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Research paper

Bidirectional association of psychopathology and cannabis use: Results from the Swiss study on recreational cannabis access via pharmacies

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ABSTRACT

Although associations between cannabis use and mental health have been widely examined, temporal relationships between cannabis use patterns and psychopathological symptoms in regulated settings remain underexplored. We investigated longitudinal associations between cannabis use patterns (frequency, quantity, and problematic use) and psychopathological symptoms (depression, anxiety, and psychosis) over one year of pharmacy-based regulated cannabis access in Switzerland among 378 adult regular cannabis users. Assessments were conducted at baseline, 6 months, and 12 months using validated instruments (PHQ-9, GAD-7, adapted ERIraos) and standardized measures of cannabis use (use days in the past 30 days, quantity per use day, CUDIT-R). Cross-lagged linear mixed-effects models and Bonferroni correction for multiple testing were applied. Problematic cannabis use (CUDIT-R) prospectively predicted higher depressive symptom load ($\beta = 0.113$, $p < 0.001$) and higher anxiety symptom load ($\beta = 0.066$, $p = 0.015$). Anxiety symptoms were associated with subsequent increased cannabis use frequency ($\beta = 1.055$, $p = 0.047$). No longitudinal associations were observed for psychosis symptoms. These findings suggest that problematic cannabis use, rather than frequency or quantity alone, may be particularly relevant for depressive and anxiety symptom trajectories in regulated cannabis access settings and should be considered in clinical assessment and public health discussions surrounding cannabis regulation.

1. Introduction

Cannabis is the most commonly used illegal drug globally, with an estimated 228 million users (UNODC, 2024). Due to legalization efforts, its user base is growing world-wide and is expected to increase further, thus raising important questions about its potential impact on public mental health (Manthey et al., 2023b; Zellers et al., 2023). Previous research efforts have linked cannabis use, to multiple adverse mental health outcomes, including depression (Gorfinkel et al., 2020), anxiety (Xue et al., 2021) and psychosis (Di Forti et al., 2019), where high potency variants appear to have the most negative impact (Hines et al., 2020).

Generally, cannabis' negative impact on mental health is assumed to be mediated via its potency, determined by the tetrahydrocannabinol (THC) concentration (Petrilli et al., 2022). Further research has shown that the frequency of cannabis consumption (Cougle et al., 2016), the quantity consumed per day (Mosandl et al., 2024), but also the duration of use (Volkow et al., 2021) are linked to negative mental health outcomes. Especially illicit-market cannabis poses risks due to potential contaminants (Jameson et al., 2022), unknown potency content as well as absence of potency limits (Hall et al., 2023), and lack of regulated purchasing controls (Mahamad et al., 2020). High potency cannabis and frequency of use increase the risk of developing cannabis use disorder (CUD) (Connor et al., 2021). Epidemiological studies have shown that approximately 10% of all cannabis users suffer from CUD (Connor et al., 2021) and one in five weekly cannabis users are estimated to suffer from the condition (Leung et al., 2020). This is particularly important as CUD was previously reported to have an increased association with

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depression, anxiety (Onaemo et al., 2021), as well as psychosis (Jefsen et al., 2023). The association between cannabis use and psychosis, especially high potency cannabis, is robust. Evidence on the relationship of depression and anxiety is equivocal, with data that hints at a certain bidirectional relationship (Petrilli et al., 2022).

Over the past two decades, a large amount of research has shown associations between cannabis use and mental health disorders (McGee et al., 2000; Urits et al., 2020). Still causal directionality remains mostly unclear. Previous investigators have mainly focused on cannabis' impact on mental health, less on the possibility that symptoms of mental disorders might further cannabis use. For instance, affective symptoms such as depression and anxiety may lead to elevated cannabis consumption as a form of self-medication, a framework that has also been extended to stress- and trauma-related symptom profiles and to developmental contexts characterized by heightened affective vulnerability (Khantzian, 1987; Hinckley et al., 2024; Rossi et al., 2023). Recent longitudinal evidence suggests that depressive symptoms during adolescence and early adulthood predict future cannabis use, while frequent cannabis consumption may exacerbate depressive symptoms, creating a potential feedback loop (Lydiard et al., 2023).

However, most existing evidence for these bidirectional relationships comes from unregulated cannabis markets, where confounding factors such as product quality and potency, as well as stress induced by illegal acquisition are difficult to control. In contrast to the well-documented hazards associated with illicit cannabis use, less is known in the setting of regulated cannabis access, which allows standardized quality control procedures. These included limits on contaminants, the transparent labeling of cannabinoid content, with limits placed on maximum product potency. Such regulatory features may plausibly mitigate certain cannabis-related risks and contribute to mental health outcomes that differ from those observed in unregulated market settings. Investigating these dynamics within regulated cannabis markets, where such factors can be standardized, could provide novel insights (Hamilton and Sumnall, 2021).

This study addresses an important gap in cannabis research by examining bidirectional relationships between mental health symptoms and cannabis use within a regulated access framework, using pharmacy-based recreational cannabis provision in Switzerland. Based on prior longitudinal and epidemiological findings, we formulated the following hypotheses. First, we hypothesized that higher psychopathological symptom load, operationalized as depressive symptoms, anxiety symptoms, and early psychosis-related symptoms, would prospectively predict increases in cannabis use patterns over time, including higher use frequency, greater quantity consumed, and greater severity of cannabis use disorder symptoms.

Second, we hypothesized that more pronounced cannabis use patterns, reflected by higher frequency and quantity of use and greater severity of cannabis use disorder symptoms, would prospectively predict increases in psychopathological symptom load across depressive, anxiety, and psychosis-related domains. We further explored whether these bidirectional associations would persist in a regulated access setting characterized by standardized product quality and constrained THC exposure.

The findings, derived from the ongoing Weed Care study in Basel, Switzerland, might improve our understanding and could help guide clinical decision-making and development of legislation, particularly in the context of increasing cannabis legalization worldwide (Baltes-Flueckiger et al., 2023).

2. Materials and methods

2.1. Design

In this longitudinal study we investigated regulated access to cannabis for recreational use via pharmacies over a one-year timespan. The project is registered as clinical trial (NCT05522205). Baseline (BL) assessments took place in January 2023 with a single follow-up (FU) one year later. The local Ethics Committee (Ethikkommission Nordwest- und Zentralschweiz (EKNZ)) and the Swiss Federal Public Health Office approved the study. The protocol adheres to the Declaration of Helsinki and ICH-GCP guidelines. Since the main goal of the study was to assess the impact of regulated cannabis access via pharmacies as a randomized clinical trial, only half of the participants were allocated in a 1:1 ratio to gain immediate access to regulated cannabis products in pharmacies in the first six months consistent with the randomized clinical trial framework of the pilot project. Thereafter, months 6–12, all participants had access for the remaining observational period, ensuring consistent quality and THC concentrations. To mirror illicit market rates and ensure realistic consumption scenarios the sold cannabis was subsidized. In online questionnaires participants were asked to answer questions on their mental and physical health, as well as cannabis consumption behaviors every six months. Accordingly, three assessment waves (baseline, 6 months, and 12 months) were available for the present longitudinal analyses. A detailed study protocol has been published elsewhere (Baltes-Flueckiger et al., 2023).

During the study, participants could purchase selected cannabis products through participating pharmacies within the regulatory framework of the Swiss pilot program. In accordance with federal requirements, products were restricted to a maximum THC content of 20% and were subject to strict contaminant testing. Individual-level purchase transactions were electronically recorded in a track-and-trace system to ensure compliance with the regulatory cap of 10 g of THC per participant per month. Analyses of purchase data are planned for separate publications. An overview of the available cannabis products is provided in Supplementary Table S1.

2.2. Eligibility criteria

Before participating in the study, individuals were screened in-person by a psychiatry-trained study physician to ensure participant safety and had to give written informed consent. Eligibility criteria included being 18 years of age or older, confirm at least monthly cannabis use for the last half year, and screen positive for THC during inclusion urinalysis. Although monthly use constituted the minimum inclusion threshold, baseline consumption in the final sample was substantially higher (Mosandl et al., 2024), corresponding to approximately four to five days per week and thus exceeding common definitions of regular cannabis users as weekly or more frequent consumption (Doggett et al., 2023). Further requirements were sufficient German language skills and internet access to partake in the questionnaires (Baltes-Flueckiger et al., 2023). To comply with local law, participants had to be residents of the canton Basel-Stadt. Individuals interested in the study who were current psychiatric inpatients, presented with acute suicidality or psychosis, pregnancy, breastfeeding or severe cognitive impairment were excluded from participation.

2.3. Recruitment

In August 2022, the Swiss public was informed about the study through a local media conference. Registration was available online for interested individuals. Eligible individuals were screened in a phone call and if eligible invited to in-person screening. During the interview, comprehensive information about the study was provided and submission of informed consent was asked. A total of 378 were included into the study. Recruitment started in September 2022 and finalized in March 2023.

Thirty-eight participants dropped out during our observational period. Four individuals withdrew before the BL assessment and were subsequently replaced. Another 10 did not complete the six-month follow-up and another 24 did not complete the twelve-month follow-up. Participant recruitment, allocation, and attrition are shown in Fig. 1.

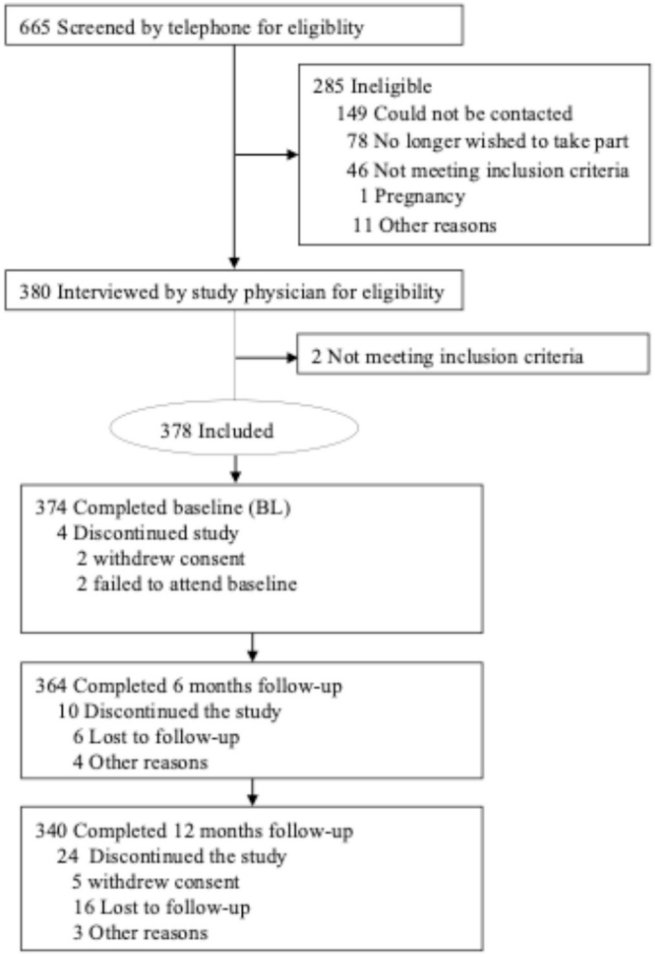

Fig. 1. Recruitment and attrition flow diagram.
A total of 38 participants dropped out during the study. Four left before the baseline (BL) assessment, and four replacement participants were recruited. Another 10 did not complete the survey at six months follow-up and another 24 did not complete the survey at the one-year follow-up (FU) in January 2024. The main reason for drop out was loss-to follow-up, as they could not be contacted despite repeated calls.

2.4. Data collection

In January 2023, we began gathering sociodemographic information on the 378 participants, which has already been published elsewhere (Mosandl et al., 2024). The baseline questionnaires on mental health and cannabis use patterns were repeated every 6 months.

Cannabis use patterns were assessed trough three measures: *Cannabis use frequency* (defined as the number of use days in the past 30 days) and *cannabis use quantity* (average grams consumed per day of use). To guide participants in estimating the amount of their consumed cannabis the questionnaire included pictures of different cannabis (flower and hashish) portions next to a 2 Francs and 2 Euro coin alongside an example of a typical hand-rolled cigarette containing tobacco and a filter with referenced values in grams (0.01, 0.05, 0.1, 0.2 and 0.5 g), in line with recommendations to improve the validity of self-reported cannabis quantity assessments through visual aids (Manthey et al., 2023a). Problematic cannabis use was assessed via the Cannabis Use Disorders Identification Test-Revised (CUDIT-R) (Adamson et al., 2010). This validated screening tool uses a score ranging from 0 to 32, where higher scores refer to a more severe problematic use.

We measured depressive, anxiety and psychosis symptom load via the Patient Health Questionnaire-9 depression scale (PHQ-9) (Kroenke et al., 2001), the Generalized Anxiety Disorder-7 scale (GAD-7) (Löwe et al., 2002) and an adapted version of the Early Recognition Inventory (ERIraos) Checklist (Maurer et al., 2006), respectively. Our version of the ERIraos contained six items on increased psychosis risk and early psychosis, with two additional items: “Impression that certain occurrences are intended only for me.” and “Diagnosis of psychosis or schizophrenia by a medical professional, psychologist, or another health care professional in the last six months.”. The internal consistency (Cronbach's α) of the adapted 8-item ERIraos was 0.53 at baseline, 0.54 at 6 months, and 0.68 at 12 months. For each psychopathological scale (PHQ-9, GAD-7, ERIraos) we calculated total scores, summing up each individual item score. Higher scores indicated greater symptom severity on each respective questionnaire. Regarding depression and anxiety, a score of 10 or greater is the recommended threshold for moderate to severe depression and moderate to severe generalized anxiety disorder, respectively (Kroenke et al., 2001; Löwe et al., 2002). Alcohol use was measured via the Alcohol Use Disorders Identification Test-Consumption (AUDIT-C) (Bradley et al., 2007), a three-item brief measure of alcohol consumption. Other drug use was assessed using selected items from the Alcohol, Smoking and Substance Involvement Screening Test (ASSIST) (Humeniuk et al., 2010), asking participants how often in the preceding six months they had used cocaine, amphetamine-type stimulants, inhalants, sedatives, hallucinogens, opioids, or other drugs; individual item scores (0 = never to 4 = daily or almost daily) were summed to produce a total score (0–42), with higher scores reflecting more frequent use.

3. Statistics

Descriptive statistics are presented as numbers (%) for categorical variables and as means (SD) or medians (IQR) for continuous variables.

To examine the bidirectional associations between psychopathological symptom load and cannabis use patterns, we estimated cross-lagged mixed-effects models. This modeling approach accounts for the nested structure of repeated measures (BL, 6 months FU and at 12 months FU), incorporates lagged values, and handles missing data.

For the analyses in which psychopathological symptom load predicted cannabis use patterns, the following scores served as independent variables: PHQ-9, GAD-7, and ERIraos. The dependent variables were cannabis use frequency, cannabis use quantity, and CUDIT-R. For example, cannabis use frequency at time *t* was predicted simultaneously by (a) its own lagged value and (b) the lagged value of PHQ-9, while adjusting for covariates. We estimated nine separate cross-lagged mixed-effects models, corresponding to three measures of psychopathological symptom load with the three measures of cannabis use patterns. Each model was adjusted for the respective lagged cannabis use variable score (use frequency, use quantity, CUDIT-R, respectively) and allocation group (immediate vs. delayed access) to account for differential access to regulated cannabis during the first six months. Random intercepts accounted for between-person differences in baseline levels.

The associations in the opposite direction - cannabis use patterns predicting psychopathological symptom load - were analyzed in the same way. Cannabis use frequency, cannabis use quantity, and CUDIT-R served as independent variables, and PHQ-9, GAD-7, and ERIraos served as dependent variables. Again, nine separate cross-lagged mixed-models were conducted; each adjusted for the respective lagged psychopathological symptom score and allocation group.

To correct for multiple testing within each direction (cannabis use patterns predicting psychopathological symptoms and psychopathological symptoms predicting cannabis use patterns), we applied a Bonferroni-corrected significance threshold ($\alpha = 0.05/9 = 0.0056$) for nine tests per direction and report corresponding 99.4% confidence intervals.

Furthermore, sensitivity analyses were conducted. First, complete case analyses were conducted assuming missing completely at random. Second, additional sensitivity analyses were conducted to rerun all models with additional covariates, including sex, age, alcohol

consumption (AUDIT-C), and use of other illicit substances (ASSIST).

As for some variables residuals were not close to normal, the following variables were logarithmically calculated for inferential analyses: cannabis use quantity, cannabis use frequency, PHQ-9, GAD-7, and ERIraos. Analyses were conducted in R version 4.2.2 (2022-10-31) using the lme function.

4. Results

4.1. Demographic characteristics

A brief sociodemographic description of the BL study population ($N = 374$) is provided in Table 1. Most participants were male (81%), with a mean age of 35.8 years, and 75% held Swiss nationality. A detailed description has been published previously (Baltes-Flueckiger et al., 2025). Four participants had missing values in sex, age, nationality and marital status. Extreme values for self-reported cannabis quantity were handled as outliers. Although very high daily quantities have been reported in online survey data (Caulkins et al., 2020), values exceeding 10 g per day of use were rare in our sample ($n = 10$) and were considered likely to reflect reporting or unit errors (e.g., confusion of grams per day vs per week/month, or misinterpretation of portion pictures) rather than typical consumption behavior within the regulated access context. Therefore, these observations were coded as missing for analyses of quantity.

4.2. Cannabis use patterns as predictors of psychopathological symptom load

Cross-lagged mixed-effects models across three waves (baseline, 6 months, and 12 months), adjusted for the respective lagged outcome and allocation group, revealed that problematic cannabis use (CUDIT-R) significantly predicted subsequent depressive and anxiety symptom load (Table 2).

Specifically, higher CUDIT-R scores were prospectively associated with higher PHQ-9 scores ($\beta = 0.113$, 99.4% CI [0.037, 0.188], $p < 0.001$) and higher GAD-7 scores ($\beta = 0.066$, 99.4% CI [0.008, 0.124], $p = 0.015$).

Neither cannabis use frequency nor cannabis use quantity predicted subsequent depressive, anxiety, or psychosis symptom load. No prospective association was observed between CUDIT-R and psychosis symptoms. Sensitivity analyses on complete cases showed comparable results after Bonferroni correction. Results are shown in Supplementary Table S4.

Table 1
Baseline characteristics of study participants.

	Total (n = 374)
Sex ($n = 370$)	
Male	299 (81%)
Female	65 (17%)
Non-binary	6 (2%)
Age (years, n = 370)	35.8 (11.4)
Swiss nationality (n = 370)	277 (75%)
Education, no. (%)	
Obligatory school	36 (10%)
Basic vocational school	113 (30%)
University qualification	57 (15%)
Higher vocational education	28 (8%)
University degree	136 (36%)
Other	4 (1%)
Employment status, no. (%)	
Paid employment	281 (75%)
Unemployed	20 (5%)
Non-working (retired, home maker, training)	73 (20%)

Data are no. (%) or mean (SD). Number of participants for whom data were available at baseline for each measure are given where different from the total for the group.

4.3. Psychopathological symptom load as predictors of cannabis use patterns

In the opposite direction, baseline psychopathological symptom load showed limited prospective associations with subsequent cannabis use patterns (Table 3).

Anxiety symptom load (GAD-7) was associated with higher subsequent cannabis use frequency ($\beta = 1.055$, 99.4% CI [−0.120, 2.145], $p = 0.047$) after Bonferroni correction.

Depressive symptoms and psychosis symptoms did not significantly predict cannabis use frequency, quantity per day of use, or CUDIT-R scores. Sensitivity analyses on complete cases showed comparable results after Bonferroni correction. Results are shown in Supplementary Table S5.

Further sensitivity analyses, which additionally adjusted for sex, age, alcohol use (AUDIT-C), and other substance use (ASSIST), yielded comparable results. The association between problematic cannabis use and depressive as well as anxiety symptom load remained statistically significant after Bonferroni correction. Similarly, the association between anxiety symptoms and cannabis use days remained significant after Bonferroni correction. Estimates are presented in Supplementary Tables S2 and S3.

5. Discussion

5.1. Bidirectional relationship between cannabis use and psychopathological symptoms

This study examined bidirectional associations between cannabis use patterns and psychopathological symptom load under regulated cannabis access. Our finding of the positive predictive capability of problematic cannabis use for depression and anxiety is consistent with a systematic review and meta-analysis by Onaemo et al. (2021), which emphasized the strong association between CUD and worsened mental health outcomes. Furthermore, our findings align with those of a large Danish cohort study showing that problematic cannabis use predicts depression (Jefsen et al., 2023). We expand upon these findings by confirming the relationship in a regulated access setting and highlighting the importance of problematic cannabis use in regular cannabis users, since we could not show a significant impact of the amount or frequency of cannabis use, as measured by CUDIT-R, on the explored psychopathological variables. This idea finds support in data provided by Danielsson et al. (2016) who could not show any association of this bidirectional relationship when examining cannabis use alone. Further, this pattern suggests that the psychosocial consequences of problematic use, such as stigma, economic strain, and interpersonal conflicts, may play a more significant role in mental health outcomes, than the pharmacological effects of cannabis itself (Brook et al., 2011; Meier, 2021). This interpretation aligns with work emphasizing resilience and psychosocial vulnerability as mediators between adverse environments and depressive symptomatology (Collazzoni et al., 2021), underscoring the relevance of the broader psychosocial context in problematic substance use. In line with this perspective, Birtel et al. (2017) demonstrated that perceived stigma related to substance use was associated with higher depressive and anxiety symptoms and highlighted the importance of social support in mitigating these effects. Complementary neurobiological evidence suggests that cannabis-related outcomes may not follow a simple dose-response pattern, heavy lifetime use, rather than recent use frequency, was associated with altered brain activation during working memory tasks (Gowin et al., 2025). Although these findings concern cognitive rather than affective outcomes, and do not imply causality, they converge with our observation that problematic use patterns may be more informative than quantity or frequency alone and point to neural correlates that may operate alongside psychosocial mechanisms in shaping affective symptom load. Although the observed effect sizes were small, reflecting modest population-level changes in

Table 2
Cross-lagged mixed-effects models examining associations of cannabis use patterns and subsequent psychopathological symptom load.

Dependent variable (DV)	Predictor	Estimate	SE	99.4% CI[a]	t-Value	P value[b]
PHQ-9	Cannabis use days in the past month (n = 362)	0.115	0.085	−0.123 to 0.353	1.343	1
	Cannabis amount per day of use (n = 361)	0.130	0.244	−0.549 to 0.808	0.533	1
	CUDIT-R (n = 365)	0.113	0.027	0.037 to 0.188	4.134	<0.001
GAD-7	Cannabis use days in the past month (n = 362)	0.057	0.066	−0.127 to 0.241	0.865	1
	Cannabis amount per day of use (n = 361)	−0.117	0.183	−0.628 to 0.393	−0.641	1
	CUDIT-R (n = 365)	0.066	0.021	0.008 to 0.124	3.162	0.015
Psychosis symptoms	Cannabis use days in the past month (n = 362)	−0.004	0.020	−0.058 to 0.051	−0.184	1
	Cannabis amount per day of use (n = 361)	0.035	0.054	−0.115 to 0.185	0.656	1
	CUDIT-R (n = 365)	0.009	0.006	−0.009 to 0.026	1.395	1

Separate cross-lagged mixed-effects models were estimated for each predictor–outcome combination across three waves (baseline, 6-month follow-up, 12-month follow-up). Models were adjusted for the respective lagged dependent variable and allocation group. All variables with skewed distributions were log-transformed prior to modeling. Estimates represent fixed effects of the lagged predictor on the subsequent outcome. CUDIT-R = Cannabis Use Disorders Identification Test – Revised. GAD-7 = Generalized Anxiety Disorder-7. PHQ-9 = Patient Health Questionnaire. Psychosis symptoms refer to the ERIraos adapted.

[a] CI were Bonferroni-corrected for multiple testing (CI = 99.4%).

[b] Bonferroni-corrected significance thresholds: α = 0.0056.

Table 3
Cross-lagged mixed-effects models examining associations of psychopathological symptom load and subsequent cannabis use patterns.

Dependent variable (DV)	Predictor	Estimate	SE	99.4% CI[a]	t-Value	P value[b]
Cannabis use days in the last 30 days	PHQ-9 (n = 357)	1.061	0.424	−0.120 to 2.145	2.501	0.116
	GAD-7 (n = 357)	1.055	0.375	0.011 to 2.099	2.815	0.047
	Psychosis symptoms (n = 357)	0.722	0.660	−1.115 to 2.561	1.095	1
Cannabis amount per average day of use	PHQ-9 (n = 352)	0.021	0.060	−0.147 to 0.189	0.352	1
	GAD-7 (n = 352)	0.012	0.054	−0.137 to 0.161	0.229	1
	Psychosis symptoms (n = 352)	0.208	0.094	−0.055 to 0.470	2.203	0.254
CUDIT-R	PHQ-9 (n = 365)	0.203	0.171	−0.273 to 0.678	1.189	1
	GAD-7 (n = 365)	0.186	0.148	−0.226 to 0.597	1.254	1
	Psychosis symptoms (n = 365)	0.342	0.253	−0.361 to 1.046	1.345	1

We adjusted for the respective lagged cannabis outcome and allocation group. Models were estimated using linear mixed-effects regression with random intercepts for participants. Variables were log-transformed where appropriate. Effect estimates reflect prospective associations between symptom load and subsequent cannabis use patterns. CUDIT-R = Cannabis Use Disorders Identification Test – Revised. GAD-7 = Generalized Anxiety Disorder-7. PHQ-9 = Patient Health Questionnaire. Psychosis symptoms refer to the ERIraos adapted.

[a] CI were Bonferroni-corrected for multiple testing (CI = 99.4%).

[b] Bonferroni-corrected significance thresholds: α = 0.0056.

symptom scores over time rather than large individual-level clinical shifts, the association between problematic cannabis use and depressive symptoms remained statistically significant after correction for multiple testing. In the present study, the absence of significant associations for cannabis use frequency and quantity across all psychopathological outcomes reinforces the specificity of the problematic use signal observed.

Turning to the reverse direction, we examined whether baseline psychopathological symptoms predicted subsequent changes in cannabis use patterns. Anxiety symptoms were associated with subsequent increased cannabis use frequency. No other psychopathological symptoms predicted changes in cannabis use patterns. These findings are partly in line with previous evidence, as prior longitudinal studies have reported inconsistent evidence for depression, anxiety, or psychosis as reliable predictors of increased cannabis use (Feingold et al., 2016; Danielsson et al., 2016). The association between baseline anxiety and subsequent cannabis use frequency is compatible with self-medication frameworks (Khantzian, 1987); however, given the observational design, causal interpretations are not warranted.

In contrast to previous literature on cannabis and psychosis risk, neither problematic use, frequency, nor quantity at BL predicted increased psychosis symptom load at follow-up in our sample. While robust evidence links cannabis use to psychosis risk (Ganesh and D'Souza, 2022), particularly with high-potency products in vulnerable individuals, our findings align with recent evidence from a large retrospective cohort study that found no significant increase in psychosis-related outcomes following cannabis legalization (Elser et al., 2023). This stands in stark contrast with findings of a large Canadian cohort study that found a significant increase in schizophrenia cases associated to CUD following cannabis legalization (Myran et al., 2025). In our sample, no such association was observed across any measure of cannabis use, albeit with important limitations due to exclusion criteria, observational period and population characteristics. Several factors may explain this apparent discrepancy: First, our regulated setting's THC content limits and quality controls may mitigate psychosis risk. Second, our exclusion criteria likely removed individuals at the highest risk of psychosis, thus limiting the study's ability to detect changes, and third, the one-year FU period may be insufficient to detect longer-term psychosis risk. Finally, the relatively older age of our sample (mean age = 36 years), composed of regular users with established consumption patterns, may also contribute. Individuals prone to severe psychosis may have already discontinued use earlier in life, as cannabis-related psychosis is more likely to emerge in younger, vulnerable individuals. Furthermore, the modest internal consistency of the adapted ERIraos (α = 0.53–0.54 at baseline and 6 months) may have additionally limited the sensitivity of our measure to detect subclinical changes.

5.2. Strengths and limitations

This study is among the first to explore bidirectional relationships between cannabis use patterns and psychopathological symptom load in a mimicked regulated setting. The longitudinal design and use of validated scales strengthen the reliability and relevance of our findings. However, the observational design limits causal inference, and self-reported data may introduce bias. Treatment-seeking behavior and medication use were not assessed. As such uncontrolled treatment effects may have attenuated symptom scores at follow-up, potentially leading to conservative estimates of the associations between cannabis use and psychopathological symptoms. The exclusion of subjects with existing, severe psychological issues, especially with acute psychosis and suicidality as well as the relatively short follow-up period may restrict the study's generalizability and capture of long-term effects. Additionally, the Swiss regulatory framework may limit the transferability of findings to other contexts. An additional limitation is that we included only active cannabis users; potential adverse effects of cannabis use on psychopathology may therefore have preceded study inclusion. Finally, regarding psychosis risk our study might be underpowered to detect changes in a population with a mean age of 36 years, as peak age for psychosis was reported to be close to 20 years (Solmi et al., 2022). Additionally, the relatively modest internal consistency of the adapted ERIraos at baseline and 6 months may have reduced sensitivity to detect associations involving psychosis-related symptoms. Despite our limitations, investigating the nuanced interplay of cannabis use and psychopathology in a study design that tries to mimic a regulated cannabis market might shed some light on an important ongoing discussion (Yimer et al., 2025). Our findings should be interpreted considering the study population, follow-up period and design. The sample consisted of adult, regular cannabis users participating in a regulated access framework and does not include adolescents, first-time users, or individuals at acute high psychiatric risk. Furthermore, the one-year follow-up limits conclusions regarding longer-term trajectories of cannabis use and psychopathology. Future research with extended follow-up periods and more diverse populations is needed to further clarify these relationships.

6. Conclusions

Our results suggest that problematic cannabis use prospectively predicted increases in depressive and anxiety symptom load among adult regular cannabis users in a regulated access setting. Furthermore, results showed associations between anxiety and later cannabis use frequency. The absence of prospective associations for cannabis use frequency and quantity underscores the importance of distinguishing problematic use from purely quantitative measures of consumption. Investigating the nuanced interplay of cannabis use and psychopathology in a regulated cannabis market might shed some light on an important ongoing discussion (Yimer et al., 2025). In the context of global legalization efforts and increasing cannabis use, these findings contribute to a more differentiated understanding of cannabis-related mental health associations. The current results suggest that the interplay between cannabis use and mental health may warrant consideration in both clinical and public health discussions surrounding cannabis regulation.

CRediT authorship contribution statement

C. Felix Mosandl: Writing – review & editing, Writing – original draft, Methodology, Investigation. **Eva-Maria Pichler:** Writing – review & editing, Writing – original draft, Methodology. **Maximilian Meyer:** Writing – review & editing, Investigation. **Adrian Guessoum:** Writing – review & editing, Investigation. **Oliver Herrmann:** Writing – review & editing, Investigation. **Jacqueline Curiger:** Writing – review & editing. **Jens Kronschnabel:** Writing – review & editing, Methodology, Formal analysis, Data curation. **Marc Vogel:** Writing – review & editing. **Marc Walter:** Writing – review & editing, Supervision, Project administration, Methodology, Funding acquisition, Conceptualization. **Lavinia Baltes-Flueckiger:** Writing – review & editing, Supervision, Resources, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization.

Declaration of Generative AI and AI-assisted technologies in the writing process

During the preparation of this work the author used Claude (Anthropic) in order to assist with cross-checking consistency between manuscript sections, Supplementary tables, rebuttal letter, and statistical output prior to submission. No AI tool was used for writing, data analysis, or generating scientific content. After using this tool/service, the author reviewed and edited the content as needed and takes full responsibility for the content of the published article.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Lavinia Baltes-Flueckiger reports financial support was provided by Canton Basel-Stadt, Switzerland. If there are other authors, they declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jad.2026.121604.

Data availability

De-identified sections of the dataset will be available from the corresponding author upon reasonable request from the time of publication.

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