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Recreational cannabis access via pharmacies: A 1-year Swiss study on cannabis use and mental health

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ABSTRACT

Background: While cannabis use has been linked to poorer mental health, the effects of regulated access remain unexplored. This study examined changes in psychopathology and cannabis-use patterns under pharmacy-based regulated access (pharmacist-dispensed, max 20% THC, ≤10 g THC/month) in Switzerland over 1 year.

Methods: Linear mixed-effects models analyzed changes in depressive and anxiety symptoms, problematic cannabis use, and cannabis-use frequency and quantity among 374 regular cannabis users with pharmacy access (mean age 35.8; 81% male), from baseline to 1-year follow-up, with subgroups by baseline problematic use (CUDIT-R ≥ 13 vs < 13).

Results: Mean depressive symptoms ($p < .0001$), anxiety ($p = .0008$), and problematic cannabis use (CUDIT-R; $p = .0002$) decreased significantly but by small amounts (PHQ-9 5.37 to 4.53). The proportion exceeding clinical thresholds did not change significantly over time (CUD: 32.7% to 28.6%, $p = .126$). Cannabis-use frequency increased modestly ($p = .0042$) and quantity was unchanged. Time explained almost none of the variance (marginal $R^2 < .01$); most of the variance reflected stable between-person differences (conditional $R^2 = .57–.70$). A group-by-time interaction showed a larger CUDIT-R reduction in the high-risk group ($p < .0001$). Adjusting for medication left all effects unchanged.

Conclusion: Over one year of pharmacy-based regulated access, psychopathological symptoms and problematic cannabis use showed small but significant mean decreases, while the proportion above clinical thresholds remained unchanged. Although the uncontrolled design precludes causal claims, these findings suggest that regulated access was not associated with deterioration in mental health or cannabis use.

1. Introduction

With over 244 million users globally, cannabis remains the most consumed controlled substance (United Nations Office on Drugs and Crime, 2025). Its consumer prevalence is growing globally and is expected to increase further because of legalization efforts, which raises concerns about related mental health consequences (Zellers et al., 2023). Research has linked cannabis use, especially of high potency variants, to several adverse mental health outcomes, including depression, anxiety, and psychosis (Di Forti et al., 2019; Hines et al., 2020; Sideli et al., 2020), and to heterogeneous effects on suicidal behaviors (Athanassiou et al., 2023). Reviews further highlight substantial risks of regular high-tetrahydrocannabinol (THC) cannabis use, including increased risks for cannabis-use disorder (CUD), psychosis, affective disorders, and suicidality (Hoch et al., 2025). These findings are part of a broader public health debate concerned with potential social and physical harms, including traffic injuries and cardiovascular disease (e.g., González-Sala et al., 2023; Mokwena, 2019). However, this

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evidence mostly comes from unregulated cannabis markets, where confounding factors, including product potency, contamination, and illicit market stressors, complicate interpretations, potentially conflating the substance's pharmacological effects with the psychosocial harms of participating in illegal markets (Hamilton and Sumnall, 2021). In the United States, for example, the potency of cannabis products increased significantly in legal markets, which has been linked to increasing adverse health consequences (Chiu et al., 2021). The mental health impact of structured, pharmacy-based regulated recreational cannabis access, however, is not well understood.

Longitudinal studies on cannabis use and mental health have produced mixed findings. Some data indicate increased risk for developing psychiatric symptoms with regular cannabis use, particularly when use was initiated in adolescence (McGee et al., 2000), whereas other findings indicate that associations between use and mental health symptoms are attenuated after accounting for confounding factors (Danielsson et al., 2016) or show stable outcomes in adults with established use patterns (Rose et al., 2024). This complexity is further highlighted by trends following recreational cannabis legalization, which show that adult consumption has increased in some jurisdictions while adolescent use has remained stable (Athanassiou et al., 2023). Overall, the mental health effects of recreational cannabis use may vary depending on the population and context, and longitudinal data from structured, public health-oriented access models remain scarce.

Cannabis consumption patterns, including frequency (Cougle et al., 2016), quantity (Mosandl et al., 2024), problematic cannabis use (Connor et al., 2021), and potency, which is often determined by the THC concentration (Petrilli et al., 2022), have been associated with mental health outcomes. These factors increase the risk of developing CUD (Connor et al., 2021). One in five weekly individuals who use cannabis (Leung et al., 2020) and approximately 10% of individuals who use cannabis are expected to develop CUD (Connor et al., 2021). Although individuals with greater problematic cannabis use tend to report greater psychiatric symptom burden (Jefsen et al., 2023; Onaemo et al., 2021), the influence of access regulation remains unclear. Emerging evidence suggests that cannabis use-related health outcomes may depend significantly on the context, including the regulatory environment (Hall et al., 2023). Reviews of the North American experience have highlighted how commercialized markets can lead to falling prices, rising product potency, and the creation of an industry interested in promoting regular use, thereby raising significant public health concerns (Hall et al., 2019). Regulated systems may reduce harm by controlling product quality, limiting access to high-risk subgroups, and enabling early health interventions. Therefore, a critical question is not simply whether regulated access increases consumption but whether it can fundamentally alter the relationship between consumption patterns and negative health outcomes, potentially decoupling use frequency from harm.

Switzerland recently introduced pharmacy-based regulated recreational cannabis access as a part of several pilot trials evaluating the effects of legalized recreational use on problematic cannabis use and related health outcomes (Baltes-Flueckiger et al., 2023, Buschner et al., 2024). Initial findings suggest reduced cannabis misuse among participants with legal access, although the results did not reach statistical significance (Baltes-Flueckiger et al., 2025). Recent reviews have highlighted post-legalization increases in cannabis-related emergency visits, CUD symptoms, and acute psychiatric presentations in Canada and the United States (Chiu et al., 2021: Farrelly et al., 2023; Yimer et al., 2025). However, treatment-seeking for CUD has declined, possibly because of fewer referrals from the justice system. These mixed findings underscore the importance of studying mental health trajectories under structured, health-focused access models.

This study examines how depressive symptoms, anxiety, and problematic use patterns can evolve over 1 year in individuals accessing cannabis through the structured system. Given previous evidence on problematic cannabis use and psychiatric burden (Leung et al., 2020), these symptoms were chosen because of their high prevalence among individuals with CUD and their significant impact on overall mental health. We further explore differences between participants in the high- and low-risk subgroups. The findings, based on the ongoing Weed Care study in Basel-Stadt, Switzerland, may help inform evidence-based policy recommendations and targeted intervention strategies, particularly in the context of increasing cannabis legalization worldwide (Baltes-Flueckiger et al., 2023; Hall et al., 2023).

2. Materials and methods

2.1. Design

This one-year longitudinal study investigated pharmacy-based regulated recreational cannabis access within the Weed Care project (NCT05522205). Baseline (BL) assessments were conducted in January 2023 with follow-up (FU) after 6 months and 1 year. The local Ethics Committee (Ethikkommission Nordwest- und Zentralschweiz [EKNZ], protocol number 2021-01670) and the Swiss Federal Public Health Office (approval number 2022/000001) approved the study. All participants provided written informed consent before undergoing any study-related procedures. This process was conducted in accordance with the Declaration of Helsinki and ICH-GCP guidelines. The Weed Care study was originally designed as a randomized controlled trial with staggered access conditions during the first 6 months (Baltes-Flueckiger et al., 2023). Because the present analysis covers the full 12-month period, during which both the intervention and the delayed-start control arm had identical access to the regulated pharmacy model, the design corresponds to a pooled within-subject pre–post analysis with allocation group as a covariate rather than a between-arm comparison. However, the current analysis focuses on the 1-year FU period; results are reported for BL and 12-month changes, consistent with the study focus. While access conditions were staggered during the first 6 months (accounted for by including allocation group as a covariate in all models), all intervention group participants had access to regulated cannabis from BL and all control group participants from 6 months onward. This design ensured comparable exposure conditions, consistent product quality, and THC concentration during the study's latter half. Cannabis pricing was subsidized to mirror illicit market rates and ensure realistic consumption scenarios. Use of the regulated pharmacy channel was non-exclusive: participants were free to obtain cannabis from the illegal market in parallel, and over the 12-month period approximately 51% of self-reported cannabis consumption was sourced from the regulated pharmacies and 49% from the illegal market. On average, participants purchased cannabis from the regulated pharmacies on 14.6 days per month (SD = 11.6). At every dispensation, trained pharmacists provided structured counseling on responsible use, lower-risk consumption practices, and the recognition of problematic use, and could refer participants to specialist services where indicated; participants did not, however, receive a structured psychotherapeutic or pharmacological intervention as part of the regulated access model. Participants completed online questionnaires on their cannabis consumption behavior, mental health, and physical health every 6 months. A detailed study protocol has been published previously (Baltes-Flueckiger et al., 2023).

2.2. Eligibility criteria

To participate in the study, individuals had to provide written informed consent, be at least 18 years old, report monthly cannabis use for the past 6 months, and test positive on a urine THC screen at BL (immunoassay, 50 ng/mL THC-COOH cut-off). Additional requirements included adequate German language skills and internet access to complete the questionnaires (Baltes-Flueckiger et al., 2023). Only Basel-Stadt canton residents were eligible for participation, in agreement with local law. Exclusion criteria included acute suicidality or

psychosis, current psychiatric hospitalization, severe cognitive impairment, and pregnancy or breastfeeding. Participation eligibility was subject to exclusion criteria and evaluated through a thorough in-person screening with a research physician to ensure the absence of serious medical issues.

2.3. Recruitment

The Swiss public was informed about the study in August 2022 through a local media conference. Interested individuals could register online and subsequently receive a phone call to undergo screening for eligibility. Eligible participants were invited to a face-to-face interview with a study physician. During this interview, they received comprehensive information about the study and were asked to provide written informed consent. The total sample size of $N = 374$ was set by the original randomized controlled trial protocol (Baltes-Flueckiger et al., 2023), which was powered for a between-arm comparison on the Cannabis Use Disorders Identification Test-Revised (CUDIT-R) at 6 months. The present 12-month analysis is a secondary, within-subject pre–post analysis of the same cohort and was not subject to a separate a priori power calculation; results should therefore be interpreted as descriptive of within-person change rather than as a confirmatory test of a between-arm intervention effect. Recruitment began in September 2022 and was completed in March 2023.

The final BL sample comprised 374 participants. Four participants withdrew before BL assessment and were replaced. Thirty-six participants (9.5%) were lost to FU at the 1-year assessment. All available data from these 36 participants were included in the final longitudinal analyses, as the linear mixed-effects models (LMMs) used can accommodate missing data.

2.4. Data collection

Data collection began in January 2023; sociodemographic information on 374 participants was collected. Participants completed online questionnaires assessing cannabis consumption, mental health, and physical health every 6 months (Mosandl et al., 2024).

Cannabis-use patterns were captured through three measures: cannabis-use frequency (defined as number of use-days in the past 30 days), cannabis-use quantity (average grams consumed per use-day), and problematic cannabis use. The questionnaire included pictures of different cannabis amounts next to a coin to help participants visually estimate their cannabis consumption. Problematic cannabis use was assessed via the CUDIT-R (Adamson et al., 2010), a validated screening tool with scores ranging from 0 to 32, where higher scores indicate more problematic cannabis use. A threshold score of 13 was used to indicate possible CUD. For clarity, we refer to participants with a CUDIT-R score ≥ 13 as "participants in the high-risk subgroup" and those below this threshold as "participants in the low-risk subgroup" throughout this paper. This classification was based on BL data.

Depressive, anxiety, and psychotic symptoms were measured with the Patient Health Questionnaire depression scale (PHQ-9; Kroenke et al., 2001), the Generalized Anxiety Disorder Screener (GAD-7; Löwe et al., 2002), and an adapted version of the Early Recognition Inventory (ERIraos) Checklist (Maurer et al., 2006), respectively. Validated German versions of the PHQ-9, GAD-7, ERIraos, and CUDIT-R were used. The German versions of these questionnaires have been widely used in clinical and research settings. For the PHQ-9 and GAD-7, validated German manuals and publications by German-speaking authors were consulted (Kroenke et al., 2001; Löwe et al., 2002). The ERIraos and CUDIT-R also have established German versions, supported by literature from German-speaking sources (Adamson et al., 2010; Maurer et al., 2006). The ERIraos checklist used in this study included six items on 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." Total scores were calculated for each psychopathological scale (PHQ-9, GAD-7, ERIraos) by summing individual item scores. Higher scores reflect greater symptom severity. A score of 10 is the recommended threshold for moderate-to-severe depression and moderate-to-severe generalized anxiety disorder (Kroenke et al., 2001; Löwe et al., 2002).

In addition, medication use was assessed at baseline and at the 6- and 12-month follow-ups with a 10-item scale on which participants rated how often they had taken each of ten medication classes, with responses ranging from 0 (never) to 4 (almost daily/daily). For the present analyses, we drew on the psychotropic classes captured by this scale — antidepressants, sedatives/benzodiazepines, antipsychotics, and stimulants — together with an item on cannabis-specific counseling.

2.5. Statistics

Descriptive statistics are presented as frequencies (%) for categorical variables and means (SD) for continuous variables. We used LMMs for analyzing the nested structure of repeated-measures data (BL, 6-month FU, and 1-year FU) and handling missing data. As the study focused on 1-year changes, only BL and 12-month results are reported. We used a two-level model, with measurements nested within participants which were included as random effects LMMs were estimated to evaluate changes from BL to FU at 6 months and FU at 1 year in depressive symptoms (PHQ-9), anxiety symptoms (GAD-7), and psychotic symptom load (ERIraos), as well as changes in cannabis-use patterns: frequency (use-days in the past 30 days), quantity (grams per use-day), and problematic cannabis use (CUDIT-R). For each variable a separate LMM was performed. To assess the variance explained, marginal R^2 (approximating variance explained by fixed effects) and conditional R^2 (approximating variance explained by both fixed and random effects) were calculated (Nakagawa and Schielzeth, 2013).

Subgroup analyses stratified participants by CUDIT-R thresholds (possible CUD, CUDIT-R ≥ 13, vs. non-CUD, CUDIT-R < 13) to examine differential outcomes in mental health symptoms and cannabis-use patterns over time. The CUDIT-R cutoff of ≥ 13 was chosen because it has been validated against DSM-IV-based clinical interviews as the threshold most strongly indicative of possible cannabis use disorder, with high sensitivity and specificity (Adamson et al., 2010), and it is the cutoff most consistently used in the recent international cannabis literature to define the high-risk/CUD subgroup. To assess whether findings were sensitive to a less conservative definition of hazardous use, a parallel set of interaction analyses was performed using the alternative CUDIT-R cutoff of ≥ 8 (hazardous cannabis use) versus < 8 (Supplementary Section S6); these analyses yielded a comparable pattern of results. For this, an interaction term between group by CUDIT-R threshold and time was added to the LMM.

All models included group allocation (intervention group with access to legal cannabis from BL vs. control group with access to legal cannabis after 6 months) as adjusting covariate. All analyses were conducted with R software version 4.2.2 (2022-10-31) using the lme4 package. All p values were two-sided, and statistical significance was set at $\alpha = 0.05$.

To examine whether concurrent psychotropic medication or cannabis counseling could account for the observed changes, we repeated the models for depressive symptoms (PHQ-9), anxiety symptoms (GAD-7), problematic cannabis use (CUDIT-R), and psychotic symptoms (ERIraos) with the four psychotropic medication classes and the cannabis-counseling item added as covariates (sensitivity analyses).

Analyses were conducted using LMMs, which include all available data under the missing-at-random assumption. This approach accounts for attrition (e.g., 9.5% at 1-year FU).

3. Results

3.1. Demographic characteristics

Table 1 provides a brief sociodemographic description of the BL study population (N = 374). Most participants were male (81%), with a mean age of 35.8 years (SD = 11.4), and 75% were of Swiss nationality. A detailed description has been published previously (Baltes-Flueckiger et al., 2025).

3.2. Changes over time

LMMs revealed significant changes from BL to 1-year FU (Table 2). Significant reductions occurred for depressive symptom load (PHQ-9; Estimate = −0.357, CI [−0.530, −0.184], p < .0001), anxiety symptom load (GAD-7; Estimate = −0.251, 95% CI [−0.396, −0.106], p = .0008), and problematic cannabis use (CUDIT-R; Estimate = −0.354, 95% CI [−0.540, −0.168], p = .0002) (Figs. 1a, 1d and 1e). In contrast, cannabis-use frequency increased significantly (Estimate = 0.690, 95% CI [0.220, 1.160], p = .0042) (Fig. 1b).

Table 1
Baseline characteristics of study participants.

Characteristic	Total (n = 374)	Low-risk subgroup (CUDIT-R < 13; n = 248)	High-risk subgroup (CUDIT-R ≥ 13; n = 126)
Sex (n = 370)	299 (81%)	198 (81%)	101 (82%)
Male	65 (17%)	44 (18%)	21 (14%)
Female	6 (2%)	4 (2%)	2 (2%)
Non-binary			
Age (years, n = 370)	35.8 (11.4)	36.3 (11.1)	35.4 (12.4)
Swiss nationality (n = 370)	277 (75%)	181 (73%)	97 (77%)
Education, no. (%)			
Obligatory school	36 (10%)	20 (8%)	16 (13%)
Basic vocational school	113 (30%)	68 (27%)	45 (36%)
University qualification	57 (15%)	35 (14%)	22 (18%)
Higher vocational education	28 (8%)	19 (8%)	9 (7%)
University degree	136 (36%)	105 (42%)	31 (25%)
Other	4 (1%)	1 (0.4%)	3 (2%)
Employment status, no. (%)			
Paid employment	281 (75%)	198 (80%)	83 (66%)
Unemployed	20 (5%)	12 (5%)	8 (6%)
Non-working (retired, home maker, training)	73 (20%)	38 (15%)	35 (28%)
CUDIT-R (possible range 0–32), mean (SD)	11.0 (4.6)	8.4 (2.8)	16.1 (2.7)
PHQ-9 (possible range 0–27), median (IQR)	4 (3, 7)	4 (2, 6)	5.5 (4, 8)
PHQ-9 ≥ 10, no. (%)	51 (14)	27 (11%)	24(19%)
GAD-7 (possible range 0–21), median (IQR)	3 (1, 5)	3 (1, 4)	4 (2.3, 6.8)
GAD-7 ≥ 10, no. (%)	23 (6%)	13 (5%)	10 (8%)
Psychotic symptoms (possible range 0–7), median (IQR)	0 (0, 1)	0 (0, 1)	0 (0, 1)
Cannabis use frequency (days per month), median (IQR)	21 (7, 30)	15 (5, 27)	30 (20, 30)
Cannabis amount per use day (in grams), median (IQR)	0.5 (0.2, 2)	0.5 (0.2, 1)	1 (0.5, 2)

Data are presented as number (%) or mean (SD). The number of participants with available baseline data for each measure is provided when it differs from the total number in the group.

No significant changes were found for psychotic symptoms (ERIraos; Estimate = −0.025, 95% CI [−0.070, 0.020], p = .283) or cannabis-use quantity (grams per day; Estimate = 0.041, 95% CI [−0.026, 0.108], p = .225) (Figs. 1c and 1 f).

For all models, the variance explained by fixed effects (marginal R^2) was consistently below .01, while the variance explained by the full models including random effects was substantial (conditional R^2 ranging from .565 to .703), indicating that most variability was attributable to stable between-participant differences (Table 2).

These time effects were robust to adjustment for concurrent treatment. In sensitivity analyses additionally including psychotropic medication (antidepressants, sedatives/benzodiazepines, antipsychotics, stimulants) and cannabis counseling as covariates, the reductions in depressive symptoms, anxiety symptoms, and problematic cannabis use remained statistically significant and essentially unchanged in magnitude, and psychotic symptoms remained non-significant.

McNemar's test showed that the proportion of participants exceeding clinical thresholds did not change significantly from BL to 1-year FU among participants with complete BL and 1-year FU data (n = 339). The proportion with possible CUD (CUDIT-R ≥ 13) decreased from 32.7 to 28.6% ($\chi^2(1) = 2.35$, p = .126); among participants classified as high-risk at BL with available FU data (n = 111), 87.4% (n = 97) remained in the high-risk category at 12 months, those with moderate-to-severe depressive symptoms (PHQ-9 ≥ 10) declined from 12.7% to 8.9% ($\chi^2(1) = 3.51$, p = .061), and those with moderate-to-severe anxiety symptoms (GAD-7 ≥ 10) declined from 5.3% to 4.4% ($\chi^2(1) = 0.21$, p = .646). Distributional properties of CUDIT-R scores in the low-risk subgroup were acceptable across time points, with only minor fluctuations in skewness (BL: skew = −0.53; 6-month FU: skew = 0.60; 12-month FU: skew = 0.13), indicating no evidence of substantial floor effects. In addition, allocation group (immediate vs. delayed access) was not significantly associated with any of the primary outcomes in the adjusted LMMs: PHQ-9 (b = 0.304, p = .353), GAD-7 (b = −0.098, p = .735), psychotic symptoms (b = 0.035, p = .658), cannabis-use frequency (b = 0.463, p = .615), and cannabis-use quantity (b = −1.144, p = .290); see Supplementary Tables S1–S5.

3.3. Subgroup analysis by baseline risk

At BL, 33.7% (126 out of 374) of participants were classified as high-risk subgroup participants (CUDIT-R ≥ 13). A significant group-by-time interaction was found for problematic cannabis use (b = −1.15, t = −5.86, p < .0001; Table 3). The fixed effects in this interaction model explained 42.3% of the variance in CUDIT-R scores (marginal R^2 =.423), while the full model explained 71.6% (conditional R^2 =.716).

Participants in the high-risk subgroup showed a significant reduction in CUDIT-R scores from BL (M = 16.11, SD = 2.74) to 1-year FU (M = 13.89, SD = 4.26). In contrast, scores for participants in the low-risk subgroup remained stable (BL: M = 8.44, SD = 2.81; FU: M = 8.48, SD = 2.81). The results of the interaction analysis are depicted in Table 3 and Fig. 1.

No significant group-by-time interactions were found for changes in cannabis-use frequency (p = .086), cannabis consumption quantity (p = .592), depressive symptom load (p = .435), anxiety symptom load (p = .643), or psychotic symptoms (p = .771), indicating similar trajectories for both risk groups on these outcomes (Supplementary Tables S1–S5).

4. Discussion

The central finding after 1 year of pharmacy-based regulated recreational cannabis access represents a divergence: while cannabis-use frequency increased significantly from an average of 18.7–20.1 days per month (p = .0042), problematic cannabis use (CUDIT-R score), as well as depressive and anxiety symptom loads, showed small but statistically significant decreases in the overall sample (Table 2). This

Table 2
Descriptive statistics on psychopathological symptoms and cannabis use at baseline and 12-month follow-up and model results.

	Baseline	12-month follow-up					
Measure	**M (SD)**	**M (SD)**	**Estimate**	**SE**	**t-value**	**p value**	**Variance (SD)**
PHQ-9 (n = 374)	5.37 (3.79)	4.53 (3.71)					
Fixed effects							
Intercept			5.489	0.295	18.593	< .001***	
Time			-0.357	0.088	-4.078	< .001***	
Random effects							
Random intercept variance (SD)							8.872 (2.979)
Model fit							
Marginal R^2	.007						
Conditional R^2	.626						
GAD-7 (n = 374)	3.81 (3.35)	3.20 (3.09)					
Fixed effects							
Intercept			4.074	0.256	15.947	< .001***	
Time			-0.251	0.074	-3.384	< .001***	
Random effects							
Random intercept variance (SD)							6.878 (2.623)
Model fit							
Marginal R^2	.005						
Conditional R^2	.643						
Psychotic symptoms (n = 374)	0.51 (0.92)	0.43 (0.96)					
Fixed effects							
Intercept			0.515	0.072	7.122	< .001***	
Time			-0.025	0.023	-1.074	.283	
Random effects							
Random intercept variance (SD)							0.474 (0.688)
Model fit							
Marginal R^2	.001						
Conditional R^2	.565						
Cannabis use-days in the past month (n = 372)	18.67 (10.91)	20.13 (10.75)					
Fixed effects							
Intercept			17.998	0.854	21.081	< .001***	
Time			0.690	0.240	2.872	.0042**	
Random effects							
Random intercept variance (SD)							79.700 (8.927)
Model fit							
Marginal R^2	.003						
Conditional R^2	.680						
Cannabis amount per use-day (n = 372)	1.18 (1.54)	1.24 (1.48)					
Fixed effects							
Intercept			1.247	0.119	10.442	< .001***	
Time			0.041	0.034	1.213	.225	
Random effects							
Random intercept variance (SD)							1.534 (1.238)
Model fit							
Marginal R^2	.004						
Conditional R^2	.675						
CUDIT-R (n = 374)	11.02 (4.58)	10.25 (4.51)					
Fixed effects							
Intercept			11.647	0.352	33.063	< .001***	
Time			-0.354	0.095	-3.746	< .001***	
Random effects							
Random intercept variance (SD)							14.532 (3.812)
Model fit							
Marginal R^2	.009						
Conditional R^2	.703						

Model results (Estimate, SE, t-value, p value) are from linear mixed-effects models assessing changes from baseline to the 12-month follow-up (utilizing baseline, 6-month, and 12-month data points), adjusted for allocation group (see Methods 2.5). Random intercept variance is the proportion of the total variability in an outcome that reflects differences in baseline levels across individuals. The marginal R^2 indicates how much of the total variance is explained by the fixed effects (i.e., the predictors) alone. The conditional R^2 indicates how much of the model's variance is explained by the full model (fixed and random effects / between-person random intercept).

Abbreviations: M = Mean; SD = Standard deviation; SE = Standard error; PHQ-9 = Patient Health Questionnaire-9; GAD-7 = Generalized Anxiety Disorder 7-item scale; ERIraos = Early Recognition Inventory for the retrospective assessment of the onset of schizophrenia; CUDIT-R = Cannabis Use Disorders Identification Test-Revised. ***p < 0.001, **p < 0.01, *p < 0.05.

finding challenges the common assumption that increased frequency of cannabis use necessarily translates into greater harm or adverse public health outcomes (Garrett et al., 2025). These mean-level improvements were small and did not correspond with statistically significant reductions in the proportion of participants exceeding clinical thresholds (PHQ-9 ≥ 10; GAD-7 ≥ 10; CUDIT-R ≥ 13). This complex pattern, especially the divergence between frequency and harm, suggests that the regulatory framework may foster safer consumption patterns, yet also highlights the continued need for targeted interventions for participants in the high-risk subgroup.

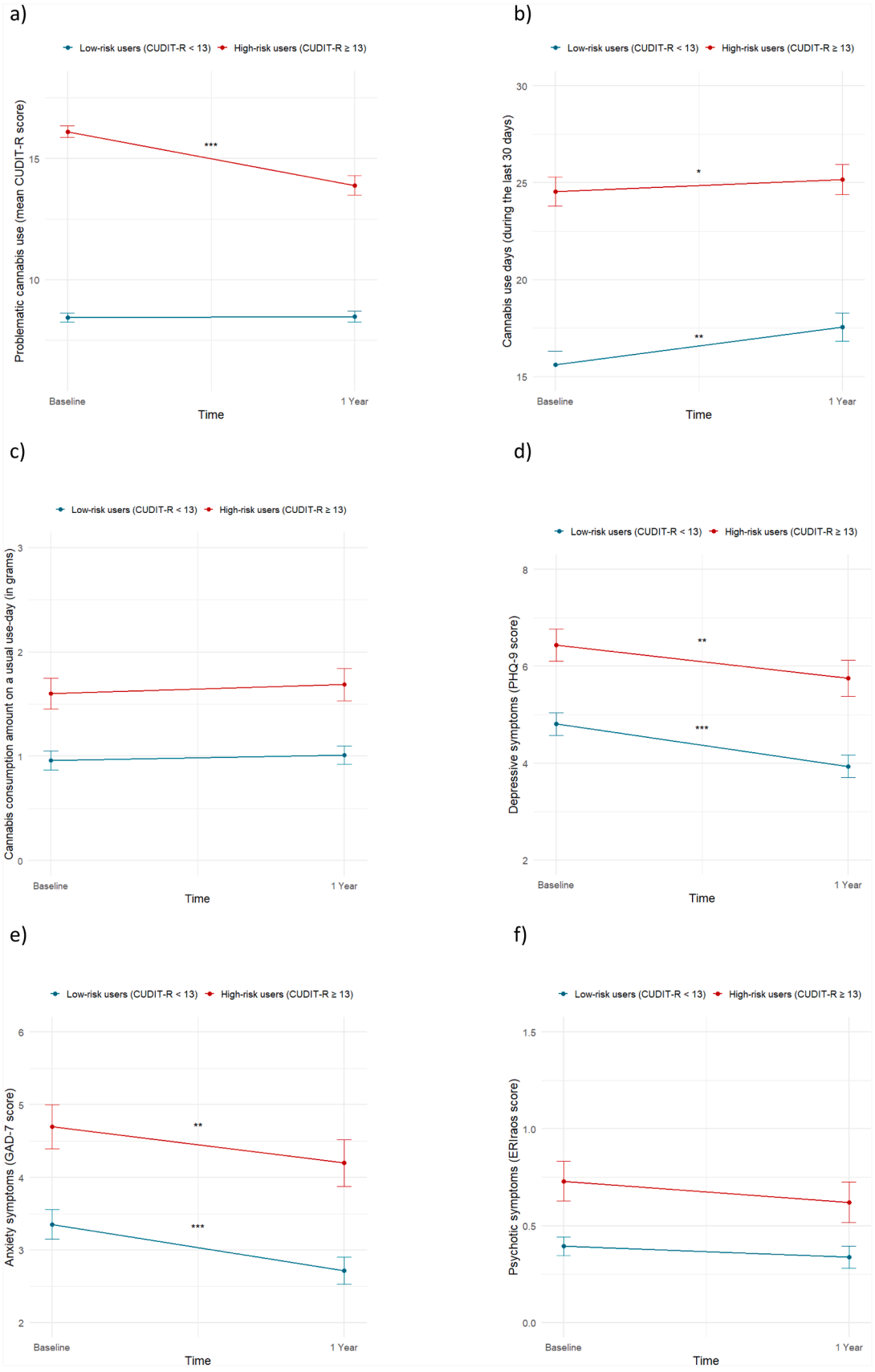

Fig. 1. Changes in cannabis use and psychopathology from baseline to 1-year follow-up, by baseline risk group (low-risk users: CUDIT-R < 13, n = 248; high-risk users: CUDIT-R ≥ 13, n = 126). (a) Problematic cannabis use (CUDIT-R score); (b) cannabis-use days during the last 30 days; (c) cannabis consumption amount on a usual use-day (in grams); (d) depressive symptoms (PHQ-9 score); (e) anxiety symptoms (GAD-7 score); (f) psychotic symptoms (ERIraos score). Data points represent group means, error bars represent standard errors of the mean. ***$p < 0.001$, **$p < 0.01$, *$p < 0.05$.

Table 3
Interaction analysis between group (high-risk vs. low-risk subgroup according to CUDIT-R) and time on problematic cannabis use.

Predictor	Estimate	SE	t-value	p value	Variance (SD)
CUDIT-R (n = 374)					
Fixed effects					
Intercept	8.634	0.326	26.495	< .001***	
Time	0.029	0.113	0.254	.799	
Group (low vs. high CUDIT-R)	8.425	0.495	17.038	< .001***	
Group (low vs. high CUDIT-R) x time	-1.149	0.196	-5.864	< .001***	
Control variable (allocation group)	-0.286	0.298	-0.960	.338	
Random effects					
Random intercept variance (SD)					6.142 (2.478)

Results from the linear mixed-effects model examining the interaction between a risk subgroup (low-risk vs. high-risk according to the CUDIT-R score at baseline) and time on problematic cannabis use (CUDIT-R score). The model was adjusted for the allocation group as a covariate. Random intercept variance is the proportion of the total variability in an outcome that reflects differences in baseline levels across individuals.
Abbreviations: SE = Standard error; CUDIT-R = Cannabis Use Disorders Identification Test-Revised. ***p < 0.001, **p < 0.01, *p < 0.05.

This heterogeneity is also reflected in the variance components. While the mean-level improvements were statistically significant, the fixed effect of time explained only a small fraction of the variance. The majority of the variance was attributable to stable, between-participant differences (see Table 2). Critically, these findings imply that regulated access did not affect all participants uniformly. This points to the value of subgroup analyses to understand who benefits most and why.

Both the high- and low-risk subgroups showed comparable reductions in depressive and anxiety symptom loads over time. In contrast, a marked difference emerged in problematic cannabis use: participants in the high-risk subgroup demonstrated a significant reduction in CUDIT-R scores (mean change from 16.11 at BL to 13.89 at 1-year FU), exceeding the two-point threshold considered a clinically reliable change (Adamson et al., 2015), a finding that parallels observations in Canada, where young adults with high-frequency cannabis use also showed significant post-legalization reductions in use and related consequences (Doggett et al., 2023). Participants in the low-risk subgroup, by comparison, showed no change (Table 3; Fig. 1). The interaction between BL risk group and time was highly significant and, together with other fixed effects, explained a considerable proportion of the variance in CUDIT-R changes, largely reflecting the influence of BL risk classification. Psychotic symptom load and cannabis-use quantity remained stable, while cannabis-use frequency increased similarly across groups.

Reductions in depressive and anxiety symptoms were of comparable magnitude in the high- and low-risk subgroups (no significant group-by-time interactions, p = .435 and p = .643), whereas the significant CUDIT-R reduction was confined to the high-risk subgroup (p < .0001). This dissociation argues against reduced problematic use as a mediator of the affective improvements; a formal mediation test would require an adequately powered longitudinal design.

Taken together, these findings indicate that regulated access may support improvements in affective symptom load across all participants, with particular benefits for reducing problematic use among individuals at high risk. However, given that the mean score in the high-risk subgroup remained close to the clinical threshold for CUD, consistent with evidence from Canada indicating that legalization alone does not substantially reduce problematic use among individuals at high risk (Hall et al., 2023), additional targeted interventions may still be required to adequately address underlying psychopathology.

One explanation for the observed decrease in problematic use and affective symptom load, despite increased consumption frequency, is that the regulatory framework itself provided protective elements that mitigated risks typically associated with higher-frequency use (Hall et al., 2023; Robinson et al., 2023). Reduced exposure to illicit market stressors, consistent product quality with known THC content, and lower stigma may have contributed to these stabilizing effects. Regular contact with healthcare professionals in pharmacies may also have supported more informed use and facilitated early identification of health needs, consistent with evidence from a recent scoping review highlighting the role of health and social service practitioners in adopting harm-reduction practices (Haddad et al., 2024).

By contrast, systematic reviews indicate that increased retail availability in commercialized markets is associated with higher use frequency and greater cannabis-related health harms (Cantor et al., 2024), a trend consistent with recent US data showing increased cannabis use post-legalization (Segura et al., 2025). These divergent outcomes underscore that effects of legalization are not monolithic but are critically shaped by the specific policy design, particularly the extent of commercialization and profit motives (Fischer et al., 2025; Kilmer, 2019). Commercial models have further been linked to falling prices, rising potency, and profit-driven promotion of frequent use, raising significant public health concerns (Hall et al., 2019). Evidence from California further supports these concerns: Bass et al. (2025) found that recreational cannabis legalization was associated with reduced treatment retention and lower rates of successful discharge among individuals in publicly funded CUD treatment. Further evidence from Canada suggests that legalization alone may not substantially alter cannabis-use trajectories among individuals with pre-existing substance use disorders. However, Britton et al. (2024) reported increases in CUD symptom severity following the expansion of edibles and other commercial products, underlining that harms may emerge particularly in the context of commercialization.

Our findings also extend prior randomized evidence from Switzerland, which showed a non-significant trend toward reduced cannabis misuse under a pharmacy-based model without changes in mental health outcomes at 6 months (Baltes-Flueckiger et al., 2025). In contrast, we observed reductions in problematic use, particularly among participants in the high-risk subgroup, alongside improvements in affective symptoms over 1 year. As highlighted in a recent commentary, such impacts of recreational cannabis regulation are likely to be model-specific, and common indicators such as the CUDIT-R may require reconsideration in the context of legal markets (Sznitman et al., 2025). Together, these findings support our interpretation that regulatory design, rather than legalization per se, is critical for public health outcomes. The non-commercial, pharmacy-based model evaluated here may therefore represent a regulatory alternative that mitigates such risks and alters the relationship between consumption patterns and adverse health outcomes.

The present findings should not be read as an endorsement of cannabis use as a treatment for depressive or anxiety symptoms. The observed associations emerge in a population of regular cannabis users within a structured regulatory framework; the magnitude of mental-health change is modest, of uncertain causal origin, and accompanied by ongoing exposure to cannabis-related harms, including dependence, cognitive impairment, and, in younger or vulnerable individuals, psychotic symptoms (Hoch et al., 2025). Established evidence-based interventions for depression and anxiety (psychotherapy and pharmacotherapy) remain the appropriate first-line approach for clinically relevant affective disorders. The pharmacy-based model evaluated here is best understood as a public-health-oriented harm-reduction framework for individuals who already use cannabis, not as a clinical alternative to psychiatric treatment.

Generalizability to other regulatory contexts is limited. The Swiss model operates within a high-income, universal-coverage health-care system with low-threshold mental-health services and comparatively

low cannabis-related stigma. Jurisdictions with substantially stricter regulation (for example China, Japan, and the Republic of Korea) differ in underlying use prevalence, stigma, criminal-justice consequences, and harm-reduction infrastructure (Kilmer, 2019; Hall et al., 2023). The present results should therefore not be transposed to such settings; they speak to the principle that specific design parameters (non-commercial dispensing, quality control, monthly limits, pharmacist counseling), rather than legalization per se, appear critical for public-health outcomes.

4.1. Stability of cannabis use and psychotic symptom load

Psychotic symptom load (ERIraos) and cannabis-use quantity remained stable over the study period, while cannabis-use frequency increased. This is an important finding, given common concerns that regulated access might lead to increased use. The stability in cannabis-use quantity and psychotic symptom load, despite increased use frequency, suggests a nuanced impact of the regulatory framework on pre-existing consumption habits and related symptoms. However, individuals at high risk for severe cannabis-related psychotic symptoms may have been underrepresented in this sample, given the study's inclusion criteria. With a mean age of 35.8 years, most participants were past the high-risk period for onset of a cannabis-precipitated psychosis, which is highest in younger, more vulnerable individuals (D'Souza et al., 2022; Elser et al., 2023). Future studies with longer follow-ups and higher-risk populations are essential to clarify long-term effects of legalization on psychosis risk.

4.2. Strengths and limitations

This study is among the first to examine longitudinal changes in cannabis-use patterns and psychopathological symptom load in a regulated market setting. The longitudinal design with 1-year FU and use of validated assessment scales strengthened the reliability and relevance of our findings. Subgroup analyses provided nuanced insights into differential effects of regulated access across risk profiles, enhancing the study's applicability to harm-reduction strategies. The proportion of participants meeting clinical thresholds for possible cannabis use disorder, depression, or anxiety did not increase over the year, and the study took place under the real-world conditions of regulated pharmacy access.

However, several limitations must be acknowledged. First, the present analysis is based on within-subject pre–post comparisons pooled across the intervention and delayed-start control arm and therefore cannot isolate the causal effect of the regulated pharmacy model from secular trends, regression-to-the-mean, and study participation effects; this is particularly relevant for the observed reductions in depressive and anxiety symptom loads, where BL severity was low and floor effects are likely. Despite including allocation group as a covariate, the unequal exposure duration at the 12-month assessment (12 months in the intervention arm vs. approximately 6 months in the delayed-start arm) introduces residual confounding that statistical adjustment cannot fully eliminate. Second, approximately 51% of cannabis consumption was sourced from the regulated pharmacy channel and 49% from the illegal market, so exposure to the regulated model was partial and co-occurred with continued illegal-market use, further limiting conclusions about the regulatory framework in isolation. Third, all cannabis-use and mental-health variables were self-reported and therefore susceptible to recall and social-desirability bias; cannabis-use frequency in particular was strongly right-skewed, and the bimodal CUDIT-R distribution reflects the predefined risk-subgroup stratification, which may affect model performance despite the robustness of LMMs. Fourth, exclusion of participants with severe pre-existing psychiatric conditions (e.g., acute psychotic or severe mood disorders, high suicidality) and the 12-month FU restrict the capture of rare adverse outcomes such as incident psychosis or chronic CUD trajectories; longer-term observation is needed to assess whether the observed short-term patterns persist or change in clinically relevant ways (Hoch et al., 2025; Yimer et al., 2025).

A further limitation concerns concurrent treatment received outside the regulated-access model. Psychotropic medication was recorded, and sensitivity analyses adjusting for antidepressants, sedatives/benzodiazepines, antipsychotics, stimulants, and cannabis counseling left the time effects essentially unchanged, indicating that the reductions are not accounted for by concurrent pharmacological treatment. Non-pharmacological treatment, such as psychotherapy, was not assessed, and therefore remains a potential confounder. Consequently the observed associations cannot be attributed to regulated access. Finally, the PHQ-9 and GAD-7 are screening instruments covering only the two weeks before each assessment; they index symptom state at three discrete time points rather than the clinical course.

A key statistical limitation relates to the models' explanatory power. Specifically, the fixed effects explained only a negligible proportion of the variance in mental health changes, such as depressive and anxiety symptoms. While the full models accounted for a substantial portion of variance through stable between-participant differences, a notable amount of residual variance remained unexplained. These trajectories are likely shaped not only by regulated access but also by unmeasured factors such as stressful life events or social support, which are established moderators of the stress–cannabis use link (Cavalli and Cservenka, 2021). Depression itself may also act as a confounder or moderator rather than solely as an outcome (Maffre Maviel et al., 2025), adding to the complexity of individual responses within a regulated access system.

Despite these limitations, this study provides valuable insights into the longitudinal development of mental health outcomes and cannabis-use patterns in pharmacy-based regulated recreational cannabis access and indicates the need for tailored interventions for participants in the high-risk subgroup.

5. Conclusions

Regulated cannabis access was associated with small but statistically significant reductions in depressive and anxiety symptom loads and with a decrease in problematic cannabis use as measured by the CUDIT-R. Cannabis-use quantity remained essentially unchanged, while cannabis-use frequency increased modestly over the 12-month period. The decline in CUDIT-R scores was most pronounced among participants in the high-risk subgroup; however, their mean CUDIT-R score at FU ($M = 13.89$) remained above the clinical threshold for possible cannabis use disorder, indicating that meaningful problematic use persisted in this subgroup. Improvements in affective symptom loads were observed across the sample but did not differ significantly between the high- and low-risk subgroups, and the magnitude of these changes is also compatible with regression-to-the-mean and floor effects given low BL severity in part of the sample. Because this analysis is uncontrolled and limited to participants who continued to access the regulated pharmacy model, no causal claims about the regulatory model itself can be made. Within these limits, the findings are consistent with the hypothesis that public health-oriented regulation in conjunction with pharmacist counseling may help to reduce specific cannabis-related harms, while underlining the need for integrated clinical support for individuals with elevated psychiatric risk. Future controlled and longer-term studies are needed to evaluate whether these associations reflect effects of the regulatory framework itself and whether the observed changes are sustained beyond one year.

CRediT authorship contribution statement

Eva-Maria Pichler: Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision. **Maximilian Meyer:** Writing – review & editing, Investigation. **Adrian Guessoum:** Writing – review & editing, Investigation. **Christoph Felix Mosandl**: Writing –

review & editing, Writing – original draft, Investigation. **Jens Kronschnabel:** Writing – review & editing, Validation, Methodology. **Marc Vogel:** Writing – review & editing, Supervision, Project administration. **Marc Walter:** Writing – review & editing, Supervision, Project administration, Methodology, Funding acquisition, Conceptualization. **Oliver Herrmann:** Writing – review & editing, Investigation. **Jacqueline Curiger:** Writing – review & editing. **Lavinia Baltes-Flückiger:** Writing – review & editing, Visualization, Validation, Supervision, Project administration, Methodology, Formal analysis, Data curation, Conceptualization.

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Ethics declaration

Written informed consent to take part in the study and to publish the article has been obtained from all participants or their legal representatives. The privacy rights of participants have been observed.

This study was performed in compliance with relevant laws, regulatory frameworks and guidelines where the research took place. This study was approved by the EKNZ. (Approval No. 2021-01670)

The results of this clinical trial and any associated work have been posted in a registry. This clinical trial was registered with number NCT05522205 (clinicaltrials.gov).

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.drugalcdep.2026.113337.

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