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Associations Between Cannabis Use and Mental Distress in Young People: A Longitudinal Study

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A B S T R A C T

Purpose: Despite a large number of studies on the relation between cannabis use and mental distress in adolescence, results are inconclusive regarding the nature of this association. The aim of the present study is to expand this body of research by analyzing the within-person association between changes in cannabis use and changes in mental distress among young people.
Methods: We used longitudinal data from a national sample of young people in Norway. The cohort was assessed in 1992 (T1), 1994 (T2), 1999 (T3), and 2005 (T4). The cumulative response rate was 60%. Respondents who participated in all four waves, aged 11–18 years at T1 (N = 1,988) were analyzed. Within-person association between changes in cannabis use and changes in mental distress in terms of symptoms of depression, anxiety, suicidal ideation, and deliberate self-harm were estimated by applying fixed-effects modeling.
Results: For males, an increase in cannabis use from no use to more than 10 times/year was significantly associated with increased risk for anxiety (relative risk [RR]: 1.72, $p = .009$), depressed mood (RR: 1.49, $p < .001$), and suicidal ideation (RR: 3.43, $p = .012$). For females, the corresponding increase in cannabis use yielded an increased risk for anxiety (RR: 1.38, $p = .023$) and suicidal ideation (RR: 2.47, $p = .002$).
Discussion: Increased cannabis use during adolescence and young adulthood seem to increase the risk for symptoms of mental distress. Although the associations appear to be more pronounced among males, it was only for depression that there was a statistically significant gender difference in the association.

IMPLICATIONS AND CONTRIBUTION

The present study lends support to the hypothesis of an association between cannabis use and mental distress. In men, increasing cannabis use was associated with increased risk for anxiety, depressed mood, and suicidal ideation. In women, increased cannabis use was associated with an increased risk for anxiety and suicidal ideation. The findings from the present study highlight that adolescent cannabis use is an important public health issue.

Many countries have liberalized their cannabis legislation since the millennium shift, and regular cannabis use has become more prevalent in jurisdictions that have legalized the drug [1]. In the European Union, 15.5% of young adults (aged 15–34 years) report past year cannabis use; in comparison, prevalence in Norway is among the lowest third, with 10.1% past year cannabis users among young adults [2]. In addition, the concentration of the main psychoactive component Δ9-tetrahydrocannabinol (THC) of cannabis has escalated [2,3].

Because cannabis may be particularly harmful to individuals whose brain development is in progress [4], studies of adolescents and young adults are important. The present study aims to

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expand this body of research by analyzing the association between cannabis use and mental distress, using panel data on young people in the Norwegian general population.

Previous research

The literature on the association between cannabis use and mental health problems is huge. However, as noted by Meier et al. (2020), a large fraction of this research is based on cross-sectional data with their well-known limitations for causal inferences [5], and many studies have assessed clinical samples or other selected groups. However, previous research provides evidence that cannabis use in adolescence is prospectively related to an increased risk of psychotic disorders [6,7].

Associations with later anxiety and depression are less clear. Gobbi and co-workers' (2019) meta-analysis showed that adolescents' use of cannabis was predictive of depression in young adulthood, while there was no statistically significant link to anxiety [8]. Similarly, Shalit and Lev-Ran (2020) reported that associations between cannabis use and anxiety generally seemed to reflect confounding, but their narrative review was not confined to studies of young people [9]. On the other hand, another recent meta-analysis, that included high-quality longitudinal studies of the general youth population, found support for an association between cannabis use and increased risk for anxiety [10]. Regarding adolescent cannabis use as a potential risk factor for later depression, yet another review concluded that "there appears to be some association [.] if there has been an early onset of cannabis use, although current results tend to be contradictory." [11].

The bulk of the studies in the aforementioned meta-analyses and literature reviews mainly relied on diagnostic outcomes. However, less severe mental health problems are also important. Since they are more common, they may contribute to the total burden of cannabis-related harm at least as much as the clinical cases. For example, among European and Canadian adolescents aged 11–15 years, one in four reported feeling nervous, irritable, or having difficulties getting to sleep every week according to the survey Health Behaviour in School-aged Children [12]. Moreover, a systematic review and meta-analysis of the global prevalence of depression and elevated depressive symptoms among adolescents showed that 34% experience elevated symptoms of depression, whereas 8% suffered from major depressive disorder [13].

Three studies of young people are particularly interesting in this context. These studies used panel data to estimate within-person associations and found that cannabis use was significantly associated with depression symptoms [5,14], major depressive disorder, and suicidal ideation [14,15]. The statistical modeling in these studies provides a strong basis for causal inferences because confounding due to time-invariant ("fixed") covariates is eliminated. However, this type of statistical model cannot eliminate confounding due to factors that vary across individuals or over time, and the model can thus be strengthened by including such factors. To our knowledge, no additional general population studies on the associations at issue have relied on such modeling.

There is also some evidence that cannabis use is associated with an increased risk of deliberate self-harm among young people [16–18]. A few other longitudinal studies have also assessed the association between cannabis use and suicidal ideation. Pedersen (2008) found that use of the drug was prospectively related to suicidal ideation in young adulthood, but not in adolescence [18]. Another longitudinal study reports a statistically significant association between adolescent cannabis use and suicidal ideation among males only [19]. Similar results, with a statistically significant association among males, have been found in the adult population [20].

Moreover, gender-specific analyses on the associations between adolescent cannabis use and anxiety and/or depression in young adulthood show mixed results. A study based on an Australian cohort of adolescents found a statistically significant association between daily cannabis use and anxiety and depression, and the risk was significantly higher among females compared to males [21]. Conversely, a study of African American adolescents found a statistically significant increased risk for depressive symptoms among males who used cannabis, but not for females using cannabis [22].

Underlying mechanisms and the issue of directionality

Various mechanisms underlying the association between cannabis use and mental health problems have been suggested. One starts out from a neurophysiological perspective, suggesting that intake of THC affects brain functions and perhaps interacts with other risk factors in a way that increases the risk of mental health symptoms. There is evidence that extensive use of cannabis high in THC increases the risk for psychosis; there is also evidence of an increased risk for suicide [23]. Another suggested explanation is common risk factors, such as parental mental health problems, affecting both cannabis use and mental distress through either genetics or environment [24]. Hence, studying the association between cannabis use and mental distress using methods that can account for such stable common risk factors is warranted. Yet another suggested pathway is that cannabis use is indirectly associated with mental distress through social mechanisms such as difficulties in the labor market [25] and school failure [26]. In line with this reasoning, it seems important to study the link between cannabis use and mental distress in various settings, for example, also in countries where prevalence is relatively low.

A critical issue in this kind of research concerns the directionality of the relations at issue. There are scattered findings suggesting that the relationship between cannabis use and mental health problems could be due to a reversed association [27,28], which underlies the so-called "self-medication hypothesis" [29]. However, the general conclusion of studies that address this issue is that the causal direction goes from cannabis use to mental distress [5,22,30].

The present study

The overarching aim of the present study is to estimate the association between changes in cannabis use and changes in mental distress during adolescence and young adulthood. Below, we outline the key features of our study, and how these can contribute to a better understanding of the association at issue.

(1) Although previous longitudinal studies of the association at issue have taken various potential confounders into account, fixed-effects modeling to assess within-person associations provides stronger basis for causal inferences. The model compares each individual to himself or herself between time points. By using this technique, time-stable characteristics of

a person such as genetic factors, family background, and personality traits are controlled for in the analysis, irrespective of whether they are measured or not [31]. To our knowledge, only three previous studies have relied on this technique to estimate the associations between cannabis use and mental health problems [5,14,15].

(2) Almost all studies in this field use a dichotomous outcome, which may be useful in a clinical setting. However, in epidemiological research, the situation is different, and a dichotomization of, for example, a depression scale is at odds with the contemporary conception of psychopathologies where depressiveness is regarded as a condition that comes in degrees rather than being a discretely delineated diagnostic category [32]. Furthermore, dichotomization yields loss of information, and decrease in statistical power, as pointed out in the methodological literature [33]. Thus, we have retained scales that are continuous as far as possible.

(3) Extant studies typically estimate the association between cannabis use and mental distress in terms of an odds ratio or relative risk. We will take this a step further by calculating the population-attributable fraction, expressing how large fraction of the outcome at issue that is attributable to cannabis use.

(4) Most studies report estimates of the association between cannabis use and mental distress for females and males together. However, as outlined above, the association between cannabis use and mental distress may differ between males and females; this is an issue that we will explore.

In this study, we will use data from a population-based cohort with data on cannabis use and mental distress at baseline (in 1992) and follow-up (in 1994, 1999, and 2005) to investigate (1) whether there is an association between changes in cannabis use and changes in mental distress, (2) if possible associations are different for males and females, and (3) how large fraction of the different types of mental distress that is attributable to cannabis use.

Data and Methods

We used data from the Young in Norway Longitudinal Study, which has followed a cohort of young people prospectively over 13 years and cover a broad range of topics (see [34] for a detailed description). The cohort was assessed in 1992 (T1), 1994 (T2), 1999 (T3), and 2005 (T4). The survey at T1 included 8th to 13th graders in 67 schools, and the sample was selected to generate a national representative cross-section of this student population (response rate: 97%). At T2, students who had left their original school received postal questionnaires, while those who were still in their original school filled in questionnaires in the classroom in the presence of a supervising teacher—as they did at T1. Only the latter group achieved a high response rate (92%). Therefore, the subsequent follow-ups were restricted to students who attended the same school at T1 and T2 (i.e., 8th and 11th graders at T1). The vast majority (91%) of these students consented to be traced for future participation in the study, of which 84% responded at T3 and 82% responded at T4. The cumulative response rate was 60%. A study analyzing the attrition in the Young in Norway Longitudinal Study found that, for example, being male, older age, having poor grades, and suburban or urban residency predicted attrition between 1992 (T1) and 2005 (T4) [35]. Our analyses were confined to respondents who participated in all four waves and who were aged 11–18 years at T1 (N = 1,988).

Ethical approval

The study was conducted in accordance with the National Guidelines for Research Ethics in the Social Sciences and approved by the Norwegian Social Science Data Services (#S-05030).

Key measures

Depressive mood was measured as an additive index based on six items from the Depressive Mood Inventory [36]. The question was: “During the past week, have you not been bothered at all, a little bit bothered, quite bothered, or extremely bothered by some of these things?: (1) Felt too tired to do things; (2) Had trouble sleeping; (3) Felt unhappy, sad, or depressed; (4) Felt hopeless about the future; (5) Felt tense or keyed up; and (6) Worried too much about things. There were four response options: Not bothered at all (coded 0); A little bit bothered (1); Quite bothered (2); and Extremely bothered (3). The reference period was the past week (The internal consistency showed little variation across the four waves; Cronbach’s alpha = 0.774–0.841).

Anxiety was measured as an additive index based on the following three items from the Hopkins Symptoms Check List [37]. The question was: “During the past week, have you not been bothered at all, a little bit bothered, quite bothered, or extremely bothered by some of these things?: (1) Suddenly scared for no reason; (2) Constantly scared or worried; and (3) Nervousness or shakiness inside. The reference period was the past week, and there were the same four response options as for depressive mood (Cronbach’s alpha: 0.679–0.771).

Suicidal ideation was measured by the following item: “[Have you] Had thoughts of ending your life?” The reference period was the past week, and there were the same four response options as for depressive mood and anxiety. The variable was coded 0 (not been bothered at all) to 3 (extremely bothered).

Deliberate self-harm was measured by the question: ‘Have you ever on purpose taken an overdose of pills or in another way tried to hurt yourself?’ Those who responded affirmatively were asked how long it had been since the (most recent) episode of deliberate self-harm. Based on the responses, a variable on the past-year incidence of deliberate self-harm (yes/no) was constructed. This measure captures both suicide attempts and nonsuicidal self-inflicted injuries and has been used in previous studies [38].

Cannabis use was measured by the following question: “During the past 12 months, have you used hashish or marihuana?” There were six response options: never (coded 0), once (1), 2 to 5 times (3.5), 6 to 10 times (8), 11 to 50 times (30), and more than 50 times (55). In the analyses, we used a three-level measure: Never; 1–10 times; and 11 times or more.

Time-varying covariates

Assessment year was controlled for by using dummy variables for each assessment year (except the first).

Heavy episodic drinking was measured by the following question: “During the past 12 months, have you had so much to drink that you felt clearly intoxicated?” There were the same six

response options as for Cannabis use: never (coded 0), once (1), 2 to 5 times (3.5), 6 to 10 times (8), 11 to 50 times (30), and more than 50 times (55).

Loneliness was measured as an additive index based on the following four items from the UCLA (University of California, Los Angeles) Loneliness Scale [39]: (1) I feel in tune with the people around me; (2) I can find companionship when I want it; (3) No one really knows me very well; and (4) People are around me but not with me. There were four response options, ranging from Never (1) to Often (4) about how often the respondent felt this way.

All measures were available for all four waves, except for deliberate self-harm, which was missing for T1.

Statistical analyses

We estimated the effect of changes in cannabis use on changes in the various outcomes by applying fixed-effects modeling [31] which is briefly described below, taking depression as an example. The following model depicts the relation at issue:

$$D_{it} = \beta_0 + \beta_1 C_{it} + U_i + \varepsilon_{it} \quad (1)$$

D is the measure of depression of individual *i* during wave *t*, C is cannabis use, and *U* represents unobserved factors that do not vary across time within individuals. The parameter of interest is β_1, capturing the effect of cannabis on depression. A potential estimation problem is the possible correlation between U and C; that is, depression and cannabis use are likely affected by stable common unobserved factors, such as genetic setup and personality traits. Estimation of model (1) on cross-sectional data will thus probably yield a biased estimate of β_1. As a remedy, we will use the longitudinal feature of our data to cancel out the distorting impact of U. First, we calculated the average of the time-varying factors for each individual across waves:

$$\overline{D}_i = \beta_0 + \beta_1 \overline{C}_i + U_i + \overline{\varepsilon}_i \quad (2)$$

(2) Next, we subtract eq. 2 from eq. 1, which yields the fixed-effects model:

$$D_{it} - \overline{D}_i = \beta_1 (C_{it} - \overline{C}_i) + (\varepsilon_{it} - \overline{\varepsilon}_i) \quad (3)$$

As can be seen, U is eliminated by this operation, and thereby that specific source of bias. Thus, this method implies that the effect estimate of cannabis use is entirely driven by the temporal variance that is induced by change over time. Although the fixed-effects technique eliminates the risk for bias caused by covariates that are stable within individuals across time, it does not remedy confounding that is due to time-varying factors that affect the outcome as well as the explanatory variable. The design can thus be strengthened by including time-varying covariates. We considered two variables as potential covariates: heavy episodic drinking and loneliness. Previous research suggests that heavy episodic drinking may be linked to mental illness [40,41] as well as cannabis use [42]. Likewise, loneliness is likely to affect the risk of mental illness [43,44], and possibly substance use, including cannabis use [45]. In addition, we controlled for time (assessment year) to eliminate bias from unobserved variables that change over time but are constant over individuals, such as, for example, the fact that all respondents are getting older.

We used Poisson regression with robust standard errors [46] to estimate the associations between cannabis use and the various outcomes. The resultant effect estimate, relative risk, is easy to interpret and serves as input in the computation of the population attributable fraction (PAF), which was computed following standard procedure [47]:

$$PAF = \frac{p^*(RR-1)}{p^*(RR-1)+1} \quad (4)$$

Where p is the proportion that is exposed to the risk factor and RR denotes the relative risk. The RR is defined as:

$$RR = \frac{Incidence\ rate\ among\ the\ exposed}{Incidence\ rate\ among\ the\ unexposed} \quad (5)$$

The PAF is often multiplied by 100, and then expresses by how many percent the incidence rate would decrease in the population if the exposure were eliminated.

To compare relative risks between females and males, we computed the ratio of relative risks (RRR):

$$RRR = \frac{RR_{males}}{RR_{females}} \quad (6)$$

To determine whether an RRR was statistically different from 1, the RR for males and the RR for females, along with their 95% confidence intervals were used as input to calculate the z-score and its *p* value. This was accomplished through the online resource: Calculator for comparing two estimated relative risk (hutchon.net) (Described in [48]).

One of the study aims is to assess whether the associations between cannabis use and mental distress differ between females and males. Methodologically, there are two basic ways to approach this issue: (1) to analyze the whole sample and include an interaction term (gender*cannabis use) and (2) to analyze females and males separately, and test whether the RRs for females and males are significantly different from each other (following the procedure described above). We applied a combination of the two approaches; that is, we first analyzed the whole sample, including an interaction term. If these analyses would suggest a statistical difference between females and males in the association between cannabis use and mental distress, we would proceed to the gender-specific analyses. This follows the recommendation of the methodological literature (e.g., [49]); finding a significant interaction term should be followed by subgroup analyses. One reason not to base the estimate of the effect of the predictor (cannabis use) on the outcome from the model including the interaction term is the following: the predictor and the interaction term will be strongly correlated (as the predictor is a constituent part of the interaction term), and the ensuing collinearity will yield interpretational problems by the interaction and predictor main effects being confounded [49].

The statistical analyses were conducted using Stata (version 17).

Results

Table 1 presents descriptive statistics. Cannabis use was more common in men, increased from T1 to T2 and peaked at T3

Table 1
Descriptive statistics

	Males (n = 836)				Females (n = 1,152)			
	T1	T2	T3	T4	T1	T2	T3	T4
Age at T1 M (SD)	14.42 (1.65)				14.51 (1.70)			
Cannabis use past 12 months. (%)	3.35	5.98	19.50	16.87	2.43	4.77	12.59	7.99
0 times (%)	96.65	94.02	80.50	83.13	97.57	95.23	87.41	92.01
1–10 times (%)	2.87	5.02	6.82	11.60	2.00	4.08	10.07	6.08
11+ times (%)	0.48	0.96	6.80	5.26	0.43	0.69	2.52	1.91
Depression, Mean (SD)	3.59 (2.93)	3.45 (2.97)	3.61 (3.22)	3.32 (3.24)	4.73 (3.39)	5.31 (3.47)	4.75 (3.69)	3.70 (3.37)
Anxiety, Mean (SD)	0.72 (1.11)	0.65 (1.06)	0.78 (1.31)	0.75 (1.29)	1.26 (1.54)	1.30 (1.55)	1.12 (1.55)	0.85 (1.37)
Suicidal ideation Mean (SD)	1.16 (0.54)	1.10 (0.39)	1.08 (0.32)	1.07 (0.31)	1.23 (0.63)	1.18 (0.56)	1.07 (0.34)	1.05 (0.27)
DSH, (%) y	–	2.39	3.47	2.87	–	5.90	8.16	4.08
HED, frequency past 12 months, Mean (SD)	*4.34 (10.75)*	7.42 (12.92)	20.38 (17.11)	17.43 (16.72)	4.06 (9.83)	6.65 (11.95)	13.92 (15.69)	10.62 (14.10)

DSH = deliberate self-harm; HED = heavy episodic drinking; SD = standard deviation.

among both men and women. Symptoms of depression, anxiety, and deliberate self-harm were more common in women. Levels of anxiety and depression were fairly stable across all four waves, whereas deliberate self-harm clearly peaked in T3; the increase between T2 and T3 was most pronounced in women. Suicidal ideation showed a slight decrease between T1 and T4 and means were similar between men and women. Like cannabis use, heavy episodic drinking was more common in men and increased from T1 to T2 and peaked at T3 among both men and women. Table 2 presents the prevalence of increased, decreased, or unchanged cannabis use, symptoms of depression, anxiety, suicidal ideation, and deliberate self-harm between T2 and T3 and between T3 and T4. The prevalence of increased cannabis use was highest between T2 and T3.

Initial analyses showed that cannabis use was not associated with any of the outcomes during the transition between T1 and T2. Subsequent analyses were thus performed on data for the three last waves, T2 to T4. Furthermore, fixed-effects modeling revealed that heavy episodic drinking had a positive and statistically significant ($p < .05$) association with cannabis use and all outcomes except suicidal ideation in females (Table 3). Thus, heavy episodic drinking was included in all models except for suicidal ideation in females. Loneliness was significantly, and positively associated with all outcomes, but not with cannabis use, and was thus not included as a covariate.

As noted above, we first analyzed the whole sample estimating models including the interaction term (gender*cannabis use), where females are coded 0 and males coded 1. Table 4 (Panel A) shows that the interaction term was statistically significant in three of the four outcomes (i.e., all except deliberate self-harm). For the sake of consistency, we proceeded to gender specific for all four outcomes. For all outcomes except deliberate self-harm, the value of the interaction term was more than 1, suggesting an excess risk for men.

Estimation of the fixed-effects models for males (Table 5) showed that increased cannabis use was significantly related to all outcomes except for deliberate self-harm. For depressed mood and suicidal ideation, it was only an increase from no use to the highest exposure level that had a statistically significant effect. For anxiety an increase from no use to either 1–10 times or 11+ times were significant. For example, males who increased their use from no use to 11+ times there was an increase in anxiety of 72%. Conversely, it means that those who reduced their use of cannabis from 11+ times to no use had reduced their risk of mental distress in terms of depression, anxiety, and suicidal ideation. For females (Table 6), increased cannabis use was only significantly associated to anxiety and suicidal ideation. Females who went from no cannabis use to 11+ times had an estimated 38% higher risk for increased symptoms of anxiety and 2.47 times higher risk for suicidal ideation. There was no significant association between changes in cannabis use and deliberate self-harm, neither among men nor among women.

Now turning to the PAFs, we note that it is less than 1% for anxiety and about 3% for suicidal ideation in females. For males, we observe the highest magnitude for suicidal ideation (10%), followed by anxiety (6%), and somewhat lower for depressed mood (about 2%).

As detailed above, we compared the estimates for females and males through computing the RRR to find out whether the gender differences were statistically significant. Although we generally found stronger associations between changes in cannabis use and mental distress for males than for females, with the exception for deliberate self-harm (Table 4, Panel B), only the effect on depression was significantly different between males and females (RRR = 1.41, $p = .005$).

Table 2
Prevalence of changes in cannabis use and the indicators of mental distress across time points

	Change from T2 to T3 (%)			Change from T3 to T4 (%)		
	Decrease	Stable	Increase	Decrease	Stable	Increase
Cannabis use	3.0	82.3	14.7	11.7	81.1	7.2
Depressed mood	47.6	13.3	39.0	50.3	16.2	33.5
Anxiety	30.9	41.9	27.2	30.7	47.7	21.6
Suicidal ideation	8.8	87.6	3.6	4.6	92.0	3.4
Deliberate self-harm	2.7	92.9	4.4	4.5	93.6	1.9

Discussion

In the present study, we assessed the within-person association between changes in cannabis use and changes in various types of mental distress during adolescence and early adulthood, using fixed-effects modeling. We found that increased cannabis use was associated with increased risk for symptoms of anxiety and suicidal ideation among both males and females. Among

Table 3
Bivariate analysis of the associations among covariates, mental distress, and cannabis use. Based on fixed-effects models estimated on three waves spanning the period 1994–2005

Outcome	Predictor	Males			95% CI		Females			95% CI	
		RR	SE	*p*	Lo.	Up.	RR	SE	*p*	Lo.	Up.
Depressed mood	Loneliness	1.10	0.01	< .001	1.08	1.13	1.09	0.01	< .001	1.07	1.11
	HED	1.01	0.00	< .001	1.00	1.01	1.01	0.00	< .001	1.00	1.01
Anxiety	Loneliness	1.16	0.03	< .001	1.10	1.21	1.15	0.02	< .001	1.13	1.18
	HED	1.01	0.00	< .001	1.01	1.02	1.01	0.00	.001	1.00	1.01
Suicidal ideation	Loneliness	1.24	0.08	< .001	1.10	1.40	1.26	0.07	< .001	1.14	1.40
	HED	1.02	0.01	.001	1.01	1.03	1.01	0.01	.190	1.00	1.02
DSH	Loneliness	1.36	0.09	< .001	1.19	1.56	1.06	0.04	.149	0.98	1.13
	HED	1.01	0.01	.183	0.99	1.03	1.01	0.00	.009	1.00	1.02
Cannabis use	Loneliness	1.04	0.03	.171	0.98	1.11	1.03	0.04	.526	0.95	1.12
Cannabis use	HED	1.03	0.00	< .001	1.02	1.03	1.03	0.00	< .001	1.03	1.04

DSH = deliberate self-harm; HED = heavy episodic drinking; RR = relative risk.

males, we also found a significant association between changes in cannabis use and changes in depressive mood.

The significant associations that we found between cannabis use and suicidal ideation for both males and females are by and large consistent with previous findings pertaining to the general youth population [8,18]. Yet some previous findings suggest associations only for males [19,20]. Regarding the association between cannabis use and anxiety, previous findings are inconclusive. Some recent studies of the association in question suggest no significant relationship between cannabis use and anxiety [8,9], whereas other studies are in line with our findings of a significant association [10]. Moreover, previous findings pertaining to the general youth population suggest an association between cannabis use and deliberate self-harm [17,18], while our results did not give any support for such an association. A possible explanation could be that the measure of deliberate self-harm was dichotomous in our study, which decreases statistical power. The association between cannabis use and depression was the only one where we also found an unequivocally significant difference in the estimates between females and males. This finding is in line with previous conclusions from some US studies [5,22]. Our study cannot establish why the association between cannabis use and depression differs between males and females but lends support for the idea that the link between cannabis use and depression is moderated by gender [22]. The outcome based on the interaction term (cannabis use*gender) suggested significantly different estimates between females and males also with respect to the association between cannabis use and the two outcomes anxiety and suicidal ideation. However, this outcome was not supported by the relative risk ratios, possibly suggesting a lower power in the latter test. We examined potential gender differences in the association between cannabis use and mental distress by performing separate analyses for females and males. However, in future research, the alternative of estimating a multiplicative interaction term should be considered, because such an approach has the potential of yielding greater statistical power compared to subgroup analyses.

Since we used fixed-effect modeling, our results strengthen the assumption of a within-person association between cannabis use and mental distress in terms of anxiety and suicidal behavior, and for men also symptoms of depression. These findings are in line with previously reported results from studies using the same statistical approach [5,14,15].

Because the model allows us to account for time-invariant characteristics of individuals, our findings indicate that the associations we observed are not due to common risk factors such as family background or genetics.

Furthermore, we calculated the PAF for each outcome, giving us an estimation of how large proportion of the outcome at issue that is attributable to cannabis use. Our results showed the highest PAF for suicidal ideation in men (9.7%) which indicates that one of 10 of the cases of increased suicidal ideation in men would have been avoided in the absence of cannabis use. Although the PAFs were lower for anxiety and depression, our findings indicate that cannabis use might play a role in the prevalence of mental distress in adolescents.

Table 4
Panel A: estimates of interaction term (Cannabis*gender); Panel B: ratio of relative risks men versus women (RRR)

	Panel A Interaction term	SE	*p*	Panel B RRR	z	*p*
Depressed mood	1.15	0.07	.018	1.41	2.57	.005
Anxiety	1.65	0.40	.041	1.39	0.58	.282
Deliberate self-harm	1.30	0.14	.011	1.25	0.88	.189
Suicidal ideation	0.92	0.26	.751	0.82	−0.29	.382

Table 5
Estimated risk ratios of within-person associations between changes in cannabis use on changes in mental distress. Based on fixed-effects models estimated on three waves spanning the period 1994–2005. Control for heavy episodic drinking and assessment year. Males

Outcome	Cannabis use	RR	SE	*p*	95% CI		PAF (%)
					Lower	Upper	
Depressed mood	0 (ref)	1					
	1 to 10	1.05	0.06	.428	0.94	1.17	
	11+	1.49	0.15	< .001	1.23	1.74	2.17
Anxiety	0 (ref)	1					
	1 to 10	1.28	0.13	.020	1.04	1.57	2.74
	11+	1.72	0.36	.009	1.14	2.56	3.14
							5.88
	0 (ref)	1					
Suicidal ideation	1 to 10	1.49	0.40	.138	0.88	2.53	
	11+	3.43	1.68	.012	1.31	8.81	9.82
	0 (ref)	1					
Deliberate self-harm	1 to 10	1.39	0.50	.361	0.67	2.70	
	11+	1.28	0.76	.675	0.32	3.53	

PAF = population attributable fraction; RR = relative risk.

Table 6
Estimated risk ratios of within-person associations between changes in cannabis use on changes in mental distress. Based on fixed-effects models estimated on three waves spanning the period 1994–2005. Control for heavy episodic drinking (except for the model for suicidal ideation) and assessment year. Females

Outcome	Cannabis use	RR	SE	*p*	95% CI		PAF (%)
					Lower	Upper	
Depressed mood	0 (ref)	1					
	1 to 10	1.09	0.06	.112	0.97	1.19	
	11+	1.06	0.10	.541	0.87	1.28	
Anxiety	0 (ref)	1					
	1 to 10	1.04	0.09	.613	0.88	1.22	
	11+	1.38	0.19	.023	1.04	1.81	0.70
Suicidal ideation	0 (ref)	1					
	1 to 10	1.19	0.36	.561	0.44	1.98	
	11+	2.47	0.73	.002	1.32	4.16	2.64
Deliberate self-harm	0 (ref)	1					
	1 to 10	1.40	0.35	.173	0.92	2.39	
	11+	1.56	0.39	.076	0.96	2.56	

PAF = population attributable fraction; RR = relative risk.

Strengths and limitations

There are some limitations to our study that need to be mentioned. Our data were collected between 1992 and 2005, and there is evidence from many countries that the concentration of the main psychoactive component (THC) of cannabis has increased substantially since then [2,3]. The link between cannabis use and mental health problems may have been affected accordingly. Indeed, a recent study of US adults showed that the association between cannabis use and depression strengthened markedly from 2005 to 2016 [50]. It is thus possible that cannabis use has grown in importance as a risk factor for mental distress since the time our data were collected.

Another limitation is that we applied a crude frequency measure of cannabis use. No data on the *quantity* of consumption were available, and it has been found that the amount consumed makes a difference as regards cannabis-related problems—above and beyond the frequency of use [51]. Furthermore, it cannot be ruled out that the panel attrition of 40% may have an over-representation of people with characteristics of importance for the present study.

Most previous studies in the current field focus on one indicator of poor mental health, for example, depression. One strength of our study is that it provides a more comprehensive assessment of the potential effect of cannabis use on mental distress by including a broad range of outcomes. Another strength of the present study is that our data allowed us to treat depressive mood, anxiety, and suicidal ideation as conditions that come in degrees rather than dichotomous outcomes. It is well known that dichotomization yields loss of information and decrease in statistical power [30]. Hence, a limitation is that deliberate self-harm was dichotomously measured. Furthermore, our analyses were based on the assumption that cannabis use increases the risk of mental distress, and not the other way around. Although this assumption seems to be well corroborated [5,22,30], others have failed to draw definite conclusions on the direction of the association [15]; thus it cannot be excluded that mental health influences cannabis use. As pointed out in the methodological literature, despite several advantages, fixed-effects modeling cannot determine the direction of causality [52].

However, a major strength of our study is indeed the analytical approach. We analyzed the data through fixed-effects modeling. Surprisingly, few previous studies have used this technique, although it is a safeguard against bias due to confounders that are temporarily stable. However, the technique is not a remedy against time-dynamic confounders. We did control for time and heavy episodic drinking, but it cannot be precluded that our estimates are biased due to other time-varying factors affecting cannabis use as well as mental distress that we were unable to control for. Hence, our results should be interpreted with some caution. By performing separate analyses for females and males, we contributed to the meager literature on gender differences in the association between cannabis use and mental distress. Although we found gender differences in the estimated cannabis effects on mental distress, it should be noted that only one of them (the effect on depression) was statistically significant, signaling a genuine absence of gender differences or insufficient power.

The findings from the present study are important in light of the recent reports of higher levels of THC in today's cannabis products [2,3] and highlight that adolescent cannabis use is an important public health issue. Moreover, our results suggested differences between males and females regarding the association between cannabis use and mental distress, in particular symptoms of depression. Hence, an important task for future research is to further probe the suggested gender differences and to uncover the mechanisms underlying such differences.

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The study was conducted in accordance with the National Guidelines for Research Ethics in the Social Sciences and approved by the Norwegian Social Science Data Services.

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