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Intermediate stable states in substance use

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ABSTRACT

Many people across the world use potentially addictive legal and illegal substances, but evidence suggests that not all use leads to heavy use and dependence, as some substances are used moderately for long periods of time. Here, we empirically examine, the stability of and transitions between three substance use states: zero-use, moderate use, and heavy use. We investigate two large datasets from the US and the Netherlands on yearly usage and change of alcohol, nicotine, and cannabis. Results, which we make available through an extensive interactive tool, suggests that there are stable moderate use states, even after meeting criteria for a positive diagnosis of substance abuse or dependency, for both alcohol and cannabis use. Moderate use of tobacco, however, was rare. We discuss implications of recognizing three states rather than two states as a modeling target, in which the moderate use state can both act as an intervention target or as a gateway between zero use and heavy use.

1. Introduction

Many people across the world use potentially addictive legal and illegal substances—especially commonly used substances such as alcohol, tobacco and cannabis (Degenhardt et al., 2008; Hasin et al., 2017; National Institute on Alcohol Abuse and Alcoholism; 2021). Substantial proportions of the population continue to use alcohol, tobacco, and cannabis throughout their lives, although typically at declining levels with increasing age (Kendler, Schmitt, Aggen, & Prescott, 2008). The last decade has seen an increased interest in understanding the causes of the key transitions in psychoactive drug use (Compton et al, 2013; Piazza & Deroche-Gamonet, 2013) including specific studies of alcohol (Rapsey et al., 2019; Flórez-Salamanca et al., 2013; Lopez-Quintero et al., 2011; Marel et al., 2019), cannabis (Van der Pol et al., 2013 Flórez-Salamanca et al., 2013; Lopez-Quintero et al., 2011; Marel et al., 2019; Feingold et al., 2020) and nicotine (Lopez-Quintero et al., 2011) It is clear that not all who use substances transition into dependence (e.g., Lopez-Quintero et al., 2011; Compton et al., 2016; Rapsey et al., 2019; Wittchen et al., 2008). In a large US epidemiologic survey following participants over several years, the transition from use to dependence differed by substance. Many people who used nicotine transitioned into dependence (67.5%), but only a minority of people who used alcohol and cannabis did (22.7% and 8.9%, respectively; Lopez-Quintero et al. 2011). Given that many individuals continue using substances throughout much of their adult life (Kendler et al., 2008), the evidence now convincingly demonstrates that many people can maintain stable moderate levels of use without having to increase their intake. Indeed, first coined in the opioid use literature, chippers (Crawford, Washington & Senay, 1983; Shiffman, 1989; Zinberg & Lewis, 1964; Powell, 1973; Stull et al., 2019) are people who use drugs regularly but moderately for years while avoiding succumbing to major drug-related problems, particularly addictive behaviors resulting in dependence. So, exposure need not lead inevitably to heavy use or strong dependence—some substances are moderately used for long periods of time without ending in disordered use. We note that heavy use has been sub-classified in different types (Leggio et al, 2009), but here we treat heavy use as one category.

Substance use behaviors are an example of a psychological system that exhibits *feedback:* the use of substances and the circumstances in which it takes place can impact one's life in both the short-term and

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long-term, creating environments that are reinforcing thereby impacting the amount of substance use. For instance, alcohol use may delay or advance marriage, whereas marriage often reduces substance use (Leonard and Eiden 2007; Salvatore et al., 2019), and alcohol inhibits self-control, and low self-control may increase intake (Hufford et al., 2003). In many natural systems, such feedback gives rise to non-linear dynamics (Thompson & Stewart, 2002), characterized by transitions between unstable and stable attractor states. Non-linear dynamical systems are a special class of dynamical systems in which the current state of the system is a nonlinear function of past states and other external factors. The dynamics of complex systems such as the weather, eco-systems, and financial markets are known to be nonlinear (Nicolis & Nicolis, 1995). Such systems are characterized by alternative stable states and sudden transitions (e.g., tipping points) between these states when some control variable is changed or surpasses a critical threshold. Several systems in nature exhibit three stable states. For example, van Nes, Hirota, Holmgren, & Scheffer (2014) describe an ecological system with three states of tree growth in the tropics: treeless, savanna, and forest, of which one to three can be stable for different levels of precipitation. Another well-known example is the walking, trotting, and galloping gait states in quadrupeds, (Aoi et al., 2013).

Nonlinear dynamical systems seem promising in the study of addictive substance use, as it may improve our insight in transitions from multiple stable states–from no use to moderate use to heavy use states—which could lead to new intervention and prevention strategies. A limited number of studies have applied nonlinear dynamical system methods (Van den Ende et al., 2022) to behavioral systems of substance use. One such study applied a nonlinear dynamical system perspective to understand relapse of alcohol use disorders in the 12 months following alcohol treatment (Witkiewitz et al. 2007). Using catastrophe and growth mixture modeling, they found a dynamic relationship between self-efficacy and drinking outcomes and identified two stable and one unstable "inconsistent drinking" classes. However, in further work, Witkiewitz, examining alcohol consumption data from the MATCH and COMBINE treatment trials, identified, respectively, three classes using latent transition analysis (nondrinking, moderate infrequent drinking and heavy drinking; Witkiewitz, 2008) and latent Markov models (infrequent, occasional and frequent heavy drinking; Witkiewitz et al, 2010). Chow et al (2015) applied cusp catastrophe model inspired mixed structural equation modeling regime switching (MSEM-RS) to MATCH alcohol use data, finding that a two class MSEM-RS medium and high use regime model fitted the data better than a low, medium and high three regime model. In aggregate, prior work suggests that, in addition to the states of abstinence and problematic/heavy use, even in individuals with prior alcohol dependence, social drinking can be a relatively stable state (Witkiewitz & Tucker, 2020; Falk et al., 2019). Further previous work mainly investigated developmental trajectories of substance use with different statistical methods, such as latent transition analysis (Choi et al., 2018), repeated-measures latent class analysis (McCarty, 2015), and parallel growth mixture modelling (Lanza 2020a; Lanza 2021). They found evidence for multiple substance use states—including infrequent or moderate use states—that were relatively stable, but also identified transitions between these states, mostly to more harmful substance use states.

Here, we compliment this work by presenting further empirical support for three stable states in substance use: zero-use (abstention), moderate use (e.g., chippers), and heavy use. Through novel descriptive data-exploration techniques, we explore two datasets to investigate the presence and/or absence of stable moderate use in three psychoactive substances–alcohol, tobacco, and cannabis. Our use of the terms "stable" and "unstable" here refers to how many consecutive person years an individuals' substance use falls into one of our three predefined categories. We make online tools available so that our results can be easily investigated and visualized, allowing the reader to explore different research questions as well as to check the sensitivity of our results based on choices we make in the analysis, such as the age ranges analyzed and the thresholds used to distinguish moderate from heavy use—the latter which is also investigated in a sensitivity analysis reported below.

2. Methods

2.1. Sample 1: Virginia adult twin study of psychiatric and substance use disorders

The first dataset analyzed in this study was from a third follow-up (MM3) of same-sex adult male twins from the **V**irginia **A**dult **T**win **S**tudy of Psychiatric and **S**ubstance **U**se **D**isorders (VATSPSUD; Kendler & Prescott, 2006). The VATSPSUD consists of Caucasian male, female, and opposite sex twin pairs from the Virginia Twin Registry (now the Mid-Atlantic Twin Registry; MATR) born between 1940 and 1974 and identified through birth records and the motor vehicle department. In data collection efforts carried out between 2000 and 2004, this subset of same-sex male twins was assessed on a range of life-time psychoactive substance usage and associated risk factors. Eligible MM3 twins were members of male–male pairs that had participated in two previous interviews. Most subjects were interviewed by trained mental health professionals by telephone with a small number interviewed in person. Each member of a twin pair was assessed by a different interviewer. All data collection protocols were approved by the Virginia Commonwealth University institutional review board. Subjects were informed about the goals of the study and provided informed consent before interviews. A Life History Calendar (LHC; Freedman, Thornton, Camburn, Alwin, & Young-demarco, 1988; Furstenberg, Brooks-Gunn, & Morgan, 1987; Kessler & Wethington, 1991) data collection approach was used to obtain detailed retrospective information on the life-span timing of changes in the amount of substances used and certain demographics (e.g., interpersonal relationships). The LHC chart format facilitates accurate recall of the timing of events by providing a person-history context that refers to salient life events such as marriage/divorce, education, and employment. Because each twin was asked to report the age at which there was a change in their consumption amount for each substance during their life, it was possible to construct a detailed sequential life-span person-year consumption record for each twin. For our analyses, multiple person-year records for each twin ranging from 0 through 61 were constructed for consumption amounts for alcohol (number of drinks per month), tobacco (cigarettes per day), cannabis (number of "unit" [e.g., joints] used per month). In a different part of the interview, they were administered a structured psychiatric assessment from which lifetime diagnoses utilizing DSM-IV (American Psychiatric Association, 2000) criteria for including alcohol and cannabis abuse and dependence. Age at onset of the abuse or dependence was also recorded. Tobacco dependence was assessed by the Fagerstrom Test for Nicotine Dependence (Heatherton, Kozlowski, Frecker & Fagerstrom, 1991). Although the VATSPSUD data consists of individuals from twin pairs, we analyze these data as individual records. Subjects reported up to a mean age of 40.3 (SD = 8.99).

2.2. Sample 2: Longitudinal Internet Studies for the Social sciences

In an attempt to replicate results from the VATSPSUD data, we analyzed the LISS (Longitudinal Internet Studies for the Social sciences) panel administered by CentERdata (Tilburg University, The Netherlands). The LISS panel is a representative sample of Dutch individuals who participate in a longitudinal online survey that is conducted every year. LISS includes measures of substance use over several years, which is similar to the VATSPSUD data, but it is also different in that the VATSPSUD twin data was assessed at a single interview retrospectively inquiring about substance use changes at specific ages across the lifespan. The LISS survey also covers a large variety of domains

including work, education, income, housing, time use, political views, values and personality.[1] We analyzed responses from 2008 to 2018 and focused on assessments of the use of tobacco and soft-drugs (cannabis).[2] Information on alcohol use was also available, but at most people could report to drink at least once per day, which does not reach our criterion for heavy use. To increase the comparability of the LISS panel and the VATSPSUD, only males in the age group 26 – 61 were included in the analysis. A detailed overview of the distribution of age in the samples analyzed can be found in Table 1. For the tobacco data, we combined measures on the number of cigarettes (including roll-your-own forms), pipes, cigars and cigarillos.

2.3. Analyses

2.3.1. Substance use state definitions

We classified, for each year, if a subject was in a zero, moderate, or heavy use state by using cut-off thresholds based on prior literature. For alcohol, tobacco, and cannabis use, we defined, respectively, moderate usage as one to 60 drinks per month (National Institute on Alcohol Abuse and Alcoholism, 2003), one to 5 cigarettes per day (Shiffman, 1989; Shiffman, Paty, Kassel, Gnys & Zettler-Segal, 1994), and one to 6 uses (e.g., joints smoked) per month (Milani et al., 2005; Patton et al., 2007).[3] Years in which less of each of these substances was used as defined above were classified as zero-use years, and years in which more substance was used above were classified as years of heavy use. We performed a sensitivity analysis in which we varied these definitions to assess how much the choice of these definitions impacted results.

2.3.2. State transitions

We investigated two types of proportions of transition (reported as percentages in the results section). A transition is defined by comparing the state of usage in two consecutive years (e.g., a transition from zero-use to moderate use in alcohol usage means a person reported zero usage in one year, and between 1 and 60 drinks per month in the next year). The first type of proportion (type A) is the relative proportion of transitions from a year in which someone was classified into a given usage state. These proportions should be understood as "after a year in which someone was classified into usage state X, how many transitioned into usage state Y", and sum to 1. For example, a year in which a substance was not used (zero-used) is followed either by a year in which the substance was not used again, a year in which the substance use was moderate, or a year in which the substance use was heavy. The second type of proportion (type B) is, for each possible transition, the proportion of subjects having that transition at least once at any point in their live. These percentages do not necessarily need to sum to 1, as subjects can have multiple transitions throughout their life. For example, for every substance 100% of the sample reported at least two consecutive zero-use years in childhood, but a smaller percentage of the sample could have reported at least one zero-use to moderate use transition.

Table 1
Descriptive statistics of the age distribution in the analyzed subset (ages 26 – 61) of the LISS dataset.

Year	n	Mean	SD
2008	1774	45.26	9.78
2009	1322	46.14	9.66
2010	1177	46.67	9.57
2011	1015	47.20	9.35
2012	947	47.38	9.48
2013	890	47.25	9.61
2015	714	47.12	9.58
2016	691	47.29	9.77
2017	596	47.70	9.85
2018	556	48.08	9.65

For all analyses, we used the statistical software R version 4.0.0 (R core team, 2020), relying primarily on the packages *dplyr* (for data handling; Wickham, François, Henry & Müller, 2020), *qgraph* (for network visualizations), and *ggplot2* (for other graphs; Wickham, 2016). The R package *shiny* was used to create interactive online platforms in which all analyses of the paper can be reproduced.[4]

3. Results

3.1. Sample 1: Virginia adult twin study of psychiatric and substance use disorders

For each substance, we classified 9 transition-types between zero, moderate use and heavy use states (i.e., for each state, people could stay in the state or transition into one of the other two states). We investigated the type A and type B transmission proportions in alcohol, tobacco and cannabis use. In addition to presenting the main results numerically in Table 2, we present results also through graphical network representations (Epskamp et al., 2012) in an online platform, which allows researchers to reproduce all findings in addition to exploring other findings (e.g., by changing the thresholds used).[5] The types of proportions are reported in brackets below. We only analyzed subjects with complete data on at least two consecutive years ($n = 1{,}695$ for alcohol use, $n = 1{,}657$ for tobacco use, and $n = 1{,}079$ for cannabis use).

Alcohol. We found a large stable moderate usage state: 94% (B) of the subjects reported having at least two consecutive years of moderate use, and 96% (A) of moderate usage years are followed by additional years of moderate use. Furthermore, most between-state transitions are *to* a state of moderate usage: 11% (A) of heavy use years are followed by years of moderate use and 5% (A) of zero-use years are followed by moderate usage years. There are only a few transitions between zero and heavy use years, as the path between these states typically occurs via the moderate usage state. We next examined the results from our model by developmental period.

Before adulthood. Investigating the onset of alcohol use (only investigating up to and including age 17), 61% (B) of the subjects report two or more consecutive years of moderate alcohol use, and very few subjects (2%; B) report a direct transition from a zero- to a heavy use year. 78% (B) of the sample reported a transition from zero to moderate use, and 12% (B) of the sample reported a transition from moderate to heavy use. During adolescence the path to heavy drinking typically goes through a moderate drinking period.

Young adults. In young adults (age 18 – 25), only 22% (B) report two consecutive zero-use years, indicating that stable zero-use of alcohol does not occur often. Moderate use is much more common and stable: 94% (A) of moderate use years are followed by additional moderate use years, with 85% (B) of the subjects reporting $\geq$ two consecutive years of moderate alcohol usage. Heavy use is also stable and common: 83% of heavy use years are followed by heavy use years, and 31% (B) report $\geq$ two consecutive heavy use years. Most people transitioning from heavy use do so to a moderate usage state: 15% (A) of heavy use years are

[1] More information about the LISS panel can be found at: www.lissdata.nl.

[2] Because the survey was not yearly on the exact same date, it could be that subjects reported to be the same age in two consecutive surveys. To adjust for this, we set up an algorithm to adjust subject's ages such that the ages are (a) consecutively increasing and (b) match the reported ages as closely as possible. For example, if a subject reported to be 40 in 2008, 41 in 2009, also 41 in 2010 and 43 in 2011, the age of 2010 was adjusted to 42 in the analysis (but not in the reported demographics of Table 1).

[3] This definition is roughly similar to "weekly" cannabis use, which is often termed "moderate" in the literature.

[4] Links to the web applications can be found at sachaepskamp.com/stable_states.

[5] https://sachaepskamp.shinyapps.io/Intermediate_Stable_States_VATSPSUD/

Table 2
Transmission proportion between different substance use states in the VATSPSUD dataset. The first proportion (type A) denotes the proportion of transitioning into a state (vertical cells) given the state (horizontal cells) a person was in in the year before; these proportions will sum to one for every row. The second proportion (type B) denotes the proportion of subjects that reported at least one transition (or two consecutive stable years). These values do not sum to 1, as subjects can report multiple types of transitions.

From	To									
	Alcohol (VATSPSUD)			Tobacco (VATSPSUD)			Cannabis (VATSPSUD)			
	Zero-use	Moderate (1-60)	Heavy (61+)	Zero-use	Moderate (1-5)	Heavy (6+)	Zero-use	Moderate (1-6)	Heavy (7+)	
Zero-use	**0.95 / 1**	0.05 / 0.93	< 0.01 / 0.04	**0.98 / 1**	0.01 / 0.27	0.01 / 0.30	**0.98 / 1**	0.02 / 0.51	< 0.01 / 0.12	Full sample
Moderate	0.01 / 0.20	**0.96 / 0.94**	0.03 / 0.39	0.05 / 0.05	**0.71 / 0.20**	0.24 / 0.23	0.09 / 0.36	**0.85 / 0.52**	0.06 / 0.24	
Heavy	0.02 / 0.07	0.11 / 0.32	**0.86 / 0.37**	0.03 / 0.25	< 0.01 / 0.03	**0.97 / 0.49**	0.06 / 0.15	0.06 / 0.17	**0.88 / 0.32**	
Zero-use	**0.95 / 1**	0.05 / 0.78	< 0.01 / 0.02	**0.98 / 1**	0.01 / 0.23	0.01 / 0.18	**0.98 / 1**	0.02 / 0.35	<0.01 / 0.07	Up to 17
Moderate	0.01 / 0.01	**0.93 / 0.61**	0.06 / 0.12	0.02 / 0.01	**0.63 / 0.14**	0.34 / 0.16	0.03 / 0.02	**0.78 / 0.25**	0.19 / 0.12	
Heavy	0.01 / < 0.01	0.11 / 0.01	**0.88 / 0.04**	0.01 / 0.01	< 0.01 / < 0.01	**0.98 / 0.25**	0.04 / 0.01	0.06 / 0.02	**0.90 / 0.13**	
Zero-use	**0.84 / 0.22**	0.14 / 0.16	0.01 / 0.01	**0.97 / 0.64**	0.01 / 0.04	0.02 / 0.09	**0.96 / 0.75**	0.03 / 0.14	0.01 / 0.04	18 – 25
Moderate	0.01 / 0.07	**0.94 / 0.85**	0.04 / 0.22	0.08 / 0.03	**0.71 / 0.08**	0.21 / 0.07	0.10 / 0.18	**0.84 / 0.38**	0.06 / 0.11	
Heavy	0.02 / 0.02	0.15 / 0.21	**0.83 / 0.31**	0.03 / 0.08	0.01 / 0.02	**0.97 / 0.46**	0.06 / 0.09	0.08 / 0.10	**0.86 / 0.27**	
Zero-use	**0.97 / 0.26**	0.03 / 0.08	< 0.01 / 0.01	**0.99 / 0.74**	< 0.01 / 0.01	0.01 / 0.06	**0.99 / 0.88**	< 0.01 / 0.05	< 0.01 / 0.01	26+
Moderate	0.01 / 0.13	**0.98 / 0.83**	0.01 / 0.09	0.07 / 0.02	**0.86 / 0.04**	0.07 / 0.02	0.10 / 0.17	**0.88 / 0.24**	0.02 / 0.03	
Heavy	0.03 / 0.04	0.08 / 0.12	**0.89 / 0.18**	0.04 / 0.18	< 0.01 / 0.02	**0.96 / 0.41**	0.05 / 0.06	0.05 / 0.05	**0.90 / 0.14**	
Zero-use	**0.94 / 1**	0.06 / 0.93	< 0.01 / 0.06	**0.94 / 1**	0.03 / 0.46	0.04 / 0.55	**0.95 / 1**	0.04 / 0.70	0.01 / 0.19	Before diagnosis
Moderate	< 0.01 / 0.02	**0.90 / 0.86**	0.1 / 0.46	0.01 / 0.01	**0.64 / 0.29**	0.36 / 0.41	0.02 / 0.03	**0.78 / 0.47**	0.20 / 0.27	
Heavy	< 0.01 / < 0.01	0.06 / 0.08	**0.94 / 0.33**	0.01 / 0.09	< 0.01 / < 0.01	**0.99 / 0.89**	0.01 / 0.01	0.02 / 0.02	**0.96 / 0.26**	
Zero-use	**0.95 / 0.29**	0.04 / 0.11	0.01 / 0.02	**0.97 / 0.41**	< 0.01 / 0.01	0.03 / 0.10	**0.98 / 0.74**	0.01 / 0.10	0.01 / 0.07	After diagnosis
Moderate	0.02 / 0.19	**0.95 / 0.83**	0.03 / 0.29	0.03 / 0.01	**0.71 / 0.04**	0.26 / 0.05	0.09 / 0.40	**0.85 / 0.59**	0.06 / 0.27	
Heavy	0.03 / 0.14	0.11 / 0.48	**0.86 / 0.59**	0.04 / 0.40	< 0.01 / 0.02	**0.96 / 0.92**	0.06 / 0.34	0.06 / 0.32	**0.88 / 0.68**	

followed by moderate use years, and 21% (B) of the sample reports at least one heavy use year followed by a moderate use year.

Adults. In adulthood (age 26 – 61), 98% (A) of years of moderate usage are followed by moderate use years, indicating that the moderate usage state is more stable than the heavy use state (89%; A). Moderate usage is a common state, 83% (B) of the subjects report at least two consecutive years of moderate use, compared to 18% (B) reporting $\geq$ two consecutive heavy use years and 26% (B) reporting $\geq$ two consecutive zero-use years. Only 1% (B) of adults 26 and over had at least one zero-use to heavy use transition, indicating that similar to young adults, in adulthood the moderate usage state seems to be common, stable, and in between zero-use and heavy use state for most subjects.

Diagnosed. Most subjects who met a diagnosis for alcohol dependence (621 subjects) had at least one zero-use to moderate use (93%; B) transition and many report at least one moderate to heavy use (46%; B) transition *before* the year in which they met criteria for an alcohol use disorder diagnosis. *After* diagnosis, the moderate usage state is still stable; 95% (A) of moderate usage years are followed by additional moderate usage years. In alcohol dependence subjects, the moderate usage state is also stable after a transition from a heavy use year to a moderate use year: 96% (A) of years of moderate use are followed by more moderate usage years. While 16% (B) of these subjects (subjects diagnosed with alcohol abuse/dependency and after reporting a heavy use to moderate use transition) report at least one transition back to a heavy use state, 98% (B) reported at least two consecutive moderate use years and 18% (B) reported a transition of moderate use to a zero-use state.

Overall, these alcohol data suggest that a moderate usage state is stable even for many subjects after meeting criteria for an alcohol use disorder. Moderate use also appears to be a "gateway" to heavy use, especially during adolescence.

Tobacco. Moderate tobacco use, as defined by smoking one to five cigarettes per day, was found to be less and common than moderate alcohol usage: 71% (A) of moderate years were followed by additional moderate years, and most between-state transitions were away from the moderate use state. 24% (A) of moderate years were followed by heavy use years and 5% (A) of moderate years were followed by zero-use years, suggesting that moderate years more commonly act as a gateway to tobacco heavy use states, than as a gateway back to zero-use. Moderate cigarette smoking is also uncommon: only 20% (B) of the subjects report at least two consecutive moderate years, compared to 49% (B) reporting at least two consecutive heavy use years. A notable portion of transitions were between zero-use and heavy use years: 25% (B) of the subjects report at least one heavy use to zero-use transition and 30% (B) report at least one zero-use to heavy use transition. As with alcohol, we then examined our results by developmental periods.

Before adulthood (0 – 17). Investigating the onset of tobacco use up to and including age 17, the moderate state seems to be very unstable, possibly serving primarily as a gateway to heavy use smoking: 34% (A) of moderate years are followed by heavy use years.

Young adults. In young adults (age 18 – 25), stable moderate use was again very uncommon. Only 8% (B) of the sample reported two consecutive moderate years, whereas 46% (B) reported at least two consecutive heavy-use years and 64% (B) reported two consecutive zero-use years. Moderate use was also less stable than zero-use and heavy use; 71% (A) of moderate use years were followed by moderate use years, versus 97% (A) for both zero-use and heavy use years. 21% (A) of moderate use years were followed by heavy use years.

Adulthood. In adulthood (age 26 – 61), the moderate state is also rare: 5% (B) of the sample report such a year, and few people transition to it; hardly any heavy use years and zero-use years are followed by moderate use years. While moderate usage is rare, it is more stable in this age group: 86% (A) of moderate years are followed by subsequent moderate years. Instead, most transitions are reported between zero-use and heavy use years: 18% (B) of the subjects report at least one heavy use to zero-use year, and 6% (B) of the subjects report at least one zero-use to heavy use year. After reporting a heavy use to zero-use transition, 24% (B) of the subjects report at least transition back from the zero-use to heavy use state, indicating a high relapse rate.

Diagnosis. Before the year in which subjects were diagnosed with nicotine dependence (470 subjects), 55% (B) of the subjects reported at least one zero-use to heavy use transition, while 46% (B) reported at least one zero-use to moderate transition and 41% (B) reported at least one moderate to heavy use transition. This indicates that many people smoked heavily very soon after initiating smoking, although others started heavier smoking via moderate smoking. *After* having met the

criteria for nicotine dependence, most subjects either stay in the heavy use state or quit and transition to the zero-use state: only 4% (B) report two consecutive moderate years, and 26% (A) of moderate years are followed by heavy use years. Rather than reducing the number of cigarettes smoked, most quit completely: 40% (B) of these male subjects report at least one heavy use to zero-use transition.

Overall, these person-year changes in cigarette smoking data in males suggests that moderate usage is unstable and mainly serves as a gateway to heavy use of nicotine. Many subjects transition within one year from zero use to heavy use.

Cannabis. Evidence pointed to a stable and common moderate usage state for cannabis. 52% (B) of the subjects report at least two consecutive moderate level usage years, and 85% (A) of moderate years are followed by another moderate year. Only 32% (B) of the subjects report two consecutive heavy use years, which is lower than with alcohol (37%; B) and tobacco (49%; B). A variety of transitions are reported in the cannabis person-year data, ranging from 12% (B) of the subjects reporting at least one zero-use to heavy use transition to 51% (B) reporting at least one zero-use to moderate transition. Notably, a large number of subjects (36%; B) reported at least one transition from moderate use to zero-use, indicating that moderate years can likely be followed up by zero-use years.

Before adulthood. Up to and including age 17, there seems to be relatively stable moderate state: 78% (A) of moderate years are followed up with moderate years. However, this state is less stable than the zero-use (98%; A) and heavy use (90%; A) states, and 19% (A) of moderate years are followed by heavy use years. Many subjects reported person year patterns of cannabis use showing a transition to heavy use via moderate use: 35% (B) reported at least one zero-use to moderate transition and 12% (B) reported at least one moderate to heavy use transition, compared to 7% (B) that reported a direct transition from zero-use years to heavy use years.

Young adults. In young adults (age 18 – 25), a relatively large portion of subjects report at least two consecutive moderate use years (38%; B), which is noteworthy as cannabis is not a legal substance in this sample. In addition, 75% (B) report at least two consecutive zero-use years. Moderate use is quite stable, as 84% (A) of moderate years are followed by subsequent moderate years. Heavy use is also stable with 86% (A) of heavy use years followed by additional heavy use years. 27% (B) reported two consecutive heavy use years.

Adulthood. In adulthood (age 26 – 61), very few subjects in the sample advanced to using more cannabis. Only 2% (A) of moderate years are followed by heavy use years and<1% (A) of zero-use years are followed by moderate use years. Instead, most subjects reduce their usage: 10% (A) of moderate years are followed by zero-use years and 5% (A) of heavy use years are followed by moderate and zero-use years. Stable moderate use is more common in adulthood than heavy use: 24% (B) of the subjects report at least two consecutive moderate years compared to 14% (B) reporting at least two consecutive heavy use years.

Diagnosis. Before the age of first meeting the criteria for cannabis abuse or dependence (321 subjects), 19% (B) of the subjects that meet criteria reported at least one zero-use to heavy use transition, compared to 70% (B) reporting at least one zero-use to moderate transition and 27% (B) of the subjects reporting at least one moderate to heavy use transition. Thus, cannabis abuse or dependence can develop with or without transitioning through moderate usage. After diagnosis, subjects either quit or diminish their usage to moderate usage: 32% (B) report at least one heavy use to moderate transition, 40% (B) report at least one moderate to zero-use transition and 34% (B) report at least one heavy use to zero-use transition. Many subjects that have met criteria for cannabis abuse or dependence report a stable moderate state in the following years: 85% (A) of moderate years are followed by moderate years and only 6% (A) of moderate years are followed by heavy use years. However, 27% (B) of the male sample do report at least one moderate to heavy use transition after meeting criteria for a diagnosis of abuse or dependence, indicating that while moderate use is stable, there is a risk of transitioning back to the heavy use state again.

Sensitivity analysis. We performed a follow-up sensitivity analysis to investigate how much the results depended on the upper cutoffs chosen to define moderate use (60 drinks per month, 5 cigarettes per day or 6 uses of cannabis per month). We varied the upper bound, and investigated the changes in transition proportions (A) per state (e.g., the proportion of moderate years that were followed by moderate years). Fig. 1 shows that these sensitivity results appear to be robust to using other cutoff values near to the ones that were originally chosen. Only for tobacco use in the form of cigarettes smoked does the chosen cutoff value appear to play an important role: moderate use defined as smoking<5 cigarettes (e.g., 3) shows lower stability levels.

3.2. Sample 2: Longitudinal Internet Studies for the Social sciences

A web application for interactively exploring the LISS panel data is available online,[6] and a summary of numeric results can be found in Table 3. We only included subjects between ages 26 and 61 and who had no missing data on at least two consecutive years ($n = 1{,}535$ for tobacco use and $n = 1{,}539$ for cannabis use).[7]

Tobacco. As found in the VATSPSUD twin sample, moderate tobacco usage in adults aged 26 − 61was less stable than zero-use and heavy use: 72% (A) of moderate years were followed by moderate years, whereas 99% (A) of zero-use years were followed by zero-use years and 87% (A) of heavy use years were followed by heavy use years. 19% (A) of moderate years were followed with zero-use years and 9% (A) of moderate years were followed by heavy use years. Stable moderate use was also an uncommon state: only 5% (B) of the sample reported at least two consecutive moderate years, versus 19% (B) for heavy use years and 80% (B) for zero-use years.

Soft-drugs. The LISS data includes items assessing how often subjects used "soft drugs such as hashish, marijuana." Comparing these assessments to those found in the VATSPSUD cannabis data in subjects aged 26–61, the LISS data revealed a less stable moderate state: 44% (A) of moderate years were followed by moderate years, compared to 78% (A) of heavy use years followed by heavy use years and 99% (A) of zero-use years followed by zero-use years. Most transitions were in the direction of reducing usage: 16% (A) of heavy use years were followed by moderate years, 6% (A) of heavy use years were followed by zero-use years, and 49% (A) of moderate years were followed by zero-use years. Therefore, most shifts from heavy use to zero-use states were via moderate use. The LISS dataset also showed that stable heavy and moderate use are uncommon: only 4% (B) of the sample report at least one moderate year, and 1% (B) of the subjects reported two consecutive heavy use years or two consecutive moderate years.

4. Discussion

In this paper, we investigated the stability of three states of substance use: zero-use or abstinence, moderate use or chipping, and heavy use. Our empirical results suggest the importance of stable moderate states, even after meeting criteria for a positive diagnosis of substance abuse or dependence, for both alcohol and cannabis use. For both substances, moderate use appears to be an important intermediate state on the path from zero-use to heavy use as well as on the path back from heavy use to zero-use. There is, however, less evidence for a stable state of moderate

[6] https://sachaepskamp.shinyapps.io/Intermediate_Stable_States_LISS/

[7] Of the total number of subjects between the ages of 26 and 61 included in the analyses, 77.9% had a Dutch background, 2% were first generation immigrants with a western background, 3.1% were first generation immigrants with a non-western background, 3.9% were second generation immigrants with a western background and 0.9% were second generation immigrants with a non-western background. The background of 12.2% of the sample were unknown (missing).

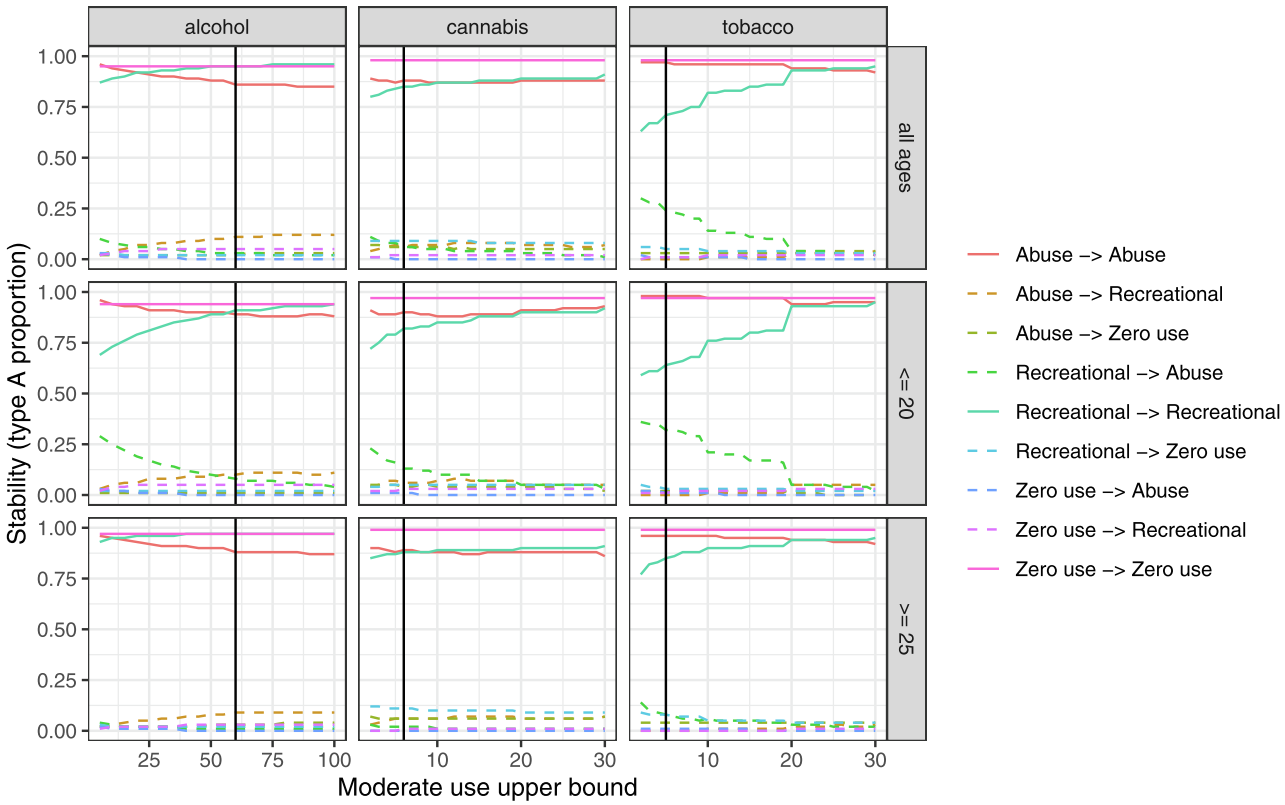

Fig. 1. Sensitivity analysis of the VATSPSUD sample results. This plot shows stability measures as function of the upper bound used to define recreational use. Stability A -> B is defined as the (type A) proportion of years in which state A was reported that reported state B in the next year. Alcohol = drinks per month; tobacco = cigarretes per day; cannabis = uses per month. The x-axis shows the threshold used to distinguish moderate use from heavy use, with vertical lines indicating the thresholds used in the paper.

Table 3
Transmission proportion between different substance use states in the LISS dataset. The first proportion (type A) denotes the proportion of transitioning into a state (vertical cells) given the state (horizontal cells) a person was in in the year before; these proportions will sum to one for every row. The second proportion (type B) denotes the proportion of subjects that reported at least one transition (or two consecutive stable years). These values do not sum to 1, as subjects can report multiple types of transitions.

From	To						
	Tobacco (LISS)			Soft-drugs (LISS)			
	Zero-use	Moderate (1–60)	Heavy (61 +)	Zero-use	Moderate (1–5)	Heavy (6 +)	
Zero-use	**0.99 / 0.83**	< 0.01 / 0.02	< 0.01 / 0.01	**0.99 / 0.97**	< 0.01 / 0.02	< 0.01 / 0.01	Full sample
Moderate	0.19 / 0.04	**0.67 / 0.05**	0.14 / 0.02	0.52 / 0.03	**0.40 / 0.01**	0.07 / < 0.01	
Heavy	0.10 / 0.07	0.04 / 0.03	**0.86 / 0.18**	0.06 / < 0.01	0.21 / 0.01	**0.72 / 0.01**	
Zero-use	**0.99 / 0.80**	< 0.01 / 0.01	< 0.01 / 0.01	**0.99 / 0.97**	< 0.01 / 0.02	< 0.01 / < 0.01	26–61
Moderate	0.19 / 0.03	**0.72 / 0.05**	0.09 / 0.02	0.49 / 0.03	**0.44 / 0.01**	0.07 / < 0.01	
Heavy	0.10 / 0.07	0.03 / 0.02	**0.87 / 0.19**	0.06 / < 0.01	0.16 / 0.01	**0.78 / 0.01**	

use for tobacco: moderate use of tobacco is not reported by many people and appears mostly to be a gateway to heavy use. Very few individuals reduce their smoking habits to moderate smoking: rather, most quit fully moving into the zero-use state, but some retain a risk of relapsing back to heavy use. These results appear to be consistent with what is expected given the addictive properties of alcohol, cannabis, and nicotine reported in previous studies (Koob & Le Moal, 2006). Our sensitivity analysis showed that these findings are robust for differences in the thresholds we used to distinguish moderate use from heavy use. The LISS dataset results mostly aligned with the VATSPSUD results. Only cannabis use showed less stable moderate use in the LISS dataset: moderate use was far less common than in VATSPSUD, and usually only a gateway to zero-use. This may be due to cultural and legal differences in these two different countries.

Including three states as targets in the theoretical modeling of substance use may therefore be more informative than considering only two states when trying to understand longitudinal patterns of substance use. Models developed for other three states systems, such as the model of van Nes, Hirota, Holmgren, & Scheffer (2014) for tree growth in the tropics can readily be re-interpreted and adapted for modeling substance use, although the interpretation of the parameters in these domains may be complicated due to the lack of unambiguous units of classification and strong inter-individual and inter-cultural differences in substance use. Another class of models that feature multiple stable states and critical transitions between these states are the so-called *catastrophe models* (Zeeman, 1976). Such models are characterized by the presence of *hysteresis:* at fixed levels of control variables two stable attractor states may be present. To obtain three stable states, while retaining behavior similar to the cusp catastrophe, we may adapt, for example, the *butterfly catastrophe model*.

While our analyses shed new light on transition rates between zero, moderate and heavy usage of different substances, our work is not without potential limitations. First, we did not statistically test differences in transition proportions. Our work is exploratory and the sample size of both datasets are large, and likely robust to outliers. In addition, the VATSPSUD dataset contains twins and therefore introduces dependencies between subjects, which could bias statistical inferences drawn from the sample (e.g., statistical power could be overstated). Therefore, we only reported descriptive statistics. If required model testing could be achieved by applying more advanced techniques such as latent Markov and latent transition modelling (Witkiewitz 2008; Witkiewitz et al., 2010). Second, we based our classification on prior literature and expert opinion rather than any statistical clustering methods. We were concerned that estimating statistical mixture models on such count data can be difficult and may not produce interpretable results. Finer grained statistically-based latent classification groupings would not, we expected, readily translate into a clearer and more informative understanding of substance use transitions. In addition, we wished to complement inferential methods through the use of descriptive data-analyses that utilize theoretical knowledge for defining class memberships. Third, we could not replicate the VATSPSUD alcohol use findings, as LISS did not have the needed data. Fourth, we only investigated transition proportions by aggregating over people, and did not investigate more fine-grained intraindividual measures. For example, future research could investigate if there are substantive differences between people who transition between these states often compare to people who only transition between these states a few times in their lives. Fifth, we only analyzed men in both samples, as the VATSPSUD data included only men, and we aimed to replicate these findings using the LISS data. In addition, the subjects analyzed were mostly Caucasian. Future analyses could focus on more heterogeneous samples, in which also at least gender specific cut-offs should probably be considered (Agrawal & Lynskey, 2007). Sixth, the same usage cutoffs were imposed across the entire sample. While our sensitivity analysis did not show a strong effect for the cutoffs used, it seems possible that there are individual differences in what amounts of each substance constitute 'moderate' or 'heavy' use from the perspective of the user. Finally, our data did not allow for investigating quantity and frequency of use separately, nor did it allow for studying variability in quantity across situations. In future research, richer datasets might lead to more refined classifications of the moderate and heavy use states studied in this paper (Caraballo et al., 2009). We note that some authors argue that use in itself is a sufficient and unbiased criterion (Rehm et al., 2013).

Our findings have three potential implications for drug dependency prevention. First, for both alcohol and cannabis, we identified relatively stable moderate use states. This suggests that, with respect to prevention of high use states and associated symptoms of dependence, abstention need not be the only public health goal. Second, a large proportion of transitions to heavy use of alcohol and cannabis came from those already engaging in moderate use. Such individuals form a target group for focused primary prevention, e.g., on the early signs of transitions from moderate to heavy use. Third, we find a qualitative different between tobacco vs. alcohol and cannabis. Moderate tobacco use is not a viable public health goal. Prevention programs might want to make this distinction especially in educational programs to youth. While moderate use of alcohol and cannabis can be reached with only modest risk of progression to heavy use states, that is not true for tobacco.

5. Author Agreement

All authors have seen and approved the final version of the manuscript being submitted. They warrant that the article is the authors' original work, hasn't received prior publication and isn't under consideration for publication elsewhere.

6. Author Statement

This project was conceptualized during the workshop "Dynamical systems, networks, and psychopathology" at the Institute for Advanced Studies, University of Amsterdam in September 2017. All authors contributed to every stage of the research process.

CRediT authorship contribution statement

Sacha Epskamp: Conceptualization, Methodology, Writing – original draft, Writing – review & editing, Software, Visualization, Formal analysis. **Han L.J. van der Maas:** Conceptualization, Methodology, Writing – original draft, Writing – review & editing. **Roseann E. Peterson:** Conceptualization, Methodology, Writing – original draft, Writing – review & editing. **Hanna M. van Loo:** Conceptualization, Methodology, Writing – original draft, Writing – review & editing. **Steven H. Aggen:** Conceptualization, Methodology, Writing – original draft, Writing – review & editing, Resources, Data curation. **Kenneth S. Kendler:** Conceptualization, Methodology, Writing – original draft, Writing – review & editing, Resources, Data curation.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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