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TITLE: Polysubstance use, mental health, and high-risk behaviours: Results from the 2012 Global Drug Survey

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ABSTRACT

Background: Polysubstance use is associated with adverse health and social outcomes, but few studies have investigated whether these associations differ between individuals engaged in different patterns of illicit drug and non-prescription medication use.

Methods: Latent Class Analysis (LCA) was used to identify patterns of drug use in the Global Drug Survey, a purposive sample collected in late 2012 and surveyed using an online questionnaire including past-year drug use, sociodemographics, mental illness, involvement in violence and sexual behaviour. The sample analyzed (N=14,869; median age 27 years; 68.5% male) included those residing in the UK (N=5,869), Australia (N=6,313), and the USA (N=2,687).

Results: LCA of cannabis, ecstasy, cocaine, stimulants, nitrous, ketamine, benzodiazepines, and opioid pain-killer use identified six classes: no polysubstance use (Class 1, 49.1%); cannabis and ecstasy (Class 2, 23.6%); all illicit drugs (Class 3, 9.4%); ecstasy and cocaine (Class 4, 8.3%); cannabis and medication (Class 5, 5.9%); all drugs (Class 6, 3.8%). Participants diagnosed with anxiety were most likely to belong to Class 5 (OR 2.66, 95% CI 2.10-3.38). Violent behaviour was most strongly associated with Class 6 membership (OR 1.9, 95% CI 1.36-2.64). Sexual risk-taking also predicted membership of this class (OR 5.79, 95% CI 4.66-7.18), and Class 4 (OR 4.41, 95% CI 3.57-5.43).

Conclusions: Five heterogeneous groups of polysubstance users were identified in this international sample covering the UK, Australia, and USA. Anxiety disorders were associated with medication and cannabis use, while high-risk behaviours predicted use of cocaine and ecstasy, or wide-ranging polysubstance use including ketamine and medications.

1 - INTRODUCTION

Polysubstance use, the use of multiple substances within a given time frame, is associated with increased risk of acute toxicity including overdose, adverse psychological experiences and engaging in high-risk behaviours such as violence and unprotected sex [1-3]. Although polysubstance use patterns are diverse [4-6], only a few studies have explored whether risk behaviours and health outcomes are the same across differing polysubstance use patterns. These studies have used latent class analysis (LCA), a technique for identifying subgroups, to characterize drug use patterns and their association with other participant attributes. LCA studies of general population samples have demonstrated that polysubstance use is associated with higher levels of drug dependence [6], mental illness [5-7], and suicidal thoughts and attempts [6, 8]. Polysubstance users also have a higher likelihood of poor physical health [7, 9, 10], sexually transmitted infections [5], being incarcerated [5], and having experienced childhood sexual, physical, or emotional abuse [6, 11].

However, few LCA studies have explored patterns of illicit polysubstance use in detail. In many studies, individuals using drugs other than alcohol, tobacco, or cannabis were combined in one group [7, 10, 12, 13], or sometimes two, with the latter group simply characterised as using a greater number of drugs [8, 11, 14]. This limited capacity to distinguish different types of polysubstance use is due to multiple factors, but the prevalence of illicit drug use is a key driver. Small samples or representative general population samples, particularly with mostly adolescent participants, will contain relatively few individuals who have used multiple illicit drugs. Including alcohol and tobacco use in the LCA polysubstance model, especially in these types of samples, produces a model which is dominated by use of these drugs due to their comparatively high prevalence, making it difficult to identify variation in illicit drug use.

LCA excluding alcohol and tobacco use and using large adult samples (>5000 participants) have identified distinct groups of polysubstance users characterised by different patterns of illicit drug use. Lynskey *et al.* [6] identified four different patterns of lifetime illicit polysubstance use in a LCA of an Australian adult twin sample. Two groups, characterised by sedative and opioid use and by high use of all substances, had approximately two-fold greater odds of major depressive disorder (MDD), suicidal ideation, and suicide attempts compared to other polysubstance groups. These two patterns of use have also been associated with MDD and generalized anxiety disorder (GAD) in large-scale studies of adults from the USA where substance use was defined using measures of abuse/dependence [15], and past-year use in those meeting criteria for alcohol dependence [5]. Additionally, these studies found an association between use of a wide range of illicit drugs and conduct disorder [6] or "deviant behaviour" (attacking others, selling illegal drugs, or stealing) [5]. These studies have demonstrated that patterns of illicit drug use are more complex than a simple increase in the number of drugs used, as are the associations between polysubstance use and mental health. However, these studies were based on data collected primarily in adults and prior to 2008; it is unclear whether the same patterns of use would be observed in more recent samples, particularly participants who use drugs that have only recently seen an increase in use, such as ketamine.

We build on this research using data from the 2012 Global Drug Survey (GDS; www.globaldrugsurvey.com) to conduct a LCA of past year illicit and prescription drug use in a large sample of teenagers and adults. This survey provides a novel perspective on polysubstance use as it has collected very large samples with higher rates of substance use than the general population, facilitating the investigation of polysubstance use involving drugs for which the population prevalence of use is relatively low. GDS conducts annual anonymous online surveys of drug and alcohol use using research tools based on work

77 conducted by the group over the last decade [16-24]. Using these data, we first characterised
78 patterns of self-reported drug use as the subgroups in the GDS sample to see if they differed
79 from previous large-scale LCA studies. We then explored associations between patterns of
80 drug use and socio-demographic characteristics, mental health problems, and high-risk
81 behaviours, particularly whether the direction or strength of these associations varied
82 between polysubstance groups.

83 ## 2 - METHODS

84 ### 2.1 - Sample

85 GDS is an anonymous, annual online survey of drug use promoted in partnership with
86 the dance music magazine Mixmag, the Guardian and Fairfax Media, and also distributed
87 through Facebook, Twitter, social news website Reddit, and drug discussion forums. The
88 sample is non-random and should not be seen as representative of drug users. Between 15th
89 November 2012 and 2nd January 2013 22,289 responses were received from participants
90 resident in 125 countries [25]. Due to the sensitive nature of the survey IP addresses were not
91 collected, consequently multiple entries from one IP address could not be eliminated.
92 However, it is unlikely that participants completed the survey multiple times due to the
93 substantial time commitment required and absence of material incentives. No identical sets
94 of responses were identified. In order to use a relatively homogeneous sample the analyses
95 reported here were limited to residents of the United Kingdom (UK), Australia, and the
96 United States of America (USA) who provided their sex and age. These countries were
97 chosen because residents of these countries made up the majority (72.5%; for most countries
98 less than 100 individuals participated), and the level of use for the illicit drugs we considered
99 is similar across countries [26]. Further discussion of the design, utility, validity, and
100 limitations of the GDS is available [11, 16-24]. Ethical approval was received from the Joint
101 South London and Maudsley and Institute of Psychiatry NHS Research Ethics Committee.

2.2 - Measures

2.2.1 - Past 12 month drug use

LCA was used to identify of distinct patterns of self-reported illicit drug and non-prescribed medication use in the previous 12 months. Respondents were asked whether they had used each of an extensive list of drugs in the past 12 months; drug categories for which at least 10% of participants endorsed use were included. Eight drugs were selected on this basis:

- Cannabis (grass, skunk, resin, and oil)
- Ecstasy (MDMA pills and powder)
- Cocaine
- Stimulants (dexamphetamine, methylamphetamine, and mephedrone)
- Nitrous oxide
- Ketamine (also including methoxetamine and N-ethylketamine)
- Benzodiazepines (non-prescription use only)
- Opioid Painkillers (non-prescription use only)

2.2.2 - Predictors of class membership

To test whether classes identified by LCA differed on other characteristics, we investigated whether class membership was associated with socio-demographic characteristics, tobacco and alcohol use, mental health diagnoses, and risk behaviours.

Socio-demographic characteristics: Gender and country of residence were used as reported. Age was collected as a continuous variable and then categorized. Sexual orientation, living

situation, and highest educational qualification were derived directly from individual questions, with some categories collapsed due to small numbers (e.g. homosexual and bisexual orientation categories were combined). Occupational status was derived from three questions on whether participants were working, studying, or unemployed, combined to categorize participants as studying only, studying and working, working only, or unemployed.

Substance use: Tobacco and alcohol use were defined as any use in the preceding 12 months. Hazardous alcohol use was assessed using the 10-item AUDIT questionnaire [27, 28]. Participants were asked whether they wanted to use less of any of illicit or non-prescribed drugs they reported using. Responses relating to drugs included in the LCA were combined to create an overall indicator of participant desire to use less of any drug.

Mental health: Participants were asked "Have you ever been diagnosed with a mental illness?" with responses combined in a single variable indicating depression, anxiety, or both (although other diagnoses could be recorded, few participants reported diagnoses other than anxiety and depression). Personality disorder was screened for using the Standardised Assessment of Personality – Abbreviated Scale (SAPAS), with a threshold of three used to indicate probable personality disorder [29, 30].

High risk behaviour: Involvement in violent incidents was indexed by self-reported participation in a fight with another adult in the last 12 months. Participants were then asked whether they had taken drugs (other than alcohol) prior to involvement in the incident. These questions were combined to create a variable indicating whether participants had been involved in a violent incident, and if so whether they had taken drugs when it occurred. Sexual risk-taking was defined as having two or more sexual partners in the past year and not using condoms on all occasions of penetrative sex (as defined in [31]). Participants were

asked to report emergency treatment due to any substances they endorsed use of; due to the low number of positive responses per drug, these were combined into a single variable indicating emergency treatment due to any illicit drug use.

2.3 - Statistical analyses

LCA identifies subgroups, or latent classes, within a sample using participant characteristics defined as categorical variables. The aim is not to represent all possible combinations of characteristics but to identify the main patterns present, assuming some measurement error [32, 33]. For this study, this translates to identifying patterns of illicit drug and medication use based on reported past-year use of these substances.

To find the likely number of subgroups, models postulating increasing numbers of latent classes were sequentially fitted, with identification of each model evaluated by refitting it using 100 sets of random starting values. Models were considered identified if at least 80% of sets converged to the same solution [32, 33]. The best-fitting model was selected by examining the Akaike Information Criterion (AIC) and Bayesian Information Criterion (BIC) for each model [34], and considering the size, distinctness, and ease of interpretation of the classes identified [33]. This was informed by the class membership probabilities, the estimated proportion of the sample belonging to each class, and the item-response probabilities for each class, which represent the likely values for the set of characteristics (i.e. probability of endorsing use of each substance), given membership of a particular class.

Multinomial logistic regression models estimated via the "one-step" approach were used to explore associations between individual covariates and subgroup membership [35, 36]. Coefficient estimates for each class were combined with the known distribution of each covariate to estimate the probability of each covariate value conditional on latent class membership. Models including adjustments for sex, age, and country of residence were then

fitted for each socio-demographic, mental health, and risk behaviour variable to examine the adjusted associations with class membership.

As this was an exploratory study without prior hypotheses regarding particular population subgroups, we did not fit grouped LCA models using, for example, sex or country of residence. All tests were two-tailed but given the number of models fitted $\alpha=0.05$ was not appropriate. A Bonferroni corrected threshold would be $P\leq0.004$, although we interpreted P-values as measures of the strength of evidence for an association [37], rather than simply applying a threshold for statistical significance. Analyses were conducted in R (version 3.0.2 for Windows) using the LCCA package (version 1.1.0) [36].

3 - RESULTS

3.1 - Sample characteristics

From the complete sample of 22,289 participants, we excluded 6,122 not resident in the three chosen countries. A further 1,298 were excluded due to missing age and/or sex (524 missing both, 723 missing sex, 51 missing age), leaving 14,869 individuals. Most participants were male (68.5%) and aged between 15 and 35 years (71.2%; Table 1). The proportions of participants endorsing past year use of the selected drugs were: cannabis (64.0%), ecstasy (37.6%), cocaine (24.8%), stimulants (10.6%), nitrous (11.7%), ketamine (14.3%), benzodiazepines (10.5%), and opioid pain-killers (11.3%).

3.2 - Latent class analysis of illicit drug use in previous 12 months

3.2.1 - Model selection

Eight latent class models (one to eight classes) were fitted but fit statistics did not unequivocally identify a best-fitting model (**Supplementary** Table 1). This discordance is not uncommon as the AIC and BIC have different strengths, but the BIC generally selects

more parsimonious models and performs better for model selection in LCA of large samples [34]. The AIC was lowest for the eight-class model, but this model was not identified (**Supplementary Figure 1**). In contrast, the BIC was lowest for the six-class model, which was identified as 98% of models had the same log-likelihood. Examination of the item-response probabilities confirmed that the subgroups identified in the six-class model had distinct characteristics (**Figure 1** and **Supplementary Table 2**), and that no class was too small (smallest class contained 4% of the sample, approximately 621 participants). These results indicated that the six-class model was most appropriate for these data.

3.2.2 - Latent class model interpretation

The item-response probabilities (**Figure 1**) suggest the classes defined by the six-class model can be characterised as follows:

1. Non-polysubstance (49.1% of the sample): No polysubstance use - moderate probability of cannabis use only;
2. Cannabis and ecstasy (23.6%): High probabilities of cannabis and ecstasy use, moderate probability of cocaine use;
3. Illicit only (9.4%): High probabilities of using most illicit drugs, but particularly cannabis, ecstasy, and ketamine;
4. Ecstasy and cocaine (8.3%): High probabilities of ecstasy and cocaine use, moderate probability of cannabis use;
5. Cannabis and medication (5.9%): High/moderate probabilities of cannabis, benzodiazepine, and opioid pain-killer use;
6. All substances (3.8%): High/moderate probabilities of using all drugs.

There were two sets of drugs that appeared to be primarily used by the same subgroups of participants. The two groups with moderate/high probabilities of endorsing ketamine use (illicit only and all substances) also had similar probabilities of endorsing nitrous oxide use (**Supplementary Table 2**). Similarly, the two groups with moderate/high probabilities of endorsing benzodiazepine use (cannabis and medication, and all substances) also had moderate/high probabilities of endorsing opioid pain-killer use. In contrast, the use of cannabis, ecstasy, cocaine, or stimulants did not display an association with use of another drug that was consistent across subgroups.

3.3 - Latent class characteristics

Compared to the polysubstance classes, participants in the non-polysubstance class were more likely to be female, and less likely to use tobacco, desire to use drugs less, have received a diagnosis of anxiety/depression, or be involved in violence or sexual risk-taking (see **Table 2**). They were also less likely to be in the 15-25 years age group compared to the polysubstance classes, with the exception of the ecstasy and cocaine class; only 7.4% of participants in this class were age 25 or younger. There were no substantial differences in past year alcohol use or hazardous alcohol use.

Participants in the cannabis and prescription medications class were more likely to report anxiety and/or depression diagnoses than members of any other class (29% compared to estimates between 11.1% and 19%), but less likely to report risky sexual behaviour (15.4% compared to estimates of 23.7% to 39.7%). Participants most likely to report risky sexual behaviour were those in the two classes defined by moderate/high probability of use of all illicit drugs (only or with prescription medications; 39.7% and 37.4% respectively). Members of these classes were also the most likely to report involvement in violent incidents, regardless of illicit drug use.

3.4 – Associations with latent class membership

Results from multinomial logistic regression models including adjustments for sex, age, and country of residence supported the majority of the associations with latent class membership suggested by the class characteristics (see **Table 3**). Sexual orientation was only associated with membership of the ecstasy and cocaine, and cannabis and medication classes; identifying as non-heterosexual increased the odds of belonging to these classes around two-fold. Having a higher degree was associated with increased odds of belonging to all polysubstance classes except those defined by use of a broad range of illicit drugs (illicit only and all drugs). Living alone increased the odds of membership of the illicit only, ecstasy and cocaine, and all drugs classes. Past year and hazardous alcohol use were not associated with class membership, but past year tobacco use was, with the strongest association identified with the all substances class (OR 28.14, 95% CI 21.43-36.94). This class also had the strongest association with reporting a desire to use drugs less (OR 70.11, 95% CI 37.7-130.4).

The adjusted multinomial logistic regression results for mental health diagnoses showed a positive association with membership of the cannabis and medication class but only for anxiety (OR 2.66, 95% CI 2.10-3.38), with similar results for personality disorder. The results for involvement in violence differed after adjustment; a strong association was still identified with the all substances class, but violence without or with drugs was also associated with the cannabis and medications class (OR 1.82, 95% CI 1.24-2.65 and OR 33.41, 95% CI 4.34-257.04 respectively). Involvement in a violent incident with drugs was also associated with membership of the ecstasy and cocaine class. Sexual risk-taking was positively associated with membership of all polysubstance classes, but particularly those defined by ecstasy and cocaine use (OR 4.41, 95% CI 3.57-5.43), and use of all drugs (OR 5.79, 95% CI 4.66-7.18).

4 - DISCUSSION

We characterised patterns of drug use in a large international sample with high levels of use, identifying five polysubstance use classes that collectively contained just over 50% of the sample and had distinct patterns of use that were more nuanced than a simple increase in the number of drugs used. These polysubstance classes were primarily distinguished by differences in use of nitrous, ketamine, benzodiazepine, and opioid pain-killers, substances that have received limited attention in LCA of general population samples. Strong associations with mental health and high-risk behaviours were identified for three of the five polysubstance classes: ecstasy and cocaine use, cannabis and medication use, and use of all drugs.

The polysubstance subgroups identified in this sample, and their associations with mental health and risk behaviours, replicate some findings from previous studies using large, general population samples. The subgroup characterised by cannabis and prescription medication use, and the association between this subgroup and mental illness that we identified, has also been found in studies from Australia and the USA [5, 6, 15]. An association between use of many illicit drugs and antisocial behaviour was also identified in these samples, although antisocial behaviour was characterised as conduct disorder and/or incarceration [5, 6]. The association between sexual risk-taking and polysubstance use has been identified in many settings [38]. Within the LCA literature, Connell *et al*. [39] identified a strong positive association between risky sexual behaviour by US adolescents and intensity of polysubstance use (alcohol, tobacco, cannabis, cocaine and inhalant use), while in adults a history of sexually transmitted infections predicted polysubstance use involving cannabis and cocaine [5].

We identified two sets of drugs which participants of certain subgroups endorsed use of to a similar level - benzodiazepines and opioid pain-killers, and nitrous oxide and ketamine – raising interesting questions about how and why individuals use these drugs. Simultaneous use of benzodiazepines and opioid pain-killers to enhance drug effects for recreational purposes is well documented [40], but it is unclear whether this is also true for nitrous oxide and ketamine. Both drugs are *N*-methyl-D-aspartate (NMDA)-antagonists and have medical uses as analgesics employed during anaesthesia [41, 42], so users could be substituting one for the other, or seeking to increase the overall effect by combining them. As the potential for adverse events, such as drug overdose or respiratory depression, is increased by simultaneous use, particularly involving drugs from the same class [41, 42], further investigation of these drug combinations is needed.

4.1 - Limitations

The major limitations of this study relate to the GDS sampling strategy and the time-frame of substance use. The non-representative sampling method used precludes estimating the extent to which these results are representative of the populations of the countries included. However, this strategy permitted recruitment of a large sample with high levels of substance use, facilitating a LCA that identified patterns of use that might have been overlooked in a representative general population sample. As GDS is cross-sectional, we cannot make causal inferences about relationships between mental health, risk behaviours, and polysubstance use. Additionally, we used data on 12-month drug use, which is not necessarily the same as simultaneous use during a small time window (e.g. 24-48 hours), although Quek *et al.* [9] found that most individuals reporting use of multiple drugs within a 12-month period also reported simultaneous use of those drugs.

5 - CONCLUSIONS

There are multiple, distinct patterns of polysubstance use involving illicit drugs and non-prescription use of medications that are more complex than a simple increase in the number of drugs used. People engaged in these different patterns of use differ in terms of both sociodemographic characteristics, and mental health and risk-taking behaviours. The clinical assessment and harm reduction implications of this work are potentially significant. Most health promotion and harm reduction activities focus on the acute intoxication-related consequences of using single drugs, but our work confirms the need to holistically address polysubstance use and drug use related activities. Longitudinal research using representative samples is needed to unravel the temporal nature of these associations, and to determine whether longer-term trajectories of drug use and health differ between latent classes. Further characterisation of simultaneous use of multiple drugs is also warranted, particularly relating to frequency of use, motivations for use, and possibilities for harm reduction.

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TABLES

Table 1: Demographic characteristics, mental health, and risk behaviours for the sample of 14,869 participants. Note that the "Missing" category is only shown for variables with missing data.

Variable	Values	Number	Percentage
Sex	Female	4685	31.5
Age	15 - 25 years	6521	43.9
	>25 - 35 years	4052	27.3
	>35 - 45 years	2143	14.4
	>45 years	2153	14.5
Country of residence	UK	5869	39.5
	Australia	6313	42.5
	USA	2687	18.1
Sexual orientation	Heterosexual	12006	80.7
	Bi/Homosexual	2508	16.9
	Missing	355	2.4
Qualifications	Higher degree	3038	20.4
	Degree	4905	33.0
	Trade/Diploma	1577	10.6
	Senior high school	3471	23.3
	Junior high school or less	1651	11.1
	Missing	227	1.5
Occupational status	Working only	6784	45.6
	Studying and working	3280	22.1
	Studying only	2880	19.4
	Unemployed	1356	9.1
	Missing	569	3.8
Living status	Partner	5353	36.0
	Shared housing	3841	25.8
	Family members	3345	22.5
	Alone	2024	13.6
	Missing	306	2.1
Tobacco use (last 12 months)	Yes	7613	51.2
Alcohol use (last 12 months)	Yes	13809	92.9
AUDIT score	Hazardous	1975	13.3
Desire to use drugs less	Yes	2601	17.5
Treatment for anxiety and/or depression	No	11386	76.6
	Anxiety	284	1.9
	Depression	1283	8.6
	Both	1443	9.7
	Missing	473	3.2
Personality disorder (SAPAS)	No	6423	43.2
	Yes	7915	53.2
	Missing	531	3.6

Variable	Values	Number	Percentage
Involvement in violent incident	No	13776	92.6
	Yes, no drugs	836	5.6
	Yes, with drugs	174	1.2
	Missing	83	0.6
Sexual risk-taking	No	10767	72.4
	Yes	2609	17.5
	Missing	1493	10.0
Emergency treatment	Yes	73	0.5

Table 2: Characteristics of Global Drug Survey 2012 participants by polysubstance use class.

Variable	Category	Non-polysubstance	Cannabis and ecstasy	Illicit only	Ecstasy and cocaine	Cannabis and medication	All drugs
Sex	Female	46.4	16.8	18.3	32.5	28.4	27.9
Age	15 - 25 years	30.9	74.4	62.6	7.4	54.2	49.3
	>25 - 35 years	33.5	12.4	18.2	45.0	22.3	24.6
	>35 - 45 years	17.7	6.6	9.6	23.8	11.8	13.0
	>45 years	17.8	6.6	9.7	23.9	11.8	13.1
Country of residence	Australia	38.6	42.3	69.5	48.6	23.3	43.6
	USA	19.3	18.1	9.6	16.1	24.1	17.7
	UK	42.1	39.6	20.9	35.2	52.6	38.7
Sexual orientation	Heterosexual	83.9	86.9	87.9	71.0	75.1	72.9
Qualifications	Higher Degree	15.1	25.4	19.6	14.1	24.0	20.5
	Degree	51.6	18.5	37.3	54.9	23.1	34.2
	Trade/Diploma	7.8	13.2	10.2	7.3	12.4	10.7
	Senior high school	17.3	29.0	22.3	16.1	27.4	23.4
	Junior high school or less	8.2	13.8	10.6	7.6	13.0	11.2
Occupational status	Working only	51.7	37.4	51.5	76.0	36.1	48.3
	Studying and working	21.1	27.3	21.2	10.5	27.9	22.6
	Studying only	18.5	24.0	18.6	9.2	24.5	19.8
	Unemployed	8.7	11.3	8.8	4.3	11.5	9.3
Living status	Partner	38.7	31.5	37.4	44.1	29.7	40.8
	Shared housing	25.6	28.6	26.1	23.3	29.3	24.7
	Family members	22.3	24.9	22.7	20.3	25.5	21.5
	Alone	13.5	15.1	13.8	12.3	15.4	13.0
Tobacco use	Yes	18.5	69.7	86.3	45.3	75.0	84.5
Alcohol use	Yes	93.3	92.7	92.5	91.0	93.6	92.6
AUDIT score	Hazardous	13.5	13.2	14.6	10.8	15.6	9.1
Desire to use drugs less	Yes	2.0	24.5	37.0	28.3	21.2	52.6
Diagnosed with anxiety and/or depression	No	79.4	88.9	87.3	84.8	61.0	79.1
	Anxiety	1.9	1.0	1.2	1.4	3.7	2.0
	Depression	8.8	4.7	5.4	6.5	16.6	8.9
	Both	9.9	5.3	6.1	7.3	18.7	10.0
Personality disorder	Yes	56.3	53.5	50.9	42.9	67.1	63.8
Violent incident	No	96.0	90.5	87.9	93.6	90.6	89.0
	Yes, no drugs	3.3	7.9	10.0	5.3	7.8	9.1
	Yes, with drugs	0.7	1.6	2.1	1.1	1.6	1.9
Sexual risk-taking	Yes	8.9	23.7	39.7	32.8	15.4	37.4
Emergency treatment	Yes	0.5	0.4	0.5	0.8	0.4	0.2

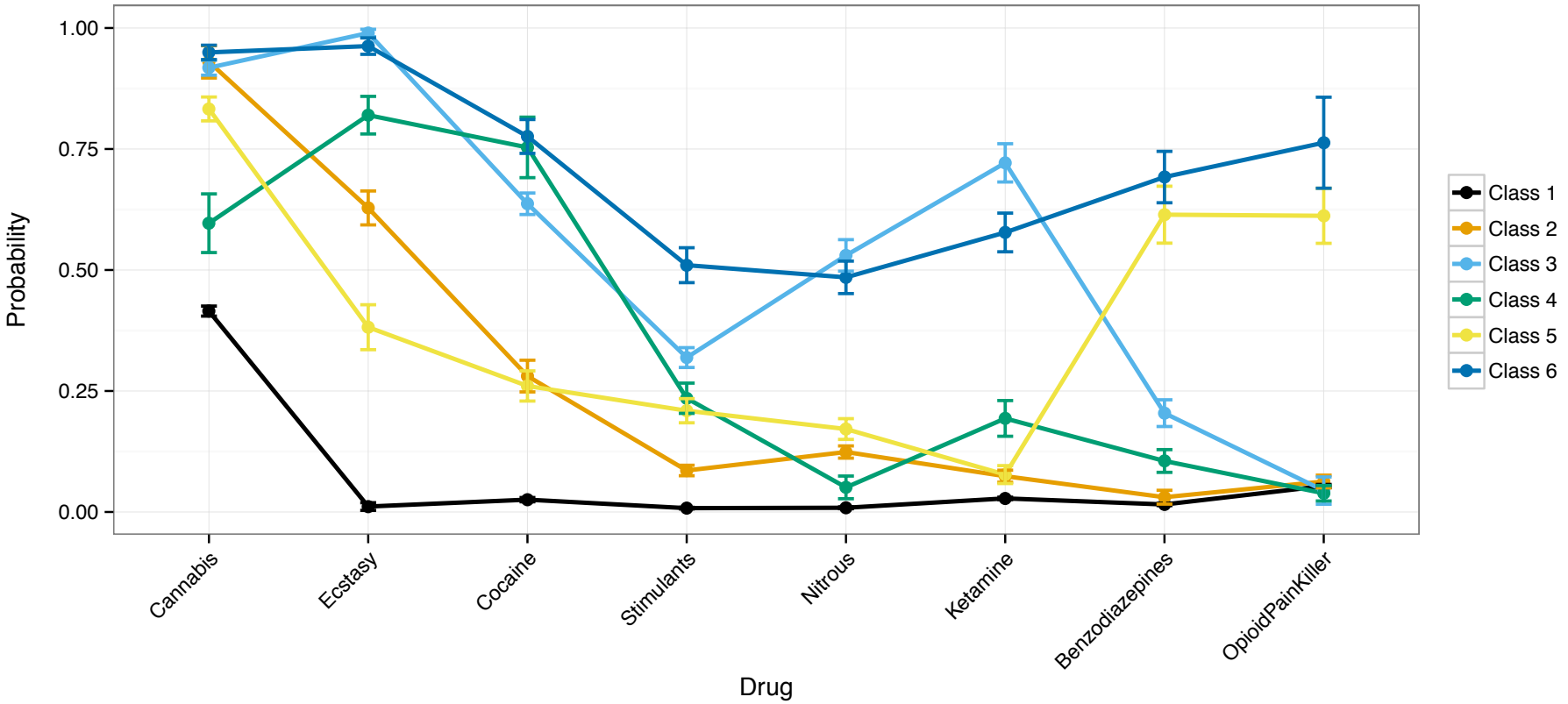
Table 3: Associations between latent class membership and participant characteristics, adjusted for sex, age, and country of residence. N indicates the number of participants included in the analysis (due to missing data for covariate). All results indicate a comparison with latent class 1 (Non-polysubstance).

Variable	Category	Cannabis and ecstasy			Illicit only			Ecstasy and cocaine			Cannabis and medication			All drugs			N
		OR	CI	P	OR	CI	P	OR	CI	P	OR	CI	P	OR	CI	P	
ɨexual rientation	Heterosexual	1			1			1			1			1			1451
	Bi/Homosexual	1.05	(0.87 - 1.26)	0.64	0.81	(0.65 - 1.01)	0.06	1.74	(1.45 - 2.09)	<0.0001	2.08	(1.65 - 2.62)	<0.0001	0.92	(0.71 - 1.2)	0.54	
)ualifications	Higher Degree	2.31	(1.94 - 2.75)	<0.0001	1.09	(0.88 - 1.33)	0.43	1.58	(1.28 - 1.94)	<0.0001	2.29	(1.81 - 2.89)	<0.0001	1.01	(0.77 - 1.32)	0.96	1464
	Degree	1			1			1			1			1			
	Trade/Diploma	0.93	(0.79 - 1.09)	0.38	0.84	(0.67 - 1.05)	0.13	1.13	(0.93 - 1.37)	0.21	1.14	(0.88 - 1.46)	0.31	0.73	(0.56 - 0.95)	0.02	
	Senior high school	0.65	(0.56 - 0.77)	<0.0001	0.55	(0.46 - 0.67)	<0.0001	0.74	(0.61 - 0.89)	0.002	0.6	(0.47 - 0.77)	0.0001	0.43	(0.35 - 0.54)	<0.0001	
	Junior high school or less	1.27	(1.07 - 1.51)	0.005	0.91	(0.71 - 1.17)	0.46	1.26	(1.04 - 1.54)	0.02	1.28	(0.96 - 1.7)	0.09	1.18	(0.92 - 1.5)	0.20	
)ccupational tatus	Working only	1			1			1			1			1			1430
	Studying and working	1.38	(1.12 - 1.69)	0.0021	0.91	(0.7 - 1.18)	0.47	0.54	(0.44 - 0.66)	<0.0001	2.11	(1.63 - 2.74)	<0.0001	1.07	(0.81 - 1.42)	0.64	
	Studying only	0.9	(0.74 - 1.09)	0.28	1.06	(0.84 - 1.34)	0.63	1.9	(1.44 - 2.51)	<0.0001	1.19	(0.93 - 1.52)	0.16	1.58	(1.18 - 2.12)	0.002	
	Unemployed	1.16	(1 - 1.36)	0.05	1.02	(0.86 - 1.21)	0.83	1.97	(1.44 - 2.72)	<0.0001	1.4	(1.14 - 1.7)	0.001	1.47	(1.13 - 1.9)	0.004	
.iving status	Partner	1			1			1			1			1			1456
	Shared housing	1.27	(1.1 - 1.46)	0.001	1	(0.8 - 1.25)	0.98	0.96	(0.82 - 1.12)	0.58	1.3	(1.03 - 1.64)	0.03	0.98	(0.75 - 1.28)	0.86	
	Family members	0.72	(0.61 - 0.86)	0.0002	0.59	(0.48 - 0.72)	<0.0001	0.71	(0.58 - 0.87)	0.001	0.73	(0.57 - 0.94)	0.01	0.33	(0.26 - 0.43)	<0.0001	
	Alone	1.05	(0.91 - 1.21)	0.50	1.73	(1.49 - 2)	<0.0001	2.2	(1.74 - 2.79)	<0.0001	1.04	(0.85 - 1.26)	0.71	1.98	(1.66 - 2.35)	<0.0001	
`obacco use	No	1			1			1			1			1			1486
	Yes	6.23	(5.12 - 7.58)	<0.0001	11.49	(9.15 - 14.42)	<0.0001	5.73	(4.8 - 6.85)	<0.0001	18.02	(13.72 - 23.66)	<0.0001	28.14	(21.43 - 36.94)	<0.0001	
.lcohol use	No	1			1			1			1			1			1486
	Yes	1.05	(0.79 - 1.38)	0.75	0.75	(0.57 - 1)	0.05	0.83	(0.64 - 1.08)	0.17	0.95	(0.64 - 1.4)	0.79	0.93	(0.66 - 1.3)	0.68	
.UDIT score	Non-hazardous	1			1			1			1			1			1486
	Hazardous	1.03	(0.83 - 1.29)	0.77	1.12	(0.89 - 1.41)	0.35	0.81	(0.65 - 1)	0.06	1.18	(0.88 - 1.57)	0.27	0.66	(0.42 - 1.02)	0.06	

Variable	Category	Cannabis and ecstasy			Illicit only			Ecstasy and cocaine			Cannabis and medication			All drugs			N
		OR	CI	P	OR	CI	P	OR	CI	P	OR	CI	P	OR	CI	P	
Desire to use drugs less	No	1			1			1			1			1			1486
	Yes	13.0	(7.0 - 24.21)	<0.0001	26.37	(14.0 - 49.63)	<0.0001	29.34	(16.2 - 53.13)	<0.0001	26.77	(14.13 - 50.72)	<0.0001	70.11	(37.7 - 130.4)	<0.0001	
Diagnosed with anxiety and/or depression	No	1			1			1			1			1			1439
	Anxiety	0.72	(0.56 - 0.92)	0.01	0.57	(0.41 - 0.8)	0.001	0.71	(0.55 - 0.9)	0.0055	2.66	(2.1 - 3.38)	<0.0001	0.97	(0.72 - 1.31)	0.85	
	Depression	1.09	(0.78 - 1.53)	0.62	1.19	(0.72 - 1.96)	0.50	1.24	(0.86 - 1.79)	0.26	0.92	(0.64 - 1.32)	0.63	0.65	(0.44 - 0.94)	0.02	
	Both	0.81	(0.53 - 1.22)	0.31	0.5	(0.27 - 0.94)	0.03	0.55	(0.34 - 0.87)	0.01	0.95	(0.6 - 1.5)	0.81	1.12	(0.71 - 1.78)	0.62	
Personality disorder	No	1			1			1			1			1			1433
	Yes	1.01	(0.87 - 1.17)	0.90	0.74	(0.63 - 0.87)	0.0002	0.74	(0.64 - 0.85)	<0.0001	1.37	(1.12 - 1.69)	0.0026	0.84	(0.7 - 1)	0.05	
Violent incident	No	1			1			1			1			1			1478
	Yes, no drugs	1.05	(0.75 - 1.47)	0.77	1.6	(1.16 - 2.19)	0.0037	1.44	(0.97 - 2.12)	0.07	1.82	(1.24 - 2.65)	0.002	1.9	(1.36 - 2.64)	0.0001	
	Yes, with drugs	6.57	(0.68 - 63.2)	0.10	2.75	(0.22 - 34.05)	0.43	26.33	(3.89 - 178.1)	0.0008	33.41	(4.3 - 257.0)	0.0007	22.07	(2.8 - 172.8)	0.0032	
Sexual risk-taking	No	1			1			1			1			1			1337
	Yes	1.48	(1.19 - 1.83)	0.0004	3.21	(2.55 - 4.03)	<0.0001	4.41	(3.57 - 5.43)	<0.0001	2.23	(1.7 - 2.93)	<0.0001	5.79	(4.66 - 7.18)	<0.0001	
Emergency treatment	No	1			1			1			1			1			1486
	Yes	1.15	(0.45 - 2.93)	0.77	0.71	(0.19 - 2.75)	0.62	1.36	(0.59 - 3.15)	0.47	0.29	(0.04 - 2.31)	0.24	1.41	(0.48 - 4.18)	0.53	

FIGURES

Figure 1: Item response probabilities (for positive endorsement of use in the last 12 months) with standard errors by latent class for the six-class model. The classes are labelled as follows: Class 1 indicates non-polysubstance; Class 2 cannabis and ecstasy; Class 3 illicit drugs only; Class 4 ecstasy and cocaine; Class 5 cannabis and medication; Class 6 indicates all drugs. Classes are shown in decreasing order of class membership probability, as per **Supplementary** Table 2.

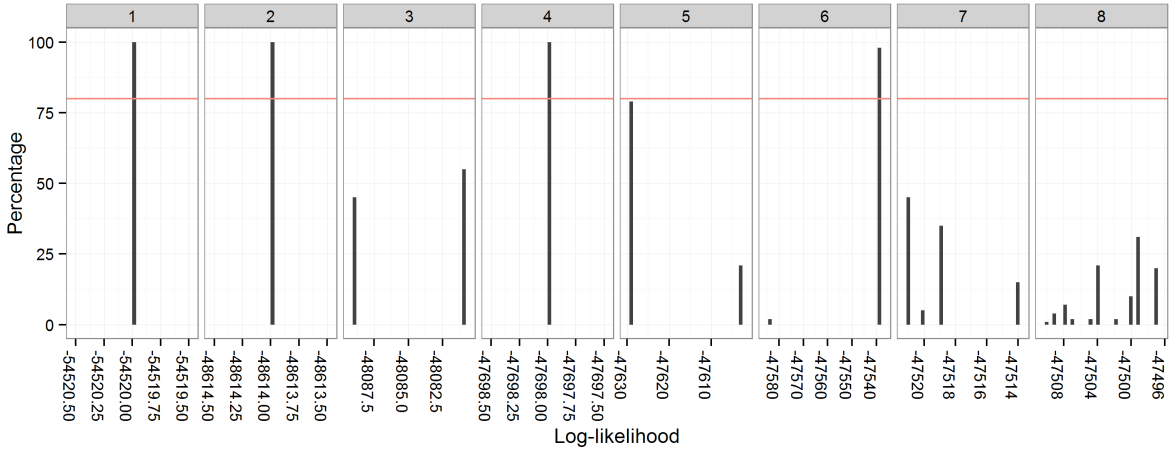


SUPPLEMENTARY TABLES AND FIGURES

Supplementary Table 1: Model fitting statistics for the ten models postulating different numbers of latent classes. BIC indicates Bayesian information criterion; AIC indicates Akaike information criterion. Best-fitting models according to each indicator are shown in bold.

Classes	Log-likelihood	BIC	AIC
1	-54519.6	109116.0	109055.1
2	-48614.3	97391.8	97262.5
3	-48080.9	96411.6	96213.9
4	-47697.8	95731.9	95465.6
5	-47629.3	95681.2	95346.5
6	-47538.8	**95586.8**	95183.7
7	-47514.4	95624.5	95152.9
8	-47499.4	95680.9	**95140.8**

Supplementary Figure 1: Results of model identification evaluation. Each panel displays the results for a model with the specified number of classes. Log-likelihood values are graphed for 100 models fitted from different starting values for each latent class model. The red horizontal line indicates the threshold of 80%.



Supplementary Table 2: Estimates and standard errors for class membership probabilities and item response probabilities (probability of endorsing substance use) from six-class latent class model for illicit and prescription drug use in the previous 12 months.

Probability	**Drug**	**Non-polysubstance**		**Cannabis and ecstasy**		**Illicit only**		**Ecstasy and cocaine**		**Cannabis and medication**		**All drugs**	
		Estimate	S.E.	Estimate	S.E.	Estimate	S.E.	Estimate	S.E.	Estimate	S.E.	Estimate	S.E.
Class membership		0.49	0.01	0.24	0.02	0.10	0.01	0.08	0.02	0.06	0.01	0.04	0.01
Item response	Cannabis	0.42	0.01	0.93	0.03	0.92	0.02	0.60	0.06	0.83	0.02	0.95	0.01
	Ecstasy	0.01	0.01	0.63	0.04	0.99	0.01	0.82	0.04	0.38	0.05	0.96	0.02
	Cocaine	0.03	0.00	0.28	0.03	0.64	0.02	0.75	0.06	0.26	0.03	0.78	0.03
	Stimulants	0.01	0.00	0.09	0.01	0.32	0.02	0.23	0.03	0.21	0.02	0.51	0.04
	Nitrous	0.01	0.00	0.12	0.01	0.53	0.03	0.05	0.02	0.17	0.02	0.48	0.03
	Ketamine	0.03	0.00	0.07	0.01	0.72	0.04	0.19	0.04	0.08	0.02	0.58	0.04
	Benzodiazepines	0.02	0.00	0.03	0.01	0.20	0.03	0.11	0.02	0.61	0.06	0.69	0.05
	Opioid Painkiller	0.05	0.00	0.06	0.01	0.04	0.03	0.04	0.02	0.61	0.06	0.76	0.09