

Medical Marijuana Users are More Likely to Use Prescription Drugs Medically and Nonmedically

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Objectives: Previous studies have found a negative population-level correlation between medical marijuana availability in US states, and trends in medical and nonmedical prescription drug use. These studies have been interpreted as evidence that use of medical marijuana reduces medical and nonmedical prescription drug use. This study evaluates whether medical marijuana use is a risk or protective factor for medical and nonmedical prescription drug use.

Methods: Simulations based upon logistic regression analyses of data from the 2015 National Survey on Drug Use and Health were used to compute associations between medical marijuana use, and medical and nonmedical prescription drug use. Adjusted risk ratios (RRs) were computed with controls added for age, sex, race, health status, family income, and living in a state with legalized medical marijuana.

Results: Medical marijuana users were significantly more likely (RR 1.62, 95% confidence interval [CI] 1.50–1.74) to report medical use of prescription drugs in the past 12 months. Individuals who used medical marijuana were also significantly more likely to report nonmedical use in the past 12 months of any prescription drug (RR 2.12, 95% CI 1.67–2.62), with elevated risks for pain relievers (RR 1.95, 95% CI 1.41–2.62), stimulants (RR 1.86, 95% CI 1.09–3.02), and tranquilizers (RR 2.18, 95% CI 1.45–3.16).

Conclusions: Our findings disconfirm the hypothesis that a population-level negative correlation between medical marijuana use and prescription drug harms occurs because medical marijuana users are less likely to use prescription drugs, either medically or

nonmedically. Medical marijuana users should be a target population in efforts to combat nonmedical prescription drug use.

Key Words: cannabis, medical marijuana, nonmedical prescription drug use, opioid abuse, risk factor

(*J Addict Med* 2018;12: 295–299)

Several peer-reviewed studies (Bachhuber et al., 2014; Bradford and Bradford, 2016; Kim et al., 2016; Bradford and Bradford, 2017), and also some working papers (Powell et al., 2016; Smart, 2016), have demonstrated that US states with medical marijuana access laws have lower rates of medical and nonmedical prescription drug use, and also associated harms, for example, opioid overdose. Some researchers have hypothesized that these ecological correlations emerge because individuals who use medical marijuana (ie, marijuana for medical purposes as recommended by a physician or other health professional) reduce their use of prescription medications (eg, opioid painkillers) and hence their risk of overdose (Bachhuber and Barry, 2016). Such an inference risks committing the “ecological fallacy” (Finney et al., 2015): the assumption that relationships between population-level data will necessarily be reflected in the behavior of individuals. As has been recognized for decades in numerous social science fields, many things that correlate in the aggregate do not do so at the individual level (Finney et al., 2011; Humphreys et al., 2015). For example, regions of France with the highest rates of smoking have the lower rates of esophageal cancer (Cohen, 1990) and US counties with the highest levels of radon exposure have the lowest rates of lung cancer (Richardson et al., 1987), but this does not mean that individuals who smoke and are exposed to radon have lower cancer risks. Different relationships between variables at the individual versus aggregate level may occur for multiple reasons, including different confounders operating at different levels of analysis and omitted variables (Portnov et al., 2007; Finney et al., 2011).

One well-known medical marijuana study illustrates the hazards of assuming that aggregate relationships are replicated at the individual level. Bradford and Bradford (2016) documented that there were fewer aggregate prescription medications from the US Medicare program (insurance for individuals who are over the age of 65 and/or disabled) in states that had legalized medical marijuana. Several journalists claimed the study was evidence that Medicare recipients are replacing prescription medications with medical marijuana, thereby saving the Medicare program over \$150

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Received for publication September 11, 2017; accepted January 29, 2018.

Conflicts of interest: TLC was supported by the George J. Mitchell Scholarship of the US-Ireland Alliance. KH was supported by a Senior Career Research Scientist Award from the Veterans Affairs Health Services Research and Development Service and by a grant from Stanford Neurosciences Institute.

Supplemental digital content is available for this article. Direct URL citation appears in the printed text and is provided in the HTML and PDF versions of this article on the journal's Web site (www.journaladdictionmedicine.com).

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ISSN: 1932-0620/18/1204-0295

DOI: 10.1097/ADM.0000000000000405

million per year (eg, Close, 2016). However, we analyzed individual-level data (ie, National Survey on Drug Use and Health [NSDUH]) and found that only approximately 2% to 3% of Medicare recipients in states with legalized medical marijuana used medical marijuana (Caputi and Humphreys, 2016). While technically possible, we believe 2% to 3% of Medicare recipients is simply too small a population to account for Bradford and Bradford's finding of reductions of 5.7% in pain prescriptions, 5.4% in nausea prescriptions, 5.2% in seizure prescriptions, 5.0% in anxiety prescriptions, 4.8% in sleep disorder prescriptions, 4.5% in psychosis prescriptions, 2.8% in depression prescriptions, and 1.5% in spasticity prescriptions. Because it is theoretically possible that such a small population could account for this large of an effect, some will disagree with our assessment that this effect is unreasonably large. However, Bradford and Bradford's paper is just 1 of many studies claiming outsized effects from this small population of medical marijuana users. When one also considers that other studies in this area attribute to medical marijuana use to sizable population decreases in alcohol sales (Baggio et al., 2017), body mass index (Sabia et al., 2017), and opioid overdoses (Bachhuber et al., 2014), it becomes increasingly difficult to sustain the idea that 2% to 3% of the population using medical marijuana truly has the enormous effects described in this literature (Caputi, under review). This suggests that population-level data do not necessarily reflect the impact of medical marijuana on prescription drug use among individuals.

State-level studies showing a negative correlation between medical marijuana and prescription drug use, and/or overdose have been shared widely and interpreted generously by journalists and marijuana policy activists (Millman, 2014; Friedersdorf, 2016; Mitman, 2016). This has convinced many researchers, policy makers, and medical practitioners that medical marijuana use is a protective factor for prescription drug nonmedical use—a conclusion ecological studies cannot prove nor disprove (Hall et al., 2018). Although a small study of Los Angeles young adults (Lankenau and Iverson, 2015) provides some support for this hypothesis at an individual level, it has never before been tested with a large, nationally-representative dataset. To provide a more robust test, we examine individual-level data from the NSDUH to determine whether medical marijuana users are at lower or higher risk for medical and nonmedical prescription drug use.

METHODS

Data Source

Data were collected from the 2015 NSDUH public use data file (Center for Behavioral Health Statistics and Quality, 2016), which contains the confidential responses of 57,146 US household residents aged 12 and older to a computer-assisted personal interview (see Supplemental Table 1, Supplemental Digital Content 1, <http://links.lww.com/JAM/A80>). The validated survey uses a complex, 4-stage survey design to create a nationally-representative sample and provide reliable estimates of the prevalence of substance use in the United States.

Measures

Participants' use of prescription drugs was measured both on the aggregate and in 4 categories of prescription drugs: pain relievers, sedatives, stimulants, and tranquilizers. For each category of drug, NSDUH asks participants about their prescription drug use behaviors, with separate questions for any (ie, medical or nonmedical use) and strictly nonmedical use. Participants report the timeframe within which they last used the drug, including an option for never having used the drug. For this study, a binomial variable is coded for whether the respondent reports a timeframe less than or equal to 12 months.

In the 2015 NSUDH and, consequently, for this study, nonmedical use is defined as the use of prescription drugs that is inconsistent with doctor's instructions, including using without a prescription, using a greater amount than directed, or using longer than prescribed. Participants who reported using marijuana in the past 12 months were asked if any of their marijuana use in the past 12 months was recommended by a doctor or other healthcare professional. Respondents were coded as medical marijuana users if they responded affirmatively. Further information on these variables and the covariates is available elsewhere (Center for Behavioral Health Statistics and Quality, 2016).

Statistical Analyses

Separate logistic regressions were conducted with medical and nonmedical prescription drug use in the past 12 months as the dependent variables, medical marijuana use in the past 12 months as the independent variable, and controls for age, sex, race, family income, health status, and living in a state that has legalized medical marijuana. The 12-month timeframe was chosen because it could be consistently observed across medical and nonmedical prescription drug use and medical marijuana use, given the NSDUH data.

In a subsidiary analysis, we also include ever cigarette use, 30-day alcohol use, and ever drug/alcohol treatment as covariates. These covariates are not included in our main analysis because they introduce possible post-treatment bias to the model, an increasingly well-recognized issue in the literature (eg, Montgomery et al., 2016).

Because odds ratios (ORs) can be confusing and, when interpreted incorrectly, biased (Davies et al., 1998), results are presented for simple interpretation as risk ratios (RRs): the ratio of estimated probability among an exposed group (ie, medical marijuana users) over the estimated probability among an unexposed group (ie, medical marijuana nonusers), where 1.00 indicates equality and 1.50 indicates a 50% greater risk among medical marijuana users compared to nonusers.

$$\text{Risk ratio} = \frac{P(\text{Outcome}|\text{Medical Marijuana Use})}{P(\text{Outcome}|\text{Medical Marijuana Non-Use})}$$

To compute these RRs, we estimated the probability of an individual exhibiting each outcome contingent upon medical marijuana use/nonuse (with covariates held at their mean) through 10,000 simulations based upon random draws from the logistic regression's variance-covariance matrix (see King et al., 2000 for a thorough description of this method).

Analyses were conducted using R ver 3.4.1 (R Core Team, 2016).

Medical marijuana users may be more likely to use prescription medications nonmedically, because, by definition, they are receiving medical attention, and may, therefore, have a medical concern and easier access to prescription medications (the reasonability of this notion can be partially explored in the first portion of our analysis). In that case, medical marijuana users would have a higher risk for non-medical prescription drug use than the general population, but much the same risk as others receiving medical attention. To explore this possibility, we replicated our analyses over the subpopulation of NSDUH respondents who had used prescription medications either medically or nonmedically in the past year, that is, people who have a medical concern and greater access to prescription medications.

Human Protections

The NSDUH is a validated protocol administered by the Research Triangle Institute. This study only used the 2015 NSDUH’s nonidentifiable, public-use data file, made available by the US Substance Abuse and Mental Health Services Administration, and was therefore exempted from review by the University of Pennsylvania Institutional Review Board.

RESULTS

Medical marijuana users were significantly more likely than medical marijuana nonusers to use prescription drugs (RR 1.62, 95% confidence interval [CI] 1.50–1.74) and to use prescription drugs nonmedically (RR 2.12, 95% CI 1.67–2.62) (Table 1). Further, when the analysis was limited to only those who had used prescription drugs in the past year, medical marijuana users were significantly more likely to

use any prescription drugs nonmedically than medical marijuana nonusers (RR 1.38, 95% CI 1.09–1.70).

When analyzed based upon specific substances, medical marijuana users were significantly more likely to use pain relievers (RR 1.66, 95% CI 1.49–1.83), sedatives (RR 1.82, 95% CI 1.26–2.51), stimulants (RR 2.23, 95% CI 1.71–2.86), and tranquilizers (RR 2.46, 95% CI 2.00–2.98) (Table 1). Further, medical marijuana users were more likely to non-medically use pain relievers (RR 1.95, 95% CI 1.41–2.62), stimulants (RR 1.86, 95% CI 1.09–3.02), and tranquilizers (RR 2.18, 95% CI 1.45–3.16). When the analysis is narrowed to only the subpopulation that reports any use of prescription drugs, the analysis becomes less clear. Although medical marijuana users are significantly more likely to engage in nonmedical use of any prescription drug, this result is not significant for any of the 4 prescription drug subcategories. The lack of significance within subcategories may be due to limited sample size and attendant loss of statistical power.

Nonmedical use of pain relievers is of particular interest because of pain relievers’ role in the opioid overdose epidemic. Medical marijuana users were more likely to use prescription pain relievers (RR 1.66, 95% CI 1.49–1.83) and also to use prescription pain relievers nonmedically (RR 1.95, 95% CI 1.41–2.62).

Our subsidiary analysis (Supplemental Table 2, Supplemental Digital Content 2, <http://links.lww.com/JAM/A81>), which included controls for tobacco use, alcohol use, and drug/alcohol treatment, showed similar results to our main analysis, except that when the sample is limited to respondents who report any use of prescription drugs, there is no evidence of a significant difference between medical marijuana users and nonusers in nonmedical prescription drug use. As mentioned in the “Methods” section, these results are subsidiary to our main analysis, because including controls for

TABLE 1. Risk Ratios of Medical Marijuana Users Relative to Medical Marijuana Nonusers

	Unadjusted RR	95% CI	Adjusted RR	95% CI
Use (medical and/or nonmedical)				
All prescription drugs	1.64*	(1.51–1.76)	1.62*	(1.50–1.74)
Pain relievers	1.69*	(1.51–1.87)	1.66*	(1.49–1.83)
Sedatives	1.70*	(1.23–2.29)	1.82*	(1.26–2.51)
Stimulants	2.50*	(2.03–3.04)	2.23*	(1.71–2.86)
Tranquilizers	2.33*	(1.98–2.69)	2.46*	(2.00–2.98)
Nonmedical use				
All prescription drugs	2.76*	(2.23–3.36)	2.12*	(1.67–2.62)
Pain relievers	2.67*	(1.99–3.49)	1.95*	(1.41–2.62)
Sedatives	2.87	(0.96–6.69)	2.45	(0.72–6.06)
Stimulants	2.62*	(1.71–3.82)	1.86*	(1.09–3.02)
Tranquilizers	2.97*	(2.00–4.24)	2.18*	(1.45–3.16)
Nonmedical use (among users)				
All prescription drugs	1.68*	(1.36–2.04)	1.38*	(1.09–1.70)
Pain relievers	1.57*	(1.19–2.02)	1.25	(0.92–1.66)
Sedatives	1.66	(0.56–3.56)	1.61	(0.43–3.96)
Stimulants	1.04	(0.68–1.47)	0.99	(0.66–1.39)
Tranquilizers	1.28	(0.87–1.78)	0.99	(0.66–1.42)

Data are drawn from the 2015 National Survey for Drug Use and Health. Each result represents a model where prescription drug use/nonmedical use in the past 12 months is the independent variable, medical marijuana use in the past 12 months is the dependent variable, and controls are added for age, sex, race, health status, family income, and living in a state with legalized medical marijuana. Estimates and confidence intervals were calculated based upon 10,000 bootstrapped simulations from random draws of the variance–covariance matrix of the logistic regression model, with covariates set at their mean. Results are presented as risk ratios, that is, the estimated probability among medical marijuana users divided by the estimated probability among medical marijuana nonusers. All estimates are adjusted for the NSDUH complex survey design.

CI, confidence interval; RR, risk ratio.

*Represents statistical significance ($P < 0.05$).

alcohol, tobacco, and drug treatment risks introducing post-treatment bias into our model. Indeed, this insignificant finding may emerge because of post-treatment bias.

DISCUSSION

Medical marijuana users were at higher risk for prescription drug use and specifically nonmedical prescription drug use than medical marijuana nonusers in a large national survey. We also found elevated risks of nonmedical prescription drug use among medical marijuana patients when analyzing only the subset of the population that used prescription drugs. This suggests that the elevated risk for prescription drug nonmedical use among medical marijuana users cannot be ascribed simply to their having a medical concern or greater access to prescription drugs.

Previous research has focused on the relationship between medical marijuana and pain relievers, because marijuana is sometimes used to treat pain (Hill, 2015) and prescription pain relievers have played a significant role in the opioid overdose epidemic. We found a significant association between medical marijuana use and not only nonmedical pain reliever use, but nonmedical stimulant and tranquilizer use as well. Further, our point estimates for relative risk were higher for nonmedical sedative and tranquilizer use than for nonmedical pain reliever use. Our findings suggest the need to explore the relationships between medical marijuana use and other types of prescription drug nonmedical use which also contribute to opioid overdose (Sun et al., 2017).

Our analysis is limited in that it is cross-sectional. As we utilize cross-sectional data, we cannot draw any conclusion on substitution effects. However, the finding that medical marijuana patients are more likely to use prescription drugs than medical marijuana nonusers is significant by itself. Medical marijuana use should not be considered a protective factor; indeed, it should be screened for as a marker for high risk of nonmedical prescription drug use. These results are in line with recent research utilizing longitudinal data (Olfson et al., 2017), which showed that marijuana use increases the risk of developing nonmedical prescription opioid use and disorder.

Few extant studies use individual-level data to examine the relationship between medical marijuana use and prescription drugs, and to our knowledge, none have used nationally-representative, individual-level data. Our analyses raise major doubts about the common interpretation of negative ecological correlations that medical marijuana users replace medical marijuana for prescription drugs (Caputi and Sabet, 2018), particularly the hypothesis that medical marijuana users are replacing prescription drug use with marijuana. Future research using longitudinal, individual-level data should be conducted to determine whether patients substitute medical marijuana for prescription drugs (Hall et al., 2018).

CONCLUSIONS

These findings suggest that healthcare professionals should screen for prescription drug nonmedical use among their patients who use medical marijuana, and, when necessary, recommend interventions. The fact that medical marijuana users are at higher risk for prescription drug nonmedical use than other prescription drug users suggests that doctors

recommending medical marijuana use should be more, rather than less, concerned about prescription drug nonmedical use among their marijuana-using patients. Caretakers should not assume that medical marijuana users are less likely to use prescription drugs. Policy makers may find it useful to explore interventions to reduce prescription drug nonmedical use interventions in this high-need population; fortunately, medical marijuana users are, by the definition set forth in the NSDUH, receiving information from a doctor, making possible interventions initiated in a medical setting.

ACKNOWLEDGMENTS

The authors would like to thank Dr Wayne Hall for his comments on an earlier version of the manuscript.

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