time since last regular use indicating that recency of use, not duration or frequency of use, had the strongest relationship with testosterone levels. When we restricted the analysis to men aged 18 – 29, the inverse relationship to time since last regular use strengthened and serum testosterone was also inversely associated with time since last use.

Prior studies of marijuana use and testosterone levels have produced inconsistent results. An influential early study by Kolodny et al. reported a significant decrease in testosterone level for marijuana users in a small, highly-selected population (Kolodny et al., 1974). While a subsequent clinical study found a similar association (Cohen, 1976), most subsequent studies reported no association (Barnett et al., 1983; Block et al., 1991; Coggins et al., 1976; Cushman, 1975; Mendelson et al., 1978; Mendelson et al., 1974; Schaefer et al., 1975). Almost all studies, however, whether observational or clinical in design, had small samples sizes. In contrast, the recent Danish study by Gundersen et al., was based on a large sample of young, healthy men and reported higher testosterone levels with greater frequency of marijuana use (Gundersen et al., 2015). Our results were similar to those of Gundersen et al., however, recency of marijuana use was better correlated with testosterone level than was frequency of use.

The biologic mechanism by which marijuana exerts an effect on hormone production likely involves the response of cannabinoid receptors, CB1 and CB2, to THC. These receptors are functional in male reproductive organs, including the Leydig cells of the testis, the principle producer of testosterone in men. Leydig cell testosterone production decreases with age, but changes in testosterone production also occur as a result of alteration of the intracellular redox environment (Beattie et al., 2015), which can lead to oxidative stress and damage to

cellular components. Environmental factors like marijuana use could play a role in this alteration. Further, Leydig cell aging may explain the more pronounced effect of marijuana among men aged 18 – 29 years compared to men ≥ 30 years. As Leydig cells age, they may be less resistant to the detrimental effects of oxidative stress.

Our results indicate that the relationship of marijuana use to serum testosterone is more pronounced among men aged 18 – 29 years, the age period of increased risk of nonseminoma. Nonseminoma has shown a stronger association with marijuana use than seminoma (Daling et al., 2009; Lacson et al., 2012; Trabert et al., 2011), however, the extent to which serum testosterone mediates this relationship is not possible without ascertainment of TGCTs in conjunction with serum testosterone and marijuana use.

A particular strength of our study is the use of a large population-based sample representative of the U.S. population with sufficient information on demographic and lifestyle factors. The use of a self-administered computer-assisted interview provided an ideal environment for collection of sensitive information, such as use of marijuana. Perhaps as a result of the confidential setting, 66.2% of the weighted study population reported ever using marijuana. The drug use questionnaire examined marijuana use in great detail, allowing differentiation of frequency, duration, and recency of marijuana use. Also, information on testosterone levels was determined using a standardized central assay with rigorous quality control measures (Botelho et al., 2013).

A limitation of this study is the cross-sectional nature of data collection in NHANES. Although there is likely a minimal effect of response bias given the frequency at which marijuana use was reported, questions about the timing and frequency of past marijuana use may be difficult to recall. Also, forms of marijuana consumption other than smoking were not captured. Factors such as the amount of sleep the previous night (Auyeung et al., 2015) and physical activity immediately before blood draw (Hakkinen & Pakarinen, 1995; Kraemer et al., 1998) may affect testosterone levels. Adjustment for these variables could not be conducted as NHANES did not collect this information. In addition, NHANES has not measured serum concentrations of other sex steroid hormones thus it was not possible to examine whether they were associated with marijuana use.

This study is the largest to examine the relationship of marijuana use to serum testosterone levels and the first study to examine the effects by age group. As marijuana use continues to rise in the US, further elucidation of its relationship to male reproductive health is warranted.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

Funding

This work was supported the intramural research program of the National Cancer Institute (NCI).

References

Auyeung TW, Kwok T, Leung J, Lee JS, Ohlsson C, Vandenput L, Wing YK, Woo J. Sleep Duration and Disturbances Were Associated With Testosterone Level, Muscle Mass, and Muscle Strength--A Cross-Sectional Study in 1274 Older Men. J Am Med Dir Assoc. 2015; 16(7):630, e631–636. DOI: 10.1016/j.jamda.2015.04.006

Barnett G, Chiang CW, Licko V. Effects of marijuana on testosterone in male subjects. J Theor Biol. 1983; 104(4):685–692. [PubMed: 6316036]

Battista N, Rapino C, Di Tommaso M, Bari M, Pasquariello N, Maccarrone M. Regulation of male fertility by the endocannabinoid system. Mol Cell Endocrinol. 2008; 286(1–2 Suppl 1):S17–23. DOI: 10.1016/j.mce.2008.01.010 [PubMed: 18328619]

Beattie MC, Adekola L, Papadopoulos V, Chen H, Zirkin BR. Leydig cell aging and hypogonadism. Exp Gerontol. 2015; 68:87–91. DOI: 10.1016/j.exger.2015.02.014 [PubMed: 25700847]

Block RI, Farinpour R, Schlechte JA. Effects of chronic marijuana use on testosterone, luteinizing hormone, follicle stimulating hormone, prolactin and cortisol in men and women. Drug Alcohol Depend. 1991; 28(2):121–128. [PubMed: 1935564]

Botelho JC, Shacklady C, Cooper HC, Tai SS, Van Uytfanghe K, Thienpont LM, Vesper HW. Isotope-dilution liquid chromatography-tandem mass spectrometry candidate reference method for total testosterone in human serum. Clin Chem. 2013; 59(2):372–380. DOI: 10.1373/clinchem.2012.190934 [PubMed: 23213081]

CBHSQ. Center for Behavioral Health Statistics and Quality. Behavioral Health Trends in the United States: Results from the 2014 National Survey on Drug Use and Health. 2015.

Cerda M, Wall M, Keyes KM, Galea S, Hasin D. Medical marijuana laws in 50 states: investigating the relationship between state legalization of medical marijuana and marijuana use, abuse and dependence. Drug Alcohol Depend. 2012; 120(1–3):22–27. DOI: 10.1016/j.drugalcdep.2011.06.011 [PubMed: 22099393]

Coggins WJ, Swenson EW, Dawson WW, Fernandez-Salas A, Hernandez-Bolanos J, Jiminez-Antillon CF, Solano JR, Vinocour R, Faerron-Valdez F. Health status of chronic heavy cannabis users. Ann N Y Acad Sci. 1976; 282:148–161. [PubMed: 1071375]

Cohen S. The 94-day cannabis study. Ann N Y Acad Sci. 1976; 282:211–220. [PubMed: 1071381]

Cushman P Jr. Plasma testosterone levels in healthy male marijuana smokers. Am J Drug Alcohol Abuse. 1975; 2(2):269–275. [PubMed: 1211384]

Daling JR, Doody DR, Sun X, Trabert BL, Weiss NS, Chen C, Biggs ML, Starr JR, Dey SK, Schwartz SM. Association of marijuana use and the incidence of testicular germ cell tumors. Cancer. 2009; 115(6):1215–1223. DOI: 10.1002/cncr.24159 [PubMed: 19204904]

du Plessis SS, Agarwal A, Syriac A. Marijuana, phytocannabinoids, the endocannabinoid system, and male fertility. J Assist Reprod Genet. 2015; 32(11):1575–1588. DOI: 10.1007/s10815-015-0553-8 [PubMed: 26277482]

Fronczak CM, Kim ED, Barqawi AB. The insults of illicit drug use on male fertility. J Androl. 2012; 33(4):515–528. DOI: 10.2164/jandrol.110.011874 [PubMed: 21799144]

Ghazarian AA, Trabert B, Devesa SS, McGlynn KA. Recent trends in the incidence of testicular germ cell tumors in the United States. Andrology. 2015; 3(1):13–18. DOI: 10.1111/andr.288 [PubMed: 25331158]

Gundersen TD, Jorgensen N, Andersson AM, Bang AK, Nordkap L, Skakkebaek NE, Priskorn L, Juul A, Jensen TK. Association Between Use of Marijuana and Male Reproductive Hormones and Semen Quality: A Study Among 1,215 Healthy Young Men. Am J Epidemiol. 2015; 182(6):473–481. DOI: 10.1093/aje/kwv135 [PubMed: 26283092]

Hakkinen K, Pakarinen A. Acute hormonal responses to heavy resistance exercise in men and women at different ages. Int J Sports Med. 1995; 16(8):507–513. DOI: 10.1055/s-2007-973045 [PubMed: 8776203]

Hasin DS, Saha TD, Kerridge BT, Goldstein RB, Chou SP, Zhang H, Jung J, Pickering RP, Ruan WJ, Smith SM, Huang B, Grant BF. Prevalence of Marijuana Use Disorders in the United States Between 2001–2002 and 2012–2013. JAMA Psychiatry. 2015; 72(12):1235–1242. DOI: 10.1001/jamapsychiatry.2015.1858 [PubMed: 26502112]

Hillard CJ. Endocannabinoids and the Endocrine System in Health and Disease. Handb Exp Pharmacol. 2015; 231:317–339. DOI: 10.1007/978-3-319-20825-1_11 [PubMed: 26408166]

Juul A, Almstrup K, Andersson AM, Jensen TK, Jorgensen N, Main KM, Rajpert-De Meyts E, Toppari J, Skakkebaek NE. Possible fetal determinants of male infertility. Nat Rev Endocrinol. 2014; 10(9):553–562. DOI: 10.1038/nrendo.2014.97 [PubMed: 24935122]

Kolodny RC, Masters WH, Kolodner RM, Toro G. Depression of plasma testosterone levels after chronic intensive marihuana use. N Engl J Med. 1974; 290(16):872–874. DOI: 10.1056/nejm197404182901602 [PubMed: 4816961]

Kraemer WJ, Hakkinen K, Newton RU, McCormick M, Nindl BC, Volek JS, Gotshalk LA, Fleck SJ, Campbell WW, Gordon SE, Farrell PA, Evans WJ. Acute hormonal responses to heavy resistance exercise in younger and older men. Eur J Appl Physiol Occup Physiol. 1998; 77(3):206–211. DOI: 10.1007/s004210050323 [PubMed: 9535580]

Lacson JC, Carroll JD, Tuazon E, Castelao EJ, Bernstein L, Cortessis VK. Population-based case-control study of recreational drug use and testis cancer risk confirms an association between marijuana use and nonseminoma risk. Cancer. 2012; 118(21):5374–5383. DOI: 10.1002/cncr.27554 [PubMed: 22965656]

McGlynn KA, Cook MB. Etiologic factors in testicular germ-cell tumors. Future Oncol. 2009; 5(9):1389–1402. DOI: 10.2217/fon.09.116 [PubMed: 19903067]

Mendelson JH, Ellingboe J, Kuehnle JC, Mello NK. Effects of chronic marihuana use on integrated plasma testosterone and luteinizing hormone levels. J Pharmacol Exp Ther. 1978; 207(2):611–617. [PubMed: 712643]

Mendelson JH, Kuehnle J, Ellingboe J, Babor TF. Plasma testosterone levels before, during and after chronic marihuana smoking. N Engl J Med. 1974; 291(20):1051–1055. DOI: 10.1056/nejm197411142912003 [PubMed: 4415097]

Rossato M, Pagano C, Vettor R. The cannabinoid system and male reproductive functions. J Neuroendocrinol. 2008; 20(Suppl 1):90–93. DOI: 10.1111/j.1365-2826.2008.01680.x [PubMed: 18426506]

Schaefer CF, Gunn CG, Dubowski KM. Letter: Normal plasma testosterone concentrations after marihuana smoking. N Engl J Med. 1975; 292(16):867–868.

Sharpe RM, Skakkebaek NE. Testicular dysgenesis syndrome: mechanistic insights and potential new downstream effects. Fertil Steril. 2008; 89(2 Suppl):e33–38. DOI: 10.1016/j.fertnstert.2007.12.026 [PubMed: 18308057]

Skakkebaek NE, Rajpert-De Meyts E, Main KM. Testicular dysgenesis syndrome: an increasingly common developmental disorder with environmental aspects. Hum Reprod. 2001; 16(5):972–978. [PubMed: 11331648]

Trabert B, Sigurdson AJ, Sweeney AM, Strom SS, McGlynn KA. Marijuana use and testicular germ cell tumors. Cancer. 2011; 117(4):848–853. DOI: 10.1002/cncr.25499 [PubMed: 20925043]

Table 1

Characteristics of the study participants by serum testosterone levels, males, NHANES 2011–2012 *

		Serum testosterone (ng/mL)		
Participant characteristic	**No. (%)[a]**	**Mean[b]**	**Median**	**IQR**
Age, years				
≤ 24	359 (18.4)	4.61	4.49	3.36 – 5.71
25 – 29	178 (11.6)	4.39	4.22	3.23 – 5.30
30 – 34	197 (11.4)	4.31	4.10	3.06 – 5.14
35 – 39	184 (10.8)	3.95	3.80	2.97 – 4.62
40 – 44	171 (12.3)	3.81	3.60	2.76 – 4.61
45 – 49	169 (12.1)	3.85	3.45	2.69 – 5.00
≥ 50	319 (23.4)	4.00	3.76	2.71 – 4.95
Race / ethnicity				
NH white	586 (65.4)	4.11	3.95	2.83 – 4.99
NH black	368 (10.2)	4.34	4.09	2.93 – 5.51
NH Asian	220 (4.6)	4.09	3.93	2.95 – 4.97
Mexican American	195 (10.0)	4.29	3.78	2.97 – 5.21
Other Hispanic	143 (6.9)	4.04	3.70	2.85 – 4.93
Other	65 (2.9)	4.16	3.59	2.78 – 4.85
BMI (kg/m^2)				
< 25.0	525 (29.9)	4.95	4.75	3.70 – 6.11
25.0 – < 30.0	542 (35.9)	4.26	4.15	2.97 – 5.15
≥ 30.0	503 (34.2)	3.33	3.26	2.49 – 4.05
Missing	7			
Physical activity per week (hours)				
< 1	275 (15.8)	3.68	3.43	2.36 – 4.82
1 – < 5	332 (19.9)	3.95	3.67	2.78 – 4.74
5 – < 10	256 (17.7)	4.18	3.98	2.85 – 4.98
10 – < 20	264 (17.8)	4.24	3.92	3.11 – 5.05
≥ 20	443 (28.7)	4.47	4.30	3.26 – 5.48
Missing	7			
Smoking status				
Never	867 (54.5)	4.10	3.86	2.82 – 5.00
Former	283 (20.4)	3.97	3.75	2.72 – 4.64
Current	424 (25.1)	4.40	4.26	3.26 – 5.46
Missing	3			
Serum cotinine (ng/mL)				
< 1	960 (62.7)	4.00	3.77	2.73 – 4.92
1 – 10	104 (6.1)	4.38	4.03	2.99 – 5.36
≥ 10	513 (31.2)	4.40	4.28	3.27 – 5.48
Diabetes status				

		Serum testosterone (ng/mL)		
Participant characteristic	**No. (%)[a]**	**Mean[b]**	**Median**	**IQR**
Positive	101 (5.0)	3.75	3.13	2.40 – 4.76
Negative	1476 (95.0)	4.17	3.96	2.95 – 5.04
Fasting length (hours)				
< 1	129 (8.3)	4.07	3.78	2.69 – 4.82
1 – < 3	325 (20.7)	3.59	3.44	2.55 – 4.33
3 – < 6	222 (13.6)	3.69	3.66	2.66 – 4.47
6 – < 12	517 (33.0)	4.57	4.44	3.33 – 5.55
≥ 12	384 (24.4)	4.33	4.22	3.04 – 5.29
Time of blood draw				
Morning	791 (50.7)	4.48	4.34	3.29 – 5.40
Afternoon	531 (31.3)	3.93	3.61	2.72 – 4.78
Evening	255 (17.9)	3.57	3.33	2.62 – 4.32

*The source population consisted of 1577 non-institutionalized U.S. males aged 18–59 years.

IQR = inter-quartile range.

NH = non-Hispanic

BMI = body mass index

[a]Proportions were determined using survey procedures to account for the sampling design of NHANES.

[b]Least squares means were used to estimate means using survey procedures to account for the sampling design of NHANES.

Table 2

Characteristics of the study participants by marijuana use, males, NHANES 2011–2012 *

Participant characteristic	Ever used marijuana, No. (%)[a]	Never used marijuana, No. (%)[a]
Age, years		
≤ 24	234 (18.5)	125 (18.4)
25 – 29	111 (11.6)	67 (11.5)
30 – 34	125 (11.3)	72 (11.5)
35 – 39	104 (9.9)	80 (12.7)
40 – 44	90 (11.9)	81 (13.2)
45 – 49	106 (11.4)	63 (13.3)
≥ 50	193 (25.5)	126 (19.4)
Race / ethnicity		
NH White	414 (70.0)	172 (56.4)
NH Black	253 (10.7)	115 (9.1)
NH Asian	78 (2.4)	142 (8.9)
Mexican American	95 (7.7)	100 (14.3)
Other Hispanic	76 (5.8)	67 (9.1)
Other	47 (3.3)	18 (2.2)
BMI (kg/m^2)		
< 25.0	313 (30.1)	212 (29.4)
25.0 – < 30.0	333 (36.3)	209 (35.3)
≥ 30.0	313 (33.6)	190 (35.3)
Missing	4	3
Physical activity per week (hours)		
< 1	145 (13.0)	130 (21.4)
1 – < 5	187 (19.9)	145 (20.0)
5 – < 10	154 (18.4)	102 (16.4)
10 – < 20	178 (18.8)	86 (15.9)
≥ 20	293 (30.0)	150 (26.2)
Missing	6	1
Cigarette smoking status		
Never	423 (44.1)	444 (74.8)
Former	198 (24.3)	85 (12.7)
Current	340 (31.6)	84 (12.4)
Missing	2	1
Serum cotinine (ng/mL)		
< 1	486 (55.2)	474 (77.2)
1 – 10	77 (7.2)	27 (4.0)
≥ 10	400 (37.5)	113 (18.9)
Diabetes status		
Positive	58 (5.3)	43 (4.5)
Negative	905 (94.7)	571 (95.5)

Participant characteristic	Ever used marijuana, No. (%)[a]	Never used marijuana, No. (%)[a]
Fasting length (hours)		
< 1	85 (9.3)	44 (6.4)
1 – < 3	194 (19.7)	131 (22.6)
3 – < 6	123 (12.1)	99 (16.7)
6 – < 12	336 (34.7)	181 (29.7)
≥ 12	225 (24.3)	159 (24.6)
Time of blood draw		
Morning	487 (52.3)	304 (47.4)
Afternoon	319 (30.8)	212 (32.5)
Evening	157 (16.9)	98 (20.0)

[*] The source population consisted of 1577 non-institutionalized U.S. males aged 18–59 years.

NH = non-Hispanic

BMI = body mass index

[a] Proportions were determined using survey procedures to account for the sampling design of NHANES

Table 3

Relationship between marijuana use and mean serum testosterone levels, males, NHANES 2011–2012

		Unadjusted		Adjusted[a]	
Participant characteristic	**No. (%)[b]**	**Mean[c]**	**95% CI**	**Mean[c]**	**95% CI**
Ever used marijuana					
No	614 (33.8)	3.70	(3.51, 3.91)	3.70	(3.45, 3.98)
Yes	963 (66.2)	3.84	(3.66, 4.02)	3.69	(3.46, 3.93)
Current or past use					
Past use	660 (73.4)	3.69	(3.50, 3.89)	3.72	(3.44, 4.03)
Current use	300 (26.6)	4.27	(4.03, 4.53)	3.96	(3.55, 4.42)
Time since last marijuana use					
> 5 years	372 (44.5)	3.59	(3.40, 3.80)	3.65	(3.35, 3.98)
> 1 year – 5 years	124 (14.4)	3.69	(3.17, 4.31)	3.73	(3.18, 4.38)
> 1 month – 1 year	163 (14.4)	3.98	(3.67, 4.33)	3.89	(3.54, 4.27)
≤ 1 month	300 (26.6)	4.27	(4.03, 4.53)	3.97	(3.56, 4.42)
p-value for trend[d]			*<0.01*		*0.19*
Ever used marijuana regularly					
No	456 (49.8)	3.64	(3.37, 3.94)	3.66	(3.31, 4.05)
Yes	506 (50.2)	4.03	(3.87, 4.21)	3.90	(3.56, 4.29)
Marijuana use frequency during regular use					
1 – 3 times per month	103 (20.2)	4.22	(3.81, 4.68)	4.54	(3.90, 5.29)
4 – 8 times per month	119 (24.7)	3.98	(3.65, 4.34)	4.07	(3.65, 4.55)
9 – 24 times per month	126 (25.4)	3.98	(3.58, 4.43)	4.05	(3.51, 4.68)
25 – 30 times per month	155 (29.7)	3.99	(3.46, 4.60)	3.96	(3.52, 4.46)
p-value for trend[d]			*0.66*		*0.24*
Number of joints / pipes per day during regular use					
1	177 (41.4)	4.05	(3.75, 4.39)	4.13	(3.72, 4.59)
2	166 (30.7)	3.94	(3.78, 4.10)	4.13	(3.67, 4.66)
3 or more	160 (27.9)	4.14	(3.64, 4.70)	4.19	(3.81, 4.60)
p-value for trend[d]			*0.74*		*0.76*

		Unadjusted		Adjusted[a]	
Participant characteristic	**No. (%)[b]**	**Mean[c]**	**95% CI**	**Mean[c]**	**95% CI**
Time since last regular marijuana use					
> 5 years	163 (38.7)	3.68	(3.39, 4.00)	3.94	(3.51, 4.42)
> 1 year – 5 years	65 (12.5)	3.67	(3.04, 4.44)	3.88	(3.18, 4.72)
> 1 month – 1 year	80 (15.5)	4.44	(3.96, 4.98)	4.63	(4.14, 5.17)
≤ 1 month	195 (33.3)	4.45	(4.05, 4.89)	4.42	(3.84, 5.09)
p-value for trend[d]			*0.03*		*0.02*
Years of regular marijuana use					
< 5 years	159 (26.2)	3.82	(3.46, 4.21)	3.86	(3.38, 4.40)
5 – < 10 years	91 (18.0)	4.50	(3.87, 5.24)	4.65	(3.97, 5.45)
10 – < 20 years	135 (28.1)	3.94	(3.59, 4.33)	4.09	(3.53, 4.73)
≥ 20 years	118 (27.7)	4.05	(3.58, 4.59)	4.35	(3.76, 5.03)
p-value for trend[d]			*0.92*		*0.51*

*The source population consisted of 1577 non-institutionalized U.S. males aged 18–59 years.

[a]Estimated using multiple linear regression with adjustment for age (continuous), race / ethnicity, BMI (continuous), physical activity per week, cigarette smoking status, diabetes status, fasting length, and time of blood draw.

[b]Proportions were determined using survey procedures to account for the sampling design of NHANES.

[c]Least squares means were used to estimate means using survey procedures to account for the sampling design of NHANES.

[d]P-value of test for trend of categorizations of marijuana use with 3 or more categories using a continuous variable.

Table 4

Relationship between marijuana use and testosterone levels by age-group, males, NHANES 2011–2012

	18–29 years					≥ 30 years				
		Unadjusted		Adjusted[a]			Unadjusted		Adjusted[a]	
Participant characteristic	**No. (%)[b]**	**Mean[c]**	**95% CI**	**Mean[c]**	**95% CI**	**No. (%)[b]**	**Mean[c]**	**95% CI**	**Mean[c]**	**95% CI**
Ever used marijuana										
No	192 (33.7)	4.19	(3.81, 4.62)	4.35	(3.40, 5.58)	422 (33.9)	3.51	(3.32, 3.72)	3.41	(3.12, 3.73)
Yes	345 (66.3)	4.10	(3.72, 4.53)	4.03	(3.26, 4.97)	618 (66.1)	3.72	(3.56, 3.90)	3.51	(3.25, 3.77)
Current or past use										
Past use	196 (64.3)	3.93	(3.52, 4.39)	3.86	(3.51, 4.25)	464 (77.3)	3.60	(3.42, 3.79)	3.55	(3.26, 3.86)
Current use	149 (35.7)	4.43	(3.95, 4.97)	4.15	(3.77, 4.58)	151 (22.7)	4.17	(3.86, 4.49)	3.81	(3.32, 4.39)
Time since last marijuana use										
> 5 years	37 (16.4)	3.60	(3.23, 4.01)	3.24	(2.88, 3.64)	335 (56.7)	3.59	(3.36, 3.83)	3.54	(3.22, 3.88)
> 1 year – 5 years	60 (20.4)	3.76	(2.91, 4.86)	3.62	(2.86, 4.58)	64 (11.9)	3.65	(2.91, 4.58)	3.57	(2.90, 4.40)
> 1 month – 1 year	99 (27.5)	4.29	(3.78, 4.87)	4.10	(3.89, 4.33)	64 (8.7)	3.61	(3.15, 4.13)	3.58	(3.08, 4.15)
≤ 1 month	149 (35.7)	4.43	(3.95, 4.97)	4.09	(3.76, 4.44)	151 (22.7)	4.16	(3.85, 4.49)	3.81	(3.31, 4.39)
p-value for trend[d]			*0.03*		*<0.01*			*0.16*		*0.49*
Ever used marijuana regularly										
No	166 (54.2)	3.96	(3.52, 4.46)	3.81	(3.27, 4.44)	290 (47.9)	3.50	(3.23, 3.79)	3.49	(3.10, 3.93)
Yes	179 (45.8)	4.28	(3.70, 4.95)	4.12	(3.68, 4.61)	327 (52.1)	3.94	(3.74, 4.16)	3.71	(3.33, 4.13)
Marijuana use frequency during regular use										
1 – 3 times per month	41 (18.3)	4.07	(3.44, 4.83)	4.15	(3.33, 5.18)	62 (20.9)	4.27	(3.77, 4.84)	4.42	(3.69, 5.28)
4 – 8 times per month	35 (22.9)	4.35	(3.66, 5.18)	4.24	(3.45, 5.21)	84 (25.4)	3.86	(3.37, 4.42)	3.88	(3.37, 4.46)
9 – 24 times per month	45 (24.1)	4.11	(3.30, 5.13)	3.74	(3.16, 4.43)	81 (25.9)	3.93	(3.45, 4.49)	3.99	(3.24, 4.92)
25 – 30 times per month	58 (34.7)	4.47	(3.59, 5.57)	4.00	(3.16, 5.06)	97 (27.8)	3.78	(3.16, 4.51)	3.65	(3.22, 4.13)
p-value for trend[d]			*0.53*		*0.49*			*0.47*		*0.21*
Number of joints / pipes per day during regular use										
1	50 (32.0)	4.13	(3.51, 4.88)	4.10	(3.38, 4.98)	127 (45.0)	4.03	(3.62, 4.50)	4.00	(3.45, 4.63)
2	65 (29.1)	4.24	(4.00, 4.49)	3.82	(3.15, 4.62)	101 (31.3)	3.84	(3.61, 4.08)	3.97	(3.48, 4.54)
3 or more	64 (38.9)	4.44	(3.41, 5.78)	4.19	(3.59, 4.89)	96 (23.7)	3.96	(3.50, 4.48)	3.89	(3.54, 4.28)

	18–29 years					≥ 30 years				
		Unadjusted		Adjusted[a]			Unadjusted		Adjusted[a]	
Participant characteristic	**No. (%)[b]**	**Mean[c]**	**95% CI**	**Mean[c]**	**95% CI**	**No. (%)[b]**	**Mean[c]**	**95% CI**	**Mean[c]**	**95% CI**
p-value for trend[d]			*0.55*		*0.48*			*0.86*		*0.69*
Time since last regular marijuana use										
> 5 years	13 (10.9)	3.18	(2.64, 3.82)	3.20	(2.50, 4.11)	150 (49.3)	3.73	(3.37, 4.12)	3.85	(3.36, 4.41)
> 1 year – 5 years	32 (18.6)	3.75	(2.88, 4.87)	3.66	(3.00, 4.47)	33 (10.2)	3.63	(2.73, 4.82)	3.54	(2.84, 4.42)
> 1 month – 1 year	36 (18.8)	4.42	(3.45, 5.67)	4.29	(3.53, 5.20)	44 (14.2)	4.45	(3.87, 5.12)	4.54	(4.02, 5.12)
≤ 1 month	98 (51.6)	4.73	(4.19, 5.33)	4.22	(3.41, 5.23)	97 (26.3)	4.24	(3.77, 4.79)	4.20	(3.59, 4.92)
p-value for trend[d]			*<0.01*		*<0.01*			*0.16*		*0.10*
Years of regular marijuana use										
< 5 years	111 (60.2)	4.13	(3.54, 4.81)	3.60	(2.92, 4.42)	48 (13.3)	3.34	(2.79, 3.99)	3.58	(3.05, 4.20)
5 – < 10 years	51 (30.3)	4.58	(3.83, 5.48)	4.24	(3.33, 5.39)	40 (13.3)	4.43	(3.56, 5.53)	4.57	(3.51, 5.95)
10 – < 20 years	17 (9.5)	4.36	(3.14, 6.06)	4.82	(3.49, 6.66)	118 (35.2)	3.90	(3.51, 4.35)	3.86	(3.31, 4.50)
≥ 20 years	–	–		–		118 (38.2)	4.05	(3.58, 4.59)	4.13	(3.53, 4.83)
p-value for trend[d]			*0.51*		*0.01*			*0.40*		*0.50*

[*] The source population consisted of 1577 non-institutionalized U.S. males aged 18–59 years.

[a] Estimated using multiple linear regression with adjustment for age (continuous), race / ethnicity, BMI (continuous), physical activity per week, cigarette smoking status, diabetes status, fasting length, and time of blood draw.

[b] Proportions were determined using survey procedures to account for the sampling design of NHANES.

[c] Least squares means were used to estimate means using survey procedures to account for the sampling design of NHANES.

[d] P-value of test for trend of categorizations of marijuana use with 3 or more categories using a continuous variable