HHS Public Access

Author manuscript

Am J Psychiatry. Author manuscript; available in PMC 2018 July 01.

Published in final edited form as:

Am J Psychiatry. 2018 January 01; 175(1): 47–53. doi:10.1176/appi.ajp.2017.17040413.

Cannabis Use and Risk of Prescription Opioid Use Disorder in the United States

Mark Olfson, M.D., M.P.H.[1], **Melanie M. Wall, Ph.D.**[1], **Shang-Min Liu, MS**[1], and **Carlos Blanco, M.D., Ph.D.**[2]

[1]Department of Psychiatry, New York State Psychiatric Institute / Columbia University, New York, NY 10032

[2]Division of Epidemiology, Services, and Prevention Research, National Institute on Drug Abuse, Bethesda, MD 20892

Abstract

Objective—To determine whether cannabis use is associated with a change in the risk of incident nonmedical prescription opioid use and opioid use disorder at 3 year follow-up.

Methods—We used logistic regression models to assess prospective associations between cannabis use at Wave 1 (2001–2002) and nonmedical opioid use and prescription opioid use disorder at Wave 2 (2004–2005) of the National Epidemiologic Survey on Alcohol and Related Conditions. Corresponding analyses were performed among adults with moderate or more severe pain and with nonmedical opioid use at Wave 1. Cannabis and prescription opioid use were measured with a structured interview (AUDADIS-IV). Other covariates included age, sex, race/ethnicity, anxiety or mood disorders, family history of drug, alcohol, and behavioral problems, and in opioid use disorder analyses, nonmedical opioid use.

Results—In logistic regression models, Wave 1 cannabis use was associated with increased incident non-medical prescription opioid use (OR=5.78, 95%CI=4.23–7.90) and opioid use disorder (OR=7.76, 95%CI=4.95–12.16) at Wave 2. These associations remained significant following adjustment for background characteristics (non-medical opioid use: AOR=2.26, 95%CI=1.86–3.69; opioid use disorder: AOR=2.18, 95%CI=1.14–4.14). Among adults with pain at Wave 1, cannabis use was also associated with increased incident non-medical opioid use (AOR=2.99, 95%CI=1.63–5.47) and approached significance with incident prescription opioid use disorder (AOR=2.14, 95%CI=0.95–4.83). Among adults with nonmedical opioid use at Wave 1, cannabis use was also associated with an increase in non-medical opioid use (AOR=3.13, 95%CI=1.19–8.23).

Conclusions—Cannabis use appears to increase rather than decrease the risk of developing nonmedical prescription opioid use and opioid use disorder.

Following more than two decades of increasing prevalence of prescription opioid use disorder in the US (1, 2), the number of people in the United States prescription opioid use

Corresponding author: Mark Olfson, MD, MPH, Department of Psychiatry, New York State Psychiatric Institute/Columbia University, 1051 Riverside Drive, Unit 24, New York, NY 10032, Phone: 646-774-6413 Fax: 646-774-6439, mo49@cumc.columbia.edu.

disorders reached 2 million in 2015 (3). Rising rates of prescription opioid use disorders have coincided with the largest epidemic of opioid overdose deaths in US history. In 2015, unintentional drug overdose deaths, most of which involved opioids, claimed over 47,000 lives (4). The crisis in nonmedical use of prescription opioids, which has exacted a heavy burden not only on individuals, but also on their families and communities, has prompted federal policy makers to consider prescription opioid use disorder a threat to public health (5).

In the wake of rising rates of nonmedical prescription opioid use, there has been increased public (6) and professional (7) interest in the possibility that cannabis might help to curb or prevent opioid use disorder. Support comes from two widely publicized ecological analyses indicating that as compared to states that do not permit medical marijuana, annual death rates due to opioid overdoses were nearly one-quarter lower in states permitting medical marijuana (8,9). Significant reductions in opioid prescribing have also been reported following passage of medical marijuana laws (10). Such ecologic analyses, however, provide no information on whether individual patients who use cannabis have a lower or higher risk of developing opioid use disorders (11).

The possibility that cannabis lowers the risk of opioid-related morbidity has fueled speculation concerning potential mechanisms. A leading hypothesis is that cannabis use tends to lower opioid use and risk of opioid use disorder through increased control of pain (8,12). A recent meta-analysis of randomized controlled trials provides a moderate level of evidence that cannabinoids improve some forms of chronic pain (13). A large Dutch study reported that just over half of adults in registered cannabis programs were also prescribed pain medications suggesting that medical marijuana is frequently used for pain control (14). In an small uncontrolled cross sectional survey of medical marijuana users with chronic pain recruited from a cannabis dispensary, cannabis use was associated with a 64% decline in opioid use (n=118) (12). Cannabis exposure has also been associated with increased analgesia among opioid-treated patients with chronic pain (15) suggesting that cannabis may potentiate anti-nociceptive effects of opioids permitting lower and presumably safer opioid dosing to achieve comparable analgesia.

Much remains to be learned about the association between cannabis use and nonmedical prescription opioid use or opioid use disorders. No prospective epidemiological or clinical studies have demonstrated that cannabis use reduces use of opioids. Moreover, epidemiologic research suggests that cannabis may actually *increase* the risk of other drug use disorders including opioids. A retrospective Australian twin study reported that early initiation of cannabis use was associated with increased risks of other drug use and abuse/dependence including opioid use and opioid abuse/dependence (16). Prospective epidemiological research further suggests that cannabis use is a risk factor for other drug use disorders (17). However, prospective epidemiological research has not previously examined the specific association between cannabis use and nonmedical opioid use or opioid use disorder to inform clinical practice and policy.

We sought to address this critical gap in knowledge with prospective data from the National Epidemiological Survey on Alcohol and Related Conditions (NESARC) a large, nationally

representative sample. We examined the association between cannabis use and incident nonmedical prescription opioid use and disorder three years later, after adjusting for several relevant demographic and clinical covariates. We also evaluated whether cannabis use among adults with nonmedical prescription opioid use was associated with a subsequent decrease in nonmedical opioid use.

Method

Sample

The 2001–2002 NESARC (Wave 1), and the 2004–2005 follow-up (Wave 2) is a nationally representative sample of the noninstitutionalized adult US population conducted by the US Census Bureau under the direction of the National Institute on Alcoholism and Alcohol Abuse (18, 19). The response rate for Wave 1 was 81%. Excluding ineligible respondents (e.g., deceased), the Wave 2 response rate was 86.7%, resulting in a cumulative response rate of 70.2% (n=34,653). Wave 2 NESARC weights include adjustments for non-response, demographic factors and psychiatric diagnoses, to ensure that the Wave 2 sample approximated the target population which was the original sample minus attrition between the two waves (18).

Assessment

All diagnoses were made according to the DSM-IV criteria using the Alcohol Use Disorder and Associated Disabilities Interview Schedule—DSM-IV version (AUDADIS-IV) for Waves 1 and 2 (19). Consistent with prior reports, non-medical use of a prescription opioid was defined as using a prescription drug “without a prescription, in greater amounts, more often, or longer than prescribed, or for a reason other than a doctor said you should use them” during the 12-months preceding the interview. Over 30 symptom items were used by the AUDADIS-IV to define 12-month prescription opioid use disorder according to DSM-IV criteria. The NESARC also collected information for other substance use disorders (nicotine dependence, alcohol use disorder and drug use disorders, including other prescription drug use disorders). The reliability of the AUDADIS-IV prescription opioid use questions (kappa values=0.66) and associated substance use disorder diagnoses (κ=0.53–0.84) are well documented in several psychometric studies including in clinical (20) and general population (21) samples. Further concurrent and predictive validity of the prescription opioid use disorder diagnosis has been documented by increased risk of related psychopathology, impairment, and probability of seeking treatment (22).

The frequency of past year use of cannabis use was assessed with an eleven level item ranging from no use in the last 12 months to use every day in the last 12 months. Following a prior convention, cannabis use was collapsed into a four level variable including 1) no use in last 12 months, 2) occasional use (at least once a year but less than once a month), 3) frequent use (from once a month or more to twice per week), and 4) very frequent use (from three times a week to every day) (23). A similar four level scale was developed for past year prescription opioid use.

Mood disorders included DSM-IV major depressive disorder, dysthymia, bipolar I, and bipolar II disorder. Anxiety disorders included DSM-IV panic disorder, social anxiety disorder, specific phobia, and generalized anxiety disorder. Test-retest reliabilities for AUDADIS-IV mood, anxiety, and personality disorders in the non-institutional population and clinical settings were fair to good. Convergent validity was good to excellent for all mood and anxiety diagnoses showed good agreement (κ=0.64–0.68) with psychiatrist reappraisals (24). Family histories of alcohol use disorder, drug use disorders, depression, and antisocial personality disorder referred to first-degree relatives. The test-retest of AUDADIS family history variables is very good to excellent (25).

Pain was assessed using the pain item of the 12-item Medical Outcomes Study Short Form version 2 (SF-12) (33), a valid measure that is commonly used in population surveys (26). The pain item uses a five-point scale (e.g., not at all, a little bit, moderately, quite a bit, and extremely) to measure the amount to which pain interferes with daily activities during the last month (28). The pain measure was collapsed into two levels depending on whether pain was associated with no or little interference (“no pain”), or with moderate to extreme interference (“pain”) (29).

Statistical Analyses

Wave 1 descriptive demographic and clinical characteristics were compared between individuals with and without any cannabis use in the year before the Wave 1 interview. Group differences were evaluated with chi-square or t-tests. Unadjusted percentages of respondents with Wave 2 incident opioid use disorders were determined by frequency of Wave 1 cannabis use.

Separate logistic regression models were fit with nonmedical opioid use and disorder outcomes at Wave 2 predicted by past year cannabis use at Wave 1. To differentiate between prevalent and incident opioid outcomes at Wave 2, we defined four outcomes: 1) prevalent nonmedical opioid use defined as any nonmedical opioid use since the Wave 1 interview; 2) incident nonmedical opioid use defined as any nonmedical opioid use since Wave 1 restricting to respondents with no lifetime nonmedical opioid use at Wave 1; 3) prevalent prescription opioid use disorder defined as meeting opioid use disorder criteria since Wave 1; and 4) incident prescription opioid use disorder defined as meeting opioid use disorder criteria since Wave 1 restricting to respondents with no lifetime opioid use disorder at Wave 1. Results are presented as unadjusted odds ratios (OR) and adjusted odds (AOR) controlling for age, sex, race/ethnicity, family history variables, antisocial personality disorder, and other substance use disorders and mood or anxiety disorders at Wave 1 (29). Adjusted models of Wave 2 opioid use disorder also controlled for Wave1 past 12 months nonmedical opioid use. Regressions were fit among the general population of NESARC Wave 1 and 2 respondents and then repeated, as a sensitivity analysis, among respondents without Wave 1 past year cannabis use disorders and among respondents with moderate or more severe pain impairment.

We further examined whether among respondents with Wave 1 past year nonmedical opioid use, cannabis use was associated with an increase or decrease in the level of opioid use at Wave 2. A separate logistic regression was fit among respondents with Wave 1 opioid use

and moderate or more severe pain. All analyses were performed using SUDAAN take into account the complex design features of the NESARC.

Results

Background characteristics of adults who use cannabis

At Wave 1, individuals with any past year cannabis use were younger than those without cannabis use, more likely to be male, and more likely to have past year opioid use disorder, cannabis use disorder, other substance use disorders, or any past year mood or anxiety disorder. They were also significantly more likely to have a family history of alcohol use disorders, drug use disorders, depression, and antisocial personality disorder. However, the two groups did not significantly differ with respect to the proportion who reported moderate or more severe pain during the month before the Wave 1 interview (Table 1).

Prospective associations between cannabis use and nonmedical prescription opioid use

Within the overall survey population, cannabis use at Wave 1 was associated with a significant increase in the odds of prevalent nonmedical prescription opioid use during the follow-up period (Table 2). After adjustment for the background demographic and clinical characteristics, a strong association persisted between Wave 1 cannabis use and Wave 2 prevalent nonmedical opioid use. These associations were also observed among adults without past year cannabis use disorder and among adults with moderate or more severe pain at Wave 1. Among individuals without nonmedical opioid use during the 12 months before the Wave 1 interview, there was a significant association between cannabis use at Wave 1 and incident nonmedical opioid use during the follow-up period. This association was also observed among adults without cannabis use disorder at Wave 1 and among adults with moderate or more severe pain at Wave 1.

In analyses restricted to individuals with past year nonmedical opioid use, Wave 1 cannabis use was significantly associated in unadjusted and adjusted regressions with an increase in the level of opioid use during the year before the Wave 2 interview. Conversely, cannabis use was associated with lower odds of decreasing the level of opioid use. When the sample was further restricted to adults with Wave 1 nonmedical opioid use and moderate or more severe pain, Wave 1 cannabis use was associated with a lower unadjusted odds of decreasing opioid use though the other regressions did not yield significant associations. Among individuals with nonmedical opioid use at Wave 1 who either used or did not use cannabis, however, decreases in opioid use at Wave 2 were markedly more common than increases in opioid use (Table 3).

Prospective associations between cannabis use and prescription opioid use disorder

In unadjusted analyses, the percentage of adults who developed a new onset opioid use disorder during the follow-up period was lowest for individuals who did not use cannabis in the year before the Wave 1 interview (0.51%) followed by occasional cannabis users (2.86%), frequent cannabis users (4.30%), and very frequent cannabis users (4.43%) (Figure 1).

In the overall survey population, cannabis use at Wave 1 was associated with a significant increase in the odds of prevalent and incident prescription opioid use disorder during the follow-up period (Table 4). After adjustment for the background demographic and clinical covariates including Wave 1 nonmedical opioid use, significant associations persisted between Wave 1 cannabis use and prevalent as well as incident nonmedical opioid use disorder at Wave 2. A similar association was observed among adults without past year cannabis use disorders and prevalent opioid use disorder, though the association with incident opioid use disorder fell below the level of statistical significance. Among adults with moderate or more severe pain at Wave 1, cannabis use was associated with prevalent and incident opioid use disorders in unadjusted analyses and with prevalent opioid use disorder in adjusted analyses (Table 4).

Discussion

In a nationally representative sample of adults evaluated three years apart, cannabis use was strongly associated with subsequent onset of nonmedical prescription opioid use and opioid use disorder. These results remained robust after controlling for the potentially confounding effects of several demographic and clinical covariates that were strongly associated with cannabis use. The association of cannabis use with development of nonmedical opioid use was evident among adults without cannabis use disorders and among adults with moderate or more severe pain. Among adults who used nonmedical opioids, cannabis use was associated with an increase in the level of opioid use at follow-up.

An independent prospective association between cannabis use and onset of prescription opioid use disorder extends results from prior epidemiological research concerning a link between cannabis use and other forms problematic drug use (15–17). Previous work in this area has either been retrospective in design (15) or focused on general associations between cannabis use and substance use disorders (17) or problems (16) rather than specifically nonmedical opioid use or opioid use disorder. Because in the present study the association was observed among adults with less than disorder-level of cannabis use and followed a dose response pattern, it suggests that some increased risk extends to a relatively large population of adult cannabis users. If cannabis use tends to increase opioid use, it is possible that the recent increase in cannabis use (31) may worsen the opioid crisis.

Several factors may contribute to a tendency for individuals with cannabis use to develop opioid use disorder or increase the frequency of opioid use among opioid users. Heroin and Δ^9 tetrahydocannabinol have similar effects on dopamine transmission through the μ_1 opioid receptor (32). As compared to controls, adolescent rats exposed to Δ^9 tetrahydocannabinol develop enhanced heroin self-administration as adults (33). Also in relation to controls, rats exposed to Δ^9 tetrahydocannabinol have a greater behavioral response to morphine challenge (34). These results are consistent with cross sensitization between cannabis and opioids. In clinical research, cannabis use can lead to behavioral disinhibition which can increase the risk of using other substances including opioids (35). Access to cannabis may also provide increased availability and social exposure to other drugs of abuse through peer affiliations (36), though such environmental influences may be less powerful in recent years with increased prevalence of cannabis use and changing public attitudes.

Ecological studies reporting fewer opioid-related deaths (8, 9) and decreased opioid prescribing following passage of medical marijuana laws (10) have been interpreted in the media (6) and scientific literature (7) as supporting cannabis as a means of reducing opioid use disorder. Yet drawing inferences about the behavior of individuals from aggregated data can be misleading. It is possible, for example, that passage of medical marijuana laws increase local clinical awareness of opioid misuse leading to earlier detection of high risk patients or more cautious opioid prescribing practices. At the individual level, cannabis use appears to substantially increase the risk of nonmedical opioid use. Moreover, the general association between cannabis use and subsequent use of illicit drugs is not explained by the legal status of cannabis. An association of early cannabis use with increased subsequent risk of other drug abuse has been reported in prospective co-twin studies in Australia (15), which has restrictive cannabis laws, and in the Netherlands where cannabis is readily available (37).

In accord with prior studies, several demographic and clinical covariates were associated with cannabis use (17). These findings converge to highlight the wide range of factors that may influence initiation of cannabis. However, because cannabis use was not associated with significant pain at baseline, relief from pain does not appear to be a strong determinant of cannabis use in the general US adult population, though we have no means of evaluating the analgesic effects of cannabis with NESARC data.

This study has several limitations. First, the NESARC sampled individuals aged 18 years and older. The relationship between cannabis and opioid use may differ in younger individuals (16). Second, information on cannabis and opioid use was based on self-report, and not confirmed with urine toxicology, which may have led to underestimates. Third, the analysis was limited to two time points three years apart which may have been too short to observe delayed consequences of cannabis use on later risk of opioid use. Fourth, the data were collected a decade ago and the social context of cannabis use may have changed during this period (31). Nevertheless, the NESARC remains the most recent nationally representative cohort of US adults. Fifth, we were unable to distinguish recreational from medical marijuana use. However, typical medical marijuana participants have been reported to be young males with histories of recreational cannabis use (38) and adults often combine medical and nonmedical cannabis use (39). Sixth, some of the associations are based on a small number of individuals and should therefore be interpreted with appropriate caution. Seventh, the NESARC did not assess inmate populations, which may have higher prevalence of substance use disorders (40). Finally, the assessment of nonmedical use of prescription opioids, although extensive, was not exhaustive and included two non-opioid medications (celecoxib and rofecoxib).

A longstanding controversy in drug research and policy concerns the extent to which use of cannabis predisposes to subsequent use of opioids and other drugs of abuse. We report that cannabis use, even among adults with moderate to severe pain, was associated with a substantially increased risk of nonmedical prescription opioid use at three year follow-up. Although a great majority of adults who used cannabis did not go on to initiate or increase their nonmedical opioid use, a strong prospective association between cannabis and opioid use disorder should nevertheless sound a note of caution in ongoing policy discussions

concerning cannabis policies and in clinical debate over authorization of medical marijuana to reduce nonmedical use of prescription opioids and fatal opioid overdoses.

Acknowledgments

Funding/support: The National Epidemiologic Survey on Alcohol and Related Conditions was sponsored by the National Institute on Alcohol Abuse and Alcoholism and funded, in part, by the Intramural Program, NIAAA, National Institutes of Health. The views and opinions expressed in this report are those of the authors and should not be construed to represent the views of any of the sponsoring organizations, agencies or the US government. Work on this manuscript was supported by grants supported by NIH grant DA019606 (Dr. Olfson) and the New York State Psychiatric Institute (Drs. Olfson and Wall). Dr. Blanco's work on this project occurred as part of his previous employment with Columbia University Medical Center. The sponsors had no additional role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; and preparation, review, or approval of the manuscript.

References

1. Han B, Compton WM, Jones CM, et al. Nonmedical prescription opioid use and use disorders among adults aged 18 through 64 years in the United States, 2003–2013. JAMA. 2015; 314(14): 1468–1478. [PubMed: 26461997]
2. Blanco C, Alderson D, Ogburn E, et al. Changes in the prevalence of non-medical prescription drug use and drug use disorders in the United States: 1991–1992 and 2001–2002. Drug Alcohol Depend. 2007 Oct 8; 90(2–3):252–60. [PubMed: 17513069]
3. Center for Behavioral Health Statistics and Quality. Key substance use and mental health indicators in the United States: Results from the 2015 National Survey on Drug Use and Health. HHS Publication No. SMA 16–4984, NSDUH Series H-51. 2016. Retrieved from http://www.samhsa.gov/data/
4. Rudd, RA., Seth, P., David, F., et al. Increases in Drug and Opioid-Involved Overdose Deaths — United States, 2010– 2015. MMWR Morb Mortal Wkly Rep. ePub: 16 December 2016. DOI: http://dx.doi.org/10.15585/mmwr.mm6550e1
5. Office of the Surgeon General. Facing Addiction in America: The Surgeon General's Report on Alcohol, Drugs, and Health. U.S. Department of Health and Human Services (HHS), Office of the Surgeon General; 2016.
6. Zhang S. Patients are ditching opioid pills for weed: can marijuana help solve the opioid epidemic? The Antlantic. Feb 2.2017
7. Miller G. Could pot help solve the US opioid epidemic? Science. Nov 3.2016
8. Bachhuber MA, Saloner B, Cunningham CO, et al. Medical cannabis laws and opioid analgesic overdose mortality in the United States, 1999–2010. JAMA Intern Med. 2014; 174:1668–1673. [PubMed: 25154332]
9. Powell D, Pacula RL, Jacobson M. Do medical marijuana laws reduce addictions and deaths related to pain killers? National Bureau of Economic Research. 2015 Working Paper 21345.
10. Bradford AC, Bradford WD. Medical marijuana laws reduce prescription medication use in Medicare Part D. Health Affairs. 2016; 25(7):1230–126.
11. Finney JW, Humphreys K, Harris AHS. What ecologic analyses cannot tell us about medical marijuana legalization and opioid pain medication mortality. JAMA Intern Med. 2015; 174:655–656.
12. Boehnke KF, Litinas E, Clauw DJ. Medical cannabis use is associated with decreased opiate medication use in a retrospective cross-sectional survey of patients with chronic pain. J Pain. 2016; 17(6):739–744. [PubMed: 27001005]
13. Whiting PF, Wolff RF, Deshpande S, et al. Cannabinoids for medical use. JAMA. 2015; 313:2456–2473. [PubMed: 26103030]
14. Hazekamp A, Heerdink ER. The prevalence and incidence of medicinal cannabis on prescription in the Netherlands. Eur J Clin Pharmacol. 2013; 69:1575–1580. [PubMed: 23588562]
15. Abrams DI, Couey P, Shade SB, et al. Cannabinoid-opioid interaction in chronic pain. Clin Pharmacol Ther. 2011; 90(6):844–851. [PubMed: 22048225]

16. Lynskey MT, Heath AC, Bucholz KK, et al. Escalation of drug use in early-onset cannabis users vs co-twin controls. JAMA. 2003; 289(4):427–433. [PubMed: 12533121]
17. Blanco C, Hasin DS, Wall MM, et al. Cannabis use and incidence of psychiatric disorders: prospective evidence from a national longitudinal study. JAMA Psychiatry. 2016; 73(4):388–395. [PubMed: 26886046]
18. Grant, BF., Kaplan, KK., Stinson, FS. Source and Accuracy Statement: The Wave 2 National Epidemiologic Survey on Alcohol and Related Conditions. National Institute on Alcohol Abuse and Alcoholism; Bethesda, MD: 2007.
19. Grant, B., Moore, T., Shepard, J., et al. Source and Accuracy Statement: Wave 1 of the 2001–2002 National Epidemiologic Survey of Alcohol and Related Conditions (NESARC). National Institute on Alcohol Abuse and Alcoholism; Bethesda, MD: 2003.
20. Hasin D, Carpenter KM, McCloud S, et al. The Alcohol Use Disorder and Associated Disabilities Interview Schedule (AUDADIS): reliability of alcohol and drug modules in a clinical sample. Drug Alcohol Depend. 1997; 44:133–141. [PubMed: 9088785]
21. Grant BF, Harford TC, Dawson DA, et al. The Alcohol Use Disorder and Associated Disabilities Interview Schedule (AUDADIS): reliability of alcohol and drug modules in a general population sample. Drug Alcohol Depend. 1995; 39:37–44. [PubMed: 7587973]
22. Hasin DS, Grant BF. The National Epidemiologic Survey on Alcohol and Related Conditions (NESARC) Waves 1 and 2: review and summary of findings. Soc Psychiatry Psychiatr Epidemiol. 2015; 50:1609–1640. [PubMed: 26210739]
23. Le Strat Y, Le Foll B. Obesity and cannabis use: results from 2 representative national surveys. Am J Epidemiol. 2011; 174(9):929–933. [PubMed: 21868374]
24. Canino G, Bravo M, Ramirez R, et al. The Spanish Alcohol Use Disorder and Associated Disabilities Interview Schedule (AUDADIS): reliability and concordance with clinical diagnoses in a Hispanic population. J Stud Alcohol. 1999; 60:790–799. [PubMed: 10606491]
25. Blanco C, Alegría A, Liu SL, et al. Differences among major depressive disorder with and without co-occurring substance use disorders and substance-induced mood disorder: results from the National Epidemiologic Survey on Alcohol and Related Conditions. J Clin Psychiatry. 2012; 73:865–873. [PubMed: 22480900]
26. Grant BF, Dawson DA, Stinson FS, et al. The Alcohol Use Disorder and Associated Disabilities Interview Schedule-IV (AUDADIS-IV): reliability of alcohol consumption, tobacco use, family history of depression and psychiatric diagnostic modules in a general population sample. Drug Alcohol Dep. 2003; 71:7–16.
27. Ware J Jr, Kosinski M, Keller SD. A 12-Item Short-Form Health Survey: construction of scales and preliminary tests of reliability and validity. Med Care. 1996; 34:220–233. [PubMed: 8628042]
28. Rubio JM, Olfson M, Villegas L, et al. Quality of life following remission of mental disorders: findings from the National Epidemiologic Survey on Alcohol and Related Conditions. J Clin Psychiatry. 2013; 74:e445–450. [PubMed: 23759465]
29. Ware, J., Snow, K., Kosinski, M., et al. SF-36 health survey: manual and interpretation guide. New England Medical Center Hospital. Health Institute, The Health Institute, New England Medical Center; 1993.
30. Blanco C, Wall MM, Okuda M, et al. Pain as a predictor of opioid use disorder in a nationally representative sample. Am J Psychiatry. 2016; 173(12):1189–1195. [PubMed: 27444794]
31. Hasin DS, Saha TD, Kerridge BT, et al. Prevalence of marijunaa use disorder in the Untied States between 2001–2002 and 2012–2013. JAMA Psychiatry. 2015; 72(12):1235–1242. [PubMed: 26502112]
32. Tanda G, Pntieri FE, Di Chiara G. Cannabinoid and heroin activation of mesolimbic dopamine transmission by a common mu1 opioid receptor mechanism. Science. 1997; 276(5321):2048–2050. [PubMed: 9197269]
33. Ellgren M, Spano SM, Hurd YL. Adolescent cannabis exposure alters opiate intake and opioid limbic neuronal populations in adult rats. Neuropsychopharmacol. 2007; 32:607–615.
34. Cadoni C, Pisanu A, Solinas M, et al. Behavioural sensitization after repeated exposure to Δ^9 -tetrahydocannabinol and cross-sensitization with morphine. Psychopharmacol. 2001; 158(3):259–266.

35. Lopez-Quintero C, Perez de los Cobos J, Hasin DS, et al. Probability and predictors of transition from first use to dependence on nicotine, alcohol, cannabis, and cocaine: results of the National Epidemiologic Survey on Alcohool and Related Conditions (NESARC). Drug Alcohol Depend. 2011; 115(1–2):120–130. [PubMed: 21145178]

36. Wilcox HC, Wagner FA, Anthony JC. Exposure opportunity as a mechanism linking youth marijuana use to hallucinogen use. Drug Alc Depend. 2002; 66:127–135.

37. Lynskey MT, Vink JM, Boomsma DI. Early onset cannabis use and progression to other drug use in a sample of Dutch twins. Behavior Genetics. 2006; 36(2):195–200. [PubMed: 16402286]

38. Bonn-Miller MO, Boden MT, Bucossi MM, et al. Self reported cannabis use characteristics, patterns and helpfulness among medical cannabis users. Am J Drug Alc Abuse. 2014; 40(1):23–30.

39. Compton WM, Han B, Hughes, et al. Use of marijuana for medical purposes among adults in the United States. JAMA. 2017; 317(2):209–211. [PubMed: 27992636]

40. Compton WM, Dawson D, Duffy SQ, et al. The effect of inmate populations on estimates of DSM-IV alcohol and drug use disorders in the United States. Am J Psychiatry. 2010; 167:473–474.

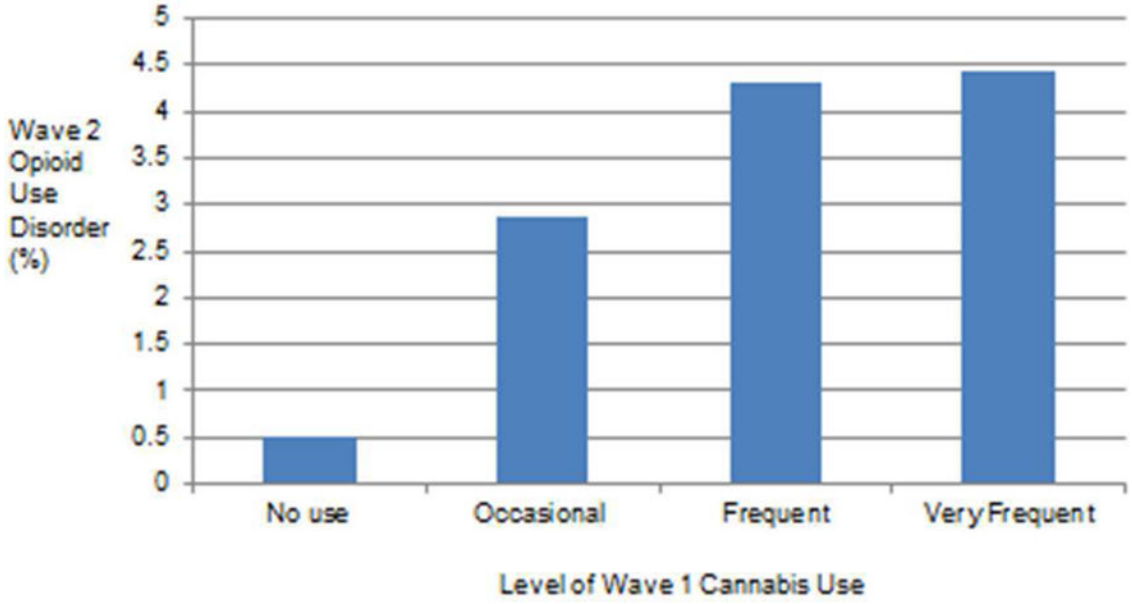

Figure 1.

Level of Wave 1 Cannabis Use and Incident Wave 2 Prescription Opioid Use Disorder

Data for Figure (Histogram):

Level of wave 1 cannabis use (N)	Wave 2Incident Opioid Use Disorder % (n)
Non-use (N=33,045)	0.51 (146)
Occasional use (N=443)	2.86 (10)
Frequent use (N=387)	4.30 (14)
Very frequent use (N=325)	4.43 (18)

Table 1

Background characteristics of NESARC respondents by any past year cannabis use at Wave 1[A]

Wave 1 Characteristics	Cannabis Use (N=1267) Mean (SD)	No Cannabis Use (N=33,352) Mean (SD)	T-score/Chi-square (p-value)
Age, years	29.91 (10.66)	45.72 (17.27)	<0.0001
	%	%	
Sex			
Male	66.49	47.14	<0.0001
Female	33.51	52.86	<0.0001
Race/Ethnicity			0.96
White, non-Hispanic	70.82	70.91	
Other	29.18	29.09	
Family History			
Alcohol Use Disorders	46.51	33.96	<0.0001
Drug Use Disorders	33.08	15.97	<0.0001
Depression	48.39	31.98	<0.0001
Antisocial Personality Disorder	21.42	2.89	<0.0001
Pain[B]	20.06	18.60	0.29
Nonmedical opioid use, past 12			<0.0001
months			
No use	81.92	98.94	
Occasional use	10.11	0.54	
Frequent use	4.37	0.32	
Very frequent use	3.61	0.21	
Mental Disorders, past 12 months			
Opioid use disorder	4.05	0.18	<0.0001
Cannabis use disorder	36.21	0	<0.0001
Other substance use disorder[C]	48.89	6.78	<0.0001
Mood or anxiety disorder	33.00	15.53	<0.0001

[A] NESARC denotes National Epidemiologic Survey on Alcohol and Related Conditions.

[B] Pain denotes moderate to extreme pain interference in past 2 weeks.

[C] Excludes cannabis use and opioid use disorder

Table 2

Prospective associations of Wave 1 cannabis use and Wave 2 prevalent and incident nonmedical prescription opioid use in the NESARC[A]

Wave 1 any past year cannabis use predicting	N in analysis	Odds Ratio	95% CI	Adjusted Odds Ratio[B]	95% CI
Overall population					
Wave 2 prevalent nonmedical opioid use	34,534	8.74	6.98–10.93	3.54	2.74–4.57
Wave 2 incident nonmedical opioid use	32,888	5.78	4.23–7.90	2.62	1.86–3.69
Population without Wave 1 cannabis use disorders					
Wave 2 prevalent nonmedical opioid use	34,091	7.43	5.59–9.87	3.35	2.48–4.52
Wave 2 incident nonmedical opioid use	32,616	5.67	3.97–8.09	2.78	1.91–4.04
Population with pain[C]					
Wave 2 prevalent nonmedical opioid use	6,920	10.30	6.89–15.39	3.97	2.44–6.46
Wave 2 incident nonmedical opioid use	6,518	6.74	4.09–11.10	2.99	1.63–5.47

[A] NESARC denotes National Epidemiologic Survey on Alcohol and Related Conditions.

[B] Adjusted for age, sex, race/ethnicity, other substance use disorders, any mood or anxiety disorder and family history of drug use disorder, alcohol use disorder, depression, and antisocial personality disorder at Wave 1. The “Overall population” and “Population without Wave 1 cannabis use disorders” analyses were also adjusted for pain at Wave 1.

[C] Pain denotes moderate to extreme pain interference in the last 2 weeks.

Table 3

Prospective associations between Wave 1 cannabis use and increase or decrease in nonmedical prescription opioid use at Wave 2 among adults with Wave 1 nonmedical prescription opioid use in the NESARC[A]

Wave 1 any past year cannabis use predicting	Percent with Change		Odds Ratio	95% CI	Adjusted Odds Ratio[B]	95% CI%
	Cannabis Use %	No Cannabis Use %				
Adults with Wave 1 nonmedical opioid use	(N=203)	(N=332)				
Increase opioid use at Wave 2	5.15	0.97	5.57	1.47–21.11	3.13	1.19–8.23
Decrease opioid use at Wave 2	81.27	93.70	0.29	0.14–0.61	0.42	0.19–0.91
Adults with Wave 1 nonmedical opioid use and pain[C]	(N=60)	(N=105)				
Increase opioid use at Wave 2	7.78	1.97	4.20	0.64–27.50	2.60	0.42–16.05
Decrease opioid use at Wave 2	79.97	93.04	0.30	0.10–0.86	0.60	0.18–2.03

[A] NESARC denotes National Epidemiologic Survey on Alcohol and Related Conditions.

[B] Adjusted for age, sex, race/ethnicity, other substance use disorders, any mood or anxiety disorder and family history of drug use disorder, alcohol use disorder, depression, and antisocial personality disorder at Wave 1.

[C] Pain denotes pain with moderate to extreme interference in the last 2 weeks.

Table 4

Prospective associations of Wave 1 cannabis use and Wave 2 prevalent and incident nonmedical prescription opioid disorder in the NESARC[A]

Wave 1 any past year cannabis use predicting	N in analysis	Odds Ratio	95% CI	Adjusted Odds Ratio[B]	95% CI
Overall population					
Wave 2 prevalent opioid use disorder	34,619	10.63	7.09–15.93	2.49	1.35–4.59
Wave 2 incident opioid use disorder	34,190	7.76	4.95–12.16	2.18	1.14–4.14
Population without Wave 1 cannabis use disorders					
Wave 2 prevalent opioid use disorder	34,176	9.03	5.21–15.64	2.15	1.16–3.99
Wave 2 incident opioid use disorder	33,798	5.42	2.99–9.82	1.72	0.81–3.63
Population with pain[C]					
Wave 2 prevalent opioid use disorder	6,934	13.21	7.03–24.83	3.70	1.70–8.08
Wave 2 incident opioid use disorder	6,772	6.70	3.08–14.55	2.14	0.95–4.83

[A] NESARC denotes National Epidemiologic Survey on Alcohol and Related Conditions.

[B] Adjusted for age, sex, race/ethnicity, other substance use disorders, any mood or anxiety disorder, nonmedical opioid use, family history of drug use disorder, alcohol use disorder, depression, and antisocial personality disorder at Wave 1. The “Overall population” and “Population without Wave 1 cannabis use disorders” were also adjusted for pain at Wave 1.

[C] Pain denotes moderate to extreme pain interference in the last 2 weeks.