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Onset of opportunity to use cannabis and progression from opportunity to dependence: Are influences consistent across transitions?

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ABSTRACT

Background: There is a developing body of research looking at cannabis use opportunity, but little research examining timing of opportunity to use cannabis.
Aims: Identify factors associated with (1) earlier opportunity to use cannabis and (2) faster progression from opportunity to cannabis dependence.
Method: Cross-sectional study of 3824 Australian twins and siblings, measuring age of onset of cannabis use opportunity and DSM-IV cannabis dependence. Survival analysis identified factors associated with faster progression to opportunity or dependence.
Results: Factors associated with both speed of progression to opportunity and dependence were conduct disorder (opportunity HR 5.57, 95%CI 1.52–20.47; dependence HR 2.49, 95%CI 1.91–3.25), parental drug problems (opportunity HR 7.29, 95%CI 1.74–30.62; dependence HR 3.30, 95%CI 1.63–6.69), weekly tobacco use (opportunity HR 8.57, 95%CI 3.93–18.68; dependence HR 2.76, 95% CI 2.10–3.64), and female gender (opportunity HR 0.69, 95%CI 0.64–0.75; dependence HR 0.44, 95%CI 0.34–0.55). Frequent childhood religious attendance (HR 0.74, 95%CI 0.68–0.80), parental conflict (HR 1.09, 95%CI 1.00–1.18), parental alcohol problems (HR 1.19, 95%CI 1.08–1.30) and childhood sexual abuse (HR 1.17, 95%CI 1.01–1.34) were uniquely associated with transition to opportunity. Depressive episode (HR 1.44, 95%CI 1.12–1.85), tobacco dependence (HR 1.36, 95%CI 1.04–1.78), alcohol dependence (HR 2.64, 95%CI 1.53–4.58), other drug use (HR 2.10, 95%CI 1.64–2.69) and other drug dependence (HR 2.75, 95%CI 1.70–4.43) were uniquely associated with progression to dependence.
Conclusion: The profile of factors associated with opportunity to use cannabis and dependence only partially overlaps, suggesting targeting of interventions may benefit from being tailored to the stages of drug use.

1. Introduction

Cannabis is widely used, with cumulative lifetime incidence of use estimated to range from 6%-20% in Europe, 3–11% in the Middle East and Africa, and to exceed 40% in the US and New Zealand (Degenhardt et al., 2008). Lifetime prevalence of cannabis use in Australian adolescents has been estimated at 60% (Patton et al., 2002). Although many individuals use cannabis infrequently and without experiencing problems, globally an estimated 13.1 million individuals meet criteria for cannabis dependence, contributing 10.3% of the illicit drug use global burden of disease (Degenhardt et al., 2014). It is estimated 10–16% of cannabis users develop dependence (Anthony, 2006), but before progressing to dependence individuals must pass through a number of preceding stages. Examining the multiple stages of drug use before dependence develops is necessary for gaining a comprehensive understanding of factors involved in drug use, and for identifying opportunities for early intervention (Hines et al., 2015a).

The first stage of drug involvement is having the opportunity to use (regardless of whether the individual uses the drug or not),

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which forms the "exposure opportunity" in the epidemiology of drug use (Wagner and Anthony, 2002). Opportunity is required for use to occur, and forms an individual's earliest necessary condition from which they are at risk of developing cannabis dependence. Recent research indicates the majority of adolescents who have an opportunity to use cannabis progress to initiation of use (Caris et al., 2009; Lopez-Quintero and Neumark, 2015; Pinchevsky et al., 2011), making the opportunity to use an important target for intervention (Neumark et al., 2012).

There is a developing body of research looking at the opportunity to use. Factors associated with opportunity to use cannabis include using alcohol, using tobacco and the combination of alcohol and tobacco use (Caris et al., 2009; Neumark et al., 2012; Wagner and Anthony, 2002). In Chile and the US, males have been found to be slightly more likely than females to have a chance to use cannabis (Caris et al., 2009; Van Etten and Anthony, 1999), but these gender differences have not been consistently observed (Wells et al., 2011). Childhood religious practices are associated with decreased likelihood of cannabis use opportunity (Chen et al., 2004), and those with externalising behaviour problems have been found to be more likely to have a cannabis use opportunity (Neumark et al., 2012; Reboussin et al., 2015). Perhaps unsurprisingly given that first cannabis use opportunity typically occurs in late childhood or early adolescence, lower parental involvement and higher levels of coercive discipline have been found to be associated with increased likelihood of cannabis use opportunity (Chen et al., 2005). The effect of parenting continues throughout adolescence, with those who reported low parental monitoring in high school more likely to have cannabis use opportunity once they started college (Pinchevsky et al., 2011).

Amongst this existing evidence, there is little research examining the timing of opportunity to use cannabis. The study of transitions, and the timing of these transitions, can provide unique insights into influences on substance use (Behrendt et al., 2012; Hines et al., 2015b; Sartor et al., 2009, 2008), but only a limited number of factors have been studied in relation to speed of transition to cannabis use opportunity (with earlier opportunity representing a faster transition) These have focussed on early childhood behaviours, with disruptive behaviour early in school in males and better reading scores in females associated with earlier cannabis use opportunity (Storr et al., 2011). Similarly, no research to date has explored whether there is overlap between factors associated with earlier opportunity and those associated with the speed of progression to dependence. These include other substance use (Behrendt et al., 2009), some mental health factors (Behrendt et al., 2011) and gender (Ridenour et al., 2006; Wittchen et al., 2008). Exploring speed of transition to cannabis opportunity will determine whether risk factors for dependence are already exerting influence on drug use behaviours at the start of an individual's cannabis involvement, which has utility for improving understanding of how dependence develops (Hines et al., 2015a). Applying survival analysis methodology to this area allows for quantification of time to cannabis use opportunity and from opportunity to dependence, and identification of what factors may impact upon the speed of these transitions.

This paper aims to:

1. Identify factors associated with earlier opportunity to use cannabis.
2. Identify factors associated with progression from cannabis use opportunity to cannabis dependence.
3. Determine whether factors associated with opportunity to use cannabis are also associated with more rapid progression from first opportunity to dependence.

2. Methods

2.1. Sample

The sample was drawn from the Australian Twin Registry. From a pool of twin pairs born between 1972 and 1979, 3348 MZ and DZ twins and 476 of their siblings (mean age at time of interview = 32.1, SD 3.04, range 21–46) completed the interview component of a study of cannabis and other drug misuse. A full description of the study methodology and of the characteristics of participants has been published previously (Lynskey et al., 2012).

2.2. Assessment

Participants were assessed through computer-assisted telephone interviews which collected information on sociodemographics, childhood experiences, drug use and common mental health disorders, including conduct disorder and major depressive disorder, assessed using the SSAGA-OZ interview (Bucholz et al., 1994; Heath et al., 1997). The SSAGA-OZ is a validated measure of mental health using DSM-IV criteria, and includes assessment of cannabis and other drug abuse and dependence. Specific measures used in the current analyses are described below.

2.3. Measures

2.3.1. Outcome measures.

2.3.1.1. Opportunity to use cannabis. Participants were asked "have you ever been offered, or had the opportunity to use cannabis, even if you did not use it at the time? How old were you the first time?" Of 3,824 individuals interviewed, 3,798 provided information on whether or not they had ever had the opportunity to use cannabis. Of these, 85% ($N = 3399$) reported they had an opportunity to use cannabis. A continuous measure of age of first opportunity was used for both survival analysis models.

2.3.1.2. Cannabis dependence. Participants were classified as meeting lifetime criteria for DSM-IV cannabis dependence (American Psychiatric Association, 2000) if they reported three or more of the following symptoms occurring within the same 12 month period: using cannabis a greater number of times/greater amount than was intended, tolerance, wanting to cut down/stop use, spending so much time obtaining/using/recovering from the effects of cannabis the participant had little time for anything else, reducing important activities as a result of cannabis use, continuing use despite it worsening health/emotional problems. Withdrawal was not included as it was not part of DSM-IV criteria for cannabis dependence. Participants were also asked the age at which they first experienced three or more of these symptoms occurring within a 12 month period.

Of those reporting lifetime opportunity to use cannabis, 10.9% ($N = 371$) met criteria for cannabis dependence, and a continuous measure of age at onset of cannabis dependence was used in survival analysis.

2.3.2. Covariates.

2.3.2.1. Gender. Gender was determined through self-report.

2.3.2.2. Parental alcohol problems. Parental alcohol problems were determined through participant self-report of their mother or father experiencing problems with health/family/job/police/other as a result of drinking, or their mother or father drinking excessively.

2.3.2.3. Parental drug problems. Parental drug problems were determined through participant self-report of their mother or father experiencing problems with health/family/job/police/other as a result of drug use, or the participant reporting they felt their mother or father had a problem with drugs.

2.3.2.4. Parental conflict. Parental conflict was determined by participant responses to the questions "how often did your parents fight or argue in front of you?" and "how much conflict and tension was there between your parents?" Both questions focused on the period when the participant was aged 6–13. Participants reporting parents 'sometimes' or 'always' fought or argued, or 'a lot' or 'some' conflict/tension, were coded as experiencing high parental conflict.

2.3.2.5. Single parent family. Single parent family was determined by participants' report of whether their mother or father was absent. Interviewers recorded whether participants lived with their mother/mother figure and/or their father/father figure for at least 4 full years between 6 and 13.

2.3.2.6. Strict parenting. Strict parenting was determined through participants response to the items "In your opinion, when you were 6–13, was your mother/mother figure more strict than most mothers?" and " In your opinion, when you were 6–13, was your father/father figure more strict than most fathers?". Those who endorsed either of these items were classified as having experienced strict parenting.

2.3.2.7. Childhood sexual abuse. Childhood sexual abuse was recorded for individuals who reported being forced into sexual intercourse or any other forms of sexual activity before age 18. Self-reported age of sexual abuse onset was used to create a time varying covariate for sexual abuse.

2.3.2.8. Frequent childhood religious attendance. Frequent childhood religious attendance was determined through participant self-report of their frequency of attendance at religious services between ages 6 and 13. Participants were coded as frequently attending religious services if they reported attendance more than once a week, once a week, once or twice a month or every couple of months.

2.3.2.9. Conduct disorder. Conduct disorder was determined by participant self-report of at least 3 of the 15 DSM-IV criteria (American Psychiatric Association, 2000) occurring within the same 12-month period, prior to age 18. Participants' self-reported age of onset of 3 symptoms occurring within a 12 month period was used to create a time varying covariate for conduct disorder.

2.3.2.10. Depressive episode. Depressive episode was recorded if participants reported a two week period where they were more irritable than usual (if under age 18 at the time), felt depressed/down/sad/blue/discouraged, or had a lot less interest in things. Self-reported age of the first occurring depressive episode was used to make time varying covariates for survival analysis.

2.3.2.11. Weekly tobacco use. Weekly tobacco use was measured through the interview item "Was there ever a time in your life when you smoked cigarettes at least once a week for at least two months in a row?" Self-reported age of onset of weekly tobacco use was used to make time varying covariates for survival analysis.

2.3.2.12. Tobacco dependence. Tobacco dependence was measured through participants reporting 3 or more of the DSM-IV tobacco dependence criteria (American Psychiatric Association, 2000) occurring within a 12 month period. Self-reported age of onset of tobacco dependence was used to make time varying covariates for survival analysis.

2.3.2.13. Monthly alcohol use. Monthly alcohol use was measured through the interview item "At what age did you start to drink regularly—that is, drinking at least once a month for 6 months or more?" Self-reported age of onset of monthly alcohol use was used to make time varying covariates for survival analysis.

2.3.2.14. Alcohol dependence. Alcohol dependence was measured through participants reporting 3 or more of the DSM-IV alcohol dependence criteria (American Psychiatric Association, 2000) occurring within a 12 month period. Self-reported age of onset of alcohol dependence was used to make time varying covariates for survival analysis.

2.3.4.15. Other drug use. Other drug use was recorded if participants reported lifetime non-prescribed use of any of the following: cocaine (all forms), stimulants, opiates and major painkillers, sedatives, hallucinogens, dissociatives, solvents or inhalants. Self-reported age of drug use onset was used to create a time varying covariate for first other drug use.

2.3.2.16. Other drug dependence. Other drug dependence was recorded if participants reported lifetime dependence on any of the following: cocaine (all forms), stimulants, opiates and major painkillers, sedatives, hallucinogens, dissociatives, solvents and inhalants. Participants were classified as meeting lifetime criteria for DSM-IV drug dependence if they reported 3 or more of the 7 DSM-IV symptoms of dependence (American Psychiatric Association, 2000) occurring within the same 12 month period. Self-reported age of onset of dependence was used to create a time varying covariate for other drug dependence. This covariate was only included in the model of progression to the development of dependence.

2.4. Statistical analyses

All analyses were conducted in Stata statistical software version 11 (StataCorp, 2009). Two separate Cox proportional hazard models were fitted to the data to test the association between a number of potential associated factors and speed of progression from (1) birth to opportunity to use cannabis and (2) opportunity to use cannabis to the development of cannabis dependence. Both were assessed as time in years. Details of the two Cox Proportional Hazards models are provided below:

Model one: To identify factors associated with hazard of the opportunity to use cannabis survival data (time in years, starting from birth) were used for analysis of 3,798 participants who had provided information on opportunity to use cannabis. Failure event was opportunity to use cannabis, and 3398 failure events were observed (one participant was excluded from analysis, see description below). Due to missing covariate data, 3,763 participants were included in the final model (3367 failure events).

Model two: To identify factors associated with hazard of the development of dependence following the opportunity to use cannabis survival data (time in years, starting from age of first opportunity to use cannabis) were used for analysis of 2,593 participants who had reported their age of opportunity to use cannabis and who had also reported lifetime cannabis use (those who had not reported lifetime cannabis use were removed from the model in order to avoid the inverse association that would exist between never-use of cannabis and cannabis dependence; additionally, one participant was omitted as their recorded age of dependence was earlier than recorded age of opportunity). The failure event was

cannabis dependence, and 371 failures were observed. Due to missing covariate data, 2,565 participants were included in the final model (363 failure events).

Person year data sets were constructed providing a separate row of participant data for each year from birth for model 1, and for each year from age of opportunity for model 2. In order to account for multiple participants experiencing failures events in the same year, the Efron adjustment for survival ties (Efron, 1977) was applied. Participants were right-censored at age of interview.

Factors described above were included in the model. Time varying measures were produced for conduct disorder, monthly alcohol use, alcohol dependence, weekly tobacco use, tobacco dependence, other drug use, other drug dependence, childhood sexual abuse, and depressive episode. These variables were coded as present for each year after the age of onset, and were only included in the model if they were positive prior to the onset of cannabis use opportunity for model one, or prior to the onset of dependence for model two (e.g., if age at opportunity to use cannabis was 13, then conduct disorder with an age of onset of 14 was coded as absent prior to the onset of opportunity).

To minimise the likelihood that the effect of childhood covariates where the specified time periods were ages 6–13 (parental conflict, single parent family, strict parenting, frequent childhood religious attendance) may have occurred after the point of cannabis use opportunity, any individuals who reported use opportunity before the age of 6 were removed from model one. This resulted in the observations of only one participant being removed from the model. Huber-White analysis for clustered data was implemented to adjust for the non-independence of observations from members of a twin pair. The assumption of proportional hazards was assessed through tests of Schoenfeld residuals and modelling of the interaction of covariates with time in the analysis (represented as '_t') ($P = \leq 0.05$). Any variables found to violate the proportional hazards assumption were reparameterized via modelling interactions between the variable and time in the analysis, resulting in an extended Cox Proportional Hazards model.

Analyses on the transition from opportunity to first use of cannabis could not be conducted due to insufficient variation in this measure (the majority of participants progressed from opportunity to first use 0 or 1 years after having the opportunity to use, data available on request).

3. Results

3.1. Sample, survival data and the proportional hazards assumption

Comparisons between those who did and did not report lifetime cannabis use opportunity, and those who did and did not progress to cannabis use following opportunity, show these groups differ on the majority of the covariates tested within the survival models (see Tables 1). Mean age of first cannabis use opportunity was 17.6 (s.d. 3.2) and the mean age of cannabis dependence 21.4 (s.d. 4.1). The mean survival time for the participants in the cannabis use opportunity model was 19.1 years (s.d. 5.1) (age at opportunity, or for those who did not report opportunity, age at interview.) This figure is higher than the mean opportunity age as individuals who have not experienced opportunity by the point of interview are also included in the survival model, with their age at time of interview in place of age of opportunity. The mean survival time for participants in the cannabis dependence model was 13.4 years (s.d. 4.9) (time from opportunity to dependence, or for those who did not develop dependence, time from opportunity to age at interview). This figure is higher than may be expected from the mean dependence age as individuals who have not developed dependence by the point of interview are also included in the survival time, with their time from opportunity to age at interview in place of time to dependence.

All covariates were tested for breach of the proportional hazards assumption, as outlined in the methods section. The following did not satisfy the proportional hazards assumption for the opportunity to use model and therefore the interaction term between the factor and analysis time was modelled in the cannabis use opportunity analysis (Bellera et al., 2010): conduct disorder, parental drug problems, weekly tobacco use and monthly alcohol use. Similarly, for the cannabis dependence analysis the following variables had the interaction with analysis time modelled in the analysis: parental drug problems, alcohol dependence and other drug use.

3.2. Factors uniquely associated with opportunity to use cannabis

Results from the Cox proportional hazards model for transition to opportunity to use cannabis are presented in Table 3. Conduct disorder, high parental conflict, parental alcohol problems, parental drug problems, childhood sexual abuse and weekly tobacco use were associated with increased hazard of earlier opportunity to use cannabis. Frequent childhood religious attendance and female gender were independently associated with slower transition to cannabis use opportunity.

3.3. Factors uniquely associated with progression to cannabis dependence

Results from the Cox proportional hazards model for transition from opportunity to use cannabis to dependence are presented in Table 3. Conduct disorder, parental drug problems, weekly tobacco use, depressive episode, tobacco dependence, alcohol dependence, other drug use and other drug dependence were associated with increased hazard of faster transition cannabis dependence. Female gender was independently associated with slower transition to cannabis dependence.

3.4. Factors consistently associated across transitions

Factors associated with increased hazard of both earlier cannabis use opportunity and faster progression to cannabis dependence were conduct disorder, parental drug problems, and weekly tobacco use (see Table 3). Female gender was associated with slower progression to both cannabis use opportunity and dependence.

4. Discussion

This paper identifies a number of factors uniquely associated with the transition to cannabis use opportunity and with the transition from opportunity to cannabis dependence, and several factors that increase hazards of both these transitions. Parental conflict, parental alcohol problems and childhood sexual abuse were uniquely associated with faster transition to opportunity, whilst frequent childhood religious attendance was associated with slower transition to opportunity. Depressive episode, tobacco dependence, alcohol dependence, other drug use and other drug dependence were uniquely associated with faster progression from opportunity to dependence. Conduct disorder, parental drug problems and weekly tobacco use were associated with faster progression to both opportunity and from opportunity and dependence, with female gender associated with slower transition for both.

Exploring a broad range of factors has identified similarities and inconsistencies with the existing literature. Frequent childhood religious attendance, associated with reduced likelihood of cannabis use opportunity, was consistent with existing literature

Table 1
Comparison of characteristics of those who reported no lifetime cannabis use opportunity with those who reported lifetime cannabis use opportunity, and those who reported cannabis use opportunity and did not progress to use with those who did progress to use (proportions and odds ratios).

	No opportunity to use cannabis *N* = 399 N (%)	Opportunity to use cannabis *N* = 3399 N (%)	Odds Ratio (95% CI)	Opportunity but did not initiate cannabis use *N* = 805 N (%)	Opportunity and initiated cannabis use *N* = 2593 N (%)	Odds ratio (95% CI)
Female gender	326 (81.7)	2099 (61.8)	0.36 (0.28–0.47)	535 (66.5)	1563 (60.3)	0.77 (0.65–0.91)
Conduct disorder	4 (1.0)	320 (9.4)	10.30 (3.82–27.76)	24 (2.98)	296 (11.4)	4.21 (2.76–6.43)
Depressive episode	185 (46.5)	1636 (48.3)	1.08 (0.87–1.32)	374 (46.5)	1262 (48.9)	1.10 (0.94–1.29)
High parental conflict†	128 (32.1)	1272 (37.4)	1.27 (1.02–1.58)	257 (31.9)	1015 (39.2)	1.37 (1.16–1.62)
Parental alcohol problems	57 (14.3)	895 (26.3)	2.15 (1.61–2.87)	183 (22.7)	712 (27.5)	1.29 (1.07–1.55)
Parental drug problems	5 (1.3)	125 (3.7)	3.03 (1.23–7.46)	19 (2.36)	106 (4.1)	1.78 (1.09–2.92)
Single parent family†	14 (3.5)	203 (6.0)	1.75 (1.01–3.03)	48 (6.0)	155 (6.0)	1.00 (0.72–1.40)
Strict parenting†	183 (45.9)	1672 (49.2)	1.14 (0.93–1.41)	371 (46.1)	1301 (50.3)	1.18 (1.01–1.38)
Frequent childhood religious attendance†	299 (74.9)	1981 (58.3)	0.47 (0.37–0.59)	512 (63.6)	1468 (56.6)	0.75 (0.63–0.88)
Childhood sexual abuse	20 (5.1)	303 (9.0)	1.86 (1.17–2.95)	48 (6.0)	255 (9.9)	1.73 (1.26–2.38)
Weekly tobacco use	30 (7.5)	1493 (44.0)	9.65 (6.61–14.09)	110 (13.7)	1382 (53.4)	7.23 (5.83–8.96)
Tobacco dependence	15 (3.8)	946 (27.8)	9.89 (5.87–16.65)	50 (6.2)	895 (34.5)	7.97 (5.92–10.73)
Monthly alcohol use	274 (68.7)	3182 (93.6)	6.72 (5.22–8.65)	682 (84.7)	2500 (96.5)	4.90 (3.69–6.51)
Alcohol dependence	19 (4.8)	928 (27.3)	7.51 (4.71–11.98)	85 (10.6)	843 (32.5)	4.08 (3.21–5.18)
Other drug use	49 (12.3)	1623 (47.8)	6.54 (4.81–8.88)	140 (17.4)	1483 (57.2)	6.36 (5.21–7.75)
Other drug dependence	0 (0.0)	178 (5.2)	–	5 (0.6)	173 (6.7)	11.51 (4.71–28.10)

† When participant was aged 6–13 years old.

Table 2
Mean age (standard deviation) of behaviour onsets of those who reported no lifetime cannabis use opportunity with those who reported lifetime cannabis use opportunity, and those who reported cannabis use opportunity and did not progress to use with those who did progress to use.

	No opportunity to use cannabis *N* = 399	Opportunity to use cannabis *N* = 3399	Opportunity but did not initiate cannabis use *N* = 805	Opportunity and initiated cannabis use *N* = 2593
Conduct disorder	12.5 (s.d. 4.20)	14.2 (s.d. 2.31)	14.0 (s.d. 2.88)	14.2 (s.d. 2.26)
Depressive episode	22.4 (s.d. 6.26)	21.8 (s.d. 6.42).	21.8 (s.d. 6.51)	21.8 (s.d. 6.40)
Childhood sexual abuse	11.9 (s.d. 4.56)	11.1 (s.d. 4.68)	10.2 (s.d. 4.58)	11.3 (s.d. 4.69)
Weekly tobacco use	17.2 (s.d. 2.64)	17.3 (s.d. 3.44).	18.3 (s.d. 3.58)	17.3 (s.d. 3.42)
Tobacco dependence	23.8 (s.d. 7.77)	21.9 (s.d. 4.47).	23.5 (s.d. 4.62)	21.8 (s.d. 4.45)
Monthly alcohol use	20.4 (s.d. 3.72)	18.0 (s.d. 2.57).	19.1 (s.d. 3.14)	17.7 (s.d. 2.31)
Alcohol dependence	22.6 (s.d. 4.79)	22.5 (s.d. 4.20).	22.7 (s.d. 4.27)	22.5 (s.d. 4.19)
Other drug use	23.7 (s.d. 6.20)	21.6 (s.d. 4.26)	21.9 (s.d. 5.45)	21.6 (s.d. 4.13)
Other drug dependence	0 (0.0)	23.0 (s.d. 4.52)	25.8 (s.d. 3.90)	22.9 (s.d. 4.52)

Table 3
Hazard ratios (95%CI) from cox regression models: factor associated with earlier opportunity to use cannabis, and for progression from opportunity to use cannabis to cannabis dependence.

Covariate	Transition to cannabis use opportunity *N* = 3763		Transition to cannabis dependence *N* = 3367	
	Unadjusted HR (95% CI)	Adjusted HR (95% CI)	Unadjusted HR (95% CI)	Adjusted HR (95% CI)
Female gender	0.70*** (0.65–0.75)	0.69*** (0.64–0.75)	0.50*** (0.40–0.62)	0.44*** (0.34–0.55)
Conduct disorder[a]	[b]7.54*** (2.39–23.76)	[b]5.57** (1.52–20.47)	4.57*** (3.63–5.75)	2.49*** (1.91–3.25)
Depressive episode[a]	1.04 (0.93–1.17)	0.98 (0.87–1.10)	1.95*** (1.55–2.42)	1.44*** (1.12–1.85)
High parental conflict†	1.09* (1.01–1.18)	1.09* (1.00–1.18)	1.16 (0.94–1.44)	1.02 (0.79–1.31)
Parental alcohol problems	1.27*** (1.16–1.38)	1.19*** (1.08–1.30)	1.29** (1.03–1.62)	1.11 (0.86–1.43)
Parental drug problems	[b]8.26** (2.12–32.15)	[b]7.29** (1.74–30.62)	[b]4.14*** (2.07–8.27)	[b]3.30*** (1.63–6.69)
Single parent family†	1.30** (1.10–1.53)	1.13 (0.95–1.35)	1.60* (1.11–2.32)	1.19 (0.78–1.81)
Strict parenting†	1.03 (0.96–1.10)	1.02 (0.95–1.09)	1.32** (1.07–1.62)	1.11 (0.88–1.39)
Frequent childhood religious attendance†	0.72*** (0.66–0.78)	0.74*** (0.68–0.80)	0.86 (0.69–1.07)	0.84 (0.67–1.06)
Childhood sexual abuse[a]	1.25** (1.08–1.42)	1.17* (1.01–1.34)	1.98*** (1.49–2.64)	1.35 (0.95–1.92)
Weekly tobacco use[a]	[b]10.17*** (5.00–20.71)	[b]8.57*** (3.93–18.68)	3.98*** (3.12–5.07)	2.76*** (2.10–3.64)
Tobacco dependence[a]	1.82* (1.29–2.56)	0.89 (0.63–1.25)	2.77*** (2.18–3.52)	1.36* (1.04–1.78)
Monthly alcohol use[a]	[b]1.65 (0.78–3.50)	[b]0.75 (0.34–1.64)	1.03 (0.75–1.41)	0.94 (0.69–1.30)
Alcohol dependence[a]	1.79*** (1.29–2.48)	1.26 (0.89–1.78)	[b]2.94*** (1.69–5.12)	[b]2.64*** (1.53–4.58)
Other drug use[a]	1.31** (1.05–1.65)	1.20 (0.94–1.52)	2.76*** (2.22–3.42)	2.10*** (1.64–2.69)
Other drug dependence[a]	–	–	5.70*** (4.77–10.94)	2.75*** (1.70–4.43)

Note: Cannabis dependence *N* = 363 (due to missing covariate data). HR = Hazard ratio.
*$P < 0.05$ **$P < 0.01$ ***$P < 0.001$.
[a] Time Varying Covariate.
[b] interaction with _t included in the model to account for breach of the proportional hazards assumption.
† When participant was aged 6 – 13 years old.

(Chen et al., 2004). In contrast to prior literature (Miller et al., 2000) this protective effect did not extend to dependence. Depressive episode was associated with increased speed of transition to dependence, which is consistent with emerging findings of an asso-

ciation between depression and cannabis use disorders (Feingold et al., 2015; Pacek et al., 2013), but was not found to be associated with earlier opportunity to use cannabis. This may be due to the age of depressive episode onset occurring after age of cannabis use opportunity for the majority of participants. Previous research has reported that childhood adversity and sexual abuse are associated with other drug use opportunity and cannabis dependence (Benjet et al., 2013; Duncan et al., 2008) but, while the present analyses identified an association between childhood sexual abuse and earlier cannabis use opportunity, there was no association between childhood sexual abuse and progression from opportunity to dependence. Differences between the present findings and existing research may be due to the relatively novel exploration of speed of transitions between stages rather than the likelihood of outcomes, which has been the focus of much existing research.

The identification of tobacco, alcohol and other drug involvement as factors associated with progression from opportunity to dependence suggests that a pattern of poly-use emerges. Although alcohol use has previously been found to be associated with early onset of cannabis use (Coffey et al., 2000) it was not associated with opportunity to use cannabis in the present analyses, which may partially reflect the high prevalence of monthly alcohol use in the current sample. The comparatively rarer outcomes of tobacco dependence, other drug use and other drug dependence were found to be associated with increased speed of progression to cannabis dependence. The use of both tobacco and cannabis has been frequently observed (Agrawal et al., 2012, 2010; Hindocha et al., 2015), and regular cigarette smokers are more likely to report earlier cannabis use opportunity (Agrawal et al., 2013). Present results strongly supported this finding, and extend it to show weekly tobacco use and dependence were significantly associated with speed of progression to cannabis dependence. The observed association between cannabis dependence and tobacco may be due to a number of factors including shared genetic and environmental influences, the co-administration of tobacco and cannabis, and smoking habituation (Agrawal et al., 2012).

A number of factors were associated with both transitions studied. Female gender was associated with slower progression to both opportunity and dependence. It is interesting to note that gender differences held across both transitions given that previous research has found males more likely to have opportunity to use cannabis, but has found these gender differences do not extend to the transition into drug use once opportunity has occurred (van Etten et al., 1999). Similarly, weekly tobacco use was associated with increased hazard of both cannabis use opportunity and progression to cannabis dependence, consistent with existing findings relating to dependence (Wagner and Anthony, 2002). Conduct disorder was associated with faster progression to both opportunity and dependence, echoing previous research showing disruptive or aggressive behaviour in both males and females is associated with earlier opportunity to use cannabis (Storr et al., 2011). Parental drug problems were significantly associated with a more rapid transition to both opportunity and dependence, in line with existing research relating to opportunity (Benjet et al., 2013). This factor most clearly demonstrated changes in the magnitude of effect size between transitions, and given the especially strong association with opportunity to use cannabis it is plausible that parental drug problems facilitate an environment in which drug access is increased, whether this is indirectly or directly through parents. Alternatively, cannabis availability has previously been shown to be influenced by genetic effects (Gillespie et al., 2009), and the present finding may represent a genetic liability to creating drug use opportunities.

The pattern of results presented in this paper demonstrates that the influence of factors differs throughout the stages of drug use progression. Research relating to early onset of drug use often calls for earlier detection and intervention (Chen et al., 2009), and the current findings have two key implications for prevention. Firstly, as factors play different roles across drug involvement, interventions may benefit from tailoring to stages of drug use. Secondly, targeting of interventions may improve by considering the consistency and differences in associated factors across the stages of drug use. Using the results of the present study may facilitate identification of populations who will benefit from targeted or indicated prevention strategies (National Research Council (US) and Institute of Medicine (US) Committee on the Prevention of Mental Disorders and Substance Abuse Among Children, Youth, and Young Adults: Research Advances and Promising Interventions, 2009).

There are certain considerations required in interpretation of this work. Firstly, analyses were conducted on retrospective self-report data, introducing the possibility of recall bias. This is a viable method of data collection (Darke, 1998; Sartor et al., 2011), and indeed recall of early experience with cannabis has been found to be especially reliable (Johnson and Mott, 2001), but as the analyses rely on accurate recall of age of onset of a number of behaviours the work would benefit from replication in longitudinal cohorts.

Secondly, analyses of the progression from opportunity to cannabis use initiation were not possible, as timing of transitions was only available as time in years, and there was not enough variation in the speed of this transition to allow for analysis (the majority of participants progressed to use within 1 year after having the opportunity to use, data available on request). Thirdly, selected covariates measured occurrence within an age range (6–13), and consequently may have occurred prior to the age of opportunity to use cannabis for a small number of individuals. Fourthly, while the prevalence of lifetime cannabis use in this sample was relatively high at 68.2% (Lynskey et al., 2012) it is important to note this estimate is consistent with previous estimates from the Australian young adult population (Australian Institute of Health and Welfare, 2014). Finally, interpretation of these analyses should be in light of the twin and sibling sample used, as there is some residual uncertainty about whether inferences from twin data have external validity with respect to what might be found in general population samples (Vitaro et al., 2009). Analyses were adjusted for clustering effects using the Huber-White estimator, which was selected over other potential analyses that can be conducted to explore within twin/sibling frailties as the most parsimonious method.

Consideration of multiple stages of drug use from non-use to dependence allows identification of factors uniquely associated with specific transitions. The current results demonstrate that different factors are influential at different stages of the development of cannabis dependence. Additionally, the differences and consistencies in factors across the stages of drug use provide an insight into which similarities and differences we may expect to see occurring through the transitions towards dependence. The findings have implications for substance use prevention efforts, as both the targeting of interventions as well as the interventions themselves may benefit from being tailored to stages of drug use.

Conflict of interest

AA has previously received peer-reviewed funding from ABMRF/Foundation for Alcohol Research which receives partial support from the brewing industry.

JS is a researcher and clinician and has worked with a range of types of treatment and rehabilitation service-providers. He has also worked with pharmaceutical companies to seek to identify new or improved treatments, and also with a range of governmental and non-governmental organisations. His employer (King's College London) is registering intellectual property on an innovative medication development with which JS is involved (not relevant

to cannabis), and JS has been named in a patent registration by a Pharma company as inventor of a potential novel overdose resuscitation product (not relevant to cannabis). A fuller account of JS's interests is on his personal web-page of the Addictions Department at http://www.kcl.ac.uk/ioppn/depts/addictions/people/hod.aspx . JS is also supported by the National Institute for Health Research (NIHR) Biomedical Research Centre for Mental Health at South London and Maudsley NHS Foundation Trust and King's College London.

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Author contributions

Lindsey A. Hines developed hypotheses, ran analysis, writing of paper.

Katherine I. Morley supervised analyses, comments throughout drafting.

John Strang comments once paper was drafted.

Arpana Agrawal comments once paper was drafted, input to design of analyses.

Elliot C. Nelson comments once paper was drafted.

Dixie Statham: organiser of original twin study, comments once paper was drafted.

Nicholas G. Martin: organiser of original twin study, comments once paper was drafted.

Michael T. Lynskey: substantive input at planning stages, comments throughout drafting.

All authors have approved the final article.

Contributors

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References

Agrawal, A., Budney, A.J., Lynskey, M.T., 2012. The co-occurring use and misuse of cannabis and tobacco: a review. Addiction 107, 1221–1233, http://dx.doi.org/10.1111/j.1360-0443.2012.03837.x.

Agrawal, A., Madden, P.A.F., Martin, N.G., Lynskey, M.T., 2013. Do early experiences with cannabis vary in cigarette smokers?? Drug Alcohol Depend. 128, 255–259, http://dx.doi.org/10.1016/j.drugalcdep.2012.09.002.

Agrawal, A., Silberg, J.L., Lynskey, M.T., Maes, H.H., Eaves, L.J., 2010. Mechanisms underlying the lifetime co-occurrence of tobacco and cannabis use in adolescent and young adult twins. Drug Alcohol Depend. 108, 49–55, http://dx.doi.org/10.1016/j.drugalcdep.2009.11.016.

American Psychiatric Association, 2000. Diagnostic And Statistical Manual Of Mental Disorders: DSM-IV-TR, Text Revision, 4th Ed. American Psychiatric Association, Washington, DC.

Anthony, J.C., 2006. The epidemiology of cannabis dependence. In: Roffman, R.A., Stephens, R.S. (Eds.), Cannabis Dependence: Its Nature, Consequences, and Treatment. Cambridge University Press, New York, pp. 58–105.

Australian Institute of Health and Welfare, 2014. National Drug Strategy Household Survey detailed report: 2013. Drug statistics series no. 28. Cat. no. PHE 183. AIHW, Canberra.

Behrendt, S., Beesdo-Baum, K., Hofler, M., Perkonigg, A., Buhringer, G., Lieb, R., Wittchen, H.U., 2012. The relevance of age at first alcohol and nicotine use for initiation of cannabis use and progression to cannabis use disorders. Drug Alcohol Depend. 123, 48–56, http://dx.doi.org/10.1016/j.drugalcdep.2011.10.013.

Behrendt, S., Beesdo-Baum, K., Zimmermann, P., Hofler, M., Perkonigg, A., Buhringer, G., Lieb, R., Wittchen, H.U., 2011. The role of mental disorders in the risk and speed of transition to alcohol use disorders among community youth. Psychol. Med. 41, 1073–1085, http://dx.doi.org/10.1017/s0033291710001418.

Behrendt, S., Wittchen, H.U., Hofler, M., Lieb, R., Beesdo, K., 2009. Transitions from first substance use to substance use disorders in adolescence: is early onset associated with a rapid escalation?? Drug Alcohol Depend. 99, 68–78, http://dx.doi.org/10.1016/j.drugalcdep.2008.06.014.

Bellera, C.A., MacGrogan, G., Debled, M., Lara, C.T., de Brouste, V., Mathoulin-Pélissier, S., 2010. Variables with time-varying effects and the Cox model: some statistical concepts illustrated with a prognostic factor study in breast cancer. BMC Med. Res. Methodol. 10, 20, http://dx.doi.org/10.1186/1471-2288-10-20.

Benjet, C., Borges, G., Medina-Mora, M.E., Méndez, E., 2013. Chronic childhood adversity and stages of substance use involvement in adolescents. Drug Alcohol Depend. 131, 85–91, http://dx.doi.org/10.1016/j.drugalcdep.2012.12.002.

Bucholz, K.K., Cadoret, R., Cloninger, C.R., Dinwiddie, S.H., Hesselbrock, V.M., Nurnberger, J., Reich, T., Schmidt, I., Schuckit, M.A., 1994. A new, semi-structured psychiatric interview for use in genetic linkage studies: a report on the reliability of the SSAGA. J. Stud. Alcohol Drugs 55, 149.

Caris, L., Wagner, F.A., Ríos-Bedoya, C.F., Anthony, J.C., 2009. Opportunities to use drugs and stages of drug involvement outside the United States : evidence from the Republic of Chile. Drug Alcohol Depend. 102, 30–34, http://dx.doi.org/10.1016/j.drugalcdep.2008.12.004.

Chen, C.-Y., Dormitzer, C.M., Bejarano, J., Anthony, J.C., 2004. Religiosity and the earliest stages of adolescent drug involvement in seven countries of Latin America. Am. J. Epidemiol. 159, 1180–1188, http://dx.doi.org/10.1093/aje/kwh151.

Chen, C.-Y., Storr, C.L., Anthony, J.C., 2009. Early-onset drug use and risk for drug dependence problems. Addict. Behav. 34, 319–322, http://dx.doi.org/10.1016/j.addbeh.2008.10.021.

Chen, C.Y., Storr, C.L., Anthony, J.C., 2005. Influences of parenting practices on the risk of having a chance to try cannabis. Pediatrics 115, 1631–1639, http://dx.doi.org/10.1542/peds.2004-1926.

Coffey, C., Lynskey, M., Wolfe, R., Patton, G.C., 2000. Initiation and progression of cannabis use in a population-based Australian adolescent longitudinal study. Addiction 95, 1679–1690, http://dx.doi.org/10.1046/j.1360-0443.2000.951116798.x.

Darke, S., 1998. Self-report among injecting drug users: a review. Drug Alcohol Depend. 51, 253–263, http://dx.doi.org/10.1016/s0376-8716(98) 00028-3.

Degenhardt, L., Chiu, W.-T., Sampson, N., Kessler, R.C., Anthony, J.C., Angermeyer, M., Bruffaerts, R., de Girolamo, G., Gureje, O., Huang, Y., Karam, A., Kostyuchenko, S., Lepine, J.P., Mora, M.E.M., Neumark, Y., Ormel, J.H., Pinto-Meza, A., Posada-Villa, J., Stein, D.J., Takeshima, T., Wells, J.E., 2008. Toward a global view of alcohol, tobacco, cannabis, and cocaine use: findings from the WHO World Mental Health Surveys. PLoS Med. 5, e141, http://dx.doi.org/10.1371/journal.pmed.0050141.

Degenhardt, L., Whiteford, H., Hall, W.D., 2014. The Global burden of disease projects: what have we learned about illicit drug use and dependence and their contribution to the global burden of disease?? Drug Alcohol Rev. 33, 4–12, http://dx.doi.org/10.1111/dar.12088.

Duncan, A.E., Sartor, C.E., Scherrer, J.F., Grant, J.D., Heath, A.C., Nelson, E.C., Jacob, T., Bucholz, K.K., 2008. The association between cannabis abuse and dependence and childhood physical and sexual abuse: evidence from an offspring of twins design. Addiction 103, 990–997, http://dx.doi.org/10.1111/j.1360-0443.2008.02210.x.

Efron, B., 1977. The efficiency of Cox's Likelihood Function for censored data. J. Am. Stat. Assoc., 557–565, http://dx.doi.org/10.2307/2286217.

Feingold, D., Weiser, M., Rehm, J., Lev-Ran, S., 2015. The association between cannabis use and mood disorders: a longitudinal study. J. Affective Disord. 172, 211–218, http://dx.doi.org/10.1016/j.jad.2014.10.006.

Gillespie, N.A., Neale, M.C., Kendler, K.S., 2009. Pathways to cannabis abuse: a multi-stage model from cannabis availability, cannabis initiation and progression to abuse. Addiction 104, 430–438, http://dx.doi.org/10.1111/j.1360-0443.2008.02456.x.

Heath, A.C., Bucholz, K.K., Madden, P.A., Dinwiddie, S.H., Slutske, W.S., Bierut, L.J., Statham, D.J., Dunne, M.P., Whitfield, J.B., Martin, N.G., 1997. Genetic and environmental contributions to alcohol dependence risk in a national twin sample: consistency of findings in women and men. Psychol. Med. 27, 1381–1396.

Hindocha, C., Shaban, N.D.C., Freeman, T.P., Das, R.K., Gale, G., Schafer, G., Falconer, C.J., Morgan, C.J.A., Curran, H.V., 2015. Associations between cigarette smoking

and cannabis dependence: a longitudinal study of young cannabis users in the United Kingdom. Drug Alcohol Depend. 148, 165–171, http://dx.doi.org/10.1016/j.drugalcdep.2015.01.004.
Hines, L.A., Morley, K.I., Mackie, C., Lynskey, M., 2015a. Genetic and environmental interplay in adolescent substance use disorders. Curr. Addict. Rep. 2, 122–129, http://dx.doi.org/10.1007/s40429-015-0049-8.
Hines, L.A., Morley, K.I., Strang, J., Agrawal, A., Nelson, E.C., Statham, D., Martin, N.G., Lynskey, M.T., 2015b. The association between speed of transition from initiation to subsequent use of cannabis and later problematic cannabis use, abuse and dependence. Addict. Abingdon Engl. 110, 1311–1320, http://dx.doi.org/10.1111/add.12963.
Johnson, T.P., Mott, J.A., 2001. The reliability of self-reported age of onset of tobacco, alcohol and illicit drug use. Addict. Abingdon Engl. 96, 1187–1198, http://dx.doi.org/10.1080/09652140120060770.
Lopez-Quintero, C., Neumark, Y., 2015. Prevalence and determinants of resistance to use drugs among adolescents who had an opportunity to use drugs. Drug Alcohol Depend. 149, 55–62, http://dx.doi.org/10.1016/j.drugalcdep.2015.01.015.
Lynskey, M.T., Agrawal, A., Henders, A., Nelson, E.C., Madden, P.A.F., Martin, N.G., 2012. An Australian twin study of cannabis and other illicit drug use and misuse, and other psychopathology. Twin Res. Hum. Genet. 15, 631–641, http://dx.doi.org/10.1017/thg.2012.41.
Miller, L., Davies, M., Greenwald, S., 2000. Religiosity and substance use and abuse among adolescents in the National Comorbidity Survey. J. Am. Acad. Child Adolesc. Psychiatry 39, 1190–1197, http://dx.doi.org/10.1097/00004583-200009000-00020.
National Research Council (US) and Institute of Medicine (US) Committee on the Prevention of Mental Disorders and Substance Abuse Among Children, Youth, and Young Adults: Research Advances and Promising Interventions, 2009. Preventing Mental, Emotional, and Behavioral Disorders Among Young People: Progress and Possibilities, The National Academies Collection: Reports funded by National Institutes of Health National Academies Press (US), Washington (DC).
Neumark, Y., Lopez-Quintero, C., Bobashev, G., 2012. Drug use opportunities as opportunities for drug use prevention: Bogota, Colombia a case in point. Drug Alcohol Depend. 122, 127–134, http://dx.doi.org/10.1016/j.drugalcdep.2011.09.022.
Pacek, L.R., Martins, S.S., Crum, R.M., 2013. The bidirectional relationships between alcohol, cannabis, co-occurring alcohol and cannabis use disorders with major depressive disorder: results from a national sample. J. Affective Disord. 148, 188–195, http://dx.doi.org/10.1016/j.jad.2012.11.059.
Patton, G.C., Coffey, C., Carlin, J.B., Degenhardt, L., Lynskey, M., Hall, W., 2002. Cannabis use and mental health in young people: cohort study. BMJ 325, 1195–1198, http://dx.doi.org/10.1136/bmj.325.7374.1195.
Pinchevsky, G.M., Arria, A.M., Caldeira, K.M., Garnier-Dykstra, L.M., Vincent, K.B., O'Grady, K.E., 2011. Marijuana exposure opportunity and initiation during college: parent and peer influences. Prev. Sci. 13, 43–54, http://dx.doi.org/10.1007/s11121-011-0243-4.
Reboussin, B.A., Ialongo, N.S., Green, K.M., 2015. Influences of behavior and academic problems at school entry on marijuana use transitions during adolescence in an African–American sample. Addict. Behav. 41, 51–57, http://dx.doi.org/10.1016/j.addbeh.2014.09.030.
Ridenour, T.A., Lanza, S.T., Donny, E.C., Clark, D.B., 2006. Different lengths of times for progressions in adolescent substance involvement. Addict. Behav. 31, 962–983, http://dx.doi.org/10.1016/j.addbeh.2006.03.015.
Sartor, C.E., Agrawal, A., Lynskey, M.T., Bucholz, K.K., Madden, P.A., Heath, A.C., 2009. Common genetic influences on the timing of first use for alcohol, cigarettes, and cannabis in young African–American women. Drug Alcohol Depend. 102, 49–55, http://dx.doi.org/10.1016/j.drugalcdep.2008.12.013.
Sartor, C.E., Bucholz, K.K., Nelson, E.C., Madden, P.A.F., Lynskey, M.T., Heath, A.C., 2011. Reporting bias in the association between age at first alcohol use and heavy episodic drinking. Alcohol. Clin. Exp. Res. 35, 1418–1425, http://dx.doi.org/10.1111/j.1530-0277.2011.01477.x.
Sartor, C.E., Xian, H., Scherrer, J.F., Lynskey, M.T., Duncan, A.E., Haber, J.R., Grant, J.D., Bucholz, K.K., Jacob, T., 2008. Psychiatric and familial predictors of transition times between smoking stages: results from an offspring-of-twins study. Addict. Behav. 33, 235–251, http://dx.doi.org/10.1016/j.addbeh.2007.09.002.
Storr, C.L., Wagner, F.A., Chen, C.Y., Anthony, J.C., 2011. Childhood predictors of first chance to use and use of cannabis by young adulthood. Drug Alcohol Depend. 117, 7–15, http://dx.doi.org/10.1016/j.drugalcdep.2010.12.023.
Van Etten, M.L., Anthony, J.C., 1999. Comparative epidemiology of initial drug opportunities and transitions to first use: marijuana, cocaine, hallucinogens and heroin. Drug Alcohol Depend. 54, 117–125.
van Etten, M.L., Neumark, Y.D., Anthony, J.C., 1999. Male-female differences in the earliest stages of drug involvement. Addiction 94, 1413–1419, http://dx.doi.org/10.1046/j.1360-0443.1999.949141312.x.
Vitaro, F., Brendgen, M., Arseneault, L., 2009. The discordant MZ-twin method: one step closer to the holy grail of causality. Int. J. Behav. Dev. 33, 376–382, http://dx.doi.org/10.1177/0165025409340805.
Wagner, F.A., Anthony, J.C., 2002. Into the world of illegal drug use: exposure opportunity and other mechanisms linking the use of alcohol, tobacco, marijuana, and cocaine. J. Epidemiol., 918–925 http://dx.doi.org/10.1093/aje/155.10.918.
Wells, J.E., Haro, J.M., Karam, E., Lee, S., Lepine, J.P., Medina-Mora, M.E., Nakane, H., Posada, J., Anthony, J.C., Cheng, H., Degenhardt, L., Angermeyer, M., Bruffaerts, R., de Girolamo, G., de Graaf, R., Glantz, M., Gureje, O., 2011. Cross-national comparisons of sex differences in opportunities to use alcohol or drugs, and the transitions to use. Subst. Use Misuse 46, 1169–1178, http://dx.doi.org/10.3109/10826084.2011.553659.
Wittchen, H.U., Behrendt, S., Hofler, M., Perkonigg, A., Lieb, R., Buhringer, G., Beesdo, K., 2008. What are the high risk periods for incident substance use and transitions to abuse and dependence? Implications for early intervention and prevention. Int. J. Methods Psychiatry Res. 17 (Suppl. 1), S16–S29, http://dx.doi.org/10.1002/mpr.254.