HHS Public Access

Author manuscript

Am J Psychiatry. Author manuscript; available in PMC 2020 July 03.

Published in final edited form as:

Am J Psychiatry. 2020 July 01; 177(7): 611–618. doi:10.1176/appi.ajp.2019.19030284.

U.S. Adults With Pain, a Group Increasingly Vulnerable to Nonmedical Cannabis Use and Cannabis Use Disorder: 2001–2002 and 2012–2013

Deborah S. Hasin, Ph.D.,
NewYork State Psychiatric Institute, NewYork; Department of Psychiatry, Columbia University Medical Center, New York; Department of Epidemiology, Columbia University Mailman School of Public Health, New York

Dvora Shmulewitz, Ph.D.,
NewYork State Psychiatric Institute, New York; Department of Psychiatry, Columbia University Medical Center, New York; Department of Epidemiology, Columbia University Mailman School of Public Health, New York

Magdalena Cerdá, Dr.P.H.,
Columbia University Mailman School of Public Health, New York; Department of Population Health, New York University, New York

Katherine M. Keyes, Ph.D.,
Department of Epidemiology, Columbia University Mailman School of Public Health, New York

Mark Olfson, M.D., M.P.H.,
NewYork State Psychiatric Institute, New York; Department of Psychiatry, Columbia University Medical Center, New York, Department of Epidemiology

Aaron L. Sarvet, M.P.H.,
Department of Epidemiology, Harvard University School of Public Health, Boston

Melanie M. Wall, Ph.D.
NewYork State Psychiatric Institute, New York; Department of Psychiatry, Columbia University Medical Center, New York; Department of Biostatistics

Abstract

Objective: Given changes in U.S. marijuana laws, attitudes, and use patterns, individuals with pain may be an emerging group at risk for nonmedical cannabis use and cannabis use disorder. The authors examined differences in the prevalence of nonmedical cannabis use and cannabis use disorder among U.S. adults with and without pain, as well as whether these differences widened over time.

Methods: Data from the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC, 2001–2002; N=43,093) and NESARC-III (2012–2013; N=36,309) were analyzed using logistic regression. Risk differences of past-year nonmedical cannabis use, frequent (at least

correspondence to Dr. Hasin (dsh2@cumc.columbia.edu).

three times a week) nonmedical use, and DSM-IV cannabis use disorder were estimated for groups with and without moderate to severe pain, and these risk differences were tested for change over time.

Results: Any nonmedical cannabis use was more prevalent in respondents with than without pain (2001–2002: 5.15% compared with 3.74%; 2012–2013: 12.42% compared with 9.02%), a risk difference significantly greater in the 2012–2013 data than in the 2001–2002 data. The prevalence of frequent nonmedical cannabis use did not differ by pain status in the 2001–2002 survey, but was significantly more prevalent in those with than without pain in the 2012–2013 survey (5.03% compared with 3.45%). Cannabis use disorder was more prevalent in respondents with than without pain (2001–2002: 1.77% compared with 1.35%; 2012–2013: 4.18% compared with 2.74%), a significantly greater risk difference in the data from 2012–2013 than from 2001–2002.

Conclusions: The results suggest that adults with pain are a group increasingly vulnerable to adverse cannabis use outcomes, warranting clinical and public health attention to this risk. Psychiatrists and other health care providers treating patients with pain should monitor such patients for signs and symptoms of cannabis use disorder.

While many individuals can use cannabis without harm, evidence indicates that regular or heavy users are at increased risk for health consequences, includingvehicle crashes, respiratory symptoms, emergency department visits, psychiatric symptoms, withdrawal, and cannabis use disorder (1). Despite this evidence, however, U.S. adults have become increasingly likely to perceive cannabis use as harmless (2), and nonmedical use of cannabis, including daily or near-daily use, has increased among U.S. adults since the early 2000s (2-4). The prevalence of adult cannabis use disorder has also increased, including among hospital inpatients (5), Veterans Health Administration patients (6), and in one general population study (4) (although not in another [2]). Given the evidence for an increase in the prevalence of cannabis use disorder, identifying characteristics that increase the risk of frequent nonmedical cannabis use and cannabis use disorder is an important public health issue. Pain may be one such characteristic.

Pain, an unpleasant sensory-emotional experience associated with actual or potential tissue damage (7), is common in U.S. adults (8), is a leading cause of disability (9), and is associated with substance use disorders (10, 11). Since 1996, 34 states have passed laws authorizing cannabis use for various medical conditions, including pain, and 11 states have legalized recreational cannabis use. Although meta-analyses of the effectiveness of cannabis to treat pain are inconsistent (12-14), 66% of adults now view marijuana as beneficial for pain management (15). Professional concerns about cannabis use for pain include the risk of unintended consequences, including frequent nonmedical use and cannabis use disorder (16, 17). Because of the many changes in the marijuana landscape (e.g., more permissive marijuana laws, more favorable public attitudes toward marijuana [2, 15], and greater nonmedical use [2–6]), people with pain may be a group at particular and growing risk for adverse cannabis outcomes, such as frequent nonmedical use and cannabis use disorder. If so, greater clinical and public health efforts to treat or prevent adverse cannabis outcomes among those with pain would be warranted.

To our knowledge, no studies have compared risk for nonmedical cannabis use and cannabis use disorder between those with and without pain in the adult general population, or ascertained whether these risks have changed over time. We used data from two nationally representative surveys of U.S. adults, the 2001–2002 National Epidemiologic Survey on Alcohol and Related Conditions (NESARC) (18) and the 2012–2013 National Epidemiologic Survey on Alcohol and Related Conditions–III (NESARC-III) (19), to examine two issues. First, within each survey, we examined whether the prevalence of any nonmedical cannabis use, frequent nonmedical use, and cannabis use disorder differed between respondents with and without pain. Second, given the many changes in the marijuana landscape, we examined whether these differences widened over time, that is, between the 2001–2002 and 2012–2013 surveys.

METHODS

Samples and Procedures

The NESARC (18) and NESARC-III surveys (19) included adults (age ≥18) in households and group quarters sampled in multistage designs. Sample weights adjusted for selection probabilities and nonresponse. The total sample analyzed was 79,402 (43,093 in NESARC, 36,309 in NESARC-III). Rigorous field procedures were similar across surveys (3, 4), including interviewer training (structured home-study and in-class training), supervision by trained supervisors, and random respondent callbacks to verify interview data. Both surveys were sponsored by the National Institute on Alcohol Abuse and Alcoholism (NIAAA), which contracted the field work to large survey organizations (NESARC: U.S. Census Bureau; NESARC-III: Westat), and participants in both surveys were informed that the survey was sponsored by NIAAA. The methodological similarities of the two surveys have facilitated examination of change over time in numerous important health outcomes (4, 20-22). The NESARC response rate was 81.0%. The protocol and written consent procedures were approved by U.S. Bureau of the Census and Office of Management and Budget institutional review boards. The NESARC-III response rate was 60.1%, similar to other contemporaneous nationally representative surveys (23, 24). The protocols and consent procedures (verbal, recorded electronically) were approved by institutional review boards at the National Institutes of Health and Westat.

Measures

The Alcohol Use Disorder and Associated Disabilities Interview Schedule (AUDADIS), a structured computer-assisted diagnostic interview, was used to assess substance use and substance use disorders in both surveys. Identical questions assessed nonmedical substance use, including cannabis.

Study outcomes included three cannabis variables: any nonmedical use, frequent nonmedical use, and DSM-IV cannabis use disorder, with the time frame specified as the past 12 months. Nonmedical use was defined to respondents as use without a prescription or other than prescribed, for example, to get high (3). Any use was defined as at least one time, and frequent use as at least three times a week. Cannabis use disorder was defined as meeting criteria for DSM-IV cannabis dependence or abuse, combined because their criteria reflect a

single condition (25). Most of the 22 cannabis use disorder symptom items used in the two surveys were identical; examination of the few slight differences showed that they could not account for the large differences in prevalence in the two surveys (3, 4).

Pain was measured in NESARC and NESARC-III with an item from the Medical Outcomes Study 12-Item Short Form Health Survey, Version 2 (SF-12) (26), a valid measure used widely in clinical (27) and general population surveys (28). This pain item uses a 5-point scale (not at all, a little bit, moderately, quite a bit, extremely) to measure how much pain interfered with "your normal work, including both work outside the home and housework" during the past 4 weeks. Consistent with a previous study (29), responses were dichotomized, coding moderate to extreme interference as positive and other responses as negative.

Control covariates included gender, age group (18–29, 30–44, 45–64, ≥65 years), race/ethnicity (Hispanic, non-Hispanic white, non-Hispanic black, Native American, Asian/Pacific Islander), education (less than high school, high school graduate or GED, at least some college), marital status (married or living together, previously married, never married), and family income ($0-$19,999, $20,000-$34,999, $35,000-$69,999, ≥$70,000). In sensitivity analyses, we used a covariate indicating whether respondents' states had a medical marijuana law, as evaluated by legal and economic experts and used in previous studies (3, 30). At the time of NESARC, California, Colorado, Hawaii, Maine, Nevada, Oregon, and Washington had medical marijuana laws. At the time of NESARC-III, these and nine additional states—Arizona, Connecticut, Maryland, Massachusetts, Michigan, Montana, New Jersey, New Mexico, and Vermont—had medical marijuana laws.

Statistical Analysis

As in other studies utilizing the two surveys (3, 4, 20, 21), we concatenated the NESARC and NESARC-III data sets, adding a variable indicating survey. Using logistic regression, we modeled cannabis outcomes as a function of pain, survey, and pain-by-survey interactions, with control covariates including sociodemographic characteristics (age, race/ethnicity, gender, education, marital status, income) and covariate-by-pain interactions, allowing covariate effects to differ between participants with and without pain. For each outcome, predictions from the logistic models were used to generate predicted marginal prevalences (i.e., prevalences standardized to the distribution of sociodemographic characteristics of the sample pooled across the two surveys) in each survey by pain status (yes or no). Group comparisons within each survey (i.e., participants with and without pain) were conducted with contrasts between those with and without pain, with risk differences indicating group differences in absolute risk and risk ratios indicating group differences in relative risk. Between-survey comparisons (2001–2002 compared with 2012–2013) were tested with pain-by-time interactions on the additive scale for risk differences and the multiplicative scale for risk ratios. Interaction on the additive scale tested whether the difference in absolute risk of cannabis outcomes between those with and without pain had changed over time (i.e., difference in risk difference), and interaction on the multiplicative scale tested whether the ratios of relative risk for cannabis outcomes between those with and without pain had changed over time (i.e., ratio of risk ratios). Estimates for differences in risk

differences and 95% confidence intervals were obtained using the PRED_EFF option in SUDAAN. Estimates for ratios of risk ratios and 95% confidence intervals were obtained using Fieller's method incorporating predicted marginal prevalences and standard errors from SUDAAN. Interactions on the additive scale are of particular interest from a public health perspective, as they point to groups that experience the greatest population-level risk (or shifts in risk) and thus may represent important targets for prevention and intervention (see the Supplemental Material section and Table S6 in the online supplement) (31-45). To yield estimates representative of the U.S. adult population, we incorporated the survey weights, and used SUDAAN 11.0.1 (46) to adjust for the complex sampling designs. All tests were two-tailed, with the significance threshold set at <0.05.

Note that in comparing groups by their pain status, interpretation of the 95% confidence intervals differs depending on whether differences in absolute risk (risk difference) or relative risk are considered. When evaluating risk differences (risk of the outcome in those with pain minus risk in those without pain), a risk difference of 0.0 indicates no group difference by pain status. Accordingly, a risk difference whose 95% confidence interval does not include 0.0 is statistically significant at $p<0.05$, as are differences in risk difference estimates whose 95% confidence intervals do not include 0.0. When evaluating group differences using risk ratios (the probability of the outcome in those with pain divided by the probability of the outcome in those without pain), a risk ratio of 1.0 indicates no difference by pain status. Accordingly, risk ratios and ratios of risk ratio whose 95% confidence intervals do not include 1.0 are statistically significant at $p<0.05$.

We conducted several sensitivity analyses of the risk difference results. First, we reran the model for cannabis use disorder after adding cannabis withdrawal to the dependence criteria (assessed identically in NESARC and NESARC-III) and requiring at least three of seven of the cannabis dependence criteria to score dependence as positive. This was done to reflect post-NESARC evidence on the validity and coherence of cannabis withdrawal with the other cannabis use disorder criteria (25). Second, we omitted the covariate-by-pain interactions to examine whether differential covariate effects on pain drove the results. Third, we ran models with age in three-way interactions with pain and survey to explore whether difference-in-difference results varied by age. Fourth, we ran models with state medical marijuana law status at the time of each survey as a covariate. In this analysis, following previous methods (3), only participants from the 42 states included in both surveys were included (41,706 from NESARC and 36,309 from NESARC-III). Finally, to explore whether state medical marijuana law status modified the results, we ran models with medical marijuana law status in three-way interaction models similar to those for age, defining the three-level medical marijuana law variable as never medical marijuana law, medical marijuana law enacted by 2001, and medical marijuana law enacted between 2002 and 2012.

RESULTS

The prevalence of pain among U.S. adults was 19.3% (SE=0.31) in the 2001–2002 survey and 20.0% (SE=0.44) in the 2012–2013 survey. Between the two surveys, overall increases occurred in the prevalence of any nonmedical cannabis use (from 4.1% [SE=0.15] to 9.5%

[SE=0.27]), frequent nonmedical use (from 1.2% [SE=0.08] to 3.7% [SE=0.15]), and cannabis use disorder (from 1.5% [SE=0.8] to 2.9% [SE=0.13]).

Pain and Any Past-Year Nonmedical Cannabis Use

The predicted prevalences of any nonmedical cannabis use among respondents with and without pain are listed in Table 1 for the 2001–2002 survey (5.15% and 3.74%) and the 2012–2013 survey (12.42% and 9.02%). As shown in Table 2, pain was associated with significantly greater absolute risk (risk difference) and relative risk (risk ratio) for any nonmedical cannabis use in both surveys. The difference-in-risk-differences test (Table 3) indicated that the risk difference for any nonmedical cannabis use between those with and without pain was greater in the 2012–2013 survey than in the 2001–2002 survey (difference in risk difference=1.99, 95% CI=0.69, 3.29). The 95% confidence interval did not include zero, indicating that the difference in risk differences between the two surveys was statistically significant. The risk ratios reflecting greater risk for any nonmedical cannabis use among those with than those without pain did not differ significantly over time (risk ratio=1.38 in both surveys [Table 2]; ratio of risk ratios=1.00, 95% CI=0.82, 1.24 [Table 3]).

Frequent Nonmedical Cannabis Use

The predicted prevalences of frequent nonmedical cannabis use among respondents with and without pain are listed in Table 1 for the 2001–2002 survey (1.35% and 1.11%) and the 2012–2013 survey (5.03% and 3.45%). In the 2001–2002 data, the predicted prevalence of frequent nonmedical cannabis use did not differ between those with and without pain on the risk difference or risk ratio scale (Table 2). However, in the 2012–2013 data, the predicted prevalence of frequent nonmedical use was significantly greater among respondents with pain than those without pain on both the risk difference and risk ratio scales (Table 2). As shown in Table 3, while the ratio of risk ratios between the two time periods did not reach significance (ratio of risk ratio=1.20, 95% CI=0.85, 1.83), the difference in risk differences indicated that the absolute risk difference between those with and without pain was significantly greater in the 2012–2013 survey than in the 2001–2002 survey (difference in risk difference=1.35, 95% CI=0.47, 2.23).

DSM-IV Cannabis Use Disorder

The predicted prevalences of DSM-IV cannabis use disorder in respondents with and those without pain (Table 1) were 1.77% and 1.35% in the 2001–2002 data and 4.18% and 2.74% in the 2012–2013 data. In the 2001–2002 data, the predicted prevalence of cannabis use disorder differed between those with and without pain on the risk difference scale but not on the risk ratio scale (Table 2). However, in the 2012–2013 survey, the predicted prevalence of cannabis use disorder was significantly greater among those with than those without pain on both the risk difference and risk ratio scales (Table 2). While the ratio of risk ratios did not reach significance between the two time periods (Table 3) (ratio of risk ratio=1.16, 95% CI=0.80, 1.83), the difference in risk differences test indicated that the absolute risk difference between those with and without pain was significantly greater in the 2012–2013 survey than in the 2001–2002 survey (difference in risk difference=1.02, 95% CI=0.18, 1.86).

Sensitivity Analyses

The results were virtually unchanged after cannabis withdrawal was added to the criteria (see Table S1 in the online supplement) and after the covariate-by-pain interaction terms were omitted (see Table S2 in the online supplement). Age did not significantly modify the results for any or frequent nonmedical use (see Table 3A in the online supplement). For cannabis use disorder, using the ≥65-year age group as the reference group, the difference-in-difference test was significantly stronger for respondents in the 18- to 29-year age group (group contrast=3.82, 95% CI=0.57, 7.07) (see Table 3B in the online supplement). The results were similar after medical marijuana law status was added to the models (see Table S4 in the online supplement), the only difference being that the risk difference for DSM-IV cannabis use disorder in those with and without pain became nonsignificant in the 2001–2002 data. No test exploring modification of change in the pain-cannabis associations over time by state medical marijuana law status was significant (see Table S5 in the online supplement).

DISCUSSION

To our knowledge, this is the first study to examine the differences in prevalence of nonmedical cannabis use and cannabis use disorder among U.S. adults with and without pain, and whether the risk differences changed over a period when the prevalence of moderate to severe pain remained similar. In the 2001–2002 survey, any nonmedical cannabis use and cannabis use disorder were more prevalent among respondents with pain than those without pain. In the 2012–2013 survey, the prevalences of all three cannabis outcomes were greater among those with pain than those without pain. Furthermore, when considered in absolute risk terms, the differences between those with and without pain increased over time. Extrapolating to the number of U.S. adults potentially affected, approximately 1.5 million more adults with pain were frequent nonmedical cannabis users in the 2012–2013 period than in the 2001–2002 period, and approximately 0.9 million more adults with pain had past-year cannabis use disorder in the 2012–2013 period than in the 2001–2002 period. These results suggest that among adults with pain, frequent nonmedical cannabis use and cannabis use disorder are growing problems.

Although the risk ratios (multiplicative scale) were unable to capture a significant pain-by-time period interaction for any of the cannabis outcomes, pain-by-time period interactions were found to be significant for all three outcomes using the risk differences (additive scale). Ours is not the first study to find a difference in interaction results depending on the scale used (44). As discussed further in the Supplemental Material section and Table S6 in the online supplement, and in a large methodological literature (31-45), for a study such as ours, results on the additive scale were the ones of interest, since we were interested in determining whether, during a period of striking changes in the U.S. marijuana landscape, adults in a particular group (i.e., those with pain) were more affected than others. The study findings suggest that in the context of the changing landscape, a shift occurred in the distribution of individuals among whom the cannabis outcomes occurred, and that those with pain are now a group particularly vulnerable to frequent nonmedical use and cannabis use disorder, thus warranting special attention.

While some may question inclusion of a variable representing “any” nonmedical cannabis use as an adverse outcome in a health study, this variable ensures consistency with many other epidemiologic studies of cannabis use that include such a variable (2, 47), and it is also analogous to the “any” drinking variable in the literature on alcohol (21, 48). At the same time, frequent nonmedical cannabis use exposes users to risk for adverse medical sequelae such as respiratory symptoms, injury due to intoxication-related impairments, onset of psychiatric disorders including psychotic disorders (49), and onset of cannabis use disorder (3, 50). Thus, frequent nonmedical cannabis use and cannabis use disorder are clearly public health concerns. With rates of frequent nonmedical use and cannabis use disorder increasing among U.S. adults (4-6, 51), identifying subgroups at particular risk for these conditions is necessary to inform clinical and public health intervention. Our results suggest that adults in pain are one such group.

Given the current U.S. opioid crisis, ecological studies of national U.S. data have examined the relationship of medical marijuana laws to state-level rates of opioid outcomes, finding decreased rates of opioid prescriptions (52-56), overdoses (57, 58), and opioid-related hospitalizations (59) after medical marijuana law enactment. These studies were interpreted as indicating that increased cannabis availability might help mitigate the opioid crisis. However, ecological studies are a weak design for investigating the causes of individual behaviors (43, 60-63), and none of these studies took individual pain or pain-related conditions into account. A large study of U.S. adults showed that among those with pain, cannabis use predicted higher incident nonmedical opioid use and opioid use disorder (63), and another national study showed that presence of a medical marijuana law predicted increased rates of nonmedical opioid use among 12th graders (64). These studies, along with the present findings, suggest the need for caution in advocating cannabis as a widespread substitute for opioids in treating chronic noncancer pain.

Sensitivity analyses showed that the results were robust to the influence of several factors, including medical marijuana law status. Results for any and frequent nonmedical cannabis use were consistent across age groups. However, for cannabis use disorder, differences between those with and without pain changed more over time among young adults (the 18- to 29-year age group) than among older groups. Replication of this finding would be useful, as would a study examining whether the result is an age, period, or cohort effect.

Popular beliefs hold that cannabis is an effective treatment for pain (15, 65), although meta-analyses of cannabis for treating pain (12, 13) show mixed efficacy, particularly for cannabis consumed in plant form (13). Further research with stronger designs may support public beliefs about cannabis or its constituent components as treatment for pain. Meanwhile, the need remains for other interventions to manage pain that do not incur the risk of another substance use disorder (i.e., cannabis use disorder) as an adverse treatment outcome.

Limitations of the study should be noted. Pain was indicated by a single variable rather than by physician assessment. However, NESARC and NESARC-III estimates of pain prevalence were nearly identical to National Health Interview Survey estimates (20.4%) (66), which are based on a well-validated pain scale (67). Future national surveys of substance use should measure pain and painful medical conditions more extensively. Cannabis variables were

based on self-report and thus subject to social desirability bias. The NESARC did not ask about cannabis use exclusively for medical purposes (i.e., no nonmedical use). NESARC-III asked about this, finding that of the 36,309 participants, 82 used cannabis exclusively for medical purposes (68). These individuals were more likely to have pain than those whose used cannabis solely for nonmedical purposes and those who used it medically and nonmedically (68). We did not include exclusively medical users in our analyses because they were not asked frequency of use or cannabis use disorder items; future studies should do so. Given the cross-sectional nature of the surveys, we could not address the possibility that cannabis use caused pain, although this appears unlikely, or that initial cannabis use for pain eventually led to cannabis use disorder, which should also be examined in the future. Future studies should also incorporate information on state prescription opioid policies and use of opioids as prescribed and nonmedically. Also, as household surveys, NESARC and NESARC-III did not include participants who were medically institutionalized (a group possibly less likely to be nonmedical marijuana users) or incarcerated (a group possibly more likely to be users), and our findings cannot be generalized to these special populations. Also, NESARC-III compensated participants for participation, whereas NESARC did not. How compensation might have affected responses is unknown, although survey methodology studies suggest little effect of compensation on data accuracy (69). Additionally, NESARC interviewers were U.S. Census Bureau employees, whereas NESARC-III interviewers were Westat employees. Some have speculated on whether participant willingness to report cannabis use varied by whether their survey interviewer was directly employed by the federal government (70). However, the fact that participants in both surveys were informed of the governmental sponsor (NIAAA) may have mitigated this possibility.

This study did not address potential mechanisms of the results, including increasingly positive attitudes toward cannabis use, increasing public beliefs that cannabis effectively treats pain, changes in state marijuana laws, and increasing prevalence of conditions that may covary with pain and cannabis use, for example, psychiatric disorders. All of these should be examined in future studies. Finally, a higher response rate in NESARC-III would have been preferable, as survey participants may be healthier than nonparticipants (71). However, the NESARC-III rate resembled other contemporaneous national surveys, and sample weights adjusted the findings to represent the overall general population.

CONCLUSIONS

This study suggests that adults with pain are a group with particular and growing vulnerability to frequent nonmedical cannabis use or cannabis use disorder, for which prevention and clinical intervention efforts are warranted. Future studies in larger samples should examine many additional questions about pain and nonmedical cannabis use, including whether pain and additional risk factors (e.g., psychiatric disorders) contribute to the risk differences in the cannabis outcomes. Meanwhile, although marijuana legalization has social justice and tax revenue advantages, state policy makers and the health departments that implement state marijuana laws should also consider and plan for potential increases in health problems if new laws and policies increase the prevalence of adult cannabis use disorder (3, 72), especially among those with pain. Also, media reports and public education

programs should provide credible public information about the risks of cannabis use, including for people with pain. A recent analysis of media reports on marijuana showed that few addressed health consequences, and of those that did, an increasing proportion focused only on favorable aspects (11% in 2012 compared with 65% in 2016) (73). Greater balance is needed in reporting marijuana issues. Finally, those developing public education programs should not assume that simple information is effective, but instead work with constituent groups to determine messaging that conveys balanced, credible information about the nature and magnitude of risks from cannabis use, including among the large group of U.S. adults with pain. Psychiatrists and other mental health professionals treating patients with moderate to severe pain should be informed about the potential risks of cannabis, including cannabis use disorder, provide information about these risks to their patients, and monitor patients for signs and symptoms of cannabis use disorder.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

Supported by NIDA grant R01DA019606 to Drs. Wall and Olfson, grants R01DA034244 and R01DA048860 to Dr. Hasin, and grant T32 MH017119 to Mr. Sarvet, and by the New York State Psychiatric Institute.

Dr. Hasin has received funding from the Campbell Alliance for the validation and use of a measure of opioid addiction among patients with chronic pain. Dr. Keyes has received compensation for consultation on behalf of plaintiff counties in the National Prescription Opioid Litigation. The other authors report no financial relationships with commercial interests.

REFERENCES

1. Hasin DS: US epidemiology of cannabis use and associated problems. Neuropsychopharmacology 2018; 43:195–212 [PubMed: 28853439]
2. Compton WM, Han B, Jones CM, et al. Marijuana use and use disorders in adults in the USA, 2002–14: analysis of annual cross-sectional surveys. Lancet Psychiatry 2016; 3:954–964 [PubMed: 27592339]
3. Hasin DS, Sarvet AL, Cerdá M, et al. US adult illicit cannabis use, cannabis use disorder, and medical marijuana laws: 1991–1992 to 2012–2013. JAMA Psychiatry 2017; 74:579–588 [PubMed: 28445557]
4. Hasin DS, Saha TD, Kerridge BT, et al. Prevalence of marijuana use disorders in the United States between 2001–2002 and 2012–2013. JAMA Psychiatry 2015; 72:1235–1242 [PubMed: 26502112]
5. Charilaou P, Agnihotri K, Garcia P, et al. Trends of cannabis use disorder in the inpatient: 2002 to 2011. Am J Med 2017;130:678–687.e7 [PubMed: 28161344]
6. Bonn-Miller MO, Harris AHS, Trafton JA: Prevalence of cannabis use disorder diagnoses among veterans in 2002, 2008, and 2009. Psychol Serv 2012; 9:404–416 [PubMed: 22564034]
7. Williams AC, Craig KD: Updating the definition of pain. Pain 2016; 157:2420–2423 [PubMed: 27200490]
8. Nahin RL: Estimates of pain prevalence and severity in adults: United States, 2012. J Pain 2015; 16:769–780. [PubMed: 26028573]
9. GBD 2016 Disease and Injury Incidence and Prevalence Collaborators: Global, regional, and national incidence, prevalence, and years lived with disability for 328 diseases and injuries for 195 countries, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016. Lancet 2017; 390:1211–1259 [PubMed: 28919117]

10. Martel MO, Shir Y, Ware MA: Substance-related disorders: a review of prevalence and correlates among patients with chronic pain. Prog Neuropsychopharmacol Biol Psychiatry 2018; 87(Pt B):245–254 [PubMed: 28669582]
11. Hefner K, Sofuoglu M, Rosenheck R: Concomitant cannabis abuse/dependence in patients treated with opioids for non-cancer pain. Am J Addict 2015; 24:538–545 [PubMed: 26246069]
12. Whiting PF, Wolff RF, Deshpande S, et al. Cannabinoids for medical use: a systematic review and meta-analysis. JAMA 2015; 313:2456–2473 [PubMed: 26103030]
13. Stockings E, Campbell G, Hall WD, et al. Cannabis and cannabinoids for the treatment of people with chronic noncancer pain conditions: a systematic review and meta-analysis of controlled and observational studies. Pain 2018; 159:1932–1954 [PubMed: 29847469]
14. De Vita MJ, Moskal D, Maisto SA, et al. Association of cannabinoid administration with experimental pain in healthy adults: a systematic review and meta-analysis. JAMA Psychiatry 2018; 75:1118–1127 [PubMed: 30422266]
15. Keyhani S, Steigerwald S, Ishida J, et al. Risks and benefits of marijuana use: a national survey of US adults. Ann Intern Med 2018; 169:282–290 [PubMed: 30039154]
16. Saxon AJ, Browne KW: Marijuana not ready for prime time as an analgesic. Gen Hosp Psychiatry 2014; 36:4–6 [PubMed: 24176513]
17. Becker WC, Tetrault JM: Medical marijuana in patients prescribed opioids: a cloud of uncertainty. Mayo Clin Proc 2016; 91:830–832 [PubMed: 27234481]
18. Grant BF, Stinson FS, Dawson DA, et al. Prevalence and co-occurrence of substance use disorders and independent mood and anxiety disorders: results from the National Epidemiologic Survey on Alcohol and Related Conditions. Arch Gen Psychiatry 2004; 61:807–816 [PubMed: 15289279]
19. Grant BF, Goldstein RB, Saha TD, et al. Epidemiology of DSM-5 alcohol use disorder: results from the National Epidemiologic Survey on Alcohol and Related Conditions III. JAMA Psychiatry 2015; 72:757–766 [PubMed: 26039070]
20. Martins SS, Sarvet A, Santaella-Tenorio J, et al. Changes in US lifetime heroin use and heroin use disorder: prevalence from the 2001–2002 to 2012–2013 National Epidemiologic Survey on Alcohol and Related Conditions. JAMA Psychiatry 2017; 74:445–455 [PubMed: 28355458]
21. Grant BF, Chou SP, Saha TD, et al. Prevalence of 12-month alcohol use, high-risk drinking, and DSM-IV alcohol use disorder in the United States, 2001–2002 to 2012–2013: results from the National Epidemiologic Survey on Alcohol and Related Conditions. JAMA Psychiatry 2017; 74:911–923 [PubMed: 28793133]
22. Olfson M, Blanco C, Wall M, et al. National trends in suicide attempts among adults in the United States. JAMA Psychiatry 2017; 74:1095–1103 [PubMed: 28903161]
23. Substance Abuse and Mental Health Services Administration: Results From the 2012 National Survey on Drug Use and Health: Summary of National Findings Appendix B: Statistical Methods and Measurement. Rockville, Md, US Department of Health and Human Services, 2013
24. Adams PF, Kirzinger WK, Martinez M: Summary health statistics for the US population: National Health Interview Survey, 2012. Vital Health Stat 10 2013, series 10, no 259:1–95
25. Hasin DS, O'Brien CP, Auriacombe M, et al. DSM-5 criteria for substance use disorders: recommendations and rationale. Am J Psychiatry 2013; 170:834–851 [PubMed: 23903334]
26. 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]
27. Kirouac M, Stein ER, Pearson MR, et al. Viability of the World Health Organization quality of life measure to assess changes in quality of life following treatment for alcohol use disorder. Qual Life Res 2017; 26:2987–2997 [PubMed: 28647889]
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–e450 [PubMed: 23759465]
29. 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; 173:1189–1195 [PubMed: 27444794]
30. Hasin DS, Wall M, Keyes KM, et al. Medical marijuana laws and adolescent marijuana use in the USA from 1991 to 2014: results from annual, repeated cross-sectional surveys. Lancet Psychiatry 2015; 2:601–608 [PubMed: 26303557]

31. VanderWeele TJ, Robins JM: The identification of synergism in the sufficient-component-cause framework. Epidemiology 2007; 18:329–339 [PubMed: 17435441]
32. Kaufman JS: Interaction reaction. Epidemiology 2009; 20:159–160 [PubMed: 19234409]
33. Knol MJ, VanderWeele TJ: Recommendations for presenting analyses of effect modification and interaction. Int J Epidemiol 2012; 41:514–520 [PubMed: 22253321]
34. Kalilani L, Atashili J: Measuring additive interaction using odds ratios. Epidemiol Perspect Innov 2006; 3:5 [PubMed: 16620385]
35. Knol MJ, van der Tweel I, Grobbee DE, et al. Estimating interaction on an additive scale between continuous determinants in a logistic regression model. Int J Epidemiol 2007; 36:1111–1118 [PubMed: 17726040]
36. Zou GY: On the estimation of additive interaction by use of the four-by-two table and beyond. Am J Epidemiol 2008; 168:212–224 [PubMed: 18511428]
37. Darnton AJ, McElvenny DM, Hodgson JT: Estimating the number of asbestos-related lung cancer deaths in Great Britain from 1980 to 2000. Ann Occup Hyg 2006; 50:29–38 [PubMed: 16126764]
38. Bally M, Nadeau L, Brophy JM: Studying additive interaction in a healthcare database: case study of NSAIDs, cardiovascular profiles, and acute myocardial infarction. PLoS One 2018; 13:e0201884 [PubMed: 30096158]
39. Kinsey TL, Sturmer T, Poole C, et al. Changing predictors of statin initiation in US women over two decades. Pharmacoepidemiol Drug Saf 2019; 28:305–314 [PubMed: 30565779]
40. Marenholz I, Kerscher T, Bauerfeind A, et al. An interaction between filaggrin mutations and early food sensitization improves the prediction of childhood asthma. J Allergy Clin Immunol 2009; 123:911–916 [PubMed: 19348926]
41. Yang X, So WY, Ma RC, et al. Low LDL cholesterol, albuminuria, and statins for the risk of cancer in type 2 diabetes: the Hong Kong diabetes registry. Diabetes Care 2009; 32:1826–1832 [PubMed: 19592629]
42. Rothman KJ, Greenland S, Walker AM: Concepts of interaction. Am J Epidemiol 1980; 112:467–470 [PubMed: 7424895]
43. Greenland S: Ecologic versus individual-level sources of bias in ecologic estimates of contextual health effects. Int J Epidemiol 2001; 30:1343–1350 [PubMed: 11821344]
44. VanderWeele TJ, Knol MJ: A tutorial on interaction. Epidemiol Methods 2014; 3:33–72
45. Greenland S, Lash TL, Rothman KJ: Concepts of interaction, in Modern Epidemiology, 3rd ed. Edited by Rothman KJ, Greenland S, Lash TL. Philadelphia, Lippincott Williams &Wilkins, 2012, pp 71–86
46. Research Triangle Institute: SUDAAN, release 11.0.1. Research Triangle Park, NC, Research Triangle Institute International
47. Han B, Compton WM, Blanco C, et al. Time since first cannabis use and 12-month prevalence of cannabis use disorder among youth and emerging adults in the United States. Addiction 2019; 114:698–707 [PubMed: 30474910]
48. White A, Castle IJ, Chen CM, et al. Converging patterns of alcohol use and related outcomes among females and males in the United States, 2002 to 2012. Alcohol Clin Exp Res 2015; 39:1712–1726 [PubMed: 26331879]
49. Hjorthøj C, Albert N, Nordentoft M: Association of substance use disorders with conversion from schizotypal disorder to schizophrenia. JAMA Psychiatry 2018; 75:733–739 [PubMed: 29710317]
50. Hasin DS, Kerridge BT, Saha TD, et al. Prevalence and correlates of DSM-5 cannabis use disorder, 2012–2013: findings from the National Epidemiologic Survey on Alcohol and Related Conditions–III. Am J Psychiatry 2016; 173:588–599 [PubMed: 26940807]
51. Gubatan J, Staller K, Barshop K, et al. Cannabis abuse is increasing and associated with increased emergency department utilization in gastroenterology patients. Dig Dis Sci 2016; 61:1844–1852 [PubMed: 26935430]
52. Bradford AC, Bradford WD: Medical marijuana laws may be associated with a decline in the number of prescriptions for Medicaid enrollees. Health Aff (Millwood) 2017; 36:945–951 [PubMed: 28424215]

53. Bradford AC, Bradford WD: Medical marijuana laws reduce prescription medication use in Medicare Part D. Health Aff (Millwood) 2016; 35:1230–1236 [PubMed: 27385238]
54. Wen H, Hockenberry JM: Association of medical and adult-use marijuana laws with opioid prescribing for Medicaid enrollees. JAMA Intern Med 2018; 178:673–679 [PubMed: 29610827]
55. Bradford AC, Bradford WD, Abraham A, et al. Association between US state medical cannabis laws and opioid prescribing in the Medicare Part D population. JAMA Intern Med 2018; 178:667–672 [PubMed: 29610897]
56. Liang D, Bao Y, Wallace M, et al. Medical cannabis legalization and opioid prescriptions: evidence on US Medicaid enrollees during 1993–2014. Addiction 2018; 113:2060–2070 [PubMed: 29989239]
57. 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]
58. Pardo B: Do more robust prescription drug monitoring programs reduce prescription opioid overdose? Addiction 2017; 112:1773–1783 [PubMed: 28009931]
59. Shi Y: Medical marijuana policies and hospitalizations related to marijuana and opioid pain reliever. Drug Alcohol Depend 2017; 173:144–150 [PubMed: 28259087]
60. Hall W, West R, Marsden J, et al. It is premature to expand access to medicinal cannabis in hopes of solving the US opioid crisis. Addiction 2018; 113:987–988 [PubMed: 29468760]
61. Finney JW, Humphreys K, Harris AH: What ecologic analyses cannot tell us about medical marijuana legalization and opioid pain medication mortality. JAMA Intern Med 2015; 175:655–656
62. McCarty D: Does medical cannabis reduce use of prescription opioids? Am J Psychiatry 2018; 175:6–7 [PubMed: 29301427]
63. Olfson M, Wall MM, Liu SM, et al. Cannabis use and risk of prescription opioid use disorder in the United States. Am J Psychiatry 2018; 175:47–53 [PubMed: 28946762]
64. Cerdá M, Sarvet AL, Wall M, et al. Medical marijuana laws and adolescent use of marijuana and other substances: alcohol, cigarettes, prescription drugs, and other illicit drugs. Drug Alcohol Depend 2018; 183:62–68 [PubMed: 29227839]
65. Gallup: Illegal drugs. 2018 https://news.gallup.com/poll/1657/illegal-drugs.aspx
66. Dahlhamer J, Lucas J, Zelaya C, et al. Prevalence of chronic pain and high-impact chronic pain among adults: United States, 2016. MMWR Morb Mortal Wkly Rep 2018; 67:1001–1006 [PubMed: 30212442]
67. Nahin RL: Categorizing the severity of pain using questions from the 2012 National Health Interview Survey. J Pain Res 2016; 9:105–113 [PubMed: 27042138]
68. Wall MM, Liu J, Hasin DS, et al. Use of marijuana exclusively for medical purposes. Drug Alcohol Depend 2019; 195:13–15 [PubMed: 30557813]
69. Singer E, Ye C: The use and effects of incentives in surveys. Ann Am Acad Pol Soc Sci 2013; 645:112–141
70. Grucza RA, Agrawal A, Krauss MJ, et al. Recent trends in the prevalence of marijuana use and associated disorders in the United States. JAMA Psychiatry 2016; 73:300–301 [PubMed: 26864618]
71. Keyes KM, Rutherford C, Popham F, et al. How healthy are survey respondents compared with the general population? Using survey-linked death records to compare mortality outcomes. Epidemiology 2018; 29:299–307 [PubMed: 29389712]
72. Wen H, Hockenberry JM, Cummings JR: The effect of medical marijuana laws on adolescent and adult use of marijuana, alcohol, and other substances. J Health Econ 2015; 42:64–80 [PubMed: 25863001]
73. Abraham A, Zhang AJ, Ahn R, et al. Media content analysis of marijuana's health effects in news coverage. J Gen Intern Med 2018; 33:1438–1440 [PubMed: 29845473]

Table 1.

Predicted prevalences of any nonmedical cannabis use, frequent nonmedical use, and DSM-IV cannabis use disorder among U S adults with and without pain 2001 –2002 and 2012–2013[a]

	2001–2002		2012–2013	
Cannabis Outcome	**Predicted Prevalence**	**SE**	**Predicted Prevalence**	**SE**
Any nonmedical use[b]				
Adults with pain	5.15	0.39	12.42	0.61
Adults without pain	3.74	0.14	9.02	0.26
Frequent nonmedical use[c]				
Adults with pain	1.35	0.19	5.03	0.43
Adults without pain	1.11	0.08	3.45	0.14
DSM-IV cannabis use disorder				
Adults with pain	1.77	0.21	4.18	0.39
Adults without pain	1.35	0.15	2.74	0.14

[a]Data are from the 2001–2002 National Epidemiologic Survey on Alcohol and Related Conditions (NESARC) survey and the 2012–2013 NESARC-III survey. Prevalences are adjusted for sociodemographic covariates (age, gender, race/ethnicity, education level, marital status, and family income) and pain-by-covariate interactions.

[b]Nonmedical use was defined as cannabis use without a prescription or other than prescribed, for example, to get high.

[c]Frequent use was defined as cannabis use at least three times a week.

Table 2.

Within-survey differences in any nonmedical cannabis use, frequent nonmedical use, and DSM-IV cannabis use disorder among U.S. adults with and without pain, 2001–2002 and 2012–2013[a]

	Comparison by Pain Status, 2001–2002				Comparison by Pain Status, 2012–2013			
Cannabis Outcome	**Risk Difference**	**95% CI[b]**	**Risk Ratio**	**95% CI[c]**	**Risk Difference**	**95% CI[b]**	**Risk Ratio**	**95% CI[c]**
Any nonmedical use[d]	**1.41**	**0.65, 2.17**	**1.38**	**1.15, 1.62**	**3.40**	**2.22, 4.58**	**1.38**	**1.22, 1.54**
Frequent nonmedical use[e]	0.24	−0.14, 0.62	1.22	0.85, 1.63	**1.59**	**0.75, 2.43**	**1.46**	**1.19, 1.74**
DSM-IV cannabis use disorder	**0.42**	**0.01, 0.84**	1.31	0.94,1.82	**1.43**	**0.63, 2.23**	**1.52**	**1.21, 1.87**

[a]Data are from the 2001–2002 National Epidemiologic Survey on Alcohol and Related Conditions (NESARC) survey and the 2012–2013 NESARC-III survey. Comparisons are adjusted for sociodemographic covariates (age, gender, race/ethnicity, education level, marital status, and family income) and pain-by-covariate interactions.

[b]Risk differences whose 95% confidence intervals do not include 0.0 are statistically significant at $p<0.05$ and are in boldface.

[c]Risk ratios whose 95% confidence intervals do not include 1.0 are statistically significant at $p<0.05$ and are in boldface.

[d]Nonmedical use was defined as cannabis use without a prescription or other than prescribed, for example, to get high.

[e]Frequent use was defined as cannabis use at least three times a week.

Table 3.

Between-survey comparisons of differences in any nonmedical cannabis use, frequent nonmedical use, and DSM-IV cannabis use disorder by pain status among U.S. adults, 2012–2013 and 2001–2002[a]

	Difference in Risk Differences, 2012–2013 Versus 2001–2002		Ratio of Risk Ratios, 2012–2013 Versus 2001–2002	
Cannabis Outcome	**Difference in Risk Differences**	**95% CI[b]**	**Ratio of Risk Ratios**	**95% CI[c]**
Any nonmedical use[d]	**1.99**	**0.69, 3.29**	1.00	0.82, 1.24
Frequent nonmedical use[e]	**1.35**	**0.47, 2.23**	1.20	0.85, 1.83
DSM-IV cannabis use disorder	**1.02**	**0.18, 1.86**	1.16	0.80, 1.83

[a] Data are from the 2001–2002 National Epidemiologic survey on Alcohol and Related conditions (NESARC) survey and the 2012–2013 NESARC-III survey. All estimates are adjusted for sociodemographic covariates (age, gender, race/ethnicity, education level, marital status, and family income) and pain-by-covariate interactions.

[b] Additive interaction: differences in risk differences whose 95% confidence intervals do not include 0.0 are statistically significant at $p<0.05$ and are in boldface.

[c] Multiplicative interaction: ratios of risk ratios whose 95% confidence intervals do not include 1.0 are statistically significant at $p<0.05$; none shown are significant.

[d] Nonmedical use was defined as cannabis use without a prescription or other than prescribed, for example, to get high.

[e] Frequent use was defined as cannabis use at least three times a week.