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Marijuana and Prescription Pain Reliever Use Among Cigarette Smokers

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Abstract

Due to marijuana's analgesic effects and its growing national legal status, it is likely that marijuana's rising prevalence will impact prescription pain reliever (PPR) use. The present study investigates the relationship between marijuana and PPR use among U.S. adult current cigarette smokers. Data were analyzed from the Tobacco and Attitudes Beliefs Survey II, with 348 current cigarette smokers, aged 24–88. Logistic regression was used to examine the likelihood of current (past 30 days) PPR use by marijuana use (never, ever, and current) among cigarette smokers. Among PPR users (N=76), we also investigated whether marijuana use frequency predicted current PPR use. Compared to never marijuana users, participants were more likely to report past 30-day PPR use if they have ever used marijuana (AOR: 2.58, 95% CI: 1.51–4.43) or have used marijuana in the past 30 days (AOR: 3.38, CI: 1.76–6.49). No significant relationship was found between marijuana use frequency and PPR use. Thus, in this sample of adult cigarette smokers, past and current marijuana users were two to three times more likely to report PPR use than never marijuana users. These findings can help inform policy makers and healthcare providers in their fight against the opioid epidemic.

Keywords

Prescription pain relievers; marijuana; dual-use; cigarettes; tobacco; substance use

INTRODUCTION

In the U.S., use of prescription pain relievers (PPRs), also known as prescription opioids and opioid pain relievers, has been increasing dramatically. Worldwide, prescriptions of PPRs have almost tripled since 1990, and the U.S. is a factor in this rise, as it has the highest per

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capita consumption of PPRs in the past ten years (International Narcotics Control Board 2016). This increase has become dangerous, as opioid use carries risks that include addiction, sedation, respiratory depression, overdose (OD) and death (Rudd et al. 2016; Benyamin et al. 2008). Between 1999 and 2010, deaths attributed to PPRs rose five times among women and 3.5 times among men (Mack, Jones & Paulozzi 2013). Of all prescription drug OD deaths in the U.S. in 2013, 71.3% involved PPRs (Mack, Jones & Paulozzi 2013).

PPRs and marijuana (i.e., cannabis) are biologically linked; like PPRs, marijuana induces analgesia, acts on some of the same brain regions, and partly exerts its effects via opioid receptors (Mack, Jones & Paulozzi 2013; Maione et al. 2011; Lynch & Campbell 2011; Cichewicz 2004). This connection is especially relevant due to the changing legal status of marijuana. As of August 2016, 24 states and Washington D.C. had legalized medical marijuana. Between 2007 and 2012, the number of past month marijuana users rose from 5.8 to 7.3% (Substance Abuse and Mental Health Services Administration (SAMHSA) 2013), and between 2001 and 2013, past year adult marijuana use increased from 4.1 to 9.5% in the U.S. (National Institute on Alcohol Abuse and Alcoholism 2015). Further, legalization of medical marijuana has been associated with increased odds of marijuana use among adults (Wang & Cataldo 2016; Martins et al. 2016; Wang et al. 2016; Cerdá et al. 2012), though no consistent association has been determined among youth/young adults (Martins et al. 2016; Wall et al. 2016).

Distinct theories attempt to explain how medical marijuana legalization affects use of substances other than marijuana. The relationship between different substances can be impacted by 1) change in cost of a substance, 2) policy alterations that influence availability of a substance, 3) shifts in legal consequences of using a substance, and/or 4) the psychoactive/pharmacological effects of a substance (Lucas et al. 2013). More U.S. states are legalizing medical marijuana (related to both policy and legal shifts), and marijuana shares some psychoactive/pharmacological effects with PPRs.

The substitution theory postulates that there is a substitution effect, whereby an increase in marijuana use coincides with a decrease in the use of other substances – in this case, PPRs (Lucas et al. 2013; Hursh et al. 2005). There are logical reasons why individuals would opt to use marijuana instead of PPRs. With the new legal status of medical marijuana, individuals can access it through medical dispensaries and enjoy a lower legal risk if they live in a state where it is legalized. Individuals also report switching to marijuana for pain control because when compared to prescription drugs, marijuana has fewer side effects and withdrawal symptoms (Lucas et al. 2013). Studies supporting the substitution effect have demonstrated that either increases in the use of marijuana or the legalization of medical marijuana is associated with reductions in opioid use, hospitalizations for opioid dependence/abuse, PPR ODs, and opioid OD mortality (Shi 2017; Boehnke, Litinas & Clauw 2016; Bachhuber et al. 2014).

In contrast to the substitution effect, there may be a complementary effect, where an increase in marijuana use is associated with an increase in the use of PPRs (Lucas et al. 2013; Hursh et al. 2005). In support of this theory, researchers using National Survey on Drug Use and Health (NSDUH) data found a positive association between marijuana and increased use of

PPRs (Novak, Peiper & Zarkin 2016). In another study, researchers focused on individuals who were prescribed long-term opioid therapy and found that those who also used medical marijuana presented with greater risk of misusing prescription opioids. (Nugent et al. 2018) Additionally, a prospective cohort study using the National Epidemiologic Survey of Alcohol and Related Conditions (NESARC) data determined that use of marijuana was associated with a greater risk of using nonmedical prescription opioids three years later (Olfson et al. 2018). However, in these studies, researchers did not analyze how co-use of other substances would impact the direction and/or strength of the relationship between marijuana and opioids/PPRs. To determine if there is either a substitution or a complementary effect between marijuana use and PPR use, co-use with other substances needs to be studied.

Additionally, there is a strong positive association between nicotine use and PPR use. When compared to non-smokers, tobacco smokers experience more intense and longer lasting chronic pain, as well as a higher frequency of PPR use (Yoon, Lane & Weaver 2015; Zale et al. 2015; Skurtveit et al. 2010). Studies have demonstrated an interaction between nicotine and opioids that is associated with an increase in the total consumption of the two substances and contributes to other effects of the drugs (Kohut 2017). The relationship between the use of these two substances has a basis in the biological connection between them, as the endogenous opioid system is an underlying mechanism for several behavioral outcomes related to nicotine (i.e., nicotine craving, anxiolytic and anxiogenic effects, and nicotine withdrawal symptoms) (Nuechterlein et al. 2016; Hadjiconstantinou & Neff 2011; Berrendero et al. 2010). Like marijuana, nicotine is involved in anti-nociception via endogenous opioid system mediation, suggesting that nicotine is used for the self-medication of pain (Kishioka et al. 2014; Ditre et al. 2016); and in fact, nicotine heightens the anti-nociceptive effects of both opioids and marijuana (Kohut 2017). Several studies have documented common use patterns among tobacco, marijuana, and opioids/PPRs (Arterberry et al. 2016; Abrahamsson & Hakansson 2015; Fiellin et al. 2013). For example, a prospective study of NESARC data demonstrated that early-onset of smoking cigarettes increased the odds of beginning opioid use and that frequency of both cigarette and marijuana use increased the odds of beginning opioid use, re-initiating opioid use after previously stopping, and continuing opioid use among current users (Arterberry et al. 2016). Thus, the three substances share anti-nociceptive actions mediated by the endogenous opioid system, and evidence indicates that marijuana and nicotine use predict opioid use among adults.

From 2003 to 2012, NSDUH data revealed a significant increase in the co-use of marijuana and tobacco (from 4.4% to 5.2% of the sample) (Schauer et al. 2015). Further, smoking tobacco is significantly associated with cannabis dependence (Agrawal and Lynskey 2009). Given the national trend toward marijuana legalization, co-use is likely to increase. Cigarette smokers and marijuana users are a crucial population to study, as nicotine and marijuana share mechanisms of action with each other and with opioids, and use of each substance has been shown to be associated with use of opioids/PPRs (Arterberry et al. 2016, Abrahamsson and Hakansson 2015, Fiellin et al. 2013, Olfson et al. 2018, Nugent et al. 2018). However, whether there is an association between prevalence of marijuana and PPR use among current smokers has not been determined. The present study addresses this gap by using the Tobacco

Attitudes and Beliefs Survey (TABS) II to investigate the relationship between marijuana use and PPR use among current cigarette smokers. This study examines (in cigarette smokers) 1) the likelihood of PPR use by marijuana use and 2) the frequency of marijuana use and current PPR use. Findings may help elucidate whether marijuana use is associated with PPR use, and if so, whether marijuana is used as a substitute or complement to PPR use.

METHODS

Data and study sample

This is a cross sectional analysis of data from the TABS II, a web-based longitudinal survey of U.S. adult former and current cigarette smokers, aged 24 years old and older. The survey included topics such as individuals' use of tobacco, tobacco-related products, marijuana, and other substances including PPRs. The present analysis used demographic data from Wave 1 (baseline) from August 2015 (see Table 1). Wave 3 data were collected in August 2016 and included survey items on marijuana use and new items on PPR use (not included in Waves 1 or 2).

Surveys were administered by Qualtrics, which uses a combination of online panels to establish national samples from which survey participants can be randomly selected. Qualtrics invited potential participants to take the survey via an email notification and offered them a $10 incentive to complete each survey wave. For Wave 1, 2,378 individuals clicked on the survey link, and 819 went on to complete the survey, yielding a completion rate of 34.4% (a rate typically seen for Qualtrics online surveys). Current smokers (n = 348) were included in the current analysis. The TABS II project was approved by the UCSF Institutional Review Board.

Measures

Cigarette use.—Participants were categorized as a current cigarette smoker if they responded "yes" to the question, "Are you a current cigarette smoker?" and if they responded with any number of days greater than 0 for the question "During the last 7 days, on about how many days did you smoke cigarettes, even 1 or 2 puffs" or to the question "During the last 7 days, on about how many days did you smoke menthol cigarettes, even 1 or two puffs." The question "On average, how many cigarettes a day do you smoke?" was used to control for cigarette consumption in the analysis of the relationship between cannabis use and PPR use.

Marijuana use.—Definitions of each user type were: "never users," never used marijuana in their lifetime; "ever" users, used marijuana at least once in their lifetime, but not in the past 30 days; and "current" users, used marijuana in the past 30 days. If participants answered the question "During the last 30 days, on about how many days did you use marijuana, even 1 or 2 puffs?" with any number above 0, they were classified as a current user. If participants responded with "I have never tried marijuana" to the question asking "Which of the following forms of marijuana have you EVER used?" then they were classified as a never user. If they responded to this question with any other option besides

"Don't know/refused" and if they were not categorized as a current user, they were classified as an ever user. For the analysis involving frequency of marijuana use as a continuous variable, responses to the question "During the last 30 days, on about how many days did you use marijuana, even 1 or 2 puffs?" were used.

Medical marijuana law (MML) status in state of residence.—Participants were categorized as: 1) no legal medical marijuana in state of residence, 2) legal medical marijuana for less than 10 years in state of residence, or 3) legal medical marijuana for 10 or more years in state of residence.

PPR use.—PPR users were categorized as "never" users if they reported they had never used PPRs in their lifetime, as "ever" users if they had used PPRs but not in the past 30 days, and "current" users if they had used PPRs in the past 30 days. If participants selected "Prescription pain relievers" for the following two questions, they were classified as current PPR users: 1) "Have you EVER used any of the following substances? Mark all that apply" and 2) "Have you used any of the following substances in the PAST 30 DAYS? Mark all that apply." If participants selected "Prescription pain relievers" in the first question (ever use), but did not select them in the second question (past 30 day use), then they were classified as ever users. If they did not select "Prescription pain relievers" in the question inquiring about ever use, they were classified as never users.

Statistical Analysis—Descriptive analyses were used to test for normality. Chi-square tests were used for categorical variables (gender, race/ethnicity, education, occupational status, type of community, MLL status in state of residence, and PPR status), and an ANOVA was used for the continuous variables (age and average cigarettes smoked per day) to compare sample characteristics between marijuana never users, ever users, and current users. For PPR status, a Bonferroni adjustment was made to account for multiple comparisons.

Logistic regression (both unadjusted and adjusted for the sample characteristics of age, gender, race/ethnicity, education, occupational status, type of community, MML status in state of residence, and average cigarettes smoked per day) was used to investigate the likelihood of PPR use in the past 30 days (reference group = current users) according to marijuana use (never, ever, and current). A logistic regression was used to examine whether the frequency of marijuana use influenced PPR use among current marijuana users. SAS University Edition, which contains SAS Studio 3.6 and SAS 9.4, was used for all analyses.

RESULTS

Sample characteristics

Participants (N=348) ranged in age from 24 to 88 years old ($\bar{X}$ = 51.28, SD = 11.04). The majority were female (n=197, 56.61%) and Caucasian (n=293, 84.20%). On average, participants smoked over 15 cigarettes per day ($\bar{X}$ = 15.81, SD= 8.66). Table 1 presents demographic information and PPR status stratified by marijuana use. Chi-square tests and an ANOVA revealed no significant differences in sample characteristics across marijuana never, ever, and current users. A significant difference was found between marijuana never, ever,

and current users for PPR status (χ^2 = 14.84, df = 4, p = 0.005). We tested three comparisons (never/ever, never/current, ever/current) using SAS proc multest, which provides Bonferroni adjusted p values. A significant difference remained for the following PPR use groups: never vs. ever (p=0.009) and never vs. current (p=0.022).

Relationship between marijuana and PPR use

As shown in Table 2, logistic regression was used to further examine the relationship between marijuana and PPR use, with PPR current use set as the reference category for the criterion variable and marijuana never use set as the reference category for the predictor variable. The model was adjusted for all sample characteristics, and compared to marijuana never users, both marijuana ever users and current users were more likely to have used PPRs in the past 30 days, with ever users having an AOR=2.58 (95% CI: 1.51–4.43) and current users having an AOR=3.38 (CI: 1.76–6.49). A logistic regression was used to investigate the relationship between the frequency of marijuana use among current marijuana users and PPR use, and no significant results were found (Table 3).

DISCUSSION

Results suggest that adult current cigarette smokers have differential use of PPRs depending on their use of marijuana. Those who were current and ever marijuana users were over 2–3 times more likely to have used PPRs in the past 30 days, respectively, when compared to cigarette smokers who never used marijuana.

Results support the findings of previous studies that addressed a possible complementary effect of marijuana use with PPR use. Novak, Peiper, and Zarkin (2016) analyzed NSDUH data in 2003 and 2013 and found that greater marijuana use was associated with more frequent PPR use. An analysis of NESARC data found higher levels of marijuana and cigarette use predicted initiation, re-initiation, and sustained opioid use (Arterberry et al. 2016); and another study using NESARC data determined that marijuana use was associated with an elevated risk of using nonmedical prescription opioids three years later (Olfson et al. 2018). Two Swedish teams found similar results. One study found a positive association between use of marijuana and unauthorized use of PPRs (Berge, Hakansson & Berglund 2014). In a re-analysis of a Swedish national household survey, non-medical PPR use was associated with both frequent cigarette smoking and marijuana use (Abrahamsson & Hakansson 2015). Studies with adolescent and young adult samples found non-medical use of PPRs is associated with marijuana use (McCabe et al. 2012; Catalano et al. 2011).

Though longitudinal studies are needed to make definitive conclusions about the nature of the relationship between marijuana and PPR use among cigarette smokers, the interface among biological effects of PPRs, marijuana, and nicotine could influence the strength and direction of this relationship. For one, PPRs and marijuana share anti-nociceptive effects, the two substances act on some of the same brain regions, and THC partly exerts its analgesic influence by relying on opioid receptors (Pacula et al. 2015; Abrams & Guzman 2015; Maione et al. 2011; Cichewicz 2004). Nicotine additionally interacts with the opioid system, and the systems have almost identical influences in key pleasure-sensing areas of the brain (McGehee 2006). Therefore, the behavioral responses to nicotine use and withdrawal

(including reward and addiction) are likely affected by the opioid system (Hadjiconstantinou & Neff 2011; Berrendero et al. 2010). As with marijuana and opioids, nicotine has anti-nociceptive actions (Kishioka et al. 2014; Ditre et al. 2016). Consequently, the interconnected neural activity and biological effects of nicotine, marijuana, and opioids could play a role in the relationship between PPR and marijuana use among cigarette smokers.

Another explanation for the higher likelihood of current PPR use among ever and current marijuana users in cigarette smokers could be that some participants had used marijuana and/or PPRs to reduce pain symptoms. Epidemiologic and prospective cohort studies point to a relationship between smoking and chronic pain, with smokers having a greater likelihood of developing chronic pain disorders than non-smokers (Shi et al. 2010). And the most frequently reported reason for adult misuse of PPRs in 2015 was to alleviate physical pain (Lipari, Williams, and Van Horn 2017).

Our results do not support prior findings of a negative association between marijuana and PPR use. Boehnke, Litinas, and Clauw (2016) report that among individuals with chronic pain, use of medical marijuana was negatively associated with opioid use. Further, legalization of medical marijuana has been correlated with a drop in the number of hospitalizations attributed to opioid dependence/abuse and PPR ODs, and a decline in opioid OD mortality rates (Shi 2017; Bachhuber et al. 2014). States with medical marijuana dispensaries also report fewer PPR ODs, a reduction in PPR treatment admissions, and a decline in opioid-related deaths (Pardo 2016; Powell 2015). However, none of these studies stratified their results by cigarette smoking status. As such, it is possible that the inclusion of only current cigarette smokers in the present study could help explain the discrepancy between the present findings and other results.

Of note, studies investigating the effect of marijuana use on opioid/PPR use vary in their sample composition (i.e., age, health status, drug use status), use of covariates (i.e., legalization of medical marijuana or specific components of medical marijuana laws), and outcome measures (i.e., use/abuse of PPRs and/or opioids in general, hospitalizations due to use of PPRs and/or opioids in general, mortality due to use of PPRs and/or opioids in general). This variation in study design is likely responsible for some of the discrepant findings in the extant literature. As previous studies have not stratified their analyses by cigarette smoking status, our study provides an important and unique contribution to current evidence, and this dynamic helps to explain why our findings differ from those that found a negative relationship between marijuana and PPR use.

We did not find a significant association between PPR use and frequency of marijuana use among current marijuana users. Our findings align with those of Lucas et al. (2013), who determined that among Canadian medical marijuana users, there was no association between frequency of marijuana use and illicit drug substitution, though this finding is attenuated because their analysis was not stratified by cigarette use status. On the other hand, our findings contrast with those of Arterberry et al. (2016), who reported that frequency of marijuana and cigarette use was predictive of opioid use among an adult sample in the NESARC. This dissimilarity may be due to differences in study design. In the work of

Arterberry et al. (2016), frequency of marijuana use was determined by asking participants how often they used marijuana in the last year, and responses were coded on a scale from 0 (never used) to 10 (used every day). In contrast, our participants reported how often they used marijuana within the past month by indicating a specific number of days from 0–30. Second, all participants in our study were current cigarette smokers, while the NESARC sample included both cigarette smokers and non-smokers.

There are several study limitations. Though the TABS II used a random sample, it is not nationally representative. All data is self-reported, and there are no biomarkers for verification of tobacco, marijuana, or PPR use. The cross-sectional nature of the analysis prevents causal inference. As there were no non-smokers included in the analysis to compare with the current smokers, further analysis of the present study is warranted. We do not have data on participants' reason for PPR use. Some participants could have medical provider-issued prescriptions for pain, yet it is possible that even patients with valid prescriptions may not actually "need" a prescription pain reliever. We did not have any information on the presence, absence, or type of pain. Studies have shown that simply asking a primary care physician for a narcotic by brand name significantly increases the likelihood of being prescribed a medication and being prescribed a strong narcotic (McKinlay 2014). Because pain is subjective, a definitive conclusion as to what level pain a patient is experiencing is not possible. Therefore, the only data available in a large data base is whether or not the participant had a prescription for use. We also did not measure the frequency of PPR use within the past 30 days, as we did with marijuana, nor did we ask respondents about the type(s) of PPRs they used. In the future, questions about these details of PPR use would be beneficial to include, as they would enable a more nuanced analysis of the data. Concerning our frequency analysis, it is possible that our sample of current marijuana users (N=76) was too small to capture a significant effect between frequency of marijuana use and PPR use. Finally, despite random sampling, our sample was predominantly Caucasian and older, limiting generalizability.

To frame conclusions about the presence of a complementary effect between marijuana and PPR use and to identify a potential causal relationship between use of these two substances, future studies should be longitudinal, with larger and more diverse samples that include both smokers and non-smokers. The incorporation of unique aspects of MMLs (i.e., home cultivation, registration requirements, and dispensaries) into future models would be useful to more accurately determine the effects of such laws.

Conclusions

Findings suggests that if adult current cigarette smokers are also current or ever marijuana users, they are more likely to be PPR users. These results can inform 1) policy changes for those who work in substance use and tobacco control to encourage prevention and increase education about the risks of using these substances and 2) practice guidelines for healthcare providers, as the combination of being a current cigarette smoker and an ever or current marijuana user increases the chances of being a current PPR user when compared to those who have never used marijuana. In light of the current national opioid epidemic (Rudd et al. 2016; SAMHSA 2013; Cai et al. 2010), clinicians should proceed with caution when

prescribing PPRs to cigarette smokers and provide patients with information about the risks of opioid use. The present results and findings from similar studies thus have important public health implications and should be followed up with additional longitudinal studies to further elucidate the interplay between marijuana, cigarette, and PPR use.

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REFERENCES

"29 legal medical marijuana states and DC: Laws, fees, and possession limits." ProCon.org, Last Modified 20 Apr 2017. http://medicalmarijuana.procon.org/view.resource.php?resourceID=000881&print=true.

Abrahamsson T & Hakansson A 2015 "Nonmedical prescription drug use (NMPDU) in the Swedish general population--correlates of analgesic and sedative use." Substance Use & Misuse 50 (2):148–55. doi: 10.3109/10826084.2014.962047. [PubMed: 25295596]

Abrams DI & Guzman M 2015 "Cannabis in cancer care." Clinical Pharmacology & Therapeutics 97 (6):575–86. doi: 10.1002/cpt.108. [PubMed: 25777363]

Agrawal A, and Lynskey MT. 2009 "Tobacco and cannabis co-occurrence: does route of administration matter?" Drug Alcohol Depend 99 (1–3):240–7. doi: 10.1016/j.drugalcdep.2008.08.007. [PubMed: 18926646]

Arterberry BJ; Horbal SR; Buu A & Lin HC 2016 "The effects of alcohol, cannabis, and cigarette use on the initiation, reinitiation and persistence of non-medical use of opioids, sedatives, and tranquilizers in adults." Drug and Alcohol Dependence 159:86–92. doi: 10.1016/j.drugalcdep.2015.11.029. [PubMed: 26710977]

Bachhuber MA; Saloner B; Cunningham CO & Barry CL 2014 "Medical cannabis laws and opioid analgesic overdose mortality in the United States, 1999–2010." JAMA Internal Medicine 174 (10):1668–73. doi: 10.1001/jamainternmed.2014.4005. [PubMed: 25154332]

Benyamin R; Trescot AM; Datta S; Buenaventura R; Adlaka R; Sehgal N; Glaser SE & Vallejo R 2008 "Opioid complications and side effects." Pain Physician 11 (2 Suppl):S105–20. [PubMed: 18443635]

Berge J; Hakansson A & Berglund M 2014 "Alcohol and drug use in groups of cannabis users: results from a survey on drug use in the Swedish general population." American Journal on Addictions 23 (3):272–9. doi: 10.1111/j.1521-0391.2014.12097.x. [PubMed: 24724885]

Berrendero F; Robledo P; Trigo JM; Martin-Garcia E & Maldonado R 2010 "Neurobiological mechanisms involved in nicotine dependence and reward: participation of the endogenous opioid system." Neuroscience & Biobehavioral Reviews 35 (2):220–31. doi: 10.1016/j.neubiorev.2010.02.006. [PubMed: 20170672]

Boehnke KF; Litinas E & Clauw DJ 2016 "Medical cannabis use is associated with decreased opiate medication use in a retrospective cross-sectional survey of patients with chronic pain." Journal of Pain 17 (6):739–44. doi: 10.1016/j.jpain.2016.03.002. [PubMed: 27001005]

Cai R; Crane E; Poneleit K & Paulozzi L 2010 "Emergency department visits involving nonmedical use of selected prescription drugs in the United States, 2004–2008." Journal of Pain & Palliative Care Pharmacotherapy 24 (3):293–7. doi: 10.3109/15360288.2010.503730. [PubMed: 20718652]

Catalano RF; White HR; Fleming CB & Haggerty KP 2011 “Is nonmedical prescription opiate use a unique form of illicit drug use?” Addictive Behaviors 36 (1–2):79–86. doi: 10.1016/j.addbeh.2010.08.028. [PubMed: 20864261]

Cerdá M, Wall M; Keyes KM; Galea S & Hasin D 2012 “Medical marijuana laws in 50 states: investigating the relationship between state legalization of medical marijuana and marijuana use, abuse and dependence.” Drug and Alcohol Dependence 120 (1–3):22–7. doi: 10.1016/j.drugalcdep.2011.06.011. [PubMed: 22099393]

Cichewicz DL 2004 “Synergistic interactions between cannabinoid and opioid analgesics.” Life Sciences 74 (11):1317–24. [PubMed: 14706563]

Ditre JW, Heckman BW, Zale EL, Kosiba JD, and Maisto SA. 2016 “Acute analgesic effects of nicotine and tobacco in humans: a meta-analysis.” Pain 157 (7):1373–81. doi: 10.1097/j.pain.0000000000000572. [PubMed: 27023418]

Fiellin LE; Tetrault JM; Becker WC; Fiellin DA & Hoff RA 2013 “Previous use of alcohol, cigarettes, and marijuana and subsequent abuse of prescription opioids in young adults.” Journal of Adolescent Health 52 (2):158–63. doi: 10.1016/j.jadohealth.2012.06.010. [PubMed: 23332479]

Hadjiconstantinou M, & Neff NH 2011 “Nicotine and endogenous opioids: neurochemical and pharmacological evidence.” Neuropharmacology 60 (7–8):1209–20. doi: 10.1016/j.neuropharm.2010.11.010. [PubMed: 21108953]

Hursh SR; Galuska CM; Winger G & Woods JH 2005 “The economics of drug abuse: A quantitative assessment of drug demand.” Molecular Interventions 5 (1):20. [PubMed: 15731502]

International Narcotics Control Board. 2016 Narcotic Drugs: Estimated World Requirements for 2017: Comments on the Reported Statistics on Narcotic Drugs New York: United Nations.

Kishioka S; Kiguchi N; Kobayashi Y & Saika F 2014 “Nicotine effects and the endogenous opioid system.” Journal of Pharmacological Sciences 125 (2):117–24. doi: 10.1254/jphs.14R03CP. [PubMed: 24882143]

Kohut SJ 2017 “Interactions between nicotine and drugs of abuse: a review of preclinical findings.” Am J Drug Alcohol Abuse 43 (2):155–170. doi: 10.1080/00952990.2016.1209513. [PubMed: 27589579]

Lipari RN, Williams M, and Van Horn SL. 2017 Why do adults misuse prescription drugs? In The CBHSQ Report Rockville, MD: Center for Behavioral Health Statistics and Quality, Substance Abuse and Mental Health Services Administration.

Lucas P; Reiman A; Earleywine M; McGowan SK; Oleson M; Coward MP & Thomas B 2013 “Cannabis as a substitute for alcohol and other drugs: A dispensary-based survey of substitution effect in Canadian medical cannabis patients.” Addiction Research & Theory 21 (5):435–442.

Lynch ME & Campbell F 2011 “Cannabinoids for treatment of chronic non-cancer pain; a systematic review of randomized trials.” British Journal of Clinical Pharmacology 72 (5):735–44. doi: 10.1111/j.1365-2125.2011.03970.x. [PubMed: 21426373]

Mack KA, Jones CM & Paulozzi LJ 2013 “Vital signs: overdoses of prescription opioid pain relievers and other drugs among women--United States, 1999–2010.” In Morbidity and Mortality Weekly Report: Centers for Disease Control and Prevention.

Maione S; Piscitelli F; Gatta L; Vita D; De Petrocellis L; Palazzo E; de Novellis V & Di Marzo V 2011 “Non-psychoactive cannabinoids modulate the descending pathway of antinociception in anaesthetized rats through several mechanisms of action.” British Journal of Pharmacology 162 (3):584–96. doi: 10.1111/j.1476-5381.2010.01063.x. [PubMed: 20942863]

Martins SS; Mauro CM; Santaella-Tenorio J; Kim JH; Cerda M; Keyes KM; Hasin DS; Galea S & Wall M 2016 “State-level medical marijuana laws, marijuana use and perceived availability of marijuana among the general U.S. population.” Drug and Alcohol Dependence 169:26–32. doi: 10.1016/j.drugalcdep.2016.10.004. [PubMed: 27755989]

McCabe SE; West BT; Teter CJ & Boyd CJ 2012 “Co-ingestion of prescription opioids and other drugs among high school seniors: results from a national study.” Drug and Alcohol Dependence 126 (1–2):65–70. doi: 10.1016/j.drugalcdep.2012.04.017. [PubMed: 22609061]

McGehee DS 2006 “Nicotinic and opioid receptor interactions in nicotine addiction.” Molecular Interventions 6 (6):311–4. doi: 10.1124/mi.6.6.4. [PubMed: 17200458]

National Institute on Alcohol Abuse and Alcoholism. 2015 Prevalence of Marijuana Use Among U.S. Adults Doubles Over Past Decade National Instititue on Alcohol Abuse and Alcoholism website: National Instititue on Alcohol Abuse and Alcoholism.

Novak SP; Peiper NC & Zarkin GA 2016 "Nonmedical prescription pain reliever and alcohol consumption among cannabis users." Drug and Alcohol Dependence 159:101–8. doi: 10.1016/j.drugalcdep.2015.11.039. [PubMed: 26748409]

Nuechterlein EB; Ni L; Domino EF & Zubieta JK 2016 "Nicotine-specific and non-specific effects of cigarette smoking on endogenous opioid mechanisms." Progress in Neuro-Psychopharmacology & Biological Psychiatry 69:69–77. doi: 10.1016/j.pnpbp.2016.04.006. [PubMed: 27095017]

Nugent SM, Yarborough BJ, Smith NX, Dobscha SK, Deyo RA, Green CA, and Morasco BJ. 2018 "Patterns and correlates of medical cannabis use for pain among patients prescribed long-term opioid therapy." Gen Hosp Psychiatry 50:104–110. doi: 10.1016/j.genhosppsych.2017.11.001. [PubMed: 29153783]

Olfson M, Wall MM, Liu SM, and Blanco C. 2018 "Cannabis Use and Risk of Prescription Opioid Use Disorder in the United States." Am J Psychiatry 175 (1):47–53. doi: 10.1176/appi.ajp.2017.17040413. [PubMed: 28946762]

Pacula RL; Powell D; Heaton P & Sevigny EL 2015 "Assessing the effects of medical marijuana laws on marijuana use: the devil is in the details." Journal of Policy Analysis and Management 34 (1): 7–31. [PubMed: 25558490]

Pardo B 2016 "Do more robust prescription drug monitoring programs reduce prescription opioid overdose?" Addiction 112 (10):1773–83. doi: 10.1111/add.13741.

Powell D; Pacula RL & Jacobson M 2015 Do Medical Marijuana Laws Reduce Addictions and Deaths Related to Pain Killers?: The National Bureau of Economic Research

Rudd RA; Aleshire N, Zibbell JE & Gladden RM 2016 Increases in Drug and Opioid Overdose Deaths--United States, 2000–2014. In Morbidity and Mortality Weekly Report: Centers for Disease Control and Prevention.

Schauer GL; Berg CJ; Kegler MC; Donovan DM & Windle M 2015 "Assessing the overlap between tobacco and marijuana: Trends in patterns of co-use of tobacco and marijuana in adults from 2003–2012." Addictive Behaviors 49:26–32. doi: 10.1016/j.addbeh.2015.05.012. [PubMed: 26036666]

Shi Y 2017 "Medical marijuana policies and hospitalizations related to marijuana and opioid pain reliever." Drug and Alcohol Dependence 173:144–150. doi: 10.1016/j.drugalcdep.2017.01.006. [PubMed: 28259087]

Skurtveit S; Furu K; Selmer R; Handal M & Tverdal A 2010 "Nicotine dependence predicts repeated use of prescribed opioids. Prospective population-based cohort study." Annals Epidemiology 20 (12):890–7. doi: 10.1016/j.annepidem.2010.03.010.

Substance Abuse and Mental Health Services Administration. 2013 Results from the 2012 National Survey on Drug Use and Health: Summary of National Findings. In H-46, edited by NSDUH Rockville, MD: Substance Abuse and Mental Health Services Administration.

Wall MM; Mauro C; Hasin DS; Keyes KM; Cerda M; Martins SS & Feng T 2016 "Prevalence of marijuana use does not differentially increase among youth after states pass medical marijuana laws: Commentary on and reanalysis of US National Survey on Drug Use in Households data 2002–2011." International Journal of Drug Policy 29:9–13. doi: 10.1016/j.drugpo.2016.01.015. [PubMed: 26895950]

Wang JB; and Cataldo JK. 2016 "Medical marijuana legalization and co-use in adult cigarette smokers." American Journal of Health Behavior 40 (2):205–14. doi: 10.5993/ajhb.40.2.5. [PubMed: 26931752]

Wang JB; Ramo DE; Lisha NE & Cataldo JK 2016 "Medical marijuana legalization and cigarette and marijuana co-use in adolescents and adults." Drug and Alcohol Dependence 166:32–8. doi: 10.1016/j.drugalcdep.2016.06.016. [PubMed: 27460859]

Yoon JH; Lane SD & Weaver MF 2015 "Opioid analgesics and nicotine: more than blowing smoke." Journal of Pain and Palliative Care Pharmacotherapy 29 (3):281–9. doi: 10.3109/15360288.2015.1063559. [PubMed: 26375198]

Zale EL; Dorfman ML; Hooten WM; Warner DO; Zvolensky MJ & Ditre JW 2015 “Tobacco smoking, nicotine dependence, and patterns of prescription opioid misuse: results from a nationally representative sample.” Nicotine & Tobacco Research 17 (9):1096–103. doi: 10.1093/ntr/ntu227. [PubMed: 25344958]

Table 1

Sample characteristics and PPR status stratified by marijuana use among current cigarette smokers (N=348).

	Marijuana use – n (%), M (SD)			p-value
	Never (n=69)	Ever (n=203)	Current (n=76)	
Age				0.157
	52.65 (11.50)	51.57 (10.80)	49.28 (11.11)	
Gender				0.546
Male	26 (17.22)	90 (59.60)	35 (23.18)	
Female	43 (21.83)	113 (57.36)	41 (20.81)	
Race/Ethnicity				0.314
Caucasian/White	56 (19.11)	176 (60.07)	61 (20.82)	
Other	13 (23.64)	27 (49.09)	15 (27.27)	
Education				0.706
High school or less	23 (21.12)	61 (58.65)	20 (19.23)	
Some college	23 (16.43)	83 (59.29)	34 (24.29)	
College graduate or higher	23 (22.12)	59 (56.73)	22 (21.15)	
Occupational status				0.096
Employed	33 (19.53)	102 (60.36)	34 (20.12)	
Unemployed	6 (12.00)	25 (50.00)	19 (38.00)	
Retired	17 (21.79)	48 (61.54)	13 (16.67)	
Other	13 (25.49)	28 (54.90)	10 (19.61)	
Type of community				0.917
Urban	18 (18.56)	56 (57.73)	23 (23.71)	
Rural	20 (20.62)	59 (60.82)	18 (18.56)	
Suburban	31(20.13)	88 (57.14)	35 (22.73)	
Cigarettes smoked per day				0.145
	17.54 (9.08)	15.60 (8.91)	14.82 (7.36)	
MML status in state of residence				0.217
Not legal	31 (18.02)	108 (62.79)	33 (19.19)	
Legal <10 years	29 (23.58)	68 (55.28)	26 (21.14)	
Legal ≥ 10 years	9 (16.98)	27 (50.94)	17 (32.08)	
PPR status				0.005 *
Never	30 (43.48)	45 (22.17)	15 (19.74)	
Ever	26 (37.68)	105 (51.72)	37 (48.68)	
Current	13 (18.84)	53 (26.11)	24 (31.58)	

Notes:

(1) p-values were calculated by using an ANOVA for the continuous variables (age and average cigarettes smoked per day) and chi-square tests for the categorical variables (gender, race/ethnicity, education, occupational status, type of community, MML status in state of residence, and PPR status)

*(2) significant at p=0.05 level

Bonferroni adjusted p-values for the chi-square test between PPR status and marijuana use status: marijuana never vs. ever p=0.009, marijuana never vs. current p=0.022, marijuana ever vs. current p=1.00

(3) Abbreviations: “PPR” = prescription pain reliever; “MML” = medical marijuana law

Table 2

Association between marijuana use status and current PPR use (N=348).

	Unadjusted		Adjusted	
	OR	**95% CI**	**AOR**	**95% CI**
Marijuana use				
Never (ref)	1	-	1	-
Ever	2.22*	1.32 – 3.74	2.58*	1.51 – 4.43
Current	2.74*	1.47 – 5.11	3.38*	1.76 – 6.49

Notes:

(1) The adjusted model incorporates sample characteristics (gender, race/ethnicity, education, occupational status, age, average cigarettes smoked per day, type of community, and MML status in state of residence)

* (2) significant at p=0.05 level

(3) Abbreviations: “PPR” = prescription pain reliever; “OR” = odds ratio; “CI” = confidence interval; “MML” = medical marijuana law

Table 3

Logistic regression results for effect of frequency of marijuana use in the past 30 days upon PPR status, among current marijuana users (N=76).

	PPR Status			Logistic Regression	
	Never (n=15)	**Ever (n=37)**	**Current (n=24)**	**OR (95% CI)**	**p-value**
Days used marijuana in past 30 days	11.20 (10.59)	15.41 (12.37)	13.21 (11.87)	1.01 (0.97–1.04)	0.796

Notes:

(1) Abbreviations: “PPR” = prescription pain reliever; “OR” = odds ratio; “CI” = confidence interval