Drug and Alcohol Dependence 194 (2019) 45–50

Contents lists available at ScienceDirect

Drug and Alcohol Dependence

journal homepage: www.elsevier.com/locate/drugalcdep

Full length article

Prevalence, incidence, recovery, and recurrence of alcohol use disorders from childhood to age 30

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ARTICLE INFO

Keywords:
Alcohol use disorders
Natural course
Onset
Recovery
Recurrence
Sex differences

ABSTRACT

Background: Little is known about the course of alcohol use disorders (AUDs) in representative samples during high-risk periods of adolescence and early adulthood. The primary objective of this research is to describe the prevalence and course of initial AUD episodes experienced between childhood and age 30 in a regionally representative cohort sample.

Methods: Study data are from an epidemiological study of 816 youth. Participants were initially selected at random from nine high schools in western Oregon, USA. Four waves of data collection were conducted between ages 16 and 30. AUD course milestones are referenced to participants' age.

Results: Results indicated that male participants (43%) were significantly more likely to be diagnosed with a lifetime AUD than female participants (28%), *OR* [CI_{95}] = 1.97 [1.47–2.65], and rate of first incidence was especially high between ages 18 and 24.9, a developmental period that also corresponded to the peak interval in prevalence rates. The rate of first AUD incidence substantially diminished beginning around age 25. Among those with an initial AUD episode, 87% recovered by age 30 and, of these, the average episode length was 23 months. Among recovered cases, 33% went on to experience a second AUD episode (i.e., a recurrence) after a minimum 12-month asymptomatic recovery period. Risk for recurrence remained relatively high within the 5 years following initial AUD offset.

Conclusions: AUDs are common lifetime conditions in representative samples, whereby most affected individuals by age 30 experience a time-limited course rather than a recurring or persistent course.

1. Introduction

Alcohol use disorders (AUDs) are prevalent globally, especially in western countries. Within the United States (U.S.), the cross-sectional 2001–2002 National Epidemiologic Survey on Alcohol and Related Conditions (NESARC-I) estimated the lifetime rate of AUD based on DSM-IV criteria to be 30% (Hasin et al., 2007). NESARC-III, a cross-sectional survey conducted during 2012–2013 and based on DSM-5 criteria, produced a 29% lifetime AUD rate estimate (Grant et al., 2015). Lifetime prevalence rates derived from multiple assessments with prospective longitudinal cohort samples also indicate that AUDs are common. In the Dunedin Multidisciplinary Health and Development Study, the lifetime rate of alcohol dependence based on DSM-III-R and DSM-IV criteria was 32% between ages 18 and 32 (Meier et al., 2013; Moffitt et al., 2010). In the Christchurch Health and Development Study (Fergusson and Horwood, 2001), lifetime rates of AUD from ages 15 to 35 based on DSM-III-R and DSM-IV criteria were 56% and 40% for male and female cohorts, respectively, or about 48% overall (Joseph M. Boden, personal communication, 2 July 2017). In the Zurich Cohort Study of Young Adults, which spanned ages 18 to 50, the estimated lifetime rate of AUD based on DSM-III, DSM-III-R, and DSM-IV was 29% (Angst et al., 2016). We (Farmer et al., 2016) earlier reported a 34% lifetime rate of DSM-IV AUD from childhood to age 30 for the Oregon Adolescent Depression Project (OADP) cohort. Despite the regional and methodological differences that characterize these studies, the overarching conclusion remains that AUDs are common in communities within Australasia, Europe, and North America.

AUDs, as defined in DSM-IV or earlier editions, typically first emerge and increase in prevalence during adolescence, peak during late adolescence and early adulthood, and gradually decline thereafter (Sher et al., 2005). Factors associated with the rapid escalation of AUD prevalence within this span include increased alcohol availability (Komro et al., 2007), reduced parental monitoring (Guilamo-Ramos et al., 2005), and peer influences (Patrick et al., 2016). Reductions in

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https://doi.org/10.1016/j.drugalcdep.2018.09.012
Received 26 March 2018; Received in revised form 13 September 2018; Accepted 17 September 2018
Available online 24 October 2018

prevalence after early adulthood are often attributed to "maturing out" and the assumption of adult life roles incompatible with excessive alcohol consumption (Sher et al., 2005). A better understanding of AUD course in representative samples, particularly during the high-risk periods spanning childhood through young adulthood, is especially important given the adverse health, social, economic, and legal consequences that often accompany AUDs (Brown et al., 2000; Parry et al., 2011; Rehm et al., 2009; Whiteford et al., 2013) which may be difficult to overcome later in life.

Views on the course of AUD have largely been shaped by studies of treated or high-risk samples, leading some to conclude that AUDs are best characterized as a chronic medical illness punctuated by alternating periods of remission and relapse (McLellan et al., 2000). A different view on the course of AUDs, however, is emerging from representative and population samples. Remission and recovery concepts in these studies have been defined variously as (a) the point at which an individual no longer meets diagnostic criteria for AUD, (b) consumption of alcohol at an amount below some threshold level of risk, or (c) complete abstinence from alcohol. Overall, these studies suggest that AUDs typically have a relatively brief course, with a large majority of baseline positive cases in remission or recovery within three years (Boschloo et al., 2012; Dawson et al., 2012; de Bruijn et al., 2006; Hasin et al., 2011; Tuithof et al., 2013). Although a large proportion of persons diagnosed with an AUD recover without participation in a treatment program (Dawson et al., 2005; de Bruijn et al., 2006; Sobell et al., 1996), those who report more severe alcohol-related problems are less likely to recover (Cunningham, 1999; de Bruijn et al., 2006).

Relapse or recurrence following a period of sustained remission represents a significant challenge to lasting change. Research on the recurrence of AUD following remission or recovery in representative samples is rare (Tuithof et al., 2014). A small number of such studies suggests that relapse or recurrence rates for remitted or recovered cases may be less than 15% within a 3–20 years follow-up interval (Dawson et al., 2007; de Bruijn et al., 2006; Tuithof et al., 2014). Altogether, the relatively few studies with representative prospective samples suggest that AUDs are common, generally of brief duration, and rarely recurrent.

Most research on the course of AUDs is based on treated samples, within which disorder severity and comorbid psychopathology are often substantially greater than in representative samples (Low et al., 2008). This investigation into the natural course of AUDs is based on data collected as part of the OADP, a longitudinal study of a regionally representative community sample. Previous OADP publications have presented AUD rates and sex distributions at ages 16 and 17 (Rohde et al., 1996), at age 24 (Rohde et al., 2001), and at age 30 (Farmer et al., 2016). The present research extends our earlier work by presenting first incidence and period prevalence data from childhood through age 30. We also examine several course indicators that signify milestones in change processes not previously reported in earlier publications, including time to onset, recovery, and recurrence when referenced to the initial (first) AUD episode. Additionally, limited indications suggest that females experience a course of AUD that is distinct from that of males, although relevant research with representative samples is sparse (e.g., Edens et al., 2008; Merikangas and McClair, 2012). We consequently conduct sex distribution comparisons of AUD for each time period or interval evaluated and in the cumulative hazard functions that describe various course indicators over time.

2. Materials and methods

2.1. Participants

OADP participants were assessed on four occasions between ages 16 and 30 (T_1-T_4). The T_1 sample consisted of 1709 adolescents randomly selected from 9 high schools representative of urban and rural districts in western Oregon (Lewinsohn et al., 1993). About one year later (T_2), 1507 (88%) were again evaluated. At T_3 (7 years after T_2), a sampling stratification procedure was introduced whereby eligible participants included all persons with a history of a psychiatric diagnosis by T_2 ($n = 644$) and a randomly selected subset of participants with no mental disorder history (NMD) by T_2 ($n = 457$ of 863 persons). Comparisons between the T_3 NMD randomly selected participants with unselected NMD participants revealed no significant differences with respect to T_2 data. Of these 1101 eligible persons, 941 (85%) completed T_3. Among those who completed T_3, 816 (87%) completed the T_4 assessment at age 30 (59% female; 89% white; 53% married; 43% at least a bachelor's degree).

An analysis of attrition included comparisons between T_4 participants to those who dropped out after T_1 with respect to a lifetime diagnosis of a DSM-defined disorder and the summated number of distinct lifetime psychiatric disorders by T_1 (Farmer et al., 2013). The T_4 panel was not statistically different from the attrition group with respect to any psychiatric disorder history ($p = .96$) or the sum of all lifetime disorders ($p = .23$) at T_1. An attrition analysis conducted for this report found that those in the attrition group, when compared to the T_4 panel, did not have significantly higher rates of AUDs at T_1 (7% vs. 5%, respectively). Across-wave analyses, however, revealed one significant difference whereby discontinuation after T_3 was more common among those with an AUD history by T_3 (lifetime AUD rates: 41% for discontinuers, 31% for T_3 participants; Pearson χ^2 [1, $n = 941$] = 4.88, $p = .027$).

Other differences across waves were noted between study continuers and dropouts. When compared to the T_2 sample, discontinuers after T_1 were more likely male, from smaller sized households, socioeconomically challenged, tobacco users, and more likely to have histories of disruptive behavior disorders and substance use disorders (SUDs) undifferentiated with respect to substance type (Lewinsohn et al., 1993). From T_2 to T_3 and T_3 to T_4, women were more likely to continue participation than men (Lewinsohn et al., 1999; Rohde et al., 2007). From T_3 to T_4, discontinuers had a higher rate of SUD undifferentiated with respect to substance. Because of the sample stratification procedures implemented at T_3 and the relatively modest attrition across waves, results presented below are based on the T_4 panel ($N = 816$).

2.2. AUD assessments

From T_1 through T_3, participants were interviewed with the Schedule for Affective Disorders and Schizophrenia for School-Age Children (K-SADS) that combined features of the Epidemiologic and Present Episode versions (Chambers et al., 1985; Orvaschel et al., 1982). T_2 and T_3 assessments also involved the administration of the Longitudinal Interval Follow-Up Evaluation (LIFE; Keller et al., 1987) that, in conjunction with the K-SADS, provided detailed information concerning the presence and course of disorders since the previous interview. The T_4 assessment included an administration of the LIFE and the Structured Clinical Interview for Axis I DSM-IV Disorders– Non-Patient Edition (First et al., 1994). Sufficient additional symptom information was collected during T_1 and T_2 to permit DSM-IV-based evaluations of substance-specific SUD categories (Rohde et al., 2007). Consequently, AUD diagnoses are based on DSM-IV diagnostic criteria. Information was collected at each assessment regarding treatment utilization for AUD, which was defined as outpatient treatment (individual, family, or alcohol support groups), inpatient treatment, hospitalizations, and medications. Agreement among raters for AUD diagnoses since the previous interview, as indexed by kappa (κ), was good to excellent (κs: $T_1 = .76$, $T_2 = .89$, $T_3 = .69$, $T_4 = .79$). When both raters agreed on the occurrence of an initial AUD episode, the intraclass correlation coefficient (ICC) associated with duration judgments (in months) was .89. ICCs corresponding to rater agreement for age (in months) of disorder onsets and offsets in instances where both raters agreed on an initial AUD episode occurrence were similarly high

(ICCs = .92 and .87 for disorder onsets and offsets, respectively).

2.3. AUD recovery and recurrence defined

Definitions of recovery and recurrence used in this study are informed by earlier descriptions of these concepts (Chung and Maisto, 2006; Frank et al., 1991), LIFE interview naming conventions (Keller et al., 1987), and DSM-IV guidelines. In the present research, *remission* refers to offset of an initial AUD episode lasting at least 1 full month but < 12 months during which the participant did not endorse any diagnostic criteria for AUD. During this remission period, however, participants may have used alcohol in the absence of alcohol-related problems as defined in AUD diagnostic criteria. The re-emergence of any AUD symptomatology during the remission period was regarded as a continuation of the initial episode (i.e., a *relapse*). Initial episode resolution, defined by a period of uninterrupted remission of at least 12 months, is considered a *recovery* from the initial episode. A *recurrence* is regarded as the emergence of a new AUD episode after a period of recovery.

2.4. Analyses

Estimates of prevalence rates, incidence rates, and odds ratios (*ORs*) accounted for the unequal stratified sampling procedure implemented at T_3 with a case weighting procedure. Age ranges used when reporting first incidence and period prevalence rates were informed by Arnett's (2007) framework: childhood through emerging adolescence (childhood to age 13.9), adolescence (ages 14.0–17.9), adolescence transitioning to emerging adulthood (ages 18.0–24.9), and emerging adulthood transitioning into young adulthood (ages 25.0–30.0).

Time-to-event analyses were implemented with Mplus statistical software (Muthén and Muthén, 1998-2012). Cumulative hazard functions were used to describe AUD onset, recovery, and recurrence functions in the presence of censorship (i.e., participants who do not experience an AUD onset, recovery, or recurrence between childhood and age 30). Time-to-event was measured in months. When cumulative hazard functions exceeded 0.5, the median survival time was reported to facilitate data interpretation.

Sex moderation of the time-to-event functions was evaluated with Cox proportional hazard (PH) models. These models assume the absence of a significant time-by-predictor interaction. Preliminary analyses involved the inclusion of the interaction term in the model as recommended by Singer and Willett (1991). On no occasion was the interaction term statistically significant (all *ps* ≥ .05), indicating that this model assumption was upheld. All models were subsequently rerun with the interaction term removed. Departures in onset curves as a function of sex were derived from hazard ratio (*HR*) estimates and accompanying 95% confidence intervals (CI_{95}).

3. Results

3.1. Prevalence rates, incidence rates, and age of onset for initial AUD episodes

3.1.1. Prevalence and incidence rates

The weighted lifetime prevalence of AUD from childhood to age 30 was 34.3%. By T_4, men (42.9%) were more likely than women (27.6%) to be diagnosed with a lifetime AUD (*OR* [CI_{95}] = 1.97 [1.47–2.65]). Only 15.3% of those with a lifetime AUD reported receiving treatment for AUD.

Table 1 presents weighted first incidence and period prevalence rate information. AUD first incidence rates were especially high between ages 18.0–24.9 and substantially diminished after age 25. Ages 18.0–24.9 also corresponded to the peak AUD prevalence period for both men and women. *First incidence rates* significantly differed by sex within the 18.0–24.9 period only (29.4% of males, 16.3% of females; *OR* [CI_{95}] = 2.14 [1.53–3.00]). *Period prevalence rates* significantly differed by sex within the 18.0–24.9 age range (36.7% of males, 22.6% of females; *OR* [CI_{95}] = 1.99 [1.46–2.70]) and the 25.0–30.0 range (21.9% of males, 12.3% of females; *OR* [CI_{95}] = 2.00 [1.37–2.91]).

3.1.2. Time to AUD onset

Among participants with a lifetime AUD, the mean onset age for the initial episode was 20.3 years (*SD* = 3.8). Mean onset ages did not significantly differ by sex (observed *Ms*: males = 20.6, *SD* = 3.4; females = 19.9). Cumulative hazard functions for AUD onset for the entire sample and separately by sex are presented in Fig. 1. The cumulative hazard functions significantly differed by sex (*HR* [CI_{95}] = 1.63, [1.30–2.03], $p < .001$), with males compared to females demonstrating a steeper rise and consistently greater cumulative rates beginning around age 18.

3.2. Recovery and non-recovery from the initial AUD episode

3.2.1. Rates of recovery

For those with a lifetime AUD, 87.1% experienced recovery from the initial episode by age 30. Recovery rates did not significantly differ by sex (84.9% for males, 89.8% for females).

3.2.2. Episode duration and time to recovery

The mean duration of the initial AUD episode for those who recovered was 23.1 months (*SD* = 23.3). A statistically significant sex difference in episode duration means was observed (males = 28.2 months, *SD* = 27.2; females = 17.3 months, *SD* = 16.1; Welch's $t[215] = -3.87$, $p < .001$, $\eta^2 = .055$).

Time-to-recovery estimates were based on the duration of the initial AUD episode plus a 12-month period of sustained remission without relapse following episode offset. Participants were right censored from the analysis if a 12-month period of sustained remission following offset of the initial AUD episode was not achieved before age 30. Cumulative hazard functions for recovery for the full subsample with AUD histories and separately by sex within this subsample are presented in Fig. 2. For those who recovered, the mean time to recovery from the initial episode was 34.9 months (*SD* = 23.3). A statistically significant sex difference in mean time to recovery was observed (males = 40.0 months, *SD* = 27.2; females = 29.1 months, *SD* = 16.1; Welch's $t[215] = -3.89$, $p < .001$, $\eta^2 = .055$). Treatment utilization was not significantly related to time to recovery (p = .598).

3.2.3. Episode duration for those who did not recover from the initial episode

In the weighted sample, 18% of those with one AUD episode remained in episode at age 30. The mean duration of that episode for these individuals through age 30 was 59.2 months (*SD* = 42.2), which was significantly longer ($t = 4.87$, $p < .001$) than the episode length for those with a single AUD episode and who achieved recovery (*M* = 23.9 months, *SD* = 22.2).

3.3. Recurrence after the initial AUD episode

3.3.1. Recurrence rates following recovery

Among participants who recovered from the initial AUD episode, 32.8% subsequently developed another AUD episode prior to age 30. Rates of recurrence were not significantly different between males (33.8%) and females (31.7%).

3.3.2. Time to recurrence

For those who experienced a second AUD episode, the mean time to recurrence was 49.2 months (*SD* = 28.0). Time to recurrence did not significantly differ between males (46.0 months) and females (53.0 months). Cumulative hazard functions are presented in Fig. 3 for time-to-recurrence for the full subsample as well as separately by sex for

Table 1
Prevalence, incidence, recovery, and recurrence rates of alcohol use disorders from childhood to age 30 by sex.

	Female Participants % [CI_{95}]	Male Participants % [CI_{95}]	*OR* [CI_{95}]
Lifetime prevalence	27.6 [23.5-31.7]	42.9 [37.8-48.0]	**1.97 [1.47-2.65]**
First incidence			
0.0 to 13.9 years	1.7 [0.5-2.9]	0.6 [0.0-1.4]	0.35 [0.08-1.57]
14.0 to 17.9 years	6.4 [4.2-8.6]	8.1 [5.4-10.8]	1.27 [0.75-2.17]
18.0 to 24.9 years	16.3 [13.0-19.6]	29.4 [24.7-34.1]	**2.14 [1.53-3.00]**
25.0 to 30.0 years	3.2 [1.6-4.8]	4.9 [2.7-7.1]	1.57 [0.77-3.21]
Period prevalence			
14.0 to 17.9 years	7.2 [4.8-9.6]	8.7 [5.8-11.6]	1.22 [0.73-2.03]
18.0 to 24.9 years	22.6 [18.7-26.5]	36.7 [31.6-41.8]	**1.99 [1.46-2.70]**
25.0 to 30.0 years	12.3 [9.4-15.2]	21.9 [17.6-26.2]	**2.00 [1.37-2.91]**
Recovery rates	89.8 [84.5-95.1]	84.9 [79.2-90.6]	0.64 [0.31-1.32]
Recurrence rates for those who recovered	31.7 [23.1-40.3]	33.8 [25.6-42.0]	1.10 [0.64-1.88]

Note. CI_{95} = 95% confidence interval. *OR* = Odds ratio. Bolded *OR*s are statistically significant at $p < .05$. All summary statistics account for sample weighting.

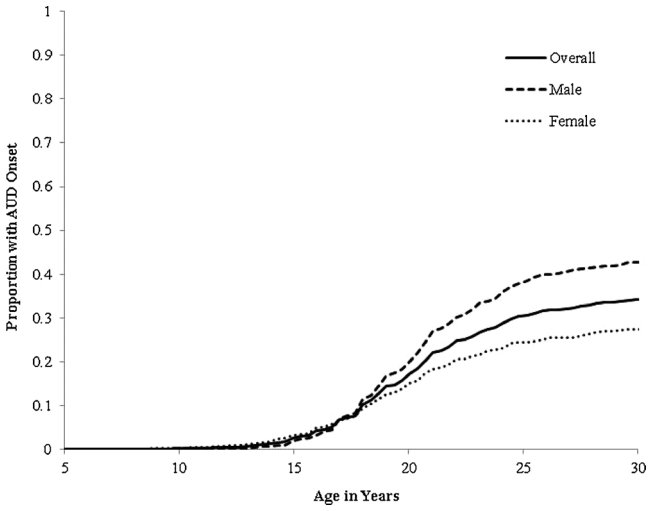

Fig. 1. Cumulative hazard functions for the onset of alcohol use disorders (AUD).

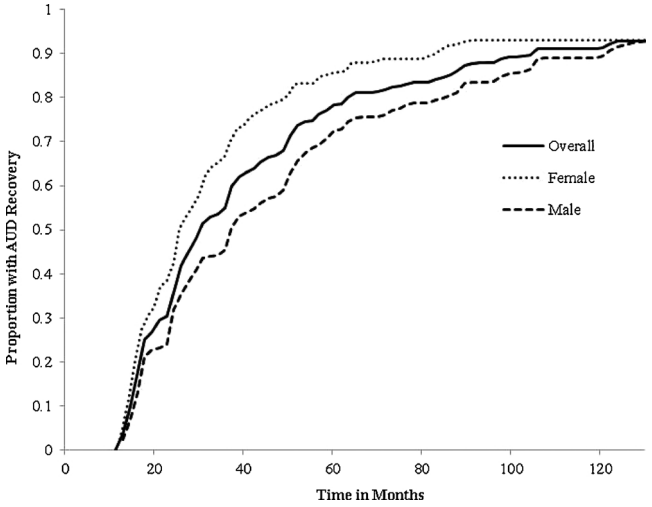

Fig. 2. Cumulative hazard functions for the recovery from alcohol use disorders (AUDs).

those who experienced a recovery from the initial AUD episode by age 30. Cumulative hazard functions that assessed time to recurrence did not differ by sex or AUD treatment received during the index episode. As depicted in Fig. 3, recurrence rates began to level off about 60 months after recovery, with recurrence becoming relatively rare after

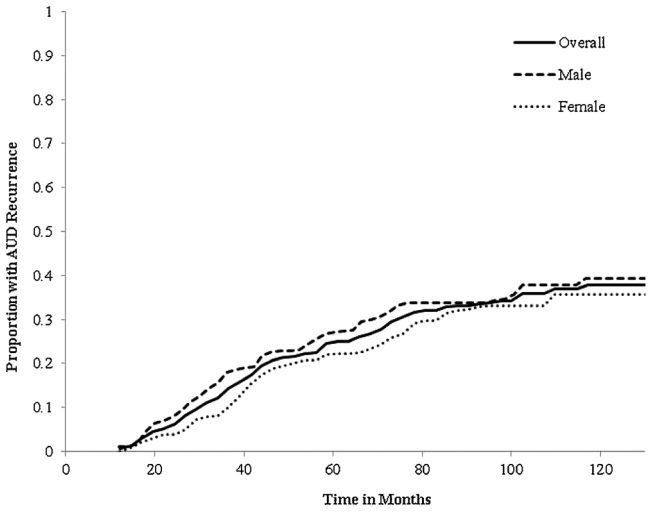

Fig. 3. Cumulative hazard functions for the recurrence of alcohol use disorders (AUD).

the 75th consecutive month after offset of the initial episode. Overall, findings reported in Fig. 3 suggest that AUD recurrence before age 30 takes place among a minority of those with a previous episode. An asymptomatic 12-month period following initial AUD offset, however, appears not to be an optimal threshold for denoting full recovery from AUDs. Rather, recurrence risk continues to be relatively high after 5 years of remission and recovery.

4. Discussion

Data on the natural course of AUDs can inform judgments about the expected prognosis of AUDs over time, influence theoretical conceptualizations of the nature of AUDs, inform the timing and design of preventive, treatment, and relapse reduction efforts, and serve as a benchmark for evaluating therapy effectiveness (Maisto et al., 2014). Our research suggests that in addition to being common among young community residents, AUDs are heterogeneous with respect to course among affected persons. AUDs are time-limited and non-recurrent for some, whereas for others AUDs constitute a persistent or recurring condition.

Sex differences in AUD rates across the age span, with the possible exception of early to mid-adolescence when rates are relatively low, have been previously noted (Wells et al., 2006). International research involving representative cross-sectional (Cheng et al., 2015; Cho et al., 2015; Grant et al., 2015; Hasin et al., 2007; Kessler et al., 2005; Subramaniam et al., 2012; Teesson et al., 2010) or community-based prospective samples (Angst et al., 2016; Meier et al., 2012; Wells et al.,

2006) consistently indicate greater rates of AUDs among male versus female participants. We similarly found an absence of significant sex differences in AUD rates prior to age 18 but generally small to moderate sex differences afterwards with men demonstrating consistently higher rates than women.

For both sexes, the peak incidence and prevalence rates for AUD occurred between ages 18 and 24.9. These findings are consistent with those reported in other studies with representative samples, where the typical age of onset for the first AUD episode was before age 30 (Grant et al., 2015; Hasin et al., 2007; Kessler et al., 2005; Subramaniam et al., 2012; Teesson et al., 2010). Cumulative hazard functions characterizing AUD onset functions in the present research differed significantly between male and female participants: males demonstrated a steeper rise beginning around age 18. For both sexes, risk for first AUD onsets substantially diminished beginning at age 25, although period prevalence rates for AUDs remained high between ages 25 and 30. Greater AUD persistence was noted for men, a finding consistent with earlier reports (Boschloo et al., 2012; Walitzer and Dearing, 2006). Overall, first incidence and period prevalence rate data in this study have strong resemblances to the "developmentally limited" patterns that have been reported earlier in cross-sectional and longitudinal studies with representative samples, whereby heavy alcohol consumption or AUDs increase during adolescence and early adulthood and then decline during the mid to late 20 s (Meier et al., 2013; Sher et al., 2005; Teesson et al., 2010; Wells et al., 2006).

Among those with AUD histories, 87% recovered from the initial episode by age 30. No significant differences in recovery rates were observed between men and women. Cumulative hazard functions significantly differed by sex, however, whereby women recovered more quickly and at a faster rate than men. For those who recovered, the average length of the initial AUD episode was relatively brief (23 months) when referenced to AUD episode durations commonly reported within treatment samples. Of those who recovered, however, 33% experienced an episode recurrence. This rate is higher than those earlier reported for representative samples with follow-up intervals of $\leq$ 3 years duration (Dawson et al., 2007; de Bruijn et al., 2006). This study's recurrence rate is also higher than that reported by Tuithof at a 20-year follow-up (Tuithof et al., 2014). This latter investigation, however, was primarily based on retrospective reports, which are known to generally underestimate lifetime disorder occurrences (Haeny et al., 2014; Moffitt et al., 2010). The absence of sex differences in recurrence rates found in the present study is generally consistent with earlier findings summarized elsewhere based on treatment samples (Walitzer and Dearing, 2006). Additional findings indicated that risk for episode recurrence remained considerable within the first five years following remission and recovery from the first episode. These observations are similar to those reported in the natural recovery literature, which generally suggests that recovery is more likely to be maintained after five years of non-recurrence (Sobell et al., 2000).

Perspective on the course of AUDs, based largely on treatment samples, has shifted in recent years from one where AUDs were regarded primarily as chronic medical illness punctuated by periods of remission and relapse (McLellan et al., 2000) to a perspective where the course of AUDs is relatively brief and largely time-limited (Boschloo et al., 2012; Dawson et al., 2012; de Bruijn et al., 2006; Hasin et al., 2011; Tuithof et al., 2013). We found evidence supportive of both of these perspectives. A third of those who recovered from the initial AUD episode experienced a recurrence, and 18% of those with a single AUD episode did not recover from that episode by age 30. For this latter subgroup, the mean AUD episode duration by age 30 was about 5 years. A majority of the sample with AUD (71%), however, recovered from the initial episode and did not experience a recurrence by age 30. Since only 15% of the OADP sample with AUD received some form of treatment during the initial episode, a large majority of cases were unaided professionally in their transition from AUD to recovery. Because a small proportion of those with AUD received treatment services, it is unlikely that most of the OADP sample with AUD matched the degree severity and psychiatric comorbidity found in treatment samples (Low et al., 2008). In other studies with representative samples, AUD recurrence or persistence has been predicted by the severity of alcohol-related problems and psychiatric comorbidity (Boschloo et al., 2012; Dawson et al., 2007; Hasin et al., 2011; Tuithof et al., 2014).

Although there are several study strengths, there are also limitations. First, the ethnic diversity of the sample, although representative of the ethnic distribution of western Oregon, is restricted. Within U.S. population samples, AUD prevalence rates and some course features demonstrate differences depending on race or ethnicity (Dawson et al., 2005; Grant et al., 2012, 2015; Hasin et al., 2007). AUD rates and course features also vary across geographic regions and cultures (Cheng et al., 2015; Cho et al., 2015; Subramaniam et al., 2012; Zavos et al., 2015). Consequently, there are some limits on the generalizability of study findings reported here. Second, study discontinuation after T_3 was more common among those with a history of an AUD, and there were some other statistically significant differences between those who discontinued or remained in the study over time. The full impact of non-random discontinuation on this study's findings is unclear. Third, the sample was followed only through 30 years of age, which limits the generalization of the study findings beyond this period of life.

Directions for future research are several. Because AUDs include a heterogeneous set of conditions with problematic alcohol use in common (Sher et al., 2005), future natural course research should better accommodate such heterogeneity into the modeling process. In DSM-5, for example, AUDs are characterized as mild, moderate, or severe based on the number of symptom features present. Greater alcohol involvement and alcohol-related problems have been found to predict a poorer AUD course (Connor et al., 2016; Dawson et al., 2005; Moyer et al., 2002); consequently, future research might evaluate whether different levels of AUD severity arise through distinct sets of processes. A greater understanding of processes that underlie transitions in the course of AUD would also have significant value in informing theory and intervention development.

Role of the funding source

National Institutes of Health grants R01MH40501, R01MH50522, and R01DA12951 to Peter Lewinsohn and R01AA020968 to Richard Farmer and John Seeley supported this research. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health. The authors thank Peter Lewinsohn for the Oregon Adolescent Depression Project dataset used in this research.

Contributors

JRS had the initial study idea and was involved in the original study protocol and data collection. RFF conducted background literature searches. DBK and JMG programmed and conducted statistical analyses. JRS, RFF and DBK wrote the first draft of the manuscript. JRS, RFF, DBK and JMG contributed to interpreting the findings and writing further drafts of the manuscript. All authors reviewed and have approved the final manuscript.

Conflict of interest

No conflict declared.

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