Original Investigation

Cannabis Use and Risk of Psychiatric Disorders
Prospective Evidence From a US National Longitudinal Study

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IMPORTANCE With rising rates of marijuana use in the general population and an increasing number of states legalizing recreational marijuana use and authorizing medical marijuana programs, there are renewed clinical and policy concerns regarding the mental health effects of cannabis use.

OBJECTIVE To examine prospective associations between cannabis use and risk of mental health and substance use disorders in the general adult population.

DESIGN, SETTING, AND PARTICIPANTS A nationally representative sample of US adults aged 18 years or older was interviewed 3 years apart in the National Epidemiologic Survey on Alcohol and Related Conditions (wave 1, 2001-2002; wave 2, 2004-2005). The primary analyses were limited to 34 653 respondents who were interviewed in both waves. Data analysis was conducted from March 15 to November 30, 2015.

MAIN OUTCOMES AND MEASURES We used multiple regression and propensity score matching to estimate the strength of independent associations between cannabis use at wave 1 and incident and prevalent psychiatric disorders at wave 2. Psychiatric disorders were measured with a structured interview (Alcohol Use Disorder and Associated Disabilities Interview Schedule–*DSM-IV*). In both analyses, the same set of wave 1 confounders was used, including sociodemographic characteristics, family history of substance use disorder, disturbed family environment, childhood parental loss, low self-esteem, social deviance, education, recent trauma, past and present psychiatric disorders, and respondent's history of divorce.

RESULTS In the multiple regression analysis of 34 653 respondents (14 564 male [47.9% weighted]; mean [SD] age, 45.1 [17.3] years), cannabis use in wave 1 (2001-2002), which was reported by 1279 respondents, was significantly associated with substance use disorders in wave 2 (2004-2005) (any substance use disorder: odds ratio [OR], 6.2; 95% CI, 4.1-9.4; any alcohol use disorder: OR, 2.7; 95% CI, 1.9-3.8; any cannabis use disorder: OR, 9.5; 95% CI, 6.4-14.1; any other drug use disorder: OR, 2.6; 95% CI, 1.6-4.4; and nicotine dependence: OR, 1.7; 95% CI, 1.2-2.4), but not any mood disorder (OR, 1.1; 95% CI, 0.8-1.4) or anxiety disorder (OR, 0.9; 95% CI, 0.7-1.1). The same general pattern of results was observed in the multiple regression analyses of wave 2 prevalent psychiatric disorders and in the propensity score–matched analysis of incident and prevalent psychiatric disorders.

CONCLUSIONS AND RELEVANCE Within the general population, cannabis use is associated with an increased risk for several substance use disorders. Physicians and policy makers should take these associations of cannabis use under careful consideration.

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Rising rates of recreational marijuana use[1] and the changing legal status of cannabis across the United States have intensified debate regarding the mental health consequences of cannabis use.[2-4] Although medical use of cannabis may benefit a selected group of patients, systematic scientific evidence supporting these claims remains limited, while the adverse consequences of cannabis use have been extensively documented.[3-6] Research highlighting the increased morbidity[7] accompanying overuse of prescription opioids[8-11] underscores potential health threats posed by broad access to drugs with addictive liability. Links between increased availability of psychoactive substances and population-level adverse health outcomes[11] raise critical public health policy questions concerning potential harms associated with expanded access to those substances.

Although the cross-sectional association between cannabis use and psychiatric disorders has been consistently documented,[12,13] longitudinal studies evaluating the association of cannabis use with incident psychiatric disorders have yielded mixed results.[14-16] Some studies have reported that cannabis use is associated with increased risk of onset of depression,[16-19] anxiety,[14,17,19] bipolar disorder,[16] substance use disorders,[20] and psychosis,[21,22] while others have not replicated these findings.[14-16,23] Discrepancies may be partly explained by a focus on varying age ranges,[14,15,17-19,23-25] geographic locations,[18,23-25] males vs females,[15] or number and type of mental disorders evaluated.[14-19,23-26] To our knowledge, no previous national study has prospectively examined the association between cannabis use and the prevalence and incidence of other mood, anxiety, and substance use disorders. National estimates of the increased incidence of major mental disorders attributable to cannabis use would critically inform clinical practice and public policy.

To help fill this gap in knowledge, we prospectively examined the associations of cannabis use with the prevalence and incidence of mood, anxiety, and substance use disorders in a large, nationally representative, longitudinal survey. With the use of propensity score–matched[27] groups of cannabis users and nonusers, we further examined whether these associations were dose dependent and whether they were robust to control for numerous confounders.[16,17]

Key Points

Question: Does cannabis use increase the risk of psychiatric disorders?

Findings: In this survey of a nationally representative sample of US adults, cannabis use was associated with significantly increased risk for developing alcohol, cannabis, and other drug use disorders as defined by the *DSM-IV* at 3 years of follow-up. However, cannabis use was not associated with increased risk for developing mood or anxiety disorders.

Meaning: Cannabis use is associated with an increased risk of developing drug and alcohol use disorders.

Methods

Sample

Two waves of the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC) were the source of data (wave 1, 2001-2002; wave 2, 2004-2005). Wave 1 targeted the civilian noninstitutionalized population 18 years or older residing in households and group quarters. Black and Hispanic individuals and young adults (aged 18-24 years) were oversampled, with data adjusted for oversampling and household- and person-level nonresponse. Wave 1 interviews were conducted with 43 093 participants by experienced lay interviewers with extensive training and supervision. The background sociodemographic characteristics[28] and rates of cannabis use disorders[29] of the NESARC sample have been presented elsewhere.

All procedures received full human subjects review and approval from the US Census Bureau and US Office of Management and Budget. Participants provided written informed consent. The wave 2 interview was conducted approximately 3 years after wave 1 (mean interval, 36.6 months). After excluding respondents ineligible for the wave 2 interview (eg, deceased), the weighted response rate was 81.5% (n = 34 653). Sample weights were developed to additionally adjust for nonresponse in wave 2, as well as demographic factors and psychiatric diagnoses, to ensure that the wave 2 sample approximated the target population, that is, the original sample minus attrition between the 2 waves.

Measures

Sociodemographic Characteristics and Cannabis Use

Sociodemographic measures included age, sex, race/ethnicity, and educational level. Cannabis use was assessed by asking respondents whether they had used cannabis in the 12 months preceding the interview. In some analyses, the following 3 levels of cannabis use were considered: no cannabis use in the past 12 months; some cannabis use in the past 12 months, but less than 1 use per month; and 1 or more uses per month.

Psychiatric Diagnoses

All diagnoses were made according to *DSM-IV* criteria using the Alcohol Use Disorder and Associated Disabilities Interview Schedule (AUDADIS-IV), waves 1 and 2 versions.[30,31] Axis I diagnoses included substance use disorders ([SUDs]; alcohol abuse and dependence, cannabis use and dependence, other drug abuse and dependence, and nicotine dependence), mood disorders (major depressive disorder, dysthymia, and bipolar disorder), and anxiety disorders (panic disorder, social anxiety disorder, specific phobia, and generalized anxiety disorder). As documented by previous national and international studies, the test-retest reliability of the AUDADIS-IV is good to excellent for SUDs (κ>0.74), good for major depressive disorder (κ, 0.65-0.73), and fair to good for other mood and anxiety disorders (κ, 0.40-0.60).[30,31] Having a new Axis I disorder was defined by the presence of a disorder at wave 2 among individuals with no lifetime history of that disorder at wave 1.

Statistical Analysis

Data analysis was conducted from March 15 to November 30, 2015. To examine the strength and independence of associations between cannabis use and psychiatric disorders, we first obtained unadjusted estimates of the observed associations. Weighted estimates and odds ratios of the prevalence and incidence of psychiatric disorders at wave 2 by cannabis use in the past 12 months at wave 1 were computed. Odds ratios are considered significant if their 95% CIs do not include 1. Incidence refers to disorders that were reported at wave 2 among respondents without a lifetime history of the disorder at wave 1. We used a linear χ^2 test to examine the existence of dose-response associations between cannabis use and prevalence and incidence of psychiatric disorders.

Second, we considered 2 different statistical methods (ie, multiple regression and propensity score matching)[27] to obtain estimates of the unconfounded association between cannabis use and psychiatric disorders. By controlling for variables that could increase the probability of both cannabis use and the prevalence and incidence of psychiatric disorders, the adjusted associations from these methods yield estimates of their independent association, assuming no unmeasured confounders. Both methods, which tend to provide similar results in large samples,[32-34] used the same set of confounders measured at wave 1 found to be highly predictive of lifetime cannabis use.[35] The confounders include a broad range of predictors from 5 tiers (childhood, early adolescence, late adolescence, adulthood, and past year) of the model described by Blanco et al.[35] To minimize the risk of reverse causality, variables in the past-year tier (comorbidity with psychiatric disorders in the year of the assessment of cannabis use, marital problems, and number of stressful life events) were not included in the model. Confounders from the childhood tier included family history of SUDs (lifetime history of alcohol or drug use disorders in the biological parents or siblings), parental loss (parent's divorce or death of at least 1 parent before the participant was 18 years old), and vulnerable family environment (parental absence or separation from a biological parent before age 18 years). The confounders for the early-adolescence tier included low self-esteem (dichotomous; scored 1 if respondents believed they were not as good, smart, or attractive as most other people), age at onset of anxiety disorders (with childhood onset before age 18 years), and social deviance (assessed as the number of conduct disorder or antisocial personality disorder behaviors in which the respondent engaged before age 15 years; range, 0-33). Confounder in the late-adolescence tier included educational level (in years), number of personality disorders, and number of Axis I disorders with onset before age 18 years. Confounders in the adulthood tier included history of divorce, history of SUD (alcohol use disorder, nicotine dependence, and drug use disorder other than cannabis use disorders), and social deviance (measured as the number of antisocial personality disorder behaviors in which the individual engaged after age 15 years but prior to the wave 1 assessment). The covariates also included age, sex, and race/ethnicity (white or nonwhite). In total, 18 covariates were considered.

Multivariable logistic regression was performed in the full sample with psychiatric disorder at wave 2 as the outcome, cannabis use in the past 12 months at wave 1 as the primary predictor of interest, and all 18 covariates included as main effects for control. The adjusted odds ratios and 95% CIs for cannabis associated with incidence and prevalence were obtained.

Propensity score matching was performed in 2 steps: first, obtaining the propensity score, and second, matching each case (ie, cannabis user) with controls (ie, nonusers) who had very similar propensity scores. Each respondent's propensity score was his or her predicted probability of cannabis use from a logistic regression model with cannabis use in the past 12 months as a binary variable (use or nonuse) at wave 1 as the outcome and all 18 potential confounders as predictors including all 2-way interactions, with final variables selected by stepwise regression. Matching was done using a caliper of variable width because the sparsity of controls with similar propensity scores allowed for only 2 matched controls per case. Balance of covariates among cannabis users and their propensity score–matched controls was checked before conducting additional analyses. Unconfounded odds ratios between psychiatric disorders at wave 2 and cannabis use in the past 12 months at wave 1 were than obtained using the matched sample. All SEs and 95% CIs in the analyses of the full sample and the propensity score–matched sample were estimated using SUDAAN (RTI International) to adjust for design characteristics of the NESARC.

Results

Analysis of the Full Sample

Distribution of Covariates

In the full sample of 34 653 respondents (14 564 male [47.9% weighted]; mean [SD] age, 45.1 [17.3] years), the 1279 individuals with cannabis use (772 male [66.4% weighted]; mean [SD] age, 29.9 [10.7] years) had greater odds of most risk predictors examined except age and history of divorce, which were lower among individuals with cannabis use, and educational level and nonwhite race/ethnicity, which did not differ across groups (eTable 1 in the Supplement). Among the individuals with cannabis use, 345 (28.4% weighted) had cannabis abuse in the past year and 99 (7.7%) had cannabis dependence in the past year (eTable 2 in the Supplement).

Prevalence and Incidence of Disorders in Wave 2

Table 1 and **Table 2**, respectively, present the prevalence and incidence of wave 2 psychiatric disorders among respondents with and without cannabis use in the past year at wave 1. In the full sample, cannabis use in the past year at wave 1 was associated with significantly greater prevalence (Table 1) and incidence (Table 2) of all disorders at wave 2, except major depressive disorder and dysthymia (as well as incidence of specific phobia). For both prevalence and incidence, the largest odds ratios were for cannabis use disorders. After adjusting for the covariates, cannabis use in wave 1 predicted increased prevalence (Table 1) and incidence (Table 2) of all wave 2 substance use disorders, including nicotine dependence,

Table 1. Cannabis Use in the Past 12 Months in Wave 1 and Prevalent Psychiatric Disorders in Wave 2 of the NESARC

Prevalent Psychiatric Disorders in Wave 2	Wave 1, % (No.)[a]		OR (95% CI)	Adjusted OR (95% CI)[b]
	Cannabis Use in Past 12 mo (n = 1279)	No Cannabis Use in Past 12 mo (n = 33 364)		
Any disorder	71.5 (892)	31.0 (10 326)	5.6 (4.7-6.6)	2.1 (1.8-2.6)
Any substance use disorder	65.6 (797)	19.3 (6103)	8.0 (6.9-9.2)	2.8 (2.4-3.4)
Any alcohol use disorder	40.2 (475)	8.4 (2663)	7.3 (6.3-8.6)	2.5 (2.1-3.0)
Abuse	17.3 (209)	4.8 (1498)	4.2 (3.4-5.1)	1.8 (1.4-2.3)
Dependence	22.9 (266)	3.6 (1165)	7.9 (6.6-9.4)	2.3 (1.9-2.9)
Any cannabis use disorder	21.4 (261)	0.8 (230)	34.7 (27.5-43.8)	12.4 (8.9-17.2)
Abuse	16.7 (206)	0.6 (172)	34.2 (26.6-44.0)	12.3 (8.9-17.0)
Dependence	4.7 (55)	0.2 (58)	25.3 (15.0-42.7)	9.0 (3.9-20.8)
Any other drug use disorder	8.9 (105)	0.8 (239)	12.5 (9.1-17.4)	3.1 (2.1-4.6)
Abuse	5.2 (61)	0.5 (137)	11.6 (7.8-17.0)	3.0 (1.9-4.7)
Dependence	4.2 (51)	0.3 (114)	12.8 (8.2-20.0)	3.0 (1.7-5.3)
Nicotine dependence	38.2 (470)	12.9 (4039)	4.2 (3.6-4.9)	1.5 (1.2-1.8)
Any mood disorder	18.0 (236)	9.3 (3296)	2.1 (1.8-2.6)	0.9 (0.7-1.2)
Major depressive disorder	6.7 (91)	5.6 (1984)	1.2 (0.9-1.6)	0.8 (0.6-1.1)
Bipolar I disorder	8.9 (112)	2.6 (910)	3.7 (2.8-4.8)	1.1 (0.7-1.5)
Bipolar II disorder	2.3 (31)	0.8 (300)	2.8 (1.7-4.7)	1.0 (0.5-1.7)
Bipolar disorder	11.1 (143)	3.4 (1210)	3.6 (2.9-4.5)	1.0 (0.8-1.4)
Dysthymia	1.0 (13)	0.8 (290)	1.3 (0.6-2.6)	0.7 (0.3-1.7)
Any anxiety disorder	21.0 (262)	12.2 (4298)	1.9 (1.6-2.3)	1.0 (0.8-1.2)
Panic disorder	5.5 (66)	2.5 (884)	2.3 (1.7-3.2)	0.8 (0.5-1.2)
Social anxiety disorder	6.6 (76)	2.4 (869)	2.9 (2.2-4.0)	1.2 (0.8-1.8)
Specific phobia	11.1 (144)	7.4 (2614)	1.6 (1.3-2.0)	0.9 (0.7-1.2)
Generalized anxiety disorder	6.6 (86)	3.7 (1276)	1.8 (1.4-2.5)	1.0 (0.7-1.4)

Abbreviations: NESARC, National Epidemiological Survey on Alcohol and Related Conditions; OR, odds ratio.

[a] Percentages are based on sample weights.

[b] Results from multiple regressions were adjusted for risk factors (see eTable 3 in the Supplement) and sociodemographic characteristics.

Table 2. Cannabis Use in the Past 12 Months in Wave 1 and Incident Psychiatric Disorders in Wave 2 of the NESARC[a]

Incident Psychiatric Disorders in Wave 2	Wave 1, % (No.)[b]		OR (95% CI)	Adjusted OR (95% CI)
	Cannabis Use in Past 12 mo (n = 1279)	No Cannabis Use in Past 12 mo (n = 33 364)		
Any disorder (n1 = 606; n2 = 7981)[c]	93.1 (606)	36.9 (7891)	23.0 (16.5-32.1)	4.4 (2.8-6.9)
Any substance use disorder (n1 = 458; n2 = 3795)	86.3 (458)	17.4 (3795)	29.9 (22.3-40.0)	6.2 (4.1-9.4)
Any alcohol use disorder (n1 = 248; n2 = 2008)	51.5 (248)	8.6 (2008)	11.3 (9.0-14.3)	2.7 (1.9-3.8)
Abuse (n1 = 153; n2 = 1149)	16.8 (153)	4.4 (1149)	4.4 (3.4-5.5)	1.5 (1.1-2.0)
Dependence (n1 = 95; n2 = 859)	14.7 (95)	3.0 (859)	5.5 (4.2-7.3)	1.9 (1.4-2.7)
Any cannabis use disorder (n1 = 120; n2 = 260)	25.0 (120)	0.9 (260)	35.4 (26.5-47.3)	9.5 (6.4-14.1)
Abuse (n1 = 73; n2 = 187)	14.1 (73)	0.7 (187)	24.2 (17.2-34.0)	7.4 (4.9-11.3)
Dependence (n1 = 47; n2 = 73)	5.1 (47)	0.2 (73)	22.2 (14.0-35.1)	6.9 (3.1-15.1)
Any other drug use disorder (n1 = 112; n2 = 339)	13.9 (112)	1.1 (339)	14.0 (10.4-18.8)	2.6 (1.6-4.4)
Abuse (n1 = 69; n2 = 199)	8.3 (69)	0.7 (199)	13.3 (9.3-18.8)	3.4 (2.1-5.4)
Dependence (n1 = 57; n2 = 155)	5.3 (57)	0.5 (155)	11.4 (7.6-17.0)	2.7 (1.6-4.5)
Nicotine dependence (n1 = 118; n2 = 1743)	17.3 (118)	6.6 (1743)	3.0 (2.2-3.9)	1.7 (1.2-2.4)
Any mood disorder (n1 = 152; n2 = 2423)	16.9 (152)	8.3 (2423)	2.3 (1.8-2.9)	1.1 (0.8-1.4)
Major depression (n1 = 55; n2 = 1442)	4.6 (55)	4.8 (1442)	1.0 (0.7-1.3)	0.9 (0.6-1.3)
Bipolar I disorder (n1 = 63; n2 = 617)	6.1 (63)	1.8 (617)	3.5 (2.5-4.9)	1.3 (0.9-1.9)
Bipolar II disorder (n1 = 23; n2 = 230)	1.5 (23)	0.6 (230)	2.5 (1.4-4.2)	1.0 (0.5-1.9)
Bipolar disorder (n1 = 86; n2 = 847)	8.0 (86)	2.5 (847)	3.4 (2.6-4.6)	1.3 (0.9-1.8)
Dysthymia (n1 = 12; n2 = 241)	1.1 (12)	0.6 (241)	1.7 (0.9-3.5)	1.2 (0.6-2.6)
Any anxiety disorder (n1 = 203; n2 = 3715)	20.0 (203)	12.4 (3715)	1.8 (1.5-2.1)	0.9 (0.7-1.1)
Panic disorder (n1 = 52; n2 = 785)	4.5 (52)	2.4 (785)	2.0 (1.4-2.8)	1.0 (0.6-1.5)
Social anxiety disorder (n1 = 53; n2 = 674)	5.2 (53)	1.9 (674)	2.8 (2.0-3.9)	1.4 (0.9-2.1)
Specific phobia (n1 = 82; n2 = 1998)	7.7 (82)	6.2 (1998)	1.3 (1.0-1.7)	0.8 (0.5-1.1)
Generalized anxiety disorder (n1 = 74; n2 = 1163)	5.9 (74)	3.6 (1163)	1.7 (1.3-2.3)	1.0 (0.7-1.5)

Abbreviations: NESARC, National Epidemiological Survey on Alcohol and Related Conditions; OR, odds ratio.

[a] Results from multiple regressions were adjusted for risk factors (see eTable 3 in the Supplement) and sociodemographic characteristics.

[b] Percentages are based on sample weights.

[c] n1 Denotes sample size with cannabis use in the past 12 mo and without index psychiatric disorder at wave 1; n2 denotes size with no cannabis use in the past 12 mo and without index psychiatric disorder at wave 1.

Table 3. Cannabis Use in the Past 12 Months in Wave 1 and Prevalent Psychiatric Disorders in Wave 2 Among Propensity Score–Matched Samples of the NESARC

Prevalent Psychiatric Disorders in Wave 2	Wave 1, % (No.)[a]		
	Cannabis Use in Past 12 mo (n = 1254)	Propensity Score Matched No Cannabis Use in Past 12 mo (n = 1254)	OR (95% CI)[b]
Any disorder	71.3 (874)	56.8 (780)	1.9 (1.5-2.4)
Any substance use disorder	65.4 (780)	45.0 (551)	2.3 (1.9-2.8)
Any alcohol use disorder	40.0 (465)	22.6 (275)	2.3 (1.8-2.8)
Abuse	17.0 (202)	11.1 (136)	1.7 (1.2-2.2)
Dependence	23.0 (263)	11.6 (139)	2.3 (1.7-3.0)
Any cannabis use disorder	21.5 (257)	3.7 (49)	7.2 (4.9-10.5)
Abuse	16.7 (202)	2.8 (31)	6.9 (4.5-10.8)
Dependence	4.8 (55)	0.9 (18)	5.8 (2.8-11.9)
Any other drug disorder	9.0 (103)	3.8 (43)	2.5 (1.6-4.0)
Abuse	5.3 (60)	2.5 (25)	2.1 (1.2-4.0)
Dependence	4.2 (50)	1.4 (20)	3.0 (1.6-5.7)
Nicotine dependence	38.2 (460)	30.6 (383)	1.4 (1.2-1.7)
Any mood disorder	17.8 (230)	16.4 (222)	1.1 (0.9-1.4)
Major depression	6.6 (89)	7.3 (92)	0.9 (0.6-1.3)
Bipolar I disorder	8.8 (110)	6.3 (95)	1.4 (1.0-2.1)
Bipolar II disorder	2.3 (30)	2.5 (32)	0.9 (0.5-1.7)
Bipolar disorder	11.1 (140)	8.8 (127)	1.3 (0.9-1.8)
Dysthymia	0.9 (12)	1.0 (14)	0.9 (0.4-2.0)
Any anxiety disorder	21.2 (260)	20.4 (261)	1.1 (0.8-1.4)
Panic disorder	5.4 (64)	4.5 (63)	1.2 (0.8-1.9)
Social anxiety disorder	6.6 (75)	4.5 (64)	1.5 (1.0-2.3)
Specific phobia	11.3 (143)	10.9 (140)	1.0 (0.8-1.4)
Generalized anxiety disorder	6.7 (86)	6.3 (82)	1.1 (0.7-1.6)

Abbreviations: NESARC, National Epidemiological Survey on Alcohol and Related Conditions; OR, odds ratio.

[a] Percentages are based on sample weights.

[b] Odds ratio results from multiple regressions adjusted for risk factors (see eTable 3 in the Supplement) and sociodemographic characteristics.

but not of mood or anxiety disorders. The pattern of findings in the adjusted and unadjusted results remained the same whether cannabis use was examined as a dichotomous or continuous (ie, frequency of use) variable (eTables 3 and 4 in the Supplement). The prevalence of any mental disorder at wave 2 tended to increase with increasing level of exposure to cannabis at wave 1, with the largest increment occurring between 0 and 1 marijuana joints per day (eTable 5 in the Supplement).

Analysis of the Propensity Matched Samples

Distribution of Covariates

After matching individuals on their propensity scores, there were no differences in the odds of any of the predictors examined, indicating that the propensity score model was successful in balancing the distribution of covariates (eTable 6 in the Supplement).

Prevalence and Incidence of Disorders in Wave 2

Individuals who used cannabis at wave 1 had greater odds than nonusers of prevalence (**Table 3**) and incidence (**Table 4**) of all SUDs, including nicotine dependence. All findings remained similar between the 2 statistical methods when cannabis use was considered as a dichotomous variable, except cannabis use was associated with significantly increased incidence of social anxiety disorder in the propensity score–matched analysis (Table 4) but not the multiple regression analysis (Table 2). Similar patterns were observed in the propensity score–matched analysis that considered frequency of cannabis use (eTables 7 and 8 in the Supplement). A greater frequency of cannabis use was also associated with significantly increased odds of incident social anxiety disorder (eTable 8 in the Supplement). The percentage of individuals with any wave 2 disorder increased with the frequency of wave 1 cannabis use, with the largest increase occurring between no cannabis use in the past 12 months and cannabis use that was less than once per month (**Figure**).

Discussion

In a large nationally representative sample, we prospectively examined associations between cannabis use and psychiatric disorders. In unadjusted analyses in the full population, cannabis use was associated with increased prevalence and incidence of a broad range of psychiatric disorders. However, after adjusting for several covariates that predicted cannabis use, multiple regression analysis and propensity score matching converged in indicating that cannabis use was associated only with increased prevalence and incidence of alcohol and drug use disorders, including nicotine dependence. For most findings, higher frequency of cannabis use was associated with greater risk of disorder incidence and prevalence.

Table 4. Cannabis Use in the Past 12 Months in Wave 1 and Incident Psychiatric Disorders in Wave 2 Among Propensity Score–Matched Samples of the NESARC

Incident Psychiatric Disorders in Wave 2	Wave 1, % (No.)[a]		
	Cannabis Use in Past 12 mo (n = 1254)	Propensity Score Matched No Cannabis Use in Past 12 mo (n = 1254)	OR (95% CI)[b]
Any disorder (n1 = 592; n2 = 478)[c]	93.0 (592)	80.2 (478)	3.3 (2.1-5.1)
Any substance use disorder (n1 = 446; n2 = 280)	86.0 (446)	57.6 (280)	4.5 (3.1-6.6)
Any alcohol use disorder (n1 = 243; n2 = 168)	51.3 (243)	34.9 (168)	2.0 (1.4-2.7)
Abuse (n1 = 150; n2 = 104)	16.7 (150)	11.6 (104)	1.5 (1.1-2.1)
Dependence (n1 = 93; n2 = 64)	14.7 (93)	9.1 (64)	1.7 (1.1-2.6)
Any cannabis use disorder (n1 = 117; n2 = 43)	24.7 (117)	4.1 (43)	7.6 (4.8-12.0)
Abuse (n1 = 71; n2 = 26)	14.0 (71)	2.8 (26)	5.7 (3.3-9.8)
Dependence (n1 = 46; n2 = 17)	4.9 (46)	0.8 (17)	6.7 (3.2-14.0)
Any other drug disorder (n1 = 108; n2 = 53)	13.7 (108)	6.9 (53)	2.1 (1.4-3.4)
Abuse (n1 = 67; n2 = 30)	8.2 (67)	4.1 (30)	2.1 (1.2-3.6)
Dependence (n1 = 55; n2 = 24)	5.2 (55)	2.2 (24)	2.4 (1.3-4.6)
Nicotine dependence (n1 = 114; n2 = 71)	17.0 (114)	10.2 (71)	1.8 (1.2-2.7)
Any mood disorder (n1 = 147; n2 = 120)	16.5 (147)	14.5 (120)	1.2 (0.8-1.6)
Major depression (n1 = 54; n2 = 57)	4.4 (54)	5.9 (57)	0.8 (0.5-1.2)
Bipolar I disorder (n1 = 61; n2 = 43)	6.0 (61)	4.1 (43)	1.5 (0.9-2.6)
Bipolar II disorder (n1 = 22; n2 = 18)	1.5 (22)	1.5 (18)	1.0 (0.5-2.1)
Bipolar disorder (n1 = 83; n2 = 61)	7.9 (83)	5.9 (57)	1.4 (0.9-2.2)
Dysthymia (n1 = 11; n2 = 9)	1.0 (11)	0.6 (9)	1.7 (0.7-4.1)
Any anxiety disorder (n1 = 201; n2 = 200)	20.3 (201)	20.5 (200)	1.0 (0.8-1.3)
Panic disorder (n1 = 50; n2 = 43)	4.4 (50)	3.3 (43)	1.4 (0.8-2.3)
Social anxiety disorder (n1 = 52; n2 = 42)	5.2 (52)	3.0 (42)	1.8 (1.1-2.8)
Specific phobia (n1 = 81; n2 = 95)	7.7 (81)	8.8 (95)	0.9 (0.6-1.3)
Generalized anxiety disorder (n1 = 73; n2 = 67)	5.9 (73)	6.0 (67)	1.0 (0.6-1.5)

Abbreviations: NESARC, National Epidemiological Survey on Alcohol and Related Conditions; OR, odds ratio.

[a] Percentages are based on sample weights.

[b] Odds ratio results from multiple regressions adjusted for risk factors (see eTable 3 in the Supplement) and sociodemographic characteristics.

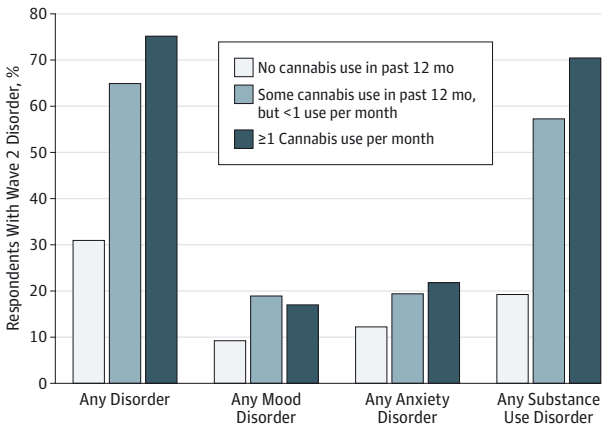
[c] n1 Denotes sample size with cannabis use in the past 12 mo and without index psychiatric disorder at wave 1; n2 denotes size with no cannabis use in the past 12 mo and without index psychiatric disorder at wave 1.

We found important contrasts between associations of cannabis use with psychiatric disorders in the unadjusted and adjusted analyses. Our findings extend previous findings that have focused on younger individuals or a restricted number of disorders to several age groups and disorders. The new results also help reconcile discrepant findings from prior studies by suggesting that most of the association of cannabis use with non-SUD psychiatric disorders is explained by differences in the distribution of confounders between cannabis users and nonusers.[14,15,17-19,23-25] In addition, our findings support a dose-response association between cannabis use and the risk of SUDs.[16,17]

A second important finding was that, even after adjusting for multiple confounders, cannabis use was associated at follow-up with increased odds of prevalence and incidence of all SUDs, including nicotine dependence, although not with other mood or anxiety disorders. The development of cross-adaptations through shared mechanisms of action or neuroadaptation[36] between cannabis and other substances, as well as greater overlap of circuitry across SUDs than overlap of the circuitry of SUDs with mood and anxiety disorders,[37-39] may contribute to the association of cannabis use with SUDs but not with most other disorders examined. Use of cannabis can also lead to behavioral disinhibition, which increases the likelihood of use of other substances and the risk of abuse or dependence on those substances.[40]

The reasons for the association of cannabis use with increased incidence of social anxiety disorder in the propensity-

Figure. Prevalence of Psychiatric Disorders in Wave 2 of the National Epidemiologic Survey on Alcohol and Related Conditions by Level of Cannabis Use in Wave 1



For respondents in the 3 past 12-month cannabis use groups in wave 1, the prevalence for any disorder in wave 2 was 31.0% (no use), 65.0% (some use but <1 use per month), and 75.3% (≥1 use per month), with $P < .001$ for all 3 pairwise comparisons. The corresponding prevalence of any mood disorder in wave 2 was 9.3%, 18.9%, and 17.1%, with $P < .001$ for the no use and some use comparison and $P < .001$ for the no use and more use comparison. The corresponding prevalence of any anxiety disorder in wave 2 was 12.2%, 19.4%, and 21.8%, with $P = .003$ for the no use and some use comparison and $P < .001$ for the no use and more use comparison. The corresponding prevalence of any substance use disorder in wave 2 was 19.3%, 57.4%, and 70.5%, with $P < .001$ for all 3 pairwise comparisons. The other pairwise comparisons had $P > .05$.

matched analysis are less obvious. Cannabis use may lead to social avoidance that over time may promote social anxiety in a subgroup of individuals.[40,41] In practice, new-onset or worsening social anxiety might prompt clinical evaluation of whether cannabis is a contributing factor. Because prior prospective research with young people also indicates that social anxiety disorder increases the risk of cannabis dependence,[42] bidirectional causality is possible. However, because the results were significant only in the propensity score matching, but not in the multiple regression analysis, they should be considered with caution pending replication.

From a perspective of prevention, the lack of association between more frequent cannabis use with increased risk of most mood and anxiety disorders does not diminish the important public health significance of the association between cannabis use and increased prevalence and incidence of drug and alcohol use disorders (including nicotine dependence). Smoking and alcohol consumption are, respectively, the first and third leading causes of preventable death,[43] and illicit drug use is associated with increased rates of incarceration and nearly $200 billion each year in costs owing to national health care, lost productivity, incarceration, and drug enforcement.[44,45]

Taken together, our findings suggest caution in the implementation of policies related to legalization of cannabis for recreational use, as it may lead to greater availability and acceptance of cannabis, reduced perception of risk of use,[25] and increased risk of adverse mental health outcomes, such as substance use disorders.[2,46-48] While the health benefits of cannabis use require further testing among patients who are unresponsive to more traditional treatments,[5] the association of cannabis use with negative mental health outcomes, such as substance use disorders, appears strong. A greater understanding of potential negative psychological effects of cannabis use may help inform the ongoing debates regarding the legal status of medical and recreational cannabis and implementation of new legislation that incorporates scientific evidence as well as political considerations. In the meantime, educational campaigns regarding the potential adverse consequences of cannabis use may help limit the expansion of recreational use.[49]

The results of this study should be interpreted in the light of several limitations. First, despite its prospective design, our study does not establish a causal association between cannabis use and new onset of disorders because of the possibility of residual confounding, particularly confounders that may vary over time across survey waves. However, prospective observational studies of large nationally representative cohorts such as the NESARC may be the strongest source of available information for the foreseeable future in light of ethical constraints on randomized clinical trials in this area. Second, the follow-up period was limited to 3 years. Longer follow-up may have revealed different patterns of incidence or prevalence. Different patterns also might have been observed if we had excluded individuals who used cannabis in the past but stopped because they developed symptoms of a mental disorder. Third, cannabis use was assessed through self-report and not confirmed with objective means. Fourth, although the NESARC is the largest prospective study with detailed psychiatric diagnostic information, sample size constraints limit our power to detect potentially meaningful significant differences in some strata. Last, despite including the most common mental disorders, some disorders were not assessed.

Conclusions

Our study indicates that cannabis use is associated with increased prevalence and incidence of substance use disorders. These adverse psychiatric outcomes should be taken under careful consideration in clinical care and policy planning.

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