Drug and Alcohol Dependence 194 (2019) 136–142

Contents lists available at ScienceDirect

Drug and Alcohol Dependence

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

Full length article

Conditional probabilities of substance use disorders and associated risk factors: Progression from first use to use disorder on alcohol, cannabis, stimulants, sedatives and opioids

Christina Marel[a,b,*], Matthew Sunderland[a,b], Katherine L. Mills[a,b], Tim Slade[a,b], Maree Teesson[a,b], Cath Chapman[a,b]

[a] National Drug and Alcohol Research Centre, University of New South Wales, NSW 2052, Sydney, Australia
[b] NHMRC Centre of Research Excellence in Mental Health and Substance Use, University of New South Wales, NSW 2052, Sydney, Australia

ARTICLE INFO

Keywords:
Substance use disorder
Transition
Alcohol
Cannabis
Opioids
Stimulants
Sedatives
Risk factors

ABSTRACT

Background: Relatively little is known about factors that may lead to the development of a substance use disorder (SUD), across a range of drug classes. This study aimed to identify factors that predict the likelihood of transition from use to SUD and the speed with which this may occur at the population level, with a focus on the impact of pre-existing mental disorders.

Methods: Data were collected as part of the 2007 Australian National Survey of Mental Health and Wellbeing, a nationally representative survey of 8841 Australian adults. A series of discrete time survival analyses were undertaken on data pertaining to the age of onset of use and symptoms of use disorder, for alcohol, cannabis, sedatives, stimulants, and opioids, as well as the impact of pre-existing mood and anxiety disorders on the likelihood of developing a SUD.

Results: Lifetime cumulative probability estimates indicated that 50.4% of stimulant, 46.6% of opioid, 39% of sedative, 37.5% of alcohol, and 34.1% of cannabis users would develop a SUD on those substances, within an estimated 14, 12, 8, 30, and 23 years after onset respectively. Pre-existing mental disorders were significantly associated with increased risk of developing a SUD for alcohol, cannabis and stimulant use disorder.

Conclusion: The relative speed associated with the transition from use to SUD emphasizes the narrow window of time available to intervene, underscoring the urgency of early identification of mental health conditions and the timely provision of appropriate evidence-based interventions, which could potentially prevent the development of secondary SUDs.

1. Introduction

Substance use is common around the world, but not everyone who uses will go on to develop a substance use disorder (SUD; i.e., DSM-IV criteria for abuse and/or dependence on alcohol or other drugs). Of the 250 million adults estimated to have used drugs at least once, in 2015, approximately 11.8% experienced a SUD (UNoDC, 2017). Findings from epidemiological research report considerable variability within and between substances in relation to the proportion of people who have used a substance that develop a SUD (i.e., conditional prevalence) and the speed of transition from use to use disorder. Conditional prevalence has been estimated for tobacco (range 8.5%–67.5%), cocaine (range 16.7%–24.2%), heroin (21.1%–23.1%), alcohol (4.2%–26.6%), and cannabis (3.9%–19.7%) (Anthony et al., 1994; Butterworth et al., 2014; Chen et al., 2005; Degenhardt et al., 2018; Flórez-Salamanca et al., 2013; Lopez-Quintero et al., 2011; Ridenour et al., 2006; Wagner and Anthony, 2002; Wittchen et al., 2008). Progression from use to SUD appears to be quickest for heroin (median 0 months), followed by cocaine (range 0–4 years), cannabis (range 1–6 years), tobacco (1–27 years), and alcohol (3–15 years) (Butterworth et al., 2014; Chen et al., 2005; Degenhardt et al., 2018; Lopez-Quintero et al., 2011; Ridenour et al., 2006; Wittchen et al., 2008).

Epidemiological evidence pertaining to the likelihood of developing a SUD and the speed of transition across drug classes is critical to guide the timing of evidence-based preventative health promotion initiatives and early interventions for those at risk. Consistent with a

* Corresponding author at: NHMRC Centre of Research Excellence in Mental Health and Substance Use, National Drug and Alcohol Research Centre, University of New South Wales, NSW, 2052, Australia.
E-mail address: c.marel@unsw.edu.au (C. Marel).

https://doi.org/10.1016/j.drugalcdep.2018.10.010
Received 11 September 2018; Received in revised form 9 October 2018; Accepted 29 October 2018
Available online 03 November 2018

biopsychosocial model of SUD, an understanding of risk and protective factors that influence the likelihood and timing of such a transition is also essential to maximize the targeting of these initiatives (Marlatt et al., 1988). Research has identified several risk factors that may impact upon the likelihood of transition from use to use disorder and the speed with which this may occur (including younger age at time of study, male sex, ethnicity, place of birth, marital status, lower income, unemployment, substance use history, and younger age of first use) (Butterworth et al., 2014; Chen et al., 2005; Degenhardt et al., 2018; Lopez-Quintero et al., 2011; Sartor et al., 2014).

Much of this previous research is limited by a constrained focus on one or two substances (predominantly alcohol and cannabis) (Butterworth et al., 2014; Chen et al., 2005; Degenhardt et al., 2018; Reboussin and Anthony, 2006; Wagner and Anthony, 2002, 2007), preventing discussion and examination across multiple drug classes, and few studies have been conducted in populations outside of the United States (Anthony et al., 1994; Chen et al., 2005; Lopez-Quintero et al., 2011; Vsevolozhskaya and Anthony, 2016; Wagner and Anthony, 2002, 2007) limiting the generalizability of findings (Mills and Marel, 2013). Critical knowledge gaps also remain.

Notably, few epidemiological studies have considered the impact of pre-existing psychiatric risk factors or other substance use (Butterworth et al., 2014; Flórez-Salamanca et al., 2013; Lopez-Quintero et al., 2011; Mills and Marel, 2013; Sartor et al., 2014), which is surprising given the strong associations found between SUDs and a range of mental health disorders, in particular, posttraumatic stress disorder (Lai et al., 2015). This is despite growing research demonstrating the temporal link between traumatic stress and the development of subsequent SUDs (Brady and Back, 2012; McCauley et al., 2012). Evidence suggests that a significant proportion of mental disorders precede the development of SUDs (De Graaf et al., 2003; Falk et al., 2008; Slade et al., 2015), highlighting the possibility of targeted interventions to prevent the development of secondary disorders. Of the few epidemiological studies that have been undertaken, there is some evidence that personality, mood, anxiety, conduct, psychotic disorders, and severe childhood physical abuse may have an effect on the transition from use to dependence (Flórez-Salamanca et al., 2013; Lopez-Quintero et al., 2011; Sartor et al., 2014). Previous research examining substance-specific predictors of dependence and SUDs, however, has highlighted inconsistencies between and across substances. For example, while being diagnosed with a mood disorder has been associated with the transition from use to dependence on alcohol and cannabis (Flórez-Salamanca et al., 2013; Lopez-Quintero et al., 2011), findings have been mixed in regards to cocaine dependence. Similarly, alcohol dependence has been associated with the transition from use to cocaine (Lopez-Quintero et al., 2011) and cannabis dependence (Flórez-Salamanca et al., 2013; Lopez-Quintero et al., 2011), but has been found to slow the progression to cocaine and alcohol dependence (Sartor et al., 2014).

Using a survival analysis approach, the present study aimed to build on the existing evidence to estimate the risk of, and identify the psychiatric predictors of, transitioning from use to use disorder in a large, nationally representative household survey of the Australian population. Specifically, this study aimed to i) estimate the conditional probability of developing a use disorder among people who use alcohol, cannabis, stimulants, sedatives or opioids and the speed of transition; ii) examine the impact of pre-existing mental health disorders and other substance use on the likelihood and speed of transition to use disorder among users of these five drug classes.

2. Methods

2.1. Sample

Data for this study came from the 2007 Australian National Survey of Mental Health and Wellbeing (NSMHWB), a nationally representative population survey with a sample size of 8841 (Slade et al., 2009). Briefly, the survey comprises a stratified, multistage probability sample of households with one household member aged 16 to 85 years selected to complete the diagnostic interview and survey questionnaire. The survey's 60% response rate was comparable with other national mental health and substance use surveys (Kerr et al., 2013; Kessler and Ustun, 2008). The focus of the current study necessitated the selection of subsamples of substance using respondents who also provided valid age of first use data: alcohol n = 5,456, cannabis n = 1,629, stimulants n = 579, opioids n = 156, and sedatives n = 137. Substance use groupings were not independent.

Diagnostic criteria for the disorders were assessed for only those respondents who indicated that they consumed a pre-determined frequency and quantity of alcohol or those who used drugs at least five times in their life: respondents had to consume alcohol 1) nearly every day or 2) 3–4 days per week at some point in their life *or* 3) consume alcohol at least 1–3 days per month at some point in their life *and* consumed at least 3 standard drinks per occasion. Age of onset was ascertained by asking each participant to provide the exact age when they first started using alcohol for each drug category. For alcohol use, respondents were asked to report the age when they first started drinking more than 12 standard drinks in any one year, which was labeled regular alcohol use. For the drug use categories, respondents who indicated that their use occurred prior to age 14 were bottom coded at 13 years of age. For each substance, the age of onset of use disorder was based on the earliest age of onset for a diagnosis of either DSM-IV abuse or dependence.

2.2. Measures

Lifetime occurrence of DSM-IV use disorder (abuse or dependence), were assessed for alcohol (AUD) cannabis (CUD), stimulants (STUD), prescribed and non-prescribed sedatives (SEUD) and opioids (OUD) using a modified version of the World Mental Health Composite International Diagnostic Interview (WMH-CIDI 3.0; (Kessler and Üstün, 2004)). This diagnostic instrument is considered a gold standard in global psychiatric epidemiology and has been previously calibrated against the structured clinical interview for DSM-IV (SCID-IV; (Kessler et al., 2004)).

To reduce the impact of recall bias in retrospective reports of age of onset, the WMH-CIDI 3.0 included probes to assist participants who could not remember the exact age when they first started using alcohol or drugs. These probes linked first use of alcohol or drugs with developmental milestones such as whether use occurred before their teens, before their twenties, or after their twenties. Those who indicated the first use occurred before their teens were bottom coded at 12, before twenties bottom coded at 19, and after twenties bottom coded at 20 years of age. Those who could not remember the age of first drug or alcohol use, those who refused to provide an age of onset, or those who indicated that the onset of disorder occurred prior to the onset of use were excluded from the analysis (n = 66 for alcohol, n = 9 for cannabis, n = 6 for stimulants, n = 6 for sedatives, n = 4 for opioids).

Lifetime diagnosis of DSM-IV major depressive episode, bipolar disorder, agoraphobia with or without panic disorder, social anxiety disorder, panic attacks, generalized anxiety disorder (GAD), obsessive-compulsive disorder (OCD), and post-traumatic stress disorder (PTSD) was also assessed with the WMH-CIDI 3.0. Diagnostic criteria were applied without DSM-IV hierarchy rules to examine the influence of comorbid conditions. Age of onset was ascertained by asking each participant the age they first experienced the core symptoms or features of each disorder. Lifetime tobacco use was also included as a covariate with the occurrence and age of onset assessed by ascertaining lifetime daily tobacco use. Other variables included in the analysis comprised: age, sex, education status (whether completed high school or tertiary education), and family history of drug or alcohol problems (with family defined as biological parents, brothers, sisters, or children).

2.3. Statistical analysis

Descriptive analyses were used to provide conditional probability estimates of AUD, CUD, STUD, SEUD, and OUD as well as the median age of disorder onset (with corresponding interquartile range; IQR) among each substance-specific subsample of users. Discrete-time survival analysis was used to model the time in years from first use to onset of use disorder for each subsample of users. Respondents who did not develop use disorder were censored at their interviewed age. The analysis commenced by comparing unconditional discrete time survival models that included increasing polynomials of time with a saturated model that included time as individual dummy-coded years. Significant reductions in model fit from the saturated model were estimated using a log-likelihood difference test using a $p < 0.01$ significance level. Conditional discrete time survival models were then utilized to examine the influence of mental health, tobacco use, and other substance use/disorder covariates on the transition from first use to onset of use disorder. Note that polysubstance use was common (e.g., 9.1% of lifetime alcohol users also had a lifetime cannabis use disorder) and thus the subsamples were not comprised of mutually exclusive groups of respondents.

The covariates were entered into the models as time-varying, meaning that the onset of the covariates was assessed at each individual person-year with a code of 0 indicating the absence of the covariate and a code of 1 indicating the onset of each covariate at that specific year. Once a covariate changed from absent to present it remained as present for all years thereafter. The proportional odds assumption for each covariate was examined by determining the significance of an interaction term between time and the covariate included in the model. There was no evidence to suggest that the interaction effects between the covariates and time included in any of the models were significant suggesting that proportional odds could be assumed. The false discovery rate was controlled across all covariates using the Benjamini-Hochberg method (Benjamini and Hochberg, 1995). All models controlled for age, sex, education, age of first substance use, family history of drug or alcohol problems, number of comorbid health conditions prior to substance use disorder, and the number of other substance use disorders prior to the specific disorder under analysis. All analyses were conducted using Stata version 14 with a sampling weight employed to obtain population-based estimates. Replicate weights and the delete-a-group jack-knife method was used to adjust standard errors for the complex sampling design of the NSMHWB.

3. Results

3.1. Sample characteristics

As illustrated in Table 1, the substance using sub-samples were predominantly male (59%–72%), with mean ages ranging from 33 to 44 years. While the majority (> 60%) of participants included in this analysis had completed high school, a substantial proportion (> 92%) across all drug classes were employed. A family history of alcohol or other drug use was common (17%–34%) as was a lifetime diagnosis of a mental health disorder (57%–92%). Inferential statistical tests were not carried out due to substantial overlap in the composition of the subsamples.

3.2. Conditional probability of SUD and age of onset

3.2.1. Discrete Time Survival Analysis

Due to the absence of onset data among respondents at 30-years after use for AUD, 23-years after use for CUD, 14 years after use for STUD, 8-years after use for SEUD, and 12-years after use for OUD, the data for each analysis were right censored at these points.

Preliminary unconditional discrete time survival models indicated that including time as a polynomial function to the power of five was the most parsimonious model relative to the saturated model for AUD ($\chi^2 = 40.70$, df = 24, p = 0.02) whereas time could be parsimoniously modeled as a linear function for the analysis of CUD (($\chi^2 = 32.94$, df = 21, p = 0.05), STUD ($\chi^2 = 14.33$, df = 12, p = 0.28), SEUD ($\chi^2 = 5.03$, df = 6, p = 0.54), and OUD ($\chi^2 = 14.73$, df = 10 p = 0.14).

The estimated conditional probabilities of developing each of the SUDs were: 45.7% for STUD (95%CI: 39.5–51.8), 44.7% for OUD (95%CI: 35.2–54.2), 39.0% for SEUD (95%CI: 27.5–50.4), 34.5% for AUD (95%CI: 32.9–36.2), and 31.8% for CUD (95%CI: 28.5–35.2). The median age of onset was 18 years for CUD (IQR 17–20), 20 years for STUD (IQR 18–24), 20 years for AUD (IQR 18–25), 20 years for OUD (IQR 18–27), and 21 years for SEUD (IQR 17–28).

3.3. Cumulative conditional probability and speed of transitioning to SUD among substance users

The cumulative probability estimates of developing SUD among users of each drug, for each year after substance use onset, are provided in the supplementary materials. Within the first year of onset, the probability of transitioning to use disorder was 13%, 12.2%, 9.6%, 7.5%, and 5.3%, for opioids, stimulants, sedatives, cannabis, and alcohol and respectively. Lifetime cumulative probability estimates indicated that 50.4% of stimulant users, 46.6% of opioid users, 39% of sedative users, 37.5% of alcohol users, and 34.1% of cannabis users would develop a use disorder for each of those substances, within an estimated 14–, 12–, 8–, 30–, and 23–years after onset respectively. The steepest transition from use to use disorder was observed for STUD and OUD followed by SEUD, CUD, and AUD respectively, with half of cases of alcohol, cannabis, stimulants, sedatives and opioid use disorder observed approximately 4 (IQR 2–9), 3 (IQR 1–6), 3 (IQR 1–5), 2 (IQR 1–5), and 2 (IQR 1–4) years after onset respectively. The estimated cumulative incidence functions for all five disorders from use to onset of disorder are provided in Fig. 1.

3.4. Predictors of transition from substance use to dependence

3.4.1. Psychiatric predictors

As shown in Table 2, pre-existing comorbid mental disorders were significantly associated with increased risk of transitioning from use to substance use disorder for AUD, CUD, and STUD. Most notably, pre-existing PTSD and GAD were significantly associated with increased risk of disorder onset across all three drug classes (PTSD: ORs 1.79–2.63; GAD: 2.28–3.89). Pre-existing major depression was associated with increased risk of transitioning from alcohol use to AUD (OR 3.22) and cannabis use to CUD (OR 2.15), as was social anxiety disorder (AUD: OR 1.59; CUD: OR 2.45).

Pre-existing agoraphobia was associated with an increased risk of transitioning from cannabis use to CUD (OR 3.06), and pre-existing bipolar disorder with an increased risk of transitioning from alcohol use to AUD (OR 2.41). The presence of GAD (OR 3.89) and PTSD (OR 2.51) were significantly associated with increased risk of transitioning from stimulant use to STUD. There was no evidence of a significant association found between pre-existing mental disorders and increased risk of transitioning from use to SEUD or OUD.

3.4.2. Substance use predictors

Table 2 also illustrates significant associations between substance use and pre-existing SUDs on the development of other SUDs across the five drug classes examined. Most notably, pre-existing CUD and STUD before AUD were associated with increased risk of developing a subsequent AUD (CUD: OR 8.03; STUD: OR 5.29). Similarly, a pre-existing STUD, AUD or SEUD was strongly associated with increased risk of transitioning from cannabis use to CUD (STUD: OR 18.29; AUD: OR 10.92; SEUD: OR 8.54).

The presence of CUD among stimulant users was significantly

Table 1
Descriptive statistics of the analyzed samples and bivariate associations with covariates[a].

	Alcohol use sub-sample (n = 5456)		Cannabis use sub-sample (n = 1629)		Stimulant use sub-sample (n = 579)		Sedative use sub-sample (n = 137)		Opioid use sub-sample (n = 156)	
	Est	95% CI	Est	95% CI	Est	95% CI	Est	95% CI	Est	95% CI
Weighted prevalence (%)	22.1	21.0–23.3	6.2	5.5–6.9	3.3	2.8–3.9	0.6	0.4–0.8	0.9	0.6–1.1
Demographics										
Age (mean)	43.6	43.2–44.0	35.9	35.1–36.7	32.6	31.5–33.6	37.3	35.0–39.7	36.4	34.4–38.5
% Male	59.1	58.0–60.2	63.2	60.5–65.8	65.0	60.0–70.0	63.1	51.6–74.6	71.8	60.9–82.7
% Unemployed	2.7	2.2–3.3	5.2	3.2–7.2	6.8	1.0–12.5	6.1	0.0–12.2	7.7	2.0–13.4
% English main language spoken at home	96.1	95.3–96.8	98.4	97.6–99.3	98.8	97.5–100.0	99.5	98.6–100.0	97.6	93.4–100.0
% Born in Australia	77.4	75.6–79.1	80.9	78.1–83.7	85.3	81.6–89.1	82.6	74.3–90.9	84.7	77.7–91.8
% Born in other English–speaking country	13.5	12.2–14.8	13.2	11.1–15.4	10.3	7.4–13.3	12.3	5.8–18.9	11.6	6.3–17.1
% Born in other country	9.1	8.0–10.2	5.8	4.2–7.5	4.3	2.6–6.0	5.0	1.2–8.8	3.5	0.8–6.3
% Completed year 12 or higher	72.1	70.2–73.9	76.6	73.4–79.8	77.4	72.7–81.2	67.1	52.8–81.3	60.1	50.9–69.4
Drug use and mental health										
% Family history of drug or alcohol problems	17.3	15.9–18.7	25.5	22.7–28.4	28.6	23.2–34.0	34.4	27.3–41.4	31.0	21.6–40.5
% Lifetime anxiety disorder	32.5	30.9–34.3	42.3	38.6–46.0	47.4	42.0–52.9	62.6	52.2–72.9	60.2	49.1–71.4
% Lifetime affective disorder	16.6	15.2–18.0	25.1	21.5–28.7	31.4	25.6–37.3	46.8	35.1–58.5	42.6	29.2–56.1
% Lifetime substance use disorder	37.0	35.3–38.7	63.0	59.8–65.9	77.7	73.2–82.3	81.0	70.4–91.5	87.0	81.2–92.8
% Lifetime mental health disorder	56.6	54.5–58.4	77.7	75.1–80.2	86.6	82.9–90.2	89.4	79.9–98.9	92.1	87.7–96.5
% 12-month anxiety disorder	15.9	14.6–17.2	22.9	19.9–25.9	28.1	23.3–32.9	41.4	29.3–53.6	38.6	28.8–48.4
% 12-month affective disorder	6.6	5.7–7.5	10.9	8.6–13.1	15.0	10.7–19.2	30.6	18.5–42.7	26.5	15.4–37.6
% 12-month substance use disorder	7.8	6.8–8.8	16.1	13.2–19.0	28.8	23.4–34.3	30.0	18.8–41.1	39.0	27.9–50.1
% 12-month mental health disorder	22.8	21.3–24.4	34.8	31.5–38.2	47.7	41.3–54.2	56.2	43.8–68.6	60.2	48.9–71.5

[a] Subsamples were not independent.

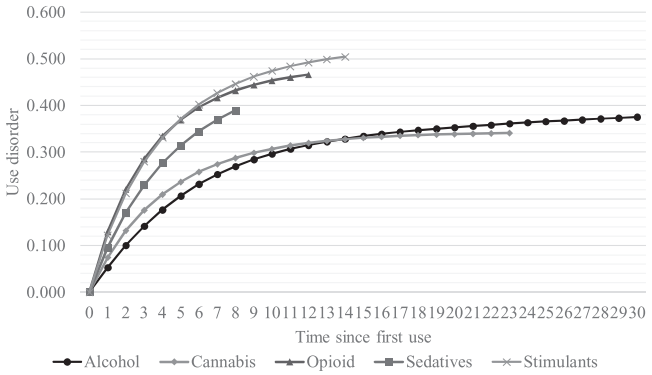

Fig. 1. Cumulative incidence curves for time from first use to disorder for each drug class[a].
Note: [a]Subsamples were not independent.

associated with increased risk of transitioning from stimulant use to STUD (OR 7.03). Opioid users with a pre-existing SEUD were significantly more likely to transition from opioid use to OUD in comparison to those without a pre-existing SEUD (OR 6.18). No significant association was found between substance use-related covariates and the transition from sedative use to SEUD.

4. Discussion

The current study estimated the risk of transitioning from regular use to use disorder across five drug classes in a nationally representative Australian sample, with a specific focus on the extent to which comorbid psychiatric disorders and other substance use influence the onset of SUD. Few studies have had the capacity to demonstrate that this relationship holds when investigating the transition from first use to SUD across multiple disorders, therefore highlighting important areas for intervention and timing of intervention/treatment seeking of substance use among different subgroups of people with psychiatric comorbidities. Consistent with much of the previous literature, the estimated cumulative conditional probability of substance use disorder was highest for stimulant users (50.4%), followed by opioid (46.6%), sedative (39%), alcohol (37.5%) and cannabis users (34.1%) (Lopez-Quintero et al., 2011; Ridenour et al., 2006; Wagner and Anthony, 2002; Wittchen et al., 2008). These estimates are, however, substantially higher than those reported in other epidemiological studies. To date, the highest estimates of cumulative probability observed have been around one-in-four for users of cocaine, opioids, and alcohol, and one-in-five for cannabis (Lopez-Quintero et al., 2011; Ridenour et al., 2006; Wagner and Anthony, 2002; Wittchen et al., 2008). This study represents the first examination of the cumulative probability of sedative use disorders.

Previous comparative epidemiological research has revealed that Australian rates of conditional dependence were substantially higher than those in the United States for all substances apart from alcohol (McBride et al., 2009). It has been suggested that social and cultural factors (e.g., differences in availability, legislation and social norms surrounding use of alcohol, prescribed and non-prescribed substances), and ideological differences in national drug strategy policy ("zero-tolerance", or abstinence-based approach versus harm minimization approach) may contribute to some of this discrepancy (McBride et al., 2009). Higher estimates of cumulative conditional prevalence in the current study may also be explained by methodological differences between this and other studies. There is considerable variability between studies in terms of how substance 'use' and 'use disorder' have been operationalized (e.g., transition from 'first use', 'regular use', 'problematic use', or 'abuse' to DSM-III-R, DSM-IV, or ICD-10 'abuse', 'dependence' or 'use disorder'. The majority of studies examining the transition from use to dependence have not included those who met criteria for abuse, and thus, have lower estimates than the current study's examination of DSM-IV use disorder.

An example of how estimates differ substantially between studies examining 'abuse', 'dependence' and 'abuse and dependence' is illustrated in a study by Wittchen and colleagues (Wittchen et al., 2008).

Table 2
Factors associated with the transition from first use to use disorder among users of each drug.

	Alcohol use disorder (AUD; n = 5456)		Cannabis use disorder (CUD; n = 1629)		Simulant use disorder (STUD; n = 579)		Sedative use disorder (SEUD; n = 137)		Opioid use disorder (OUD; n = 156)	
Covariate	OR[g]	95%CI[h]	OR	95%CI	OR	95%CI	OR	95%CI	OR	95%CI
Mental health										
MDE[a]	**3.22**	**2.49 – 4.15**	**2.15**	**1.44 – 3.20**	1.25	0.73 – 2.13	0.98	0.39 – 2.46	0.36	0.12 – 1.06
Bipolar	**2.41**	**1.57 – 3.69**	1.95	1.02 – 3.71	2.08	0.92 – 4.70	0.89	0.23 – 3.40	1.10	0.24 – 4.94
GAD[b]	**2.28**	**1.76 – 2.96**	**2.60**	**1.55 – 4.35**	**3.89**	**2.01 – 7.53**	4.24	0.95 – 18.82	2.31	0.61 – 7.33
Panic attacks	**1.64**	**1.32 – 2.03**	**1.97**	**1.41 – 2.75**	1.36	0.84 – 2.19	2.14	1.00 – 4.59	1.67	0.71 – 3.89
Social anxiety	**1.59**	**1.18 – 2.14**	**2.45**	**1.72 – 3.50**	1.23	0.65 – 2.34	1.67	0.48 – 5.80	1.74	0.48 – 6.30
Agoraphobia	1.39	0.70 – 2.74	**3.06**	**1.65 – 5.66**	2.23	0.90 – 5.57	3.00	0.81 – 11.06	4.70	1.49 – 14.83
PTSD[c]	**2.63**	**1.92 – 3.62**	**1.79**	**1.16 – 2.72**	**2.51**	**1.58 – 3.99**	2.19	0.74 – 6.49	1.27	0.27 – 5.99
OCD[d]	1.49	0.98 – 2.26	1.25	0.65 – 2.40	1.06	0.45 – 2.48	1.21	0.34 – 4.25	0.98	0.26 – 3.69
Any affective	**3.30**	**2.55 – 4.28**	**2.32**	**1.62 – 3.32**	1.29	0.72 – 2.31	1.13	0.42 – 3.02	0.36	0.12 – 1.13
Any anxiety	**2.17**	**1.75 – 2.68**	**2.90**	**2.11 – 3.99**	**2.13**	**1.35 – 3.36**	2.55	1.02 – 6.36	2.35	0.85 – 6.46
Substance use										
Daily smoking	**1.56**	**1.36 – 1.80**	**1.56**	**1.09 – 2.23**	1.25	0.73 – 2.16	0.87	0.29 – 2.56	3.22	0.86 – 12.11
Alcohol use	–	–	1.16	0.72 – 1.86	1.07	0.43 – 2.72	0.71	0.13 – 4.00	0.85	0.28 – 7.80
Cannabis use	**2.23**	**1.92 – 2.59**	–	–	0.60	0.36 – 1.02	0.80	0.24 – 2.74	4.82	0.83 – 27.89
Stimulant use	**2.57**	**1.84 – 3.58**	**3.28**	**2.31 – 4.65**	–	–	3.59	1.03 – 12.51	4.51	0.41 – 49.24
Sedative use	**2.68**	**1.56 – 4.63**	**3.66**	**2.12 – 6.35**	1.91	1.08 – 3.40	–	–	1.77	0.81 – 3.88
Opioid use	**2.73**	**1.93 – 3.84**	**3.85**	**2.42 – 6.12**	1.28	0.68 – 2.39	1.69	0.54 – 4.46	–	–
AUD	–	–	**10.92**	**6.00 – 19.90**	1.58	0.98 – 2.56	1.96	0.57 – 6.72	2.10	0.99 – 4.47
CUD	**8.03**	**5.17 – 12.46**	–	–	**7.03**	**4.02 – 12.29**	3.31	1.02 – 10.79	4.65	1.56 – 13.90
STUD	**5.29**	**3.15 – 8.90**	**18.29**	**9.77– 34.23**	–	–	9.04	1.43 – 57.08	5.05	1.54 – 16.53
SEUD	2.12	0.83 – 5.41	**8.54**	**3.51 – 20.75**	2.44	0.74 – 8.03	–	–	**6.18**	**2.26 – 16.89**
OUD	**3.37**	**1.65 – 6.86**	**6.88**	**2.82 – 16.79**	2.37	1.04 – 5.46	10.31	2.31 – 46.04	–	–
Any other SUD[e,f]	**3.37**	**2.69 – 4.21**	**3.43**	**2.49 – 4.74**	**5.09**	**3.26 – 7.94**	4.53	1.06 – 19.34	**5.57**	**1.93 – 16.07**

Note: All models controlled for age, sex, education, age first alcohol/drug use, family history of drug or alcohol problems, number of comorbid mental health conditions with onset prior to that of the target alcohol or drug use disorder, number of other alcohol or drug use disorders with onset prior to that of the target alcohol or drug use disorder. Bold indicates significant after adjusting for false discovery rate using Benjamini–Hochberg method. [a]Major depressive episode; [b]Generalized anxiety disorder; [c]Post traumatic stress disorder; [d]Obsessive compulsive disorder; [e]Any SUD other than the dependent variable of the analysis; [f]The number of other alcohol or drug use disorders prior to that of the target alcohol or drug use disorder was excluded as a control variable; [g]odds ratio; [h]95% confidence interval.

Investigating the proportion of those who transitioned from first use of alcohol, cannabis and other (unspecified) illicit drugs to DSM-IV abuse, in addition to those who transition from first use to DSM-IV dependence on these substances, this paper found higher estimates for abuse than dependence (abuse ranging from 9.6% to 38.6%; dependence ranging from 4.6% to 17.9%). Estimates of abuse/dependence were more comparable to the current study, with the proportion who transitioned from first use to alcohol abuse/dependence: 56.5% males, 17.1% females; cannabis abuse/dependence: 32.6% males, 13.7% females; other illicit substance abuse/dependence: 23.2% males, 16.1% females (Wittchen et al., 2008). The examination of 'use disorder' in the present study is in line with the current DSM-5 conceptualizations where the concepts of 'abuse' and 'dependence' categories have been merged (APA, 2013).

Consistent with previous research, the current study found that transition from use to use disorder occurred fastest for opioids, stimulants, closely followed by sedatives, cannabis and alcohol (Flórez-Salamanca et al., 2013; Lopez-Quintero et al., 2011; Ridenour et al., 2006, 2005). The findings indicate that of those who will go on to develop a use disorder, half will do so within the first two to four years of first use. Ultimately, these findings emphasize the very narrow window of time available in which effective, evidence-based interventions may be implemented to prevent the transition from regular use to use disorder. A combination of prevention of use, as well as early intervention once use begins to halt the progression to disorder, is important (NSW Health, 2015).

Previous research has documented high rates of comorbid mental disorders and polysubstance use among people with SUDs (Bierut et al., 2008; Brooner et al., 1997; Kessler, 2004; Kessler et al., 1996). The current study found that the presence of particular pre-existing mood and anxiety disorders significantly increased the likelihood of developing a subsequent alcohol, cannabis or stimulant use disorder. GAD and PTSD were the only psychiatric disorders found to significantly increase the risk of transitioning to use disorder across these three drug classes: that is, AUD, CUD and STUD. The strongest associations were observed between GAD and STUD, where pre-existing GAD more than trebled the risk of transitioning from use to STUD. Similarly, the presence of any affective disorder and major depressive episode (MDE) in particular more than trebled the risk of transitioning to AUD. The lack of a statistically significant relationship between pre-existing psychiatric disorders and subsequent SEUD or OUD is likely due to the small number of respondents in each of these categories. Nonetheless, the estimates derived from this study may be useful in informing future research, and it is worth noting that the confidence intervals are, for the most part heavily weighted towards a positive association, rather than no relationship. Examination of the absolute size of the odds ratios in Table 2 shows that many associations in the SEUD and OUD models are of a similar magnitude to those for the AUD, STUD and CUD models.

The finding that nearly every mood and anxiety disorder examined was significantly associated with transitioning to AUD and CUD emphasizes the need to assess symptoms of co-occurring mental disorders among people who use alcohol or cannabis use, as these may herald an increased risk of transitioning to these disorders. Conversely, this finding also highlights the need to ask about the use of alcohol or cannabis among people with mood or anxiety disorders, as the risk of transitioning to SUD may be elevated among these people. These findings are consistent with previous research from the National Epidemiological Survey on Alcohol and Related Conditions (NESARC), which found pre-existing affective disorders more than doubled the risk of transitioning from first use to alcohol, cannabis, or cocaine dependence, and pre-existing anxiety disorders doubled the risk of transitioning to alcohol or cannabis dependence (Lopez-Quintero et al., 2011). These and the current study findings highlight the need to focus intervention efforts towards those with mood (particularly MDE), and

anxiety (particularly GAD and PTSD) disorders, who are at risk of regular alcohol, cannabis or stimulant use to prevent the development of secondary SUDs.

A pre-existing SUD had the strongest association with transitioning from use to SUD on other substances. This finding is in line with previous research, which has found an increased risk of dependence was associated with prior substance use and SUD (Butterworth et al., 2014; Chen et al., 2005; Flórez-Salamanca et al., 2013). The strongest relationships were found in relation to transitioning from cannabis use to CUD: pre-existing STUD increased the risk of transitioning to CUD by more than 18 times; a history of AUD increased the risk of CUD onset more than ten-fold; pre-existing SEUD increased the risk of CUD onset more than eight times, and a history of OUD increased the risk of transitioning to CUD more than six times. These findings are consistent with previous epidemiological research from NESARC, which observed the strongest association for transitioning from cannabis use to dependence for prior cocaine dependence, which more than quadrupled this risk (Lopez-Quintero et al., 2011). A history of CUD was also found to increase the risk of transitioning from stimulant use to STUD by more than seven times, in line with the findings from NESARC, which demonstrated a history of cannabis dependence more than trebled the risk of transitioning to cocaine dependence (Lopez-Quintero et al., 2011). From a theoretical perspective, these findings suggest common underlying mechanisms that may contribute to the transition from use to disorder than are not explained by the specific action of a given drug class. These findings further emphasize the need for assertive prevention and early intervention efforts among stimulant users.

Of all the covariates examined, only pre-existing SEUD significantly increased the risk of transitioning from opioid use to OUD, increasing this risk by more than six times. Benzodiazepine use among opioid users has been extensively documented, and its use associated with poorer outcomes across several domains (Darke, 1994; Darke et al., 2010; Ghitza et al., 2008; Ross et al., 1996). These and the current findings highlight the need for healthcare providers to exercise caution in prescribing benzodiazepines and other sedatives to patients who use opioids.

The present findings should be interpreted within the context of several limitations common to many large-scale surveys. Firstly, the cross-sectional nature of the survey relied on retrospective recall of age of first substance use and disorder onset and may be subject to bias (Shillington et al., 2012; Simon and VonKorff, 1995). Although the survey utilized methodology similar to the World Mental Health Surveys to maximize accuracy of recall (Kessler et al., 2007), potential memory limitations should be borne in mind. Secondly, the small sizes for sedative and opioid samples resulted in wide confidence intervals, and as such, significant findings should be interpreted with caution. However, the magnitude and direction of the odds ratios suggest that similar findings would be observed in larger samples. The nature of the study meant there was overlap between substance using samples, with a relatively high amount of polysubstance use. As such, the groups were not independent, and direct comparison between substances was not possible. Furthermore, there may be other factors associated with the transition from use to SUD that has not been examined in the current study, for example, socioeconomic status, area-level deprivation, and externalizing spectrum disorders, which may also play a role in these relationships.

5. Conclusion

Findings from the current study suggest that between one-third and one-half of people who use substances go on to develop a SUD, with the highest rates of transition observed with stimulant and opioid users. The rapidity with which people transition from use to use disorder emphasizes the narrow window of opportunity available to intervene, underscoring the urgency of early identification, particularly among those with pre-existing mood or anxiety disorders. The timely provision of appropriate evidence-based treatments may prevent the development of secondary comorbid substance use disorders.

Role of funding source

The 2007 National Survey of Mental Health and Wellbeing (NSMHWB) was funded by the Australian Government and conducted by the Australian Bureau of Statistics. The Centre of Research Excellence in Mental Health and Substance Use is funded by the National Health and Medical Research Council. The National Drug and Alcohol Research Centre is supported by funding from the Australian Government under the Substance Misuse Prevention and Service Improvements Grants Fund. This work is also supported by NHMRC Fellowships to Maree Teesson and Katherine Mills, and Society for Mental Health Research Fellowship to Christina Marel.

Contributors

CM conceived the topic, drafted and finalized the manuscript. MS conducted the analysis, contributed to writing the first draft, and was involved in editing the manuscript. MS, KM and CC assisted with topic refinement. MS, KM, TS, MT and CC contributed to substantial editing of the manuscript. All authors have approved the final article.

Conflict of interest

No conflict declared.

Acknowledgments

The authors would like to thank the NSMHWB reference group for their input in the survey's design. The authors would also like to thank all those who participated in the survey.

Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.drugalcdep.2018.10.010.

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