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Risk of readmission among individuals with cannabis use disorder during a 15-year cohort study: The impact of socioeconomic factors and psychiatric comorbidity

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ABSTRACT

Background and aim: Cannabis use disorder (CUD) is one of the main reasons for seeking substance treatment in the Nordic countries, yet there are few studies on readmission to care. We aimed to characterize CUD readmission and estimate the magnitude of how socioeconomic factors and psychiatric comorbidity influence the risk of CUD readmission.

Design: A nation-wide cohort study between 2001 and 2016.

Setting: Sweden.

Participants: Individuals with CUD, aged 17 years and above (N = 12 143).

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Measurements: Information on predictors was obtained from registers and included education, income, and psychiatric comorbidity assessed by six disease groups. The outcome measure was readmission, defined as a CUD visit to healthcare *at least* six months after initial CUD diagnosis. Hazard ratios were estimated using Cox survival analyses and flexible parametric survival analyses to assess risk of readmission and how the risk varied with age.

Findings: The vast majority of CUD visits took place in outpatient care (~80%). About 23% of the included individuals were readmitted to care during follow-up. The fully adjusted model showed an increased risk of readmission among those with schizophrenia and other psychotic disorders (HR = 1.54, 1.29–1.84 95% CI), low education (HR=1.40, 1.24-1.57), personality disorders (HR = 1.27, 1.05–1.54), or mood disorders (HR = 1.27, 1.12–1.45). Flexible parametric modeling revealed increased risk of readmission mainly in individuals aged 18–35 years.

Conclusions: The risk of readmission was highest among those with low education, schizophrenia and other psychotic disorders, mood-related disorders, or personality disorders. Individuals aged 18–35 years showed the highest risk of readmission. Our findings highlight individuals with complex healthcare needs.

INTRODUCTION

While cannabis use disorder (CUD) – i.e., the *harmful use of or dependence on* cannabis – is one of the leading causes of seeking substance treatment [1,2], knowledge about the course of this disorder is limited.

Roughly a third of cannabis users may develop CUD [3–5], with estimates showing 22 million people worldwide meet the criteria for cannabis dependence alone [4]. As decriminalization and legalization of cannabis use continues, CUD is expected to further increase, as shown in settings where such legislative changes have occurred [6,7].

Alongside this development, a recent review on the healthcare utilization of people who use drugs found that studies focusing on cannabis are scarce, US-dominated, and limited follow-ups [8]. Thus, the question of how CUD develops over time merits further investigation, and studies from multiple countries, with longer follow-up times, are needed [9]. The few existing studies show high CUD remission rates of around 80% [10,11]. One study showed that approximately 67% of individuals with a self-reported CUD remitted within 3 years [12]. The mean duration from CUD onset to recovery has been reported at around 32 months, with women recovering more quickly than men [11] and being more likely to remit [10]. Also, one previous study showed the risk of relapse to be higher among those with low education or income [13].

Furthermore, studies report that approximately 50–70% of individuals with CUD also have another psychiatric disorder [3,14,15]. This comorbidity may expose individuals with CUD for poorer clinical outcomes such as suicide attempts [16]. In addition to illustrating the complexity in the mental health of individuals with CUD, a recent review found men to be more likely to have CUD together with most psychiatric disorders, except anxiety disorders and anti-social personality disorders – for which women were more likely to present with CUD [17].

An increase in hospitalizations due to CUD in recent years has been shown in the US [18,19], but less is known about the situation in other countries. A recent study from Germany showed an almost five-fold increase in the number of inpatient cases due to cannabis-related diagnoses between 2000 and 2018 [20]. However, this study lacked any information on the individuals receiving care. Swedish dependency care is available both in primary and specialized care, which operate on either local or regional level [21] and the largest proportion of patients are treated in outpatient care [22]. Considering the increase in both prevalence of CUD and hospitalizations due to CUD, it is important

to better understand this population in order to prepare healthcare systems. We aimed to examine the risk of CUD readmission, focusing on the following research questions:

a) What characterizes CUD readmission with regard to frequency, CUD severity, socioeconomic factors, psychiatric disorders, and healthcare provider of first CUD diagnosis (outpatient/inpatient care)?
b) What is the risk of readmission after an initial CUD diagnosis?
c) To what extent do socioeconomic factors and psychiatric disorders influence the risk of CUD readmission?
d) How does the risk of readmission vary with age?

METHODS

Study design and population

We conducted a cohort study, including individuals with a CUD diagnosis, born 1950–1999, and registered as living in Sweden sometime between 2001 and 2016 (N = 15 283). Individuals were included upon their first CUD diagnosis.

Individuals were identified through the Swedish National Patient Register (NPR), held by the Swedish National Board of Health and Welfare (Figure 1) [23]. The study population was linked to Statistics Sweden's Longitudinal integrated database for health insurance and labour market studies (LISA) [24], which includes socioeconomic variables for all individuals aged ≥ 16 years, starting in 1990. Register linkages were possible through use of each individual's unique personal identification number, assigned at birth or migration to Sweden. The study protocol was not pre-registered, our analyses should thus be considered exploratory.

Assessment of CUD

Our population of interest was individuals aged ≥ 17 years with CUD as a primary diagnosis in the NPR (in- and outpatient care), wherever the CUD diagnosis was recorded first (i.e., unique records). Younger individuals were excluded due to lack of sociodemographic information. We included ICD-10 codes F12.1 (harmful use) and F12.2 (dependence). We chose to combine the in- and outpatient care since the majority of visits occurred in outpatient care and the proportion diagnosed with either harmful use or dependence was similar in both registers.

Outcome – CUD readmission

We measured CUD readmission as any visit with CUD as primary diagnosis registered in the in- or outpatient care (NPR) *at least* six months after first CUD diagnosis. Upon examining the data, we found that most CUD visits occurred soon after a first visit (58% occurred within 60 days from first CUD diagnosis) and then rapidly decreased in frequency (Supplementary Figure S1 for further details). Since our data did not specify the purpose of the visits (e.g., initial assessment, treatment, relapse), we used this 6-month time limit to capture visits that could be indicative of relapses or initiations of new courses of treatment – essentially readmissions non-coherent with prior CUD visits. To assess our definition, we conducted sensitivity analyses with other time periods (3, 9, and 12 months).

Predictors

We obtained information on the following variables from LISA in the year before CUD diagnosis. *Disposable family income*, based on all income sources in the family (salaries, wages, welfare benefits, pensions, etc.), was categorized into quartiles: low income ≤ 117 400 SEK, lower-middle income 117 401–232 600 SEK, upper-middle income 232 601–430 500 SEK, high income ≥ 430 501 SEK (100 SEK ≈ £10). *Highest attained educational level* was based on number of school years completed and grouped into three categories: primary education (≤ 9 years), secondary education (12 years), and post-

secondary education (> 12 years). We used highest attained parental education for individuals aged ≤ 25 years at entry.

Healthcare provider indicated if individuals received their first CUD diagnosis in outpatient or inpatient care. *CUD severity*: based on first CUD diagnosis individuals were grouped as harmful users (ICD-10 F12.1), or cannabis-dependent (ICD-10 F12.2).

For *psychiatric comorbidity*, we focused on diagnoses that have been found to correlate with cannabis use in previous studies [25,26] and identified psychiatric diagnoses registered as primary or secondary in the NPR before an individual's CUD diagnosis. We included unique records of each psychiatric diagnosis, which meant each individual could have multiple diagnoses. The disorders included in our study were: 1) other substance-related disorders, 2) schizophrenia and other psychotic disorders, 3) mood-related disorders, 4) neurotic and stress-related disorders, 5) personality disorders, and 6) behavioral disorders. We also dichotomized having any of the disorders (yes/no) and used this variable in model adjustment. The included ICD codes are detailed in the supplementary material (Table S1).

Statistical analysis

We performed survival analyses with Cox proportional hazards model to estimate hazard ratios (HRs) with 95% confidence intervals (CIs) to assess the potential associations between the predictors and time to CUD readmission, and flexible parametric modeling [27] to examine how HRs varied over time. We used age as the timescale, where the time to event was measured from an individual's age at entry to whichever of the following occurred first: readmission, death, or end of follow-up. The survival analyses were stratified by birth cohort (categorized into five-year groups) to control for calendar time (i.e., period effects) [28].

First, we conducted descriptive analyses (chi-square and t-tests) to examine bivariate associations between the predictors and CUD readmission. Second, we used Cox proportional hazards models to assess associations between predictors and CUD readmission. We applied five models to sequentially compare the effect of the predictors: model 1 – univariable analyses, model 2 – adjustment for sex,

education and income, model 3 – adding healthcare provider and CUD severity, model 4 – adding any other psychiatric disorder, and model 5 – fully adjusted model (i.e., adding all psychiatric disorders respectively to model 4 and removing the general yes/no variable). For all models, we present the results with and without weighted birth cohort stratification [28]. The proportional hazards assumption was tested and assessed with Kaplan-Meier curves. Based on the results, we also examined how the HRs varied over time (i.e., with age) for predictors that did not satisfy the assumption of proportionality. We did this by applying a flexible parametric survival model with restricted cubic splines, which enables fitting both proportional and non-proportional hazard models [27]. The number of knots for the cubic splines in each analysis was determined based on the number of events and the pattern of the graph, to prevent potential overfitting or collapse of non-linear patterns.

Data management, descriptive analyses, and Cox regression model analyses were conducted in SAS software 9.4 [29], while the flexible parametric modeling was conducted in Stata 15 [30].

RESULTS

Descriptive results

We excluded individuals who received their CUD diagnosis before the age of 17 years (n = 2 540) and individuals with missing information on education (n = 357), income (n = 214), or both (n = 29). Thus, our final study population comprised 12 143 individuals. Mean follow-up time was 3.6 years but lower for those who readmitted (1.6 years).

– Insert Figure 1 here –

The number of CUD visits during follow-up ranged from 1–76 with a mean of 3.4 – slightly higher for individuals with cannabis dependence (4.1) than for individuals with harmful use (2.7). Fifty-three percent of visits occurred within 30 days from first CUD diagnosis.

In the study population of 12 143 individuals, 2 807 (23.1%) were readmitted during follow-up (Table 1). The proportion readmitted was similar among men and women (23.2% and 22.6% respectively, P =

0.502), but differed across educational groups (26.3% for those with primary education vs. 20.1% for those with post-secondary education, P <0.001) and income levels (25.3% for those with low income vs. 20.5% for those with high income, P <0.001). Individuals with neurotic and stress-related disorders or behavioral disorders showed slightly higher proportions of readmission than those not diagnosed with those disorders (P = 0.004). Diagnosis of harmful use of cannabis was more common than cannabis dependence (55.3%, P <0.001). The majority of CUD diagnoses were registered in outpatient care (~80%, P <0.001), irrespective of severity.

– Insert Table 1 here –

Risk of readmission

The univariable analyses (model 1) showed elevated HRs for readmission among individuals with primary education compared to those with post-secondary education (HR = 1.49, 1.33–1.67 95% CI) or with low income compared to those with high income (HR=1.23, 1.09–1.38). We found no significantly elevated risk for readmission among men compared with women (1.07, 0.97–1.17). Individuals diagnosed with cannabis dependence had higher risk for readmission than those diagnosed with harmful use (1.46, 1.34–1.61). Having any other psychiatric disorder increased the risk for readmission (1.49, 1.37–1.61); the highest risk was observed for those with schizophrenia and other psychotic disorders (1.81, 1.53–2.13), personality disorders (1.69, 1.41–2.02), or mood-related disorders (1.55, 1.38–1.73). When including socioeconomic factors and adding CUD severity and healthcare provider to the analyses, the HRs of readmission were marginally attenuated. When also taking other psychiatric disorders into account, a slight increase in risk of readmission was observed among men compared with women (1.11, 1.01–1.22). In the fully adjusted model, estimates for individuals with schizophrenia and other psychotic disorders, personality disorders, or mood-related disorders were somewhat attenuated although still significant.

The results of the survival analyses where fairly similar whether stratified by birth cohort or not (Table 2).

– Insert Table 2 here –

Sensitivity analyses

We conducted sensitivity analyses to test different time periods of readmission. Based on the distribution of visits (Supplementary Figure S1), we changed the measure of readmission to at least 3, 9, or 12 months after first CUD visit, respectively. Our results revealed minimal differences (Supplementary Table S4). In general, the estimates for readmission at least 3 months after first CUD diagnosis were modestly higher (e.g., HR_{mood} = 1.30, 1.16-1.46), and at 9 and 12 months slightly lower (HR_{mood} = 1.22, 1.06-1.41 and HR_{mood} = 1.20, 1.03-1.41 respectively) compared to the estimates calculated at 6 months. The risk of readmission among individuals with schizophrenia and other psychotic disorders, or mood-related disorders remained largely intact irrespective of timeframe to readmission, whereas individuals with personality disorders showed no significant risk increase for readmission 12 months after initial CUD diagnosis.

Risk of readmission by age

Individuals aged 18–35 years showed a consistently elevated risk of CUD readmission (Figures 2-4). The risk was elevated in a wider age range (18–40 years) among individuals with neurotic and stress-related disorders or mood-related disorders.

– Insert Figures 2-4 here –

DISCUSSION

Main findings

We found that most CUD-related visits took place in outpatient care (~80%), irrespective of CUD severity. Most visits occurred within the first two months after initial diagnosis, and the average number of visits during follow-up was 3.4. Overall, 23.1% were readmitted to care at least six months after their initial CUD diagnosis. Individuals with only primary education had an elevated risk of CUD readmission, as did those diagnosed with schizophrenia and other psychotic disorders, mood-related

disorders, or personality disorders. The risk of readmission was highest in younger ages, especially 18–35 years.

In line with what has been shown previously, we found no difference in risk of CUD readmission between men and women [11,13], but an increased risk among those with low education or income [13]. Moreover, unlike the study by Flórez-Salamanca et.al. (2013), we found that the association between low income and CUD readmission persisted also after adjusting for other covariates [13]. Our results are also in line with previous findings showing individuals diagnosed with mood-related disorders, personality disorders, or neurotic and stress-related disorders to have an increased risk of CUD readmission [13].

Interestingly, we found no impact of healthcare provider (in-/outpatient care) on the risk of readmission. However, we did find differences with regard to CUD severity, where individuals diagnosed with cannabis dependence had higher risk of readmission than those diagnosed with harmful use.

Like studies on the course of substance use disorders in general [12], the majority of previous studies on CUD have primarily focused on remission rather than on relapse or readmission [8,31]. We were unable to assess remission, since our healthcare data did not comprise information on type of treatment, cannabis consumption, or any information about the individuals between visits. Thus, although our results showed 77% non-readmission during follow-up, we cannot say if this is to be considered remission. Factors shown to influence remission rates may be similar to those protecting from risk of relapse, such as somatic diagnoses that may serve as incentives for remission in order to improve physical health [12]. In our study, 15% reappeared in healthcare due to other psychiatric disorders than CUD during follow-up (not shown), meaning that close to 40% were in fact readmitted to care. Still, this means that more than half of our participants did not reappear in specialized

psychiatric care during follow-up after their first CUD diagnosis. Potential explanations include that they instead appeared in primary healthcare settings or treatment/rehab clinics, or social services, or that they in fact recovered. Actually, data from social services indicate an increase in recent years of individuals reporting cannabis as their main substance use problem [32]. Consequently, while we are able to identify a group with frequent healthcare utilization, we know less about those not readmitted, in particular those not present in any of our registers. In general, substance use disorders are cyclical (with regard to remission, recovery, and relapse), making them difficult to assess without more detailed information about the affected individuals (e.g., assessments of consumption, remission, symptoms of craving, withdrawal etc.) [33].

The increased risk of readmission among younger individuals shown in our study was expected, since most individuals diagnosed with CUD are young. It is also in line with previous studies showing individuals developing CUD in their early-to-mid-twenties [e.g. 10,11]. In Sweden, most individuals receiving healthcare for cannabis-related diagnoses are 15–29 years [32]. However, during the past ten years, the proportion of individuals aged 30–49 years who receive cannabis-related healthcare has more than doubled [32].

Methodological considerations

This study has limitations that need to be addressed.

The inherent uncertainty of studying a concept with no definition, let alone standardized and validated operationalization, introduces difficulties – not only within the current study but also, importantly, when comparing with previous research. A recent review highlighted the inconsistency regarding relapse definitions, especially with regard to time period, showing ranges from two months to three years [33]. Our definition of readmission was based on the number of CUD admissions during a specified time period. Thus, our definition may merely serve as a proxy for either continued care, or

relapse. However, our sensitivity analysis of readmission after at least 3, 9, and 12 months, respectively, showed fairly small changes in results. As illustrated by the histogram, our choice of at least six months was restrictive, as most visits occurred during the first couple of months. Nevertheless, the lack of a coherent definition complicates research on readmission and relapse – ultimately rendering work on treatment and prevention difficult to tackle [33].

While we adjusted for psychiatric disorders at baseline, it may still be the case that individuals developed one of the included disorders during follow-up. This means we may have underestimated their impact on the risk of CUD readmission. Further, the models for the survival analyses included adjustment for predictors that showed insignificant differences between those who were readmitted during follow-up and those who were not. We chose to include them because of their documented association with CUD in previous research [e.g., 7,17]. Still, running the models with the significant predictors only had minimal impact on the results (Supplementary Table S3). This study may be considered exploratory in nature, where the research questions were not pre-registered – although these, the predictors, and outcome were determined prior to performing any analyses. We did not correct for multiple comparisons – although we present results from all examined associations [34,35].

Another limitation is that we did not have sufficient information on the type of treatment the patients received after being diagnosed with CUD. Our registers contained elemental care-related information for each patient (e.g., general and psychological screenings, suicide risk assessment, and urine samples) for less than half of those individuals diagnosed with CUD. These are broad measures and do not clarify how individuals with this disorder are cared for, making it impossible to evaluate the treatment offered. In spite of the increase in prevalence of and treatment-seeking for CUD [32,36], evidence-based CUD treatment is scarce, consisting mainly of psychotherapy [33] not developed specifically for CUD [37]. Generally, CUD treatment in Sweden is supposed to consist of various

psychotherapeutic approaches [32]. Nevertheless, information about what treatment is actually taking place is lacking.

It would have been preferable to also include individuals with CUD aged < 17 years. However, our data were limited by register linkage to socioeconomic variables – which are only available for those aged ≥ 16 years. Nevertheless, our subgroup analyses of those aged < 17 years (excluding socioeconomic factors) showed similar risk estimates, although with mainly insignificant results in the fully adjusted models (not shown). Regarding representativeness, we were able to study only those who sought and/or required specialized healthcare. Consequently, the results are indicative of healthcare utilization. Our results may have been affected by the fact that we do not capture those receiving support from primary healthcare or social services, and may not be generalizable to the broader group of individuals with CUD [38]. Although likely towards underestimation, as we thus captured fewer individuals with CUD, this it is important to consider when assessing the findings.

The inpatient data in the NPR had high coverage, but the outpatient data had slightly lower coverage at the beginning of the study period, in particular for psychiatric care [39,40]. We observed lower proportions of CUD diagnoses in the first ten years of the study period (not shown). The increase in later years may be due to improved reporting or increased demand and diagnosing, perhaps due to increased awareness, decreased stigma, or changed care-seeking behaviors. Still, our results are in line with findings in other countries such as the US and Germany [18,20].

The strengths of this study include the use of comprehensive, nation-wide registers covering the total Swedish population [23,39]. We are able to answer important questions regarding the healthcare of individuals with CUD – an insufficiently studied group, especially in Sweden. Our findings contribute to the understanding of individuals' frequency in care. Additionally, we are able to identify predictors

that impact the risk of readmission, further emphasizing comorbidity, which can aid healthcare systems in planning future care of individuals with CUD.

CONCLUSION

Most CUD visits took place in outpatient care, irrespective of CUD severity, and during the first two months from initial CUD diagnosis. About twenty-three percent were readmitted to CUD-related care during follow-up. The risk of readmission was highest among those with low education, schizophrenia and other psychotic disorders, mood-related disorders, or personality disorders. Individuals aged 18–35 years showed the highest risk of readmission. Our findings have clinical relevance by highlighting individuals with complex healthcare needs, as well as underscoring the importance of comorbidity within psychiatric care.

Declaration of Conflicting Interests

The Authors declare that there are no conflicts of interest.

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TABLES & FIGURES

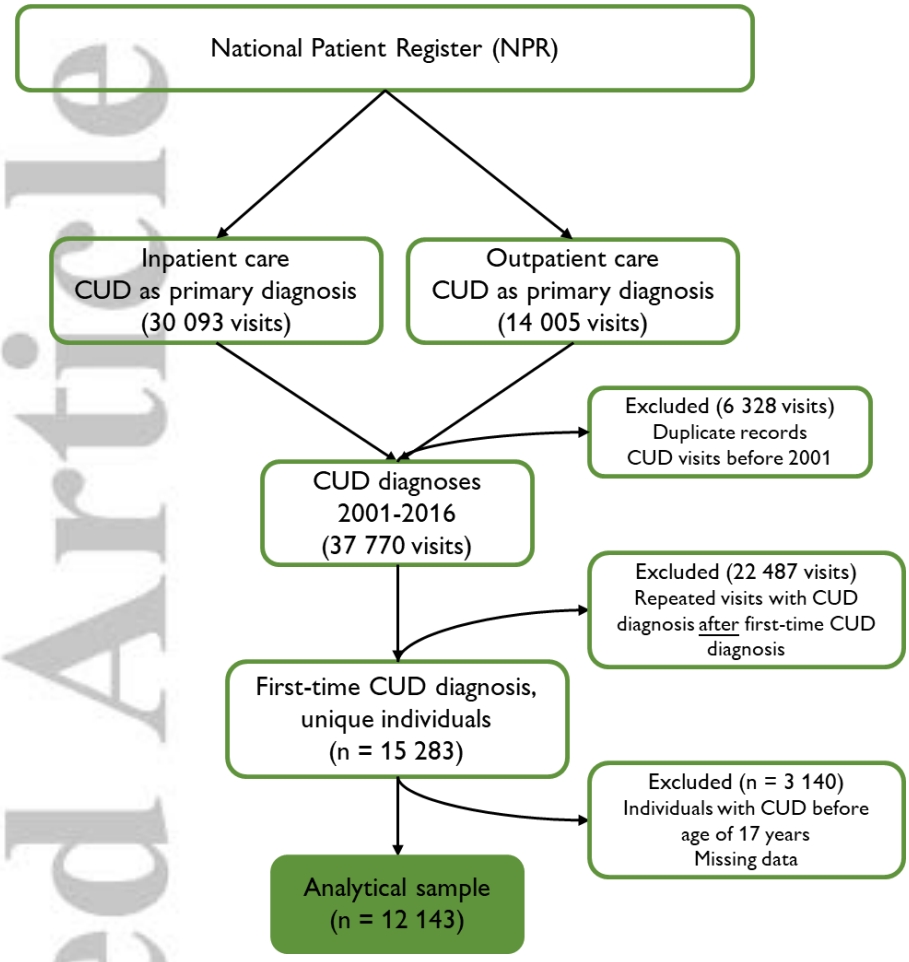

Figure 1. Flowchart of analytical sample.

Table 1. Distribution of covariate frequencies (%) among individuals in the study population readmitted for cannabis use disorder (CUD) compared with those not readmitted.

Covariates	Sample (N = 12 143)		Chi-square
	No readmission (n = 9 336)	Readmission (n = 2 807)	
Sex			0.502
Men	7520 (76.8%)	2277 (23.2%)	
Women	1816 (77.4%)	530 (22.6%)	
Age at entry (years)			0.441[a]
Median (IQR)	22.9 (9.5)	22.9 (9.9)	
Educational level			< 0.001
Primary education (≤ 9 years)	1979 (73.7%)	705 (26.3%)	
Secondary education (12 years)	4617 (76.6%)	1411 (23.4%)	
Post-secondary education (> 12 years)	2740 (79.9%)	691 (20.1%)	
Disposable family income level			< 0.001
Low income (≤ 117 400 SEK)	2271 (74.7%)	769 (25.3%)	
Lower-middle income (117 401–232 600 SEK)	2309 (76.1%)	727 (24.0%)	
Upper-middle income (232 601-430 500 SEK	2343 (77.3%)	690 (22.8%)	
High income (≥ 430 501 SEK	2413 (79.5%)	621 (20.5%)	
Healthcare provider – first CUD diagnosis			< 0.001
Outpatient care	7738 (78.1%)	2175 (21.9%)	
Inpatient care	1598 (71.7%)	632 (28.3%)	
CUD Severity			< 0.001

Harmful use of cannabis	5341 (79.6%)	1373 (20.5%)	
Cannabis dependence	3995 (73.6%)	1434 (26.4%)	
Any other psychiatric disorder			0.409
No	6074 (76.7%)	1850 (23.4%)	
Yes	3262 (77.3%)	957 (22.7%)	
Other substance-related disorders			0.653
No	7012 (76.8%)	2120 (23.2%)	
Yes	2324 (77.2%)	687 (22.8%)	
Schizophrenia and other psychotic disorders			0.118
No	8898 (77.0%)	2655 (23.0%)	
Yes	438 (74.2%)	152 (25.8%)	
Mood-related disorders			0.206
No	8103 (76.7%)	2462 (23.3%)	
Yes	1233 (78.1%)	345 (21.9%)	
Neurotic and stress-related disorders			0.004
No	7844 (76.4%)	2421 (23.6%)	
Yes	1492 (79.5%)	386 (20.6%)	
Personality disorders			0.208
No	8967 (77.0%)	2681 (23.0%)	
Yes	369 (74.6%)	126 (25.5%)	
Behavioral disorders			0.004
No	8358 (76.5%)	2565 (23.5%)	
Yes	978 (80.2%)	242 (19.8%)	

[a] Mann-Whitney-Wilcoxon U-test

Table 2. Hazard ratios (HR) for readmission following baseline diagnosis of cannabis use disorder (CUD) during 15-year follow-up.

	HR (95% CI) N= 12 143									
	Model 1[a]		Model 2[b]		Model 3[c]		Model 4[d]		Model 5[e]	
	Age as timescale	Age as timescale with birth cohort stratification	Age as timescale	Age as timescale with birth cohort stratification	Age as timescale	Age as timescale with birth cohort stratification	Age as timescale	Age as timescale with birth cohort stratification	Age as timescale	Age as timescale with birth cohort stratification
Men	1.07 (0.97–1.18)	1.07 (0.97–1.17)	1.09 (0.99–1.20)	1.08 (0.99–1.19)	1.06 (0.96–1.16)	1.06 (0.96–1.16)	1.11 (1.01–1.22)	1.11 (1.01–1.22)	1.13 (1.02–1.24)	1.13 (1.02–1.24)
Women	1	1	1	1	1	1	1	1	1	1
Primary education	1.50 (1.35–1.68)	1.49 (1.33–1.67)	1.47 (1.31–1.65)	1.46 (1.30–1.63)	1.43 (1.28–1.61)	1.42 (1.27–1.60)	1.42 (1.26–1.59)	1.40 (1.25–1.57)	1.41 (1.26–1.58)	1.40 (1.24–1.57)
Secondary education	1.22 (1.11–1.33)	1.21 (1.10–1.33)	1.20 (1.09–1.32)	1.20 (1.09–1.32)	1.19 (1.08–1.30)	1.18 (1.07–1.30)	1.18 (1.07–1.29)	1.17 (1.06–1.29)	1.18 (1.08–1.30)	1.18 (1.07–1.29)
Post-secondary education	1	1	1	1	1	1	1	1	1	1
Low income	1.24 (1.11–1.39)	1.23 (1.09–1.38)	1.16 (1.03–1.31)	1.16 (1.03–1.31)	1.13 (1.00–1.27)	1.13 (1.00–1.27)	1.12 (0.99–1.26)	1.11 (0.98–1.25)	1.11 (0.99–1.25)	1.10 (0.98–1.24)
Lower-middle income	1.17 (1.04–1.31)	1.17 (1.04–1.31)	1.10 (0.98–1.23)	1.11 (0.99–1.25)	1.09 (0.97–1.22)	1.10 (0.98–1.24)	1.10 (0.98–1.23)	1.10 (0.98–1.23)	1.09 (0.97–1.22)	1.09 (0.97–1.22)
Upper-middle income	0.99 (0.89–1.11)	1.00 (0.90–1.12)	0.95 (0.85–1.06)	0.96 (0.86–1.07)	0.94 (0.84–1.05)	0.95 (0.85–1.06)	0.95 (0.85–1.07)	0.96 (0.86–1.07)	0.96 (0.86–1.07)	0.96 (0.86–1.07)
High income	1	1	1	1	1	1	1	1	1	1
Outpatient care	1	1	---	---	1	1	1	1	1	1
Inpatient care	0.93 (0.84–1.01)	0.91 (0.83–0.99)	---	---	0.93 (0.85–1.02)	0.93 (0.84–1.01)	0.93 (0.85–1.01)	0.91 (0.83–1.00)	0.93 (0.85–1.01)	0.91 (0.83–1.00)
Harmful use of cannabis	1	1	---	---	1	1	1	1	1	1
Cannabis dependence	1.46 (1.35–1.57)	1.46 (1.35–1.58)	---	---	1.41 (1.30–1.53)	1.42 (1.31–1.53)	1.42 (1.31–1.54)	1.42 (1.31–1.53)	1.43 (1.32–1.55)	1.43 (1.32–1.55)

Any other psychiatric disorder	1.46 (1.35–1.58)	1.48 (1.37–1.61)	---	---	---	---	1.47 (1.36–1.59)	1.49 (1.37–1.61)	---	---
Other substance-related disorders	1.43 (1.31–1.56)	1.45 (1.33–1.58)	---	---	---	---	---	---	1.18 (1.06–1.30)	1.18 (1.06–1.31)
Schizophrenia and other psychotic disorders	1.80 (1.52–2.12)	1.81 (1.53–2.13)	---	---	---	---	---	---	1.54 (1.29–1.83)	1.54 (1.29–1.84)
Mood-related disorders	1.50 (1.34–1.68)	1.55 (1.38–1.73)	---	---	---	---	---	---	1.26 (1.10–1.43)	1.27 (1.12–1.45)
Neurotic and stress-related disorders	1.44 (1.29–1.60)	1.48 (1.33–1.65)	---	---	---	---	---	---	1.16 (1.02–1.32)	1.18 (1.03–1.34)
Personality disorders	1.65 (1.38-1.98)	1.69 (1.41-2.02)	---	---	---	---	---	---	1.25 (1.03-1.52)	1.27 (1.05-1.54)
Behavioral disorders	1.31 (1.15–1.50)	1.34 (1.18–1.54)	---	---	---	---	---	---	1.02 (0.89–1.18)	1.03 (0.89–1.19)

[a] Model 1: univariable estimates.
[b] Model 2: adjusted for sex, education, income.
[c] Model 3: adjusted for sex, education, income, healthcare provider, CUD severity.
[d] Model 4: adjusted for sex, education, income, healthcare provider, CUD severity, any other psychiatric disorder.
[e] Model 5: full adjustment, includes all variables in Table 1 excluding *'Age at entry'* and *'Any other psychiatric disorder'*.

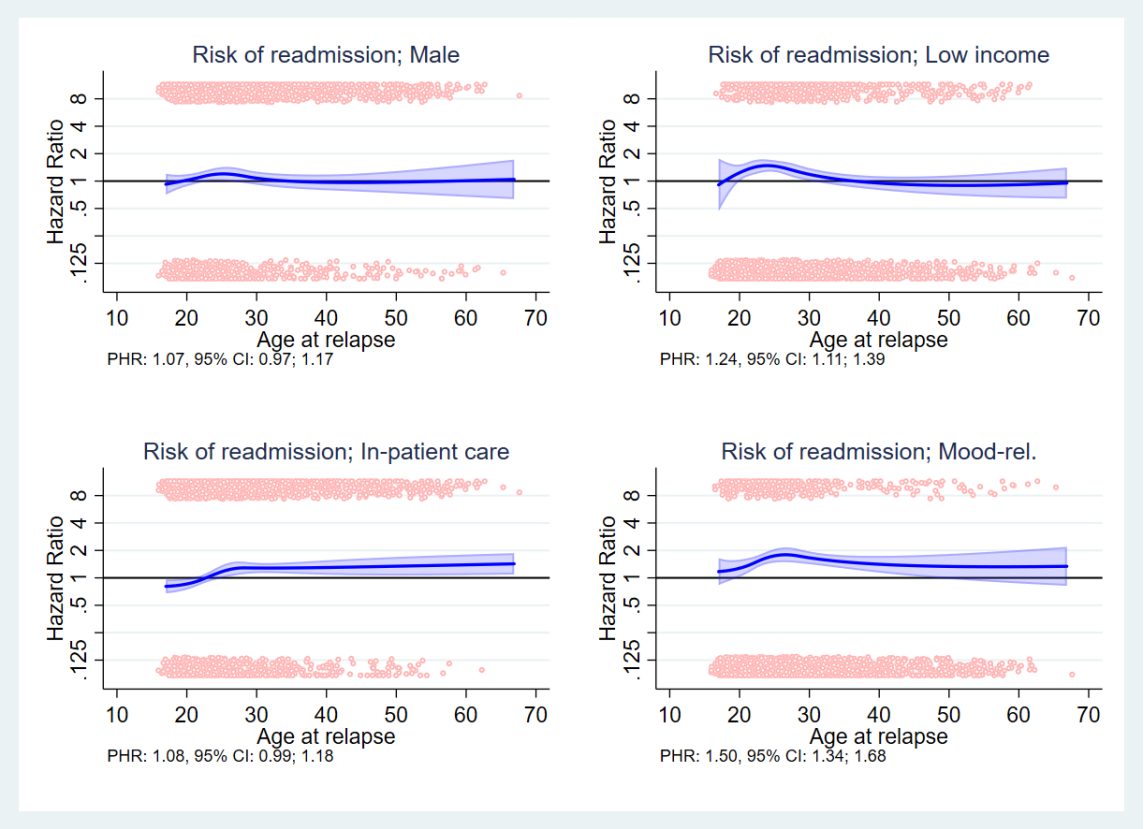

Figure 2. The results from the flexible parametric models for sex, income, in- or outpatient care, and mood-related disorders. The red points at the top of the graphs represent the exposed individuals with readmission for cannabis use disorder and those at the bottom represent the unexposed individuals with readmission for cannabis use disorder. The graphs show the hazard ratio by age, with the proportional hazard ratio (i.e., a weighted mean hazard ratio over the time period) presented in the bottom left corner of each graph.

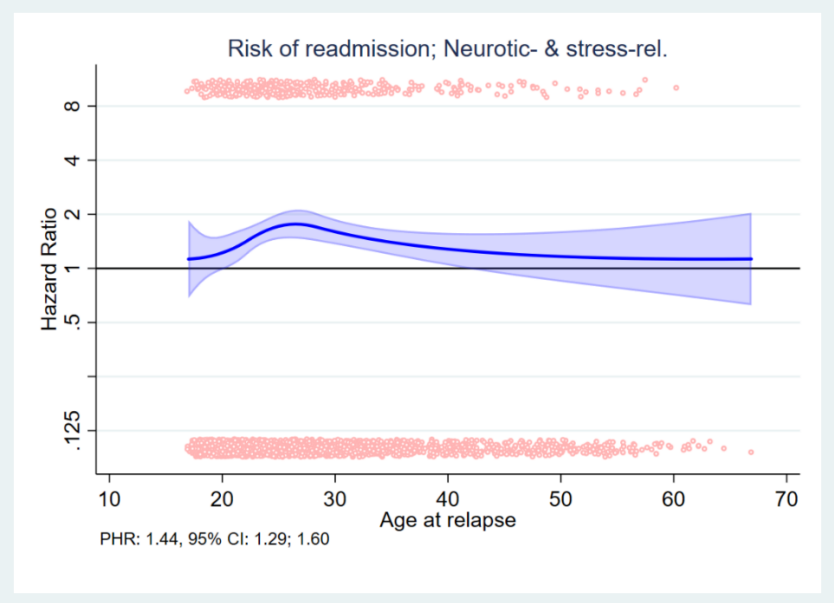

Figure 3. The results from the flexible parametric models for neurotic and stress-related disorders. The red points at the top of the graphs represent the exposed individuals with readmission for cannabis use disorder and those at the bottom represent the unexposed individuals with readmission for cannabis use disorder. The graphs show the hazard ratio by age, with the proportional hazard ratio (i.e., a weighted mean hazard ratio over the time period) presented in the bottom left corner of each graph.

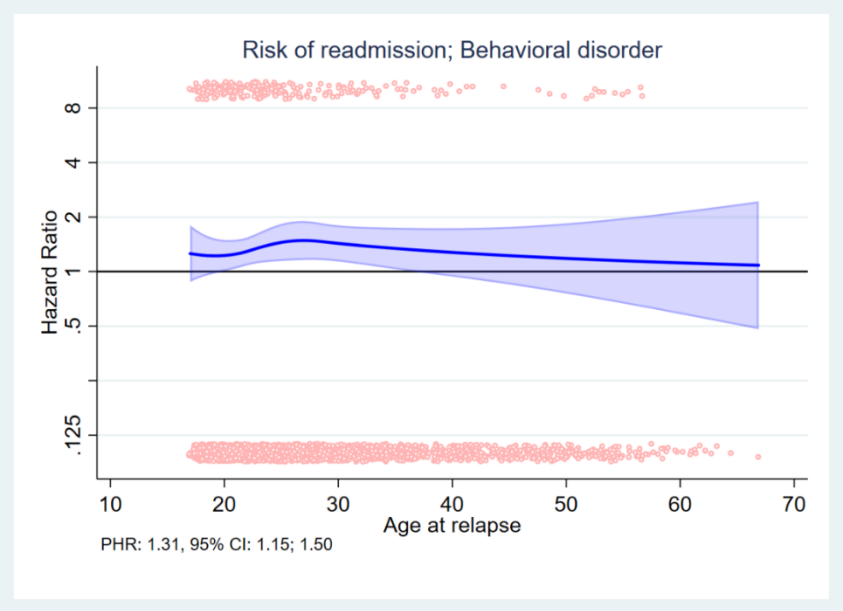

Figure 4. The results from the flexible parametric models for behavioral disorders. The red points at the top of the graphs represent the exposed individuals with readmission for cannabis use disorder and those at the bottom represent the unexposed individuals with readmission for cannabis use disorder. The graphs show the hazard ratio by age, with the proportional hazard ratio (i.e., a weighted mean hazard ratio over the time period) presented in the bottom left corner of each graph.