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Prospective associations between cannabis use and depressive symptoms across adolescence and early adulthood

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ABSTRACT

Cannabis use and occurrences of depression during adolescence are common. However, the temporal relationship between the two is less understood. Does depression lead to cannabis use, or does cannabis use lead to depression, or is it a combination of both? Furthermore, this directionality is confounded by other substance use, specifically binge drinking, which is common during adolescence. This study aimed to examine the temporal directionality of cannabis use and depression among a prospective, longitudinal, sequential cohort of 15 to 24-year-olds. Data were drawn from the National Consortium on Alcohol and Neurodevelopment in Adolescence (NCANDA) study. The final sample included 767 participants. Multilevel regression models were run to assess concurrent (at the same time point) and prospective (1 year later) associations between cannabis use and depression. When measured concurrently, depressive symptoms did not significantly predict past-month cannabis use but did significantly predict more days of use among cannabis users. Prospective associations indicated that depressive symptoms significantly predicted cannabis use 1 year later and cannabis use significantly predicted depressive symptoms 1 year later. We found no evidence that these associations varied by age or binge drinking. Overall, the relationship between cannabis use and depression appears to be complex and not unidirectional.

1. Introduction

Adolescence is a critical period in neurodevelopment and many adolescents experiment with drugs and alcohol during this period. Depression often emerges during adolescence, but the link between substance use and depression is not well understood. In 2020, 35% of 12th graders in the US reported using cannabis and 55% reported using alcohol in the last 12 months (Patrick et al., 2022). Approximately 16% of adolescents report having at least one depressive episode in 2019 (Substance Abuse and Mental Health Services Administration, 2021), and evidence suggests depression is more common in adolescents who have substance use disorders (SUDs) (Armstrong and Costello, 2002; Feingold and Weinstein, 2021). Given that cannabis and alcohol are commonly used substances during adolescence, it is crucial to understand their potential impact, alone or in combination, on the development of depression in this age group.

Understanding the temporal relationship between substance involvement and the development of depressive symptoms is crucial to unpack this complex yet common comorbidity. The self-medication hypothesis suggests that people with depression use substances to relieve their symptoms (Khantzian, 1985; Markou et al., 1998), while another proposes that substance use during adolescence could increase the risk of developing depression through changes in the brain, reduced goal-oriented behavior, and increased social stressors arising from poor academic performance, conflict with parents or peers, and health and legal consequences (Markou et al., 1998; Pacheco-Colón et al., 2019; Wilkinson et al., 2016). Both pathways may contribute to the link between depression and substance use, as they share common environmental, neurobiological, and genetic factors (Feingold and Weinstein, 2021; Kendler, 2012; Quello et al., 2005).

Evidence indicates adolescent cannabis use precedes depression. A meta-analysis of 11 longitudinal studies found that adolescent cannabis users (≤18 years) were 1.4 times more likely to develop depression in young adulthood (18–32 years), adjusting for baseline depression

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(Gobbi et al., 2019). Additionally, from 24 trajectory-based studies, 18 showed a positive correlation between adolescent cannabis use and later depression, while 6 found no correlation (Gobbi et al., 2019). In contrast, limited evidence indicates depression preceding cannabis use. One cross-sectional study found that major depressive disorder preceded SUDs (Deykin et al., 1987), while a small longitudinal study found that academic performance, depressive symptoms, and popularity predicted subsequent cannabis use among high school adolescents (Diego et al., 2003). Overall, systematic reviews suggest a complex bidirectional relationship between cannabis use and depression, with mixed evidence for both directions (Farooqui et al., 2022; Urits et al., 2020; White et al., 2022).

With the bidirectional relationship between adolescent cannabis use and depression, it is important to consider factors that may modify the relationship. Age is one such factor, as older adolescents may be more vulnerable to using cannabis to self-medicate (Zucker et al., 2015). In a large U.S. sample, the association between adolescent depression and cannabis use symptoms strengthened as youth grew older (Wilkinson et al., 2016). However, research on age as a moderator is limited because it requires longitudinal data spanning multiple developmental phases. Concurrent alcohol use or binge drinking may also modify the link between adolescent cannabis use and depression. Using both alcohol and cannabis during adolescence is associated with poorer outcomes in several domains linked to the development of depression. Among Californian adolescents ($N = 6509$), higher alcohol use was associated with greater delinquency and academic unpreparedness, while higher cannabis use was associated with greater delinquency, academic unpreparedness, lower academic performance, and poorer mental health (D'Amico et al., 2016). The use of both substances may harm neurodevelopment and leave adolescents vulnerable to multiple depressogenic factors.

Finally, to study the link between depression and cannabis use, it is important to distinguish between factors influencing the decision to use *any* cannabis and those influencing the *amount* of use. For example, greater depressive symptoms may prompt more cannabis use among those who already use it, but are unlikely to result in non-users starting to use cannabis. Typical modeling strategies combine effects on users and non-users of a substance, but zero-inflated models can help investigate these separate processes among users and non-users (Atkins et al., 2013).

The current study aimed to investigate how cannabis use and depressive symptoms are related concurrently and prospectively in a diverse cohort followed for up to 8 years. Specifically, we examined both directions of the relationship and whether age or binge drinking modified this relationship.

2. Methods

2.1. Participants

The National Consortium on Alcohol and Neurodevelopment in Adolescence (NCANDA) participants were 831 adolescents aged 12–21 years using an accelerated cohort design (Brown et al., 2015). Youth were recruited at five sites: University of California, San Diego, SRI International, Duke University Medical Center, University of Pittsburgh, and Oregon Health & Science University. Recruitment was primarily conducted through school mailers, community fliers and advertisements, and announcements at local universities. Each site provided independent IRB approval with parent approval and assent for youth participants under age 18. As of 20th December 2022, ethics approval was centralized to the UCSD site (#120915). Refer to Fig. 1 for an illustration of the recruitment for NCANDA and additional exclusion criteria for the current study. The data were part of the public data release NCANDA_PUBLIC_6Y_REDCAP_V02 (Pohl et al., 2022), distributed according to the NCANDA Data Distribution agreement (https://www.niaaa.nih.gov/ncanda-data-distribution-agreement).

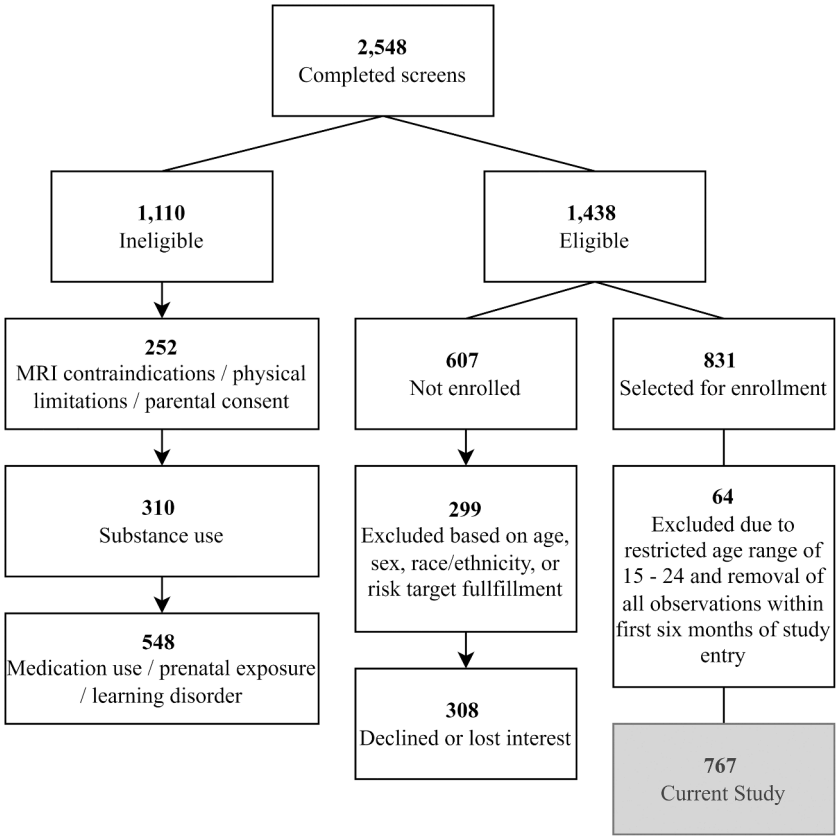

Fig. 1.

The current study drew data from 767 participants observed at ages 15–24 years old. Two restrictions were imposed to arrive at this subsample. First, we had relatively few observations occurring beyond age 24, and very low rates of cannabis use before age 15, so we restricted the observations to ages 15–24. Second, because very little cannabis use was reported at study entry, observations occurring within the first six months of study entry were excluded. Both restrictions were necessary to improve convergence given the complex statistical models being fit (Brumback et al., 2021). Of the 767 participants contributing data, 51% of participants were female. 12% identified as Hispanic; 72% as White, 12% as Black, 7% as Asian, and 8% as Alaskan Native or Pacific Islander. 81% of participants had at least one parent with a Bachelor's degree. Across ages, prevelance of past-month cannabis use changed curvilinearly by age with 9% of 15-year-olds, 37% of 19-year-olds, and 26% of 24-year-olds endorsing past-month use. A similar pattern is observed with depressive symptoms, with 7% of 15-year-olds, 9% of 20-year-olds, and 5% of 24-year-olds meeting criteria for probable clinical diagnosis of depression.

2.2. Procedures

A standardized protocol was followed at every site in which data was first collected at the baseline visit, and subsequent follow-up data were collected in annual appointments for up to 8 years (Brown et al., 2015). At baseline and follow-up assessments, family, health and environmental information was obtained and youth completed a neuroimaging session, neuropsychological battery, and an assessment of substance use, past psychiatric diagnoses as well as current symptoms, and overall functioning in major life domains (e.g., school, peers, work, etc.). For more information regarding recruitment and assessment protocol, please refer to Brown et al. (2015). In order to enhance accuracy of self-report, youth were assured that their information would remain confidential and would not be revealed to parents except in the case of serious risk to self or others (e.g. suicidal/homicidal ideation or abuse), to which parents offered their consent.

2.3. Measures

Past and current substance use was measured via interview using the Customary Drinking and Drug-Use Record (CDDR; Brown et al., 1998), which facilitates recall of the frequency of alcohol, cannabis and seven other substances used within the past 30 days, past year, and since the last interview (range 6–12 months depending on the follow-up timepoint). Binge drinking (also known as heavy episodic drinking) was defined as $\geq$4/$\geq$5 standard drinks per occasion for females/males, respectively. Depressive symptoms were measured using the depressive problems subscale of the Achenbach rating system, a well-validated self-report measure of emotional difficulties among adolescents and adults (Achenbach and Rescorla, 2003, 2001). During adolescence, participants completed the Youth Self-Report (YSR) form; during young adulthood, they completed the corresponding Adult Self-Report (ASR) form. The forms contained 13 (youth) or 14 (adult) items, rated on a 3-point Likert Scale from *never true* to *very true*, assessing depressive symptoms such as often feeling sad, worthless, or guilty, enjoying little, lacking energy, having trouble making decisions, or thinking of suicide or self-harm. The mean response across items was computed for analysis.

2.4. Analytic plan

Models were fit in *M*plus v8.2 (Muthén and Muthén, 2017). Multilevel regression models with a random intercept for participants were utilized to examine associations between cannabis use and depressive symptoms over time. Linear models were used when the dependent variable was depressive symptoms. We used zero-inflated, negative-binomial models when the dependent variable was cannabis use to account for the fact that cannabis use was a count (number of days) and that at each timepoint, a significant portion of the sample reported zero days of use (Atkins et al., 2013).[1] As noted in the Introduction, this modeling strategy allowed separate investigation of the effects of depressive symptoms on the probability of using cannabis at all and the extent of use among users. As described above, the present analysis included observations between the ages of 15 and 24 years old, excluding any observations that occurred within the first six months of study entry. These restrictions resolved issues with model convergence arising from the very low rates of cannabis use at the baseline assessment (Brumback et al., 2021). We used the robust maximum likelihood estimator in *M*plus and the rescaled chi-square difference test for comparing nested models (Satorra and Bentler, 2010). To address participant age within the accelerated longitudinal design (Thompson et al., 2011), we covaried three parameters: age at study entry ("age--cohort"), change in age from study entry to the current observation ("age-change"), and a quadratic term for the change in age from study entry to the current observation ("age-change^2"). The age-cohort term captures differences between participants of different birth cohorts, which may have been exposed to different national contexts for cannabis use or depression. The age-change and age-change^2 terms capture maturation, or developmental changes in cannabis or depression as participants grow older. We also covaried youth sex and past-month frequency of binge drinking, both of which predict both cannabis use and depression. Depressive symptoms were scaled by the mean standard deviation across waves (*SD*=0.27) and cannabis use was scaled in number of days.

2.4.1. Analysis 1: concurrent associations

First, we examined associations between cannabis use frequency and depressive symptoms when measured concurrently at the same wave. Longitudinal data were structured with multiple observations per participant (i.e., "long" format). The dependent variable was predicted by time-invariant controls (youth sex, age-cohort), time-varying controls (age-change, age-change^2), frequency of binge drinking, and either depressive symptoms (when the dependent variable was cannabis use) or cannabis use (when the dependent variable was depressive symptoms). After fitting the initial model, we used likelihood ratio tests for nested models to test whether adding product terms for the interaction between (a) age-change and age-change^2 or (b) frequency of binge drinking with either cannabis use frequency or depressive symptoms significantly improved model fit.

2.4.2. Analysis 2: prospective associations

Next, we examined prospective associations between cannabis use frequency and depressive symptoms. Longitudinal data were structured in long format and the dependent variable was predicted by time-invariant controls (youth sex, age-cohort), time-varying controls (age-change, age-change^2), and lagged variables measured at the visit one year earlier (the dependent measure [cannabis or depression], the variable of interest [the other one of cannabis or depression]).

3. Results

3.1. Concurrent associations

Table 1 reports the sample characteristics. Table 2 reports the regression models for concurrent associations. Table 3 reports the tests of statistical significance of putative moderators. Past-six-month depressive symptoms were not significantly associated with the odds of any past-month cannabis use ($\beta = -0.02$, SE= 0.46, Odds Ratio [OR]

[1] The rate of reporting zero days of cannabis use in the past month ranged from a minimum of 63% at age 19 years to a maximum of 91% at age 15 years. No more than 3% of participants endorsed the ceiling (30 days of use) at any age.

Table 1
Sample Characteristics.

Wave (years)	Sample Size (N)	Age (years)	% Female	Externalizing Symptoms
1.0	587	18.1	51	44.8
1.5	609	18.4	51	
2.0	648	18.5	51	44.3
2.5	629	18.9	51	
3.0	701	19.2	51	44.0
3.5	578	19.7	50	
4.0	639	20.0	50	44.5
4.5	499	20.4	51	
5.0	598	20.7	50	45.3
5.5	493	21.1	50	
6.0	565	21.4	49	44.6
6.5	489	21.7	50	
7.0	451	22.1	51	
7.5	270	22.3	50	
8.0	121	22.7	50	
8.5	12	23.1	75	

Note: Wave represents the yearly assessment time points from baseline (i.e., 1.0 is the 1-year follow-up after baseline); sample size indicates the number of participants who completed the relevant measures; age is represented by the mean age in years at each wave; % female represents the percentage of the sample that identified as female from sex at birth at each wave; externalizing symptoms are the t-score on the externalizing symptoms subscale from the Youth Self-Report (Achenbach and Rescorla, 2003, 2001).

= 0.98, p = .97) but were associated with a greater number of days of cannabis use among users (β = 1.19, SE= 0.24, p < .001). We did not find evidence that either age-change or binge drinking moderated the associations between depressive symptoms and cannabis use (*p*s from 0.36 to 0.92).

3.2. Prospective associations

Prospective relations were evaluated in regression models between depression and cannabis use to determine the directionality of the substance use and depression relationships (presented in Table 3).

3.2.1. Depressive symptoms predicting cannabis use

When adjusting for current frequency of cannabis use, current depressive symptoms were significantly, positively, and prospectively associated with the likelihood of any cannabis use measured 1 year into the future (β = 0.74, SE= 0.32, p = .02), but not with frequency of cannabis use among only those who were users (β = 0.15, SE= 0.23, p = .51).

3.2.2. Cannabis use predicting depressive symptoms

While adjusting for current depressive symptoms, current frequency of cannabis was significantly, positively, and prospectively associated with depressive symptoms measured 1 year into the future (β = 0.002, SE= 0.001, p = .08).

3.3. Moderation of cannabis-depressive symptoms associations by age and binge drinking

Next, we fit models with interaction terms to evaluate if the cannabis-depression association was impacted by concurrent alcohol use and participant age. No tested interactions were statistically

Table 2
Regression Models for Associations Between Cannabis Use and Depressive Symptoms When Measured Concurrently.

	Dependent variable: Cannabis use Logistic component (any cannabis use [>0 days] in past month)				Negative binomial component (# days using cannabis in past month)			Dependent variable: Depressive symptoms Linear regression		
Term	OR	B	SE	*p*	B	SE	*p*	B	SE	*p*
Intercept	.00	−11.211	19.080	.56	.743	.763	.33	.489	.183	.008
Female	.38	-0.971	.367	.008	-0.431	.246	.08	.112	.017	<0.001
Age-cohort	.00	−21.912	23.583	.35	−1.443	.608	.02	-0.381	.207	.06
Age-change	(omitted)	34.069	20.215	.09	2.450	.982	.01	.505	.185	.006
Age-change^2	9145.34	9.121	7.362	.21	-0.118	.259	.65	.117	.060	.051
Binge drinking	562.28	6.332	26.435	.81	.061	.025	.01	-0.001	.002	.68
Depressive symptoms	.98	-0.016	.458	.97	1.185	.241	<0.001	–	–	–
Cannabis use	–	–	–	–	–	–	–	.005	.001	<0.001

Note. OR = odds ratio, *B* = coefficient, SE = standard error, *p* = *p*-value for coefficient. Female was coded as 0/1. Age was scaled in decades (10 years) before creating age-cohort and age-change variables. Binge drinking was scaled in number of days (0–30). Depressive symptoms were scaled in standard deviation units. Models fit to 2901 observations of 767 youth.

Table 3
Regression Models for Prospective Associations Between Cannabis Use and Depressive Symptoms When Measured 12 Months Apart.

	Dependent variable: Cannabis use Logistic component (any cannabis use [>0 days]in past month)				Negative binomial component (# days using cannabis in past month)			Dependent variable: Depressive symptoms Linear regression		
Term	OR	B	SE	*p*	B	SE	*p*	B	SE	*p*
Intercept	.02	−3.987	2.687	.14	3.081	1.351	.02	.264	.133	.047
Female	1.23	.207	.201	.30	-0.688	.215	.001	.045	.014	.002
Age-cohort	.00	−6.106	3.195	.06	−3.070	1.576	.051	-0.199	.154	.20
Age-change	162.71	5.092	2.942	.08	4.653	1.987	.02	.219	.144	.13
Age-change^2	4.99	1.607	.982	.10	.946	.571	.10	.054	.046	.24
Lag(Binge drinking)	2.00	.692	.277	.01	-0.016	.016	.32	-0.002	.003	.57
Lag(Depressive symptoms)	2.10	.740	.320	.02	.153	.229	.51	.612	.109	<0.001
Lag(Cannabis use)	18.82	2.935	.460	<0.001	.035	.009	<0.001	.002	.001	.08

Note. OR = odds ratio, *B* = coefficient, SE = standard error, *p* = *p*-value for coefficient. Female was coded as 0/1. Age was scaled in decades (10 years) before creating age-cohort and age-change variables. Binge drinking was scaled in number of days (0–30). Depressive symptoms were scaled in standard deviation units. Models fit to 2901 observations of 767 youth.

significant. We did not find evidence that either age-change or binge drinking moderated the concurrent or prospective associations between depressive symptoms and cannabis use, regardless of which construct predicted which (*ps* from 0.39 to 0.89).

4. Discussion

We investigated the associations between cannabis use and depressive symptoms in a prospective, longitudinal, sequential cohort design with repeated observations of 767 participants spanning ages 15–24 years old. When measured concurrently, depressive symptoms did not predict the odds of past-month cannabis use but did predict more days of use among cannabis users. These contrasting findings indicate mixed support for the "self-medication" hypothesis, which was supported among cannabis users, but not among the general population (Feingold and Weinstein, 2021; Pacheco-Colón et al., 2019).

When we examined prospective (vs. concurrent) associations in a more rigorous design that adjusted for initial levels of depressive symptoms and cannabis use, depressive symptoms predicted a greater likelihood of subsequent any cannabis use during the following year, and cannabis use frequency predicted greater subsequent depressive symptoms. The former finding again provides some support for the "self-medication" hypothesis. However, in contrast to our cross-sectional findings, the self-medication hypothesis was supported among the general population but not among cannabis users. The difference between our cross-sectional and prospective findings could be explained by a difference in the timescale of action and the non-linearity of mood disorders as they happen episodically (Leadbeater et al., 2019). Perhaps depressive symptoms drive individuals toward cannabis use, but this effect only unfolds over a longer period (e.g., 1 year as examined herein). However, one way to interpret the data on more proximal use is that depressive symptoms do not drive individuals to cannabis use but do drive increased use among established users. Our results indicate that individuals who endorse elevated depressive symptoms, but not concurrent cannabis use may be more likely to use cannabis use later. Among individuals who are already using cannabis, they may be more vulnerable to elevated depressive symptoms if not intervened early on.

Regarding the effect of cannabis use on subsequent depressive symptoms, consistent with other recent literature (Feingold and Weinstein, 2021; Pacheco-Colón et al., 2019), the present study found evidence supporting cannabis use prospectively predicting depressive symptoms. One of these reviews noted stronger evidence to support depression predicting cannabis use but found support for both mechanisms. The studies reviewed varied in their measures of concurrent substance use. While most controlled for concurrent substance use in some way, it was difficult to draw any conclusions about the impact of concurrent use of specific substances on outcomes. There are several explanatory mechanisms for cannabis use predicting depressive symptoms. Cannabis use may have led to worse psychosocial outcomes, which can increase the risk of developing depressive symptoms (D'Amico et al., 2016). In addition, introducing exogenous cannabinoids, such as THC, could disrupt the endogenous endocannabinoid system. The endocannabinoid system impacts neurotransmitter function and disruption could impact neurodevelopment and increase vulnerability to developing depression (Paruk and Burns, 2016).

We did not find evidence that the associations between cannabis use and depressive symptoms varied by age between ages 15 and 24, indicating age may not be playing a significant role in this bidirectional relationship and regardless of age, the likelihood as to whether cannabis use will increase as a function of depressive symptoms or vice versa remains. However, our findings contrast Wilkinson et al. (2016). Though, one explanation for the discrepancy could be that we tested the concurrent and 1-year prospective associations, whereas they tested whether depressive symptoms measured once in adolescence predicted changes in the levels of cannabis across subsequent ages. Tests of this question in additional samples seems warranted, but at present, our data suggest similar dynamic relations between cannabis and depressive symptoms are detectable across middle adolescence, late adolescence, and early adulthood.

Likewise, we did not find evidence that concurrent associations between cannabis use and depressive symptoms varied by binge drinking concurrent to cannabis use. In prospective models, we found evidence for additive effects of binge drinking and depressive symptoms on subsequent cannabis use—more binge drinking predicted greater likelihood of using any cannabis 12 months later, adjusting for initial levels of cannabis use. Individuals engaging in binge drinking while reporting depressive symptoms may be more likely to engage in cannabis use if not intervened early. We did not find additive effects of cannabis use and binge drinking in predicting subsequent depressive symptoms. After adjusting for cannabis use, binge drinking was no longer a statistically significant predictor. These results indicate that among this sample, engaging in concurrent binge drinking and cannabis use, binge drinking does not increase the likelihood of elevated depressive symptoms. The varied pattern of findings on the role of binge drinking across the concurrent and prospective models underscores the importance of considering this contextual factor when examining the link between cannabis and depressive symptoms.

Although our design provided more rigorous prospective evidence of an association, results do not conclusively demonstrate causality. There may have been systematic differences between cannabis users and non-users and those with or without depression symptoms that remain (e.g., being bullied, family history of mood disorders, etc.) even after adjusting for pre-existing levels of cannabis, depression, and other covariates. In addition, a more precise and specific measure of depression would have helped give more confidence in the level of depressive symptoms reported. Variability in assessment instruments, and context, sample selection criteria across studies may also influence the findings. Finally, the quantification of cannabis use remains imprecise, making it difficult to precisely examine the association of depression with the level of use. Our sample provided data on the number of days of cannabis use but did not specify how much cannabis was used on any particular day. Given the variety of cannabis products available, it would also be helpful to have biochemical measures of exposure, the potency of cannabis consumed, method of use (vape, flower, concentrate, edibles), secondary exposure, number of people smoking (if shared), etc.

Conclusion

In this longitudinal study of a large sample of adolescents and young adults, we found that cannabis use is positively associated with depression, but the relationship appears to be complex and not unidirectional. Depressive symptoms were associated with more cannabis use in those already using cannabis, and frequency of use predicted greater depression symptoms 1 year later, even after adjusting for current levels of cannabis use. As cannabis use is becoming legal in an increasing number of states, it is more accessible and the prevalence of use is rising. More information about the relationship between youth cannabis use and other psychiatric and cognitive outcomes, including depression, is vital in informing prevention and public health efforts.

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CRediT authorship contribution statement

Jessie B. Lydiard: Conceptualization, Formal analysis, Writing – original draft, Writing – review & editing. **Herry Patel:** Writing – original draft, Writing – review & editing. **Yoni Strugatsky:** Writing – original draft, Writing – review & editing. **Wesley K. Thompson:** Formal analysis, Data curation, Writing – review & editing. **William E. Pelham:** Formal analysis, Supervision, Writing – original draft, Writing – review & editing. **Sandra A. Brown:** Formal analysis, Supervision, Writing – review & editing, Funding acquisition.

Declaration of Competing Interest

The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health. All authors have no conflicts of interest to disclose.

References

Achenbach, T.M., Rescorla, L.A., 2003. Manual for the ASEBA adult forms & profiles. University of Vermont, Research Center for Children, Youth, & Families.

Achenbach, T.M., Rescorla, L.A., 2001. Manual for the ASEBA school-age forms & profiles. University of Vermont, Research Center for Children, Youth, & Families.

Armstrong, T.D., Costello, E.J., 2002. Community studies on adolescent substance use, abuse, or dependence and psychiatric comorbidity. J. Consult. Clin. Psychol. 70, 1224–1239. https://doi.org/10.1037/0022-006X.70.6.1224.

Atkins, D.C., Baldwin, S.A., Zheng, C., Gallop, R.J., Neighbors, C., 2013. A tutorial on count regression and zero-altered count models for longitudinal substance use data. Psychol. Addict. Behav. 27, 166–177. https://doi.org/10.1037/A0029508.

Brown, S.A., Brumback, T., Tomlinson, K., Cummins, K., Thompson, W.K., Nagel, B.J., Bellis, M.D.D., Hooper, S.R., Clark, D.B., Chung, T., Hasler, B.P., Colrain, I.M., Baker, F.C., Prouty, D., Pfefferbaum, A., Sullivan, E.V., Pohl, K.M., Rohlfing, T., Nichols, B.N., Chu, W., Tapert, S.F., 2015. The National Consortium on Alcohol and Neuro Development in Adolescence (NCANDA): a multisite study of adolescent development and substance use. J Stud Alcohol Drugs 76, 895. https://doi.org/10.15288/JSAD.2015.76.895.

Brown, S.A., Myers, M.G., Lippke, L., Tapert, S.F., Stewart, D.G., Vik, P.W., 1998. Psychometric evaluation of the Customary Drinking and Drug Use Record (CDDR): a measure of adolescent alcohol and drug involvement. J. Stud. Alcohol 59, 427–438. https://doi.org/10.15288/jsa.1998.59.427.

Brumback, T., Thompson, W., Cummins, K., Brown, S., Tapert, S., 2021. Psychosocial predictors of substance use in adolescents and young adults: longitudinal risk and protective factors. Addict. Behav. 121, 106985 https://doi.org/10.1016/J.ADDBEH.2021.106985.

D'Amico, E.J., Tucker, J.S., Miles, J.N.V., Ewing, B.A., Shih, R.A., Pedersen, E.R., 2016. Alcohol and marijuana use trajectories in a diverse longitudinal sample of adolescents: examining use patterns from age 11 to 17 years. Addiction 111, 1825–1835. https://doi.org/10.1111/ADD.13442.

Deykin, E.Y., Levy, J.C., Wells, V., 1987. Adolescent depression, alcohol and drug abuse. Am. J. Public Health 77, 178–182. https://doi.org/10.2105/AJPH.77.2.178.

Diego, M.A., Field, T.M., Sanders, C.E., 2003. Academic performance, popularity, and depression predict adolescent substance use. Adolescence 38, 35.

Farooqui, M., Shoaib, S., Afaq, H., Quadri, S., Zaina, F., Baig, A., Liaquat, A., Sarwar, Z., Zafar, A., Younus, S., 2022. Bidirectionality of smoking and depression in adolescents: a systemic review. Trends Psychiatry Psychother. https://doi.org/10.47626/2237-6089-2021-0429.

Feingold, D., Weinstein, A., 2021. Cannabis and depression. Adv. Exp. Med. Biol. 1264, 67–80. https://doi.org/10.1007/978-3-030-57369-0_5/FIGURES/1.

Gobbi, G., Atkin, T., Zytynski, T., Wang, S., Askari, S., Boruff, J., Ware, M., Marmorstein, N., Cipriani, A., Dendukuri, N., Mayo, N., 2019. association of Cannabis Use in Adolescence and Risk of Depression, Anxiety, and Suicidality in Young Adulthood: a Systematic Review and Meta-analysis. JAMA Psychiatry 76, 426–434. https://doi.org/10.1001/jamapsychiatry.2018.4500.

Kendler, K.S., 2012. Levels of explanation in psychiatric and substance use disorders: implications for the development of an etiologically based nosology. Mol. Psychiatry 17, 11–21. https://doi.org/10.1038/mp.2011.70.

Khantzian, E.J., 1985. The self-medication hypothesis of addictive disorders: focus on heroin and cocaine dependence. AJP 142, 1259–1264. https://doi.org/10.1176/ajp.142.11.1259.

Leadbeater, B.J., Ames, M.E., Linden-Carmichael, A.N., 2019. Age-varying effects of cannabis use frequency and disorder on symptoms of psychosis, depression and anxiety in adolescents and adults. Addiction 114, 278–293. https://doi.org/10.1111/ADD.14459.

Markou, A., Kosten, T.R., Koob, G.F., 1998. Neurobiological similarities in depression and drug dependence: a self-medication hypothesis. Neuropsychopharmacology 18, 135–174.

Muthén, L.K., Muthén, B.O., 2017. Mplus User's Guide (No. Eight Edition). Muthén & Muthén, Los Angeles, CA.

Pacheco-Colón, I., Ramirez, A.R., Gonzalez, R., 2019. Effects of adolescent cannabis use on motivation and depression: a systematic review. Adolesc./Young Adult Addict. 6, 532–546. https://doi.org/10.1007/s40429-019-00274-y.

Paruk, S., Burns, J.K., 2016. Cannabis and mental illness in adolescents: a review. South Afr. Fam. Pract. 58, 18–21. https://doi.org/10.1080/20786190.2014.978106.

Patrick, M.E., Schulenberg, J.E., Miech, R.A., Johnston, L.D., O'malley, P.M., Bachman, J.G., 2022. Monitoring the future panel study annual report. doi:10.7826/ISR.

Pohl, K.M., Sullivan, E.V., Podhajsky, S., Baker, F.C., Brown, S.A., Clark, D.B., Colrain, I. M., DeBellis, M., Goldston, D., Nagel, B.J., Nooner, K.B., Tapert, S.F., Pfefferbaum, A., 2022. NCANDA_PUBLIC_6Y_REDCAP_V04" data release of the national consortium on alcohol and neurodevelopment in adolescence (NCANDA). Sage Bionetw. Synap. https://doi.org/10.7303/syn26951066.

Quello, S.B., Brady, K.T., Sonne, S.C., 2005. Mood disorders and substance use disorder: a complex comorbidity. Sci. Pract. Perspect. 3, 13–21.

Satorra, A., Bentler, P.M., 2010. Ensuring positiveness of the scaled difference chi-square test statistic. Psychometrika 75, 243–248. https://doi.org/10.1007/S11336-009-9135-Y.

Substance Abuse and Mental Health Services Administration, 2021. Key substance use and mental health indicators in the United States: results from the 2020 National Survey on Drug Use and Health (No. HHS Publication No. PEP21-07-01-003). NSDUH Series H-56. Center for Behavioral Health Statistics and Quality. Substance Abuse and Mental Health Services Administration, Rockville, MD.

Thompson, W.K., Hallmayer, J., O'Hara, R., 2011. Design considerations for characterizing psychiatric trajectories across the lifespan: application to effects of APOE-ε4 on cerebral cortical thickness in Alzheimer's disease. https://doi.org/10.1176/appi.ajp.2011.10111690 168, 894–903. doi:10.1176/APPI.AJP.2011.10111690.

Urits, I., Gress, K., Charipova, K., Li, N., Berger, A.A., Cornett, E.M., Hasoon, J., Kassem, H., Kaye, A.D., Viswanath, O., 2020. Cannabis use and its association with psychological disorders. Psychopharmacol. Bull. 50, 56–67.

White, C.T., Shamim, H., Shouli, R.A., Habbal, A.B., Mohammed, L., 2022. Cannabis use and the development of depression in adolescents: is there an established linear relationship between the two? Cureus 14. https://doi.org/10.7759/CUREUS.27394.

Wilkinson, A.L., Halpern, C.T., Herring, A.H., Shanahan, M., Ennett, S.T., Hussey, J.M., Harris, K.M., 2016. Testing longitudinal relationships between binge drinking, marijuana use, and depressive symptoms and moderation by sex. J. Adolesc. Health 59, 681–687. https://doi.org/10.1016/J.JADOHEALTH.2016.07.010.

Zucker, R.A., Brown, S.A., Peterson, S.J., Smith, G.T., 2015. Application of the expectancy concept to substance use. The Oxford Handbook of Adolescent Substance Abuse, pp. 372–386. https://doi.org/10.1093/OXFORDHB/9780199735662.013.017.