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ORIGINAL ARTICLE

Natural course of cannabis use disorders

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Background. Despite its importance as a public health concern, relatively little is known about the natural course of cannabis use disorders (CUDs). The primary objective of this research was to provide descriptive data on the onset, recovery and recurrence functions of CUDs during the high-risk periods of adolescence, emerging adulthood and young adulthood based on data from a large prospective community sample.

Method. Probands (n=816) from the Oregon Adolescent Depression Project (OADP) participated in four diagnostic assessments (T_1–T_4) between the ages of 16 and 30 years, during which current and past CUDs were assessed.

Results. The weighted lifetime prevalence of CUDs was 19.1% with an average onset age of 18.6 years. Although gender was not significantly related to the age of initial CUD onset, men were more likely to be diagnosed with a lifetime CUD. Of those diagnosed with a CUD episode, 81.8% eventually achieved recovery during the study period. Women achieved recovery significantly more quickly than men. The recurrence rate (27.7%) was relatively modest, and most likely to occur within the first 36 months following the offset of the first CUD episode. CUD recurrence was uncommon after 72 months of remission and recovery.

Conclusions. CUDs are relatively common, affecting about one out of five persons in the OADP sample prior to the age of 30 years. Eventual recovery from index CUD episodes is the norm, although about 30% of those with a CUD exhibit a generally persistent pattern of problematic use extending 7 years or longer.

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Introduction

In many countries cannabis is the most widely used illicit drug (Copeland & Swift, 2009). In the USA, cross-sectional studies suggest that adolescence and early adulthood are particularly critical developmental periods for the initiation of cannabis use and the development of cannabis use disorders (CUDs; defined as a diagnosis of cannabis abuse or dependence disorders). Findings from the 2012 Monitoring the Future Survey (Johnston *et al.* 2013), for example, indicated that 15% and 45% of 8th- and 12th-grade youth in the USA, respectively, have used cannabis. The National Survey on Drug Use and Health (Substance Abuse and Mental Health Services Administration, 2012) documented that in 2011, 2.6 million US residents aged 12 years or older initiated cannabis use, with most initiates (57.7%) younger than the age of 18 years. There were an estimated 18.1 million past-year cannabis users aged 12 years or older during 2011, or about 7% of the general US population. In this same year, 1.6% of the US population (4.2 million persons) was estimated to have met criteria for cannabis abuse or dependence. Despite indications that rates of frequent cannabis users among US adolescents are among the highest worldwide (ter Bogt *et al.* 2006), relatively little is known about the natural development and course of CUDs in the USA.

Limited international and domestic longitudinal research with community samples indicates that cannabis initiation, experimentation, frequent use and CUD emergence are most likely between the ages of 15 and 24 years (Cohen *et al.* 1993; Chen & Kandel, 1995; Brook *et al.* 1999; Poulton *et al.* 2001; Boden *et al.* 2006; Perkonigg *et al.* 2008; Roxburgh *et al.* 2010). Most individuals who try cannabis, however, either cease use altogether within a short period following initiation or remain occasional users (Flory *et al.* 2004; Windle & Wiesner, 2004; Lynskey *et al.* 2006; Perkonigg *et al.* 2008; Brook *et al.* 2011*b*). Others, however, increase their usage with age or maintain frequent or heavy use (Newcomb *et al.* 2001; Perkonigg *et al.* 2008; Calabria *et al.* 2010; Brook *et al.* 2011*b*). Estimates from community-based

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prospective samples from Australasia and Europe suggest that 13% to 21% of adolescents are at risk for developing a CUD by early adulthood (Boden *et al.* 2006; Perkonigg *et al.* 2008; Moffitt *et al.* 2010), although actual percentages are probably higher given the reluctance of some individuals to answer questions about illicit drug use (Perkonigg *et al.* 2008). Findings reported from different geographical regions are mixed as to whether CUD prevalence rates decline or remain stable between late adolescence and the mid-20s (Poulton *et al.* 2001; Newcomb *et al.* 2001; Perkonigg *et al.* 2008; Calabria *et al.* 2010).

Despite the importance of CUDs as a public health concern, important gaps in knowledge remain concerning the development and course of CUDs in the general population. To address these gaps, the present research provides descriptive data on the natural course of CUDs based on data collected as part of the Oregon Adolescent Depression Project (OADP; Lewinsohn *et al.* 1993), a longitudinal study of a community-based cohort. Specifically, we report the first incidence and prevalence (point, period and lifetime) of CUDs from childhood to age 30.0 years, which encompasses the developmental periods within which cannabis initiation, problematic use and cessation of problematic use are most common (Chen & Kandel, 1995). We also report data on time to recovery from the index CUD episode and time to CUD recurrence. Outcomes from these analyses are expected to highlight developmental periods within which the risk for CUD onset and recurrence are especially high, as well as threshold points by which initial recovery is likely to be sustained. Because gender differences in cannabis use, abuse and dependence often emerge during late adolescence and early adulthood, with males tending to use more frequently than females (Brook *et al.* 1999; Kandel & Chen, 2000; Poulton *et al.* 2001; Coffey *et al.* 2003; Perkonigg *et al.* 2008; Griffith-Lendering *et al.* 2012), we also evaluate possible gender differences in onset, recovery and recurrence functions.

Method

Participants

Current and past Diagnostic and Statistical Manual of Mental Disorders (DSM)-defined cannabis abuse or dependence and other psychiatric diagnostic categories were assessed with OADP probands on four occasions between the ages of 16 and 30 years (T_1 to T_4). The T_1 sample (initiated between 1987 and 1989; n=1709; mean age=16.6 years, S.D.=1.2 years) was randomly drawn from nine high schools in two urban and three rural communities in western Oregon, and subsequently found to be representative of the regional population from which it was drawn (Lewinsohn *et al.* 1993). At 1 year following T_1, T_2 was initiated, and 1507 (88%) probands were reassessed.

At T_3, which was initiated about 7 years after T_2, a stratified sampling procedure was implemented whereby eligible participants included all persons with a positive history of a substance abuse or psychiatric diagnosis by T_2 (n=644) and a randomly selected subset of never mentally ill (NMI) probands (457 of 863 persons). Of these 1101 eligible persons, 941 (85%) completed T_3. Comparisons between the T_3 NMI participants who were randomly selected for further participation with unselected NMI probands revealed no significant differences with respect to T_2 data. Of the 941 T_3 probands, 816 (87%) participated in T_4 about 6 years after T_3 (59% female, 89% white, 53% married).

In our recent analysis of proband attrition across waves (Farmer *et al.* 2013), we compared the T_4 panel with those who dropped out from the study after T_1 with respect to psychiatric history (i.e. any lifetime DSM-defined disorder diagnosis) and the cumulative number of lifetime psychiatric disorders at T_1. The T_4 panel was not statistically different from the attrition group with respect to positive psychiatric histories (p=0.96) or the cumulative number of lifetime disorders (p=0.23) at T_1. Similarly, when we performed an attrition analysis based exclusively on CUDs for this report, those in the attrition group, when compared with the T_4 panel, did not have significantly higher rates of CUDs at T_1 [8% *v.* 7%, respectively; Pearson χ^2 (1, n=1299)=0.39, p=0.532]. Wave-to-wave analyses, however, revealed one significant difference: discontinuation from T_3 to T_4 was more common among those with a history of a CUD by T_3 (18% for discontinuation group *v.* 12% for those who participated in T_4, p=0.03). Given the sample stratification procedures implemented at T_3, the relatively modest attrition over successive waves, and evidence that analyses based on T_3 and T_4 panels produced highly similar outcomes[1]†, results presented in the following section are based on the T_4 panel (n=816).

Assessment of CUDs

During T_1, T_2 and T_3, participants were interviewed with a version of the Schedule for Affective Disorders and Schizophrenia for School-Age Children (K-SADS) that combined features of the Epidemiologic and Present Episode versions (Orvaschel *et al.* 1982; Chambers *et al.* 1985). Follow-up psychiatric disorder

† The notes appear after the main text.

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assessments at T_2 and T_3 also involved the joint administration of the Longitudinal Interval Follow-Up Evaluation (LIFE; Keller *et al.* 1987) that, in conjunction with the K-SADS, provided detailed information related to the presence and course of disorders since participation in the previous diagnostic interview. The T_4 assessment included administration of the LIFE and the Structured Clinical Interview for Axis I DSM-IV Disorders–Non-Patient Edition (SCID-NP; First *et al.* 1994). Symptom reports related to cannabis use were evaluated in accordance with DSM-III-R diagnostic criteria (APA, 1987) at T_1 and T_2 and DSM-IV diagnostic criteria (APA, 1994) at T_3 and T_4.

DSM-III-R and DSM-IV hierarchically arrange substance use disorders into abuse and dependence categories, whereby dependence takes precedence over abuse when criteria for both conditions are satisfied. This hierarchical taxonomic approach has been challenged by data that fail to support the cannabis abuse/dependence distinction as operationalized in DSM (Langenbucher *et al.* 2004; Blanco *et al.* 2007; Hartman *et al.* 2008; Beseler & Hasin, 2010). This hierarchical organization has also been discontinued in DSM-5 (APA, 2013) in favor of a single 'use disorder' category. Consequently, for the analyses described below, we combine cannabis abuse and dependence diagnoses into a single category (CUDs) to indicate problematic cannabis use that has resulted in a symptomatic presentation coupled with significant impairment in functioning that rises to the threshold of diagnosis and, consequently, warrants clinical attention.

All interviews were recorded and randomly selected for reliability assessments by a second interviewer. Inter-rater reliability was indexed by κ. Diagnostic agreement among raters for CUD diagnoses since the previous interview was good to excellent (κ's: T_1=0.72, T_2=0.93, T_3=0.83, T_4=0.82).

CUD recovery and recurrence

Definitions of recovery and recurrence in the present research are informed by previous conceptualizations of these concepts (Frank *et al.* 1991; Chung & Maisto, 2006), LIFE interview naming conventions (Keller *et al.* 1987) and by guidelines provided in DSM-IV (APA, 1994). Given our emphasis on the natural course of disorders rather than symptoms, and the elimination of the abuse/dependence distinction with respect to CUDs in DSM-5 (APA, 2013), we applied the following definitions regardless as to whether the index episode was cannabis abuse or cannabis dependence. 'Remission' as used here refers to offset of an initial CUD episode lasting at least 1 full month but less than 12 months during which the individual no longer meets diagnostic criteria for the index CUD episode but may continue to use cannabis at subthreshold levels. The re-emergence of an index CUD episode during the remission period is regarded as a continuation of the index episode (i.e. a 'relapse'). The resolution of the index episode, defined as a period of uninterrupted remission lasting at least 12 months, is regarded as a 'recovery' from the index episode. Recovery is only achieved after a 12-month period following the sustained offset of the index CUD episode, during which there is no relapse of the index episode. A 'recurrence' is regarded as a new CUD episode after a period of recovery.

Statistical analyses

Because of the unequal stratified sampling strategy implemented at T_3, weighting procedures were used to estimate prevalence rates, incidence rates and odds ratios (ORs). Time-to-event analyses were implemented using SUDAAN statistical software (RTI International, USA), and standard errors were estimated using the Taylor series linearization method to appropriately account for the unequal stratified sampling procedure implemented at T_3. In the analyses that follow, rate, ratio and proportion values are based on weighted data.

Potential gender moderation of the time-to-event functions was tested using Cox proportional hazards (PH) models. An assumption of Cox PH models is the absence of a significant time × predictor interaction. Consistent with recommendations (Singer & Willett, 1991), we initially included a time × gender interaction term in the model. Subsequent findings indicated that in no instance was the interaction term statistically significant. Given that this assumption of the PH model was met, the interaction term was removed and the models rerun, with data from these analyses reported. Hazard ratio (HR) estimates, which index differences in onset curves as a function of gender, were calculated along with 95% confidence intervals (CIs). Cumulative hazard functions were used to describe CUD onset, recovery and recurrence functions in the presence of censorship (i.e. participants who did not experience a CUD onset, recovery or recurrence during the observation period). Time-to-event was measured in months. In instances where the cumulative hazard functions exceeded 0.5, the median survival time was reported to facilitate data interpretation. The demarcation of age ranges in the reporting of first incidence and period prevalence rates was based on a developmental framework outlined by Arnett (2007). Within this framework, developmental periods analysed were childhood to emerging adolescence (childhood to age 13.9 years), adolescence

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Table 1. *Natural course of cannabis use disorders from childhood to age 30 years: gender comparisons*[a]

	Female probands (95% CI)	Male probands (95% CI)	OR (95% CI)
Lifetime prevalence, %	16.4 (13.1–19.7)	22.5 (18.2–26.8)	1.48 (1.04–2.09)*
First incidence, %			
0.0–13.9 years	1.9 (0.7–3.1)	2.4 (0.8–4.0)	1.29 (0.50–3.36)
14.0–17.9 years	6.0 (3.8–8.2)	7.6 (4.9–10.3)	1.30 (0.75–2.25)
18.0–24.9 years	7.1 (4.7–9.5)	11.6 (8.3–14.9)	1.71 (1.06–2.77)*
25.0–30.0 years	1.4 (0.2–2.6)	0.8 (0.0–1.8)	0.56 (0.14–2.26)
Period prevalence, %			
14.0–17.9 years	7.2 (4.8–9.6)	9.9 (6.8–13.0)	1.40 (0.85–2.30)
18.0–24.9 years	11.4 (8.5–14.3)	19.0 (14.9–23.1)	1.83 (1.24–2.71)*
25.0–30.0 years	5.7 (3.5–7.9)	11.9 (8.6–15.2)	2.25 (1.35–3.74)*
Point prevalence, %			
T_1 (about age 16 years)	1.1 (0.1–2.1)	2.0 (0.6–3.4)	1.84 (0.58–5.83)
T_2 (about age 17 years)	0.6 (0.0–1.4)	1.8 (0.4–3.2)	2.90 (0.72–11.72)
T_3 (about age 24 years)	2.1 (0.7–3.5)	6.7 (4.2–9.2)	3.42 (1.59–7.36)*
T_4 (about age 30 years)	2.8 (1.2–4.4)	7.3 (4.6–10.0)	2.68 (1.36–5.29)*
Recovery rate, %	86.5 (78.7–94.3)	77.4 (68.4–86.4)	0.54 (0.23–1.25)
Recurrence rates for those who recovered, %	25.4 (14.8–36.0)	30.0 (18.6–41.4)	1.26 (0.57–2.74)

CI, Confidence interval; OR, odds ratio.

[a] All summary statistics account for sample weighting.

* Statistically significant ($p<0.05$).

(14.0–17.9 years), adolescence transitioning to emerging adulthood (18.0–24.9 years) and emerging adulthood transitioning into young adulthood (25.0–30.0 years).

Results

Prevalence rates, incidence rates and age of onset for index CUD episodes

Prevalence and incidence rates

The weighted lifetime prevalence of CUD from childhood to age 30.0 years in the OADP sample was 19.1%. Men (22.5% of T_4 male proband sample) were more likely than women (16.4% of T_4 female proband sample) to be diagnosed with a lifetime CUD [likelihood ratio (LR) χ^2 (1, n=816)=4.74, p=0.030, OR 1.48, 95% CI 1.04–2.09].

Weighted first incidence and period prevalence rates, presented in Table 1, highlight age ranges during which CUD risk is greatest. Findings presented in this table highlight the significance of ages 14.0 to 24.9 years as a period of exceptional risk for initial CUD onset. This risk, however, is substantially diminished after the age of 25 years. Ages 18.0 to 24.9 years additionally correspond to a period where the prevalence of CUDs reaches its peak.

Table 1 also includes ORs to illustrate how first incidence and prevalence rates for CUDs differ by gender. First incidence rates significantly differed by gender within the 18.0 to 24.9 years period only [11.6% of males compared with 7.1% of females; LR χ^2 (1, n=816)=4.84, p=0.024, OR 1.71, 95% CI 1.06–2.77]. Period prevalence rates also significantly differed by gender within the 18.0 to 24.9 years developmental period [19.0% of males compared with 11.4% of females; LR χ^2 (1, n=816)=9.34, p=0.002, OR 1.83, 95% CI 1.24–2.71], and within the 25.0 to 30.0 years period as well [11.9% of males compared with 5.7% of females; LR χ^2 (1, n=816)=10.14, p=0.001, OR 2.25, 95% CI 1.35–3.74]. Similarly, point prevalence rates significantly differed by gender at T_3 [6.7% of males compared with 2.1% of females; LR χ^2 (1, n=816)=11.09, p<0.001, OR 3.42, 95% CI 1.59–7.36] and T_4 [7.3% of males compared with 2.8% of females; LR χ^2 (1, n=816)=8.66, p=0.003, OR 2.68, 95% CI 1.36–5.29].

Time to CUD onset

For those with a lifetime CUD diagnosis, the average age of onset for the first episode was 18.6 years (S.D.=4.2 years), which did not differ by gender (observed mean values: males=18.6, S.D.=4.1 years; females=18.7, S.D.=4.3 years; t_{153}=0.13, p=0.901). Cumulative hazard functions for CUD onset for the combined sample and separately by gender are presented in Fig. 1. The cumulative hazard functions

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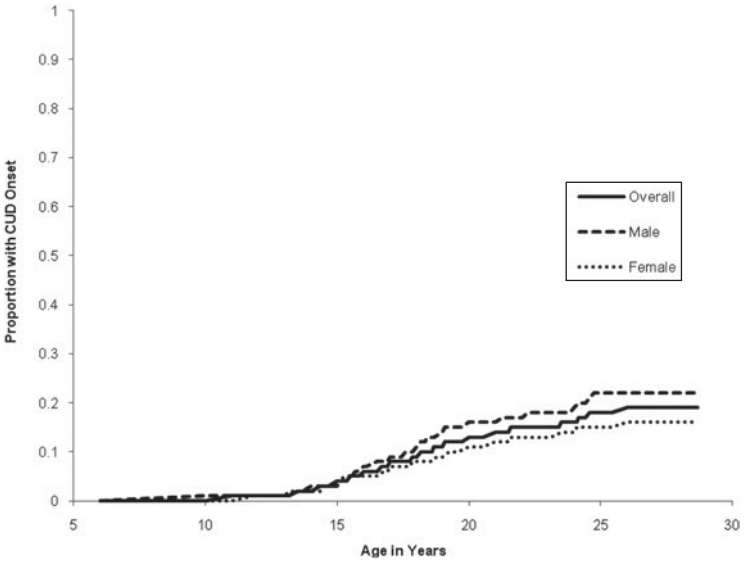

Fig. 1. Cumulative hazard functions for cannabis use disorder (CUD) onset by age in years.

significantly differed by gender (HR 1.42, 95% CI=1.03–1.95, p=0.033).

Recovery following the index CUD episode

Rates of recovery

Among the persons with a lifetime CUD, 81.8% experienced recovery from the index CUD episode by the age of 30 years. Rates of recovery did not differ by gender [77.4% of males and 86.5% of females recovered; LR χ^2 (1, n=155)=2.17, p=0.141, OR 0.54, 95% CI 0.23–1.25].

Time to recovery

Among those who recovered from the index CUD episode, the mean duration of the index CUD episode was 32.5 months (S.D.=35.6 months), which significantly differed with respect to gender (males=41.2, S.D.=42.7 months; females=24.2, S.D.=24.8 months; t_{125}=−2.77, p=0.006). Time to recovery is based on the full duration of the index CUD episode plus a 12-month period of sustained remission following episode offset, during which CUD symptomatology does not again rise to the level of diagnosis. If, for example, an individual met CUD criteria for 14 consecutive months and did not again meet criteria for a CUD in the 12 months following the offset of the index episode, the time to recovery would be 26 months. Participants that did not experience 12 months of sustained remission for their index CUD episode prior to the T_4 diagnostic interview were right censored from the survival analysis. Cumulative hazard functions for recovery from a CUD episode for the complete subsample with a lifetime diagnosis and separately by gender are presented in Fig. 2. Hazard rates were estimated for recovery in 1-month intervals commencing with the onset of the first CUD episode. The cumulative hazard functions that assessed time to recovery from the initial CUD episode significantly differed by gender (HR 0.57, 95% CI 0.39–0.82, p=0.003). The median recovery time (i.e. survival time) was 61 months for males and 31 months for females.

Recurrence following the first CUD episode

Recurrence rates following a period of recovery

Of the participants who recovered from their index CUD episode, 27.7% developed another CUD episode before the age of 30 years. Recurrence rates were not significantly different between male and female probands [30.0% of males, 25.4% of females; LR χ^2 (1, n=127)=0.33, p=0.564, OR 1.26, 95% CI 0.57–2.74].

Time to recurrence

Among those with a second CUD, the mean time to recurrence was 46.1 months (S.D.=35.6 months), which did not significantly differ with respect to gender (males=51.9, S.D.=39.0 months; females=40.1, S.D.=31.6 months; t_{35}=−1.00, p=0.326). Cumulative hazard functions for recurrence for the complete subsample with CUD recovery and separately by gender are presented in Fig. 3. Hazard rates were estimated for recurrence in 1-month intervals, with recurrence defined as a second CUD episode occurring after a period of at least 12 months of remission from the index CUD episode. The cumulative hazard functions that assessed time to recurrence did not differ by gender

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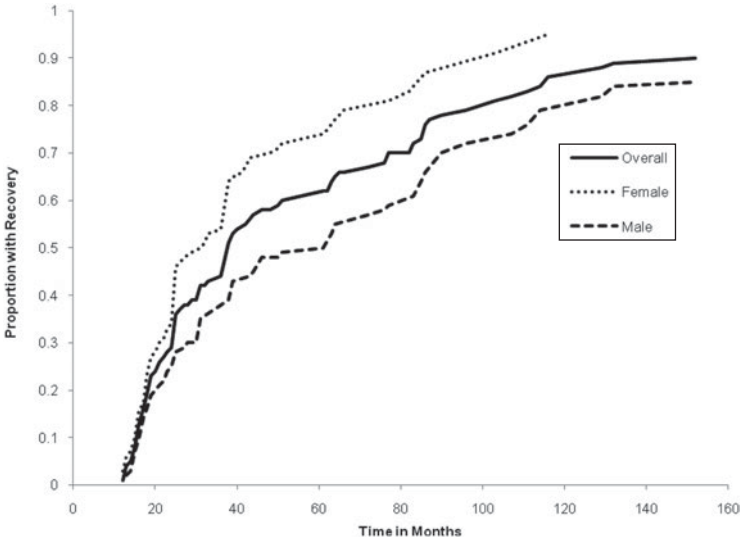

Fig. 2. Cumulative hazard functions for cannabis use disorder recovery by time since disorder onset.

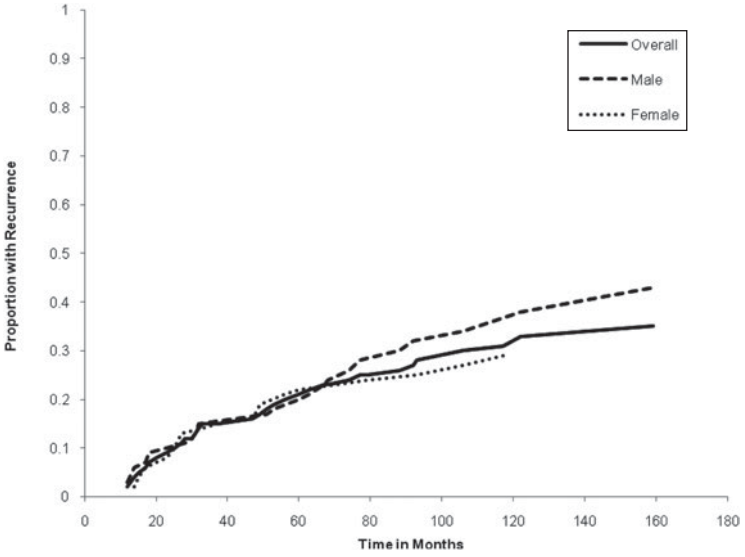

Fig. 3. Cumulative hazard functions for cannabis use disorder recurrence by time since initial disorder offset.

(HR 1.21, 95% CI 0.66–2.22, p=0.539). Data presented in Fig. 3 indicate that the highest rates of recurrence occurred within 24 months after recovery. CUD recurrence for females is rare after the 60th consecutive month since offset of the initial episode. For males, however, there is no clear recovery threshold evident within the interval surveyed. Overall, there is little support from Fig. 3 that a disorder-free period of 12 months is an optimal threshold for denoting recovery from CUDs.

Discussion

Although prevalence of cannabis initiation and frequency of use have been well documented in adolescent and young adult samples (e.g. Johnston *et al.* 2013), comparatively little is known about the course of prolonged cannabis use that rises to the threshold of a CUD diagnosis. Previous research indicates that the progression from cannabis experimentation or use to CUD is comparatively rare (Chen *et al.* 2005; Wittchen *et al.* 2007). In the current study, the weighted lifetime prevalence of a CUD from childhood to the age of 30 years was 19.1%. Consistent with findings from other prospective community samples (Coffey *et al.* 2003; Perkonigg *et al.* 2008), men were 1.5 times more likely than women to be diagnosed with a lifetime CUD. Findings further indicate that initial CUD incidence and period prevalence rates peaked between the ages of 18 and 25 years for both

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men and women, and declined sharply thereafter. Point prevalence rates, however, were highest at T_4 (about age 30 years), and mostly influenced by individuals who exhibited a more chronic course.

Although cannabis use appears to be quite stable during the adolescent, emerging adulthood and young adulthood developmental periods (Perkonigg *et al.* 2008), data presented here indicate that there are moderate rates of both cessation and persistence of CUDs across these same periods. Whereas 54% of those with an index CUD episode fully recovered without a subsequent recurrence by the age of 30 years, the remaining 46% never recovered, remitted less than 12 months prior to the end of the study, or recovered only to experience a subsequent recurrence. When lifetime CUD rates for female and male probands (16.4% and 22.5%, respectively) are compared with CUD point prevalence rates at T_4 (about age 30 years; 2.8% and 7.3%, respectively), however, it is apparent that a majority of individuals, especially women, who develop CUDs during the developmental periods studied recovered by the age of 30 years. Rather than a chronic and relapsing condition, CUDs for many appear to be developmentally limited (see also Flory *et al.* 2004; Windle & Wiesner, 2004; Lynskey *et al.* 2006).

Although total recovery rates did not significantly differ between men and women, time to CUD recovery was significantly more rapid for women than men. In DSM-5 (APA, 2013), the 'recovery' course specifier is not used. Instead, the interval following CUD offset is specified as 'early remission' or 'sustained remission', with the main distinction being the timeframe within which CUD-defining criteria are absent after disorder offset (>3 months but <12 months *v.* $\geqslant$12 months, respectively). Sustained remission in DSM-5 is analogous with the concept of recovery used in the present research, with the main difference being the emphasis placed on the absence of all CUD-defining criteria except craving (DSM-5) *v.* the absence of a symptom presentation that rises to the threshold of diagnosis (present study). Remission and recovery functions in the current research did not reveal abrupt discontinuities or sudden shifts in hazard functions over time; therefore, at the CUD disorder-level of specification, a continuum of behavior change processes rather than distinct recovery stages also appears to be evident. Future refinements in the terminology used to describe the course of CUDs should jointly consider not only disorder thresholds and time since disorder offset, but also the degree of subthreshold symptomatology evident during the remission and recovery periods, the frequency or quantity of cannabis use, and the associated level of functional impairment (cf. Rush *et al.* 2006).

Rates of recurrence did not significantly differ by gender, and were relatively uncommon following the offset of the index CUD episode, occurring in slightly more than one-quarter of participants with CUD who recovered. Recurrences, when observed, were most likely to occur within 36 months following offset of the first CUD episode, and were relatively rare after 60 months. Based on their comprehensive review of the natural recovery literature, Sobell *et al.* (2000) recommended a period of at least 5 years as the minimal threshold for a recovery designation given accumulated findings which indicate that recovery processes usually stabilize by this time and that subsequent recurrence is uncommon. Findings from the present research are consistent with this recommendation.

Although the incidence and point prevalence of CUDs peak during the emerging adulthood period, developmental pathways for CUDs and other forms of substance abuse probably emerge long before problematic cannabis use begins (Clark, 2004; Zucker *et al.* 2008). Furthermore, significantly lower lifetime prevalence rates of CUDs for women compared with men, coupled with significantly quicker times to recovery among women, suggest possible gender-related risk mechanisms associated with CUD onset and offset. Cannabis use and CUDs are heritable (Agrawal & Lynskey, 2006), and associated with latent liabilities for externalizing disorders (which include attention-deficit hyperactivity disorder, oppositional defiant disorder, conduct disorder, adult antisocial behavior and other substance use disorders; see Krueger & Markon, 2006; Farmer *et al.* 2009). Externalizing disorders and associated liabilities are also more commonly observed among males (e.g. Kessler *et al.* 2005; Hicks *et al.* 2007) and are heritable (Young *et al.* 2000; Hicks *et al.* 2004). The extent to which transmitted risk factors are specific to CUDs *v.* broad temperamental factors inclusive of CUDs, or the extent to which these mechanisms are gender-related, requires additional study.

There are a few noteworthy study limitations that must be considered in conjunction with findings from this research. First, the ethnic diversity of the OADP sample, although representative of the ethnic distribution of western Oregon, is limited. A majority of the sample (89%) was Caucasian. Some studies (e.g. Brook *et al.* 2011*a*) suggest that rates of CUDs might vary considerably as a joint function of race and gender. Second, this research was conducted with a community sample of western Oregon youth. Cannabis is probably more readily available in the Pacific Northwest region compared with other US regions, and cannabis availability has been associated with an increased risk for cannabis initiation and abuse (Gillespie *et al.* 2009). The lifetime prevalence

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rates of CUDs reported here, however, are generally consistent with findings reported in international prospective samples (Boden *et al.* 2006; Perkonigg *et al.* 2008; Moffitt *et al.* 2010). Third, there was sample attrition across assessment waves, and it is possible that this attrition may have biased some findings. Analyses to determine whether distributions of CUDs at T_1 differed between the attrition group and the reference sample revealed no evidence of selective bias based on adolescent CUD history. Wave-to-wave attrition analyses, however, indicated a significantly higher rate of attrition between T_3 and T_4 for those with a CUD history by T_3. Parallel analyses to those reported here were conducted with the T_3 panel, and few differences were noted in the findings observed (see Note 1). Fourth, data collection and diagnostic coding procedures adopted for this study precluded us from estimating CUD course transition rates (i.e. recovery and recurrence rates) for time intervals less than those specified (e.g. rate comparisons when recovery was defined as an uninterrupted remission lasting at least 6 months *v.* 12 months). Cumulative hazard functions (Figs. 2 and 3), however, provide information about the implications for rate data when recovery and recurrence transition points are extended beyond this study's definitional parameters.

To illuminate possible mechanisms that underlie CUD onset, maintenance, recovery and recurrence processes, future research might examine the predictive value of proximal and distal factors associated with each of these events. Additionally, as suggested by limited longitudinal research (Kandel & Chen, 2000; Flory *et al.* 2004; Windle & Wiesner, 2004, Wittchen *et al.* 2009; Brook *et al.* 2011*b*), individuals who currently or historically met criteria for a CUD might be quite heterogeneous along a number of important dimensions. To clarify the heterogeneity among those with CUDs, future research might attempt to identify distinct developmental trajectories based on patterns of cannabis use or abuse over time, and evaluate the extent to which the resultant trajectories overlap with those associated with other forms of substance use (e.g. alcohol use, abuse of other illicit drugs). Although each substance appears to have a unique developmental trajectory (Rohde & Andrews, 2006), it might be that the distinctiveness of trajectories associated with different substances is diminished among more problematic users.

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Declaration of Interest

None.

Notes

1 To evaluate if differential rates of attrition between T_3 and T_4 for those with a lifetime CUD by T_3 had an effect on the conclusions reached in the present research, we repeated the analyses presented in the Results section with the T_3 panel (n=941). Only modest differences were observed between samples, and in only two instances did non-significant findings for the T_4 panel emerge as significant in the T_3 panel. These exceptions were noted in gender comparisons for the first incidence and period prevalence rates for ages 14.0 to 17.9 years. When rates based on T_3 and T_4 panel data were compared for this age interval, male probands demonstrated higher CUD first incidence and period prevalence rates in the T_3 panel compared with the T_4 panel (9.3% *v.* 7.6% for first incidence, 11.5% *v.* 9.9% for period prevalence, respectively). These higher rates for males resulted in statistically significant OR comparisons between female and male probands for this age interval when based on T_3 panel data (first incidence: OR 1.70, 95% CI 1.04–2.80; period prevalence: OR 1.71, 95% CI 1.09–2.68), with males having higher rates of lifetime CUDs than females in each instance.

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