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Typologies of illicit drug use in mid-adulthood: a quasi-longitudinal latent class analysis in a community-based sample of twins

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ABSTRACT

Aims To identify drug use typologies based on substances used and persistence of use over two time points, use a genetically informed design to explore twin concordance of and genetic influence on the use typologies and compare patterns of declined/discontinued ("desistant") and persistent drug use on drug use correlates. **Design** Latent class analysis was applied to data from a cross-sectional self-report survey on current and past drug use. Use characteristics, use disorder, and psychiatric problems were compared across classes. **Setting** Computer-assisted telephone interview in respondents' homes. **Participants** A total of 3785 individual twins and siblings (1365 men, 2420 women; M_{age} = 32) from the Australian Twin Registry Cohort III. **Measurements** A comprehensive interview assessed prior to past year and past year use of cannabis, stimulants, cocaine/crack, hallucinogens, opioids, sedatives, inhalants, dissociatives, and solvents; age of first use; opportunity to use; peer drug use; attention deficit/hyperactivity, conduct, antisocial personality, depressive, and substance use disorders; and suicidality. **Findings** A five-class solution emerged: no/low use (50%), desistant cannabis use (23%), desistant party drug use (18%), persistent prescription drug misuse (4%), and persistent polydrug use (5%). Twin concordances were higher among monozygotic (k = 0.30–0.35) than dizygotic pairs (same-sex k = 0.19–0.20; opposite sex k = 0.07), and biometric modeling suggested that the persistent polydrug use class, in particular, was highly heritable (a^2 = 0.94). Conduct disorder (OR = 2.40), antisocial personality disorder (OR = 3.27), and suicidal ideation (OR = 1.98) increased persistent polydrug use risk; depression (OR = 2.38) and lifetime suicide attempt (OR = 2.31) increased persistent prescription misuse risk. Relative to persistent prescription drug misuse, persistent polydrug use was associated with higher rates of cannabis and stimulant use disorder (OR = 6.14–28.01), younger first substance use (OR = 0.82–0.83), more drug use opportunity (OR = 10.66–66.06), and more drug-using peers (OR = 4.66–9.20). **Conclusions** Unique patterns of declined/discontinued ("desistant") and persistent drug use are differentially heritable and differentially associated with risk factors, psychiatric symptoms, and substance use disorder outcomes.

Keywords Illicit drugs, latent class analysis, persistent drug use, polydrug use, quasi-longitudinal, twin study.

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INTRODUCTION

Longitudinal research on the initiation and persistence of drug use through the third decade of life suggests that there are distinct trajectories of use over time. For example, one study of substance use persistence and decline/discontinuation ("desistance") identified four temporal typologies of substance use: consistent abstention, light alcohol use with rare illicit drug use, moderate alcohol use with experimental illicit drug use, and persistent heavy alcohol with heavy illicit drug use that continued into the 30s [1]. There is also evidence that trajectories vary across different drugs. Although it is not uncommon for cannabis and cocaine use to persist into the late 20s, there is minimal initiation of illicit drug use after age 25; when drug use is initiated at this point, it is most often with cocaine or psychoactive prescription medications [2]. However, focusing on the use of specific drugs

in isolation overlooks potentially meaningful patterns of polysubstance use; despite this, many studies combine all non-cannabis illicit drugs into a single category [1,3], include only a subset of more common drug types [4], or focus on a single drug type (e.g. illegal opioids, prescription drugs, club drugs) [5–7]. A more useful approach might be to examine multiple addictive substances in a single multivariate model that would conceptualize their use as a complete pattern of interrelated behaviors.

A germane example comes from a latent class analysis (LCA) of data from a study of Australian twins that included a comprehensive inventory of lifetime use of illicit drugs: cannabis, stimulants, cocaine/crack, hallucinogen, opioids, sedatives, inhalants, and solvents [8]. Five typologies of drug use were identified: "low use" (some cannabis use); "moderate use" (cannabis use, some stimulant and hallucinogen use); "party drug" (cannabis use, some cocaine/crack, stimulant, hallucinogen, and inhalant use); "opioid/sedative" (sedative and opioid use, some cannabis use); and "polydrug" (use of all drugs) [8]. However, these typologies were defined by use measured at only a single time point. Although valuable work on illicit drug use has been conducted using LCA [8], twin designs [9,10] and longitudinal analysis [11], research on illicit drug use that marries the strengths of these designs is, to our knowledge, nearly nonexistent.

Present study

The present study extends this previous research by using a novel twin sample to model the persistence of illicit drug use within an LCA framework [8] with the goals of (i) examining temporal characteristics of drug use patterns by including retrospective cross-sectional reports of prior to past year and past year drug use as indicators of latent classes, (ii) comparing classes on important drug use correlates, (iii) assessing heritable influences on class membership, and (iv) contrasting desistant and persistent use classes. We hypothesized that the "low use" class, as defined in the previous LCA study, would represent a consistently low-using class, the "moderate use" and "party drug" classes would represent desistant drug use trajectories (experimental use/"maturing out") [1,12], and "polydrug use" would represent a persistent trajectory. The trajectory of the opioid/sedative class is unclear but is of particular interest and importance in light of the current opioid epidemic in the United States (US) and substantial risk for post-prescription opioid misuse [13]. Although this study presents data from Australia, population-level trends in Australia have shown increases in opioid prescribing and related harms over the past two to three decades, including during the period of data collection for the present study [14]; as such, these data may help inform research and policy regarding the US opioid epidemic.

METHODS

Participants and procedure

Participants were 3298 individual twins and 487 non-twin siblings from the Australian Twin Registry (M_{age} = 32.13 [SD = 3.04], range = 21–46 [94% between age 28 and 38]; 64% female) [15]. The twin subsample included 169 monozygotic (MZ) male pairs, 396 MZ female pairs, 116 dizygotic (DZ) male pairs, 298 DZ female pairs, and 225 DZ opposite-sex pairs. Participants were surveyed via computer-assisted telephone interview in 2005–2009 (participation rate = 76%) [15]. Original data collection was approved by the Institutional Review Boards at Washington University and Berghofer QIMR; secondary analysis of these data was deemed exempt by the University of Missouri Institutional Review Board. Analyses were not pre-registered and results should be considered exploratory.

Measurements

Substance use

The assessment of substance use was facilitated by providing participants with a booklet that contained nine lists of substances, with each list corresponding to a class of drug (i.e. cannabis, stimulants [amphetamines], cocaine/crack, hallucinogens, opioids, sedatives, inhalants, dissociatives, and solvents). For each list, participants were asked if they (i) ever had the opportunity to use, and (ii) had ever used any of the substances listed. Those who endorsed having used were asked their age at first use, the recency of their last use, and to identify the specific substances(s) on the list they had used. Over-the-counter and prescription medications with abuse potential were counted if taken not as directed or without a prescription. Responses were coded positive for "past use" if first use occurred prior to the past year. Responses were coded positive for "current use" if last use occurred within the past year. Lifetime use and age of first use of alcohol and nicotine were also assessed.

Perceived peer drug use

Participants were queried regarding the proportion of their current male friends, female friends, and co-workers that have ever used illicit drugs. Responses were rated on a 1–100 percentile scale.

Substance use and mental health problems

Assessments of DSM-IV SUD and psychiatric disorders were from the Australian version of the Semi-Structured Assessment of the Genetics of Alcoholism [16]. Diagnoses of lifetime SUDs were obtained by combining abuse and dependence diagnoses. Attention deficit/hyperactivity disorder (ADHD), conduct disorder, and lifetime antisocial

personality disorder (ASPD), major depression, and suicidality (ideation, attempt) were also assessed [16–18].

Analytic plan

Analyses were conducted in Mplus Version 8 [19]. Missing data were minimal (2.4%) and handled using full information maximum likelihood estimation. First, a replication of the previous LCA model [8] was run to verify its replicability before expanding upon it. The model was successfully replicated (Supporting information Table S1). We then performed an additional check by rerunning the replication model with thresholds of 3 and 10 lifetime uses to confirm that the single-use threshold was not producing spurious results. The same class solution was produced.

The quasi-longitudinal model was built using past and current use of cannabis, stimulants, cocaine/crack, hallucinogens, opioids, sedatives, inhalants, dissociatives, and solvents as indicators of the latent classes. The purpose of this analysis was twofold: (i) to identify discrete classes of drug use trajectory based on the specific types of drugs used (or not used) prior to the past year and in the past year, and, relatedly, (ii) to identify "persistent" classes of drug use. Gender was included as a covariate in all models. Maximum likelihood ratio sandwich estimation was applied to adjust standard errors for familial non-independence. Akaike's Information Criterion (AIC), the Bayesian Information Criterion (BIC), and Lo–Mendell–Rubin adjusted likelihood ratio tests (LMR LRTs) assessed model fit [20–22]. All external validators (demographics, age of first use, opportunity to use, perceived peer use, SUD, and psychiatric disorder) were modeled as auxiliary variables using the Bolck–Croon–Hagenaars (BCH) method [23,24]. This method outperforms other approaches for modeling distal outcomes, using a weighted multiple group analysis to avoid shifts in latent class that can occur when distal outcomes are included in the LCA model; it is also robust in cases in which the variance of an auxiliary variable differs substantially across classes [23]. Although most often used to model continuous variables, the BCH method is also appropriate for modeling binary outcomes [23]; the expected value can be interpreted as the proportion of 1 s in the class (or the probability of a 1 rather than a 0 for a randomly selected class member) [25,26]. Descriptive statistics and tests of omnibus differences across classes were generated within the auxiliary model.

After class identification, three sets of contrasts were conducted using logistic regression to examine differences between latent classes. Multivariate models were built for each "cluster" of variables (i.e. demographics, age of first use, opportunity to use, perceived peer use, SUD, and psychiatric disorder). Two contrasts compared pairs of desistant and persistent use classes, and were selected a priori with the aim of identifying factors associated specifically with persistent use; desistant and persistent classes were matched for comparison based on relative similarity of drug use probabilities at the prior to past year time point to better isolate factors potentially related to persistence. The third contrast compared persistent use classes and was identified after observing their divergent use probability patterns.

Twin analyses

Twin similarity for latent class membership was estimated in SAS software version 9.4 [27]. For each zygosity group, twin concordance for most probable class membership was evaluated using the kappa coefficient. Significant twin similarity would provide evidence for the validity of the latent classes, and greater MZ than DZ twin similarity would provide evidence for a genetic contribution to latent class membership.

These omnibus tests of twin similarity were followed with biometric modeling applied individually to each latent class. These analyses partitioned the variation in class membership liability into additive genetic, common environmental, and unique environmental influences. Models were fitted directly to the raw twin data by the method of robust weighted least squares; bias-corrected bootstrapped confidence intervals were estimated. These analyses were conducted in Mplus Version 8 [19].

RESULTS

In line with past research, use of any one illicit drug increased odds of use of all others [28], supporting a multivariate approach (see Supporting information Table S2 for OR ratios and use rates). Cannabis and hallucinogens were typically initiated earliest (M_{age} = 17.91, 19.95, respectively), while other drugs were initiated in the early- to mid-20s (M_{age} = 20.67–24.89). Cocaine, opioids, and stimulants were, on average, the most recently used substances (M = 4.89–4.98 years since last use), followed by dissociates and sedatives (M = 5.33–5.64), and cannabis, hallucinogens, and inhalants (M = 7.37–8.99). Among respondents who reported use in the past year, last use was, on average, 3–4 months prior (except hallucinogens [7 months]). Solvents were an exception, with first and last use occurring relatively early (M_{age} = 14.96, 16.10).

Latent class solution

A 5-class solution best fit the data, producing the lowest AIC and BIC values (Table 1). The 6-class solution was the first with a highly nonsignificant LMR LRT, indicating that it was the largest viable solution and likely did not add information above and beyond the 5-class model [29]. The 5-class solution is theoretically sound, replicating

Table 1 Model fit indices for quasi-longitudinal model class solutions

Information criteria								LMR LRT	
Model	*Likelihood ratio* χ^2	χ^2 P	χ^2 df	*AIC*	*BIC*	*SSBIC*	*Entropy*	*Value*	P
2-Class	2432.80	1.00	262035	28508.21	28745.29	28624.54	0.91	6783.00	<0.0001
3-Class	2023.62	1.00	262035	27661.27	28023.12	27838.83	0.85	881.59	<0.0001
4-Class	1713.15	1.00	262024	27238.91	27725.53	27477.69	0.86	459.58	<0.0001
5-Class	**1584.32**	**1.00**	**262010**	**27036.35**	**27647.75**	**27336.36**	**0.76**	**241.09**	**0.0003**
6-Class	1413.16	1.00	261986	26946.03	27682.21	27307.26	0.77	129.54	0.34

Bold indicates preferred solution; AIC = Akaike's Information Criterion; BIC = Bayesian Information Criterion; SSBIC = sample size-adjusted Bayesian Information Criterion; LMR LRT = Lo–Mendell–Rubin adjusted likelihood ratio test; entropy is reported for descriptive purposes and should not be used for model selection.

past findings [8] without identifying any overly small, difficult-to-define classes.

Based on the drug use endorsement probabilities (Supporting information Table S3), the classes were interpreted as follows: (i) no/low use (NL; 50%), with near-zero drug use overall (Fig. 1a); (ii) desistant cannabis use (DC; 23%), with near-universal past cannabis use, slightly elevated probability of past stimulant use, and

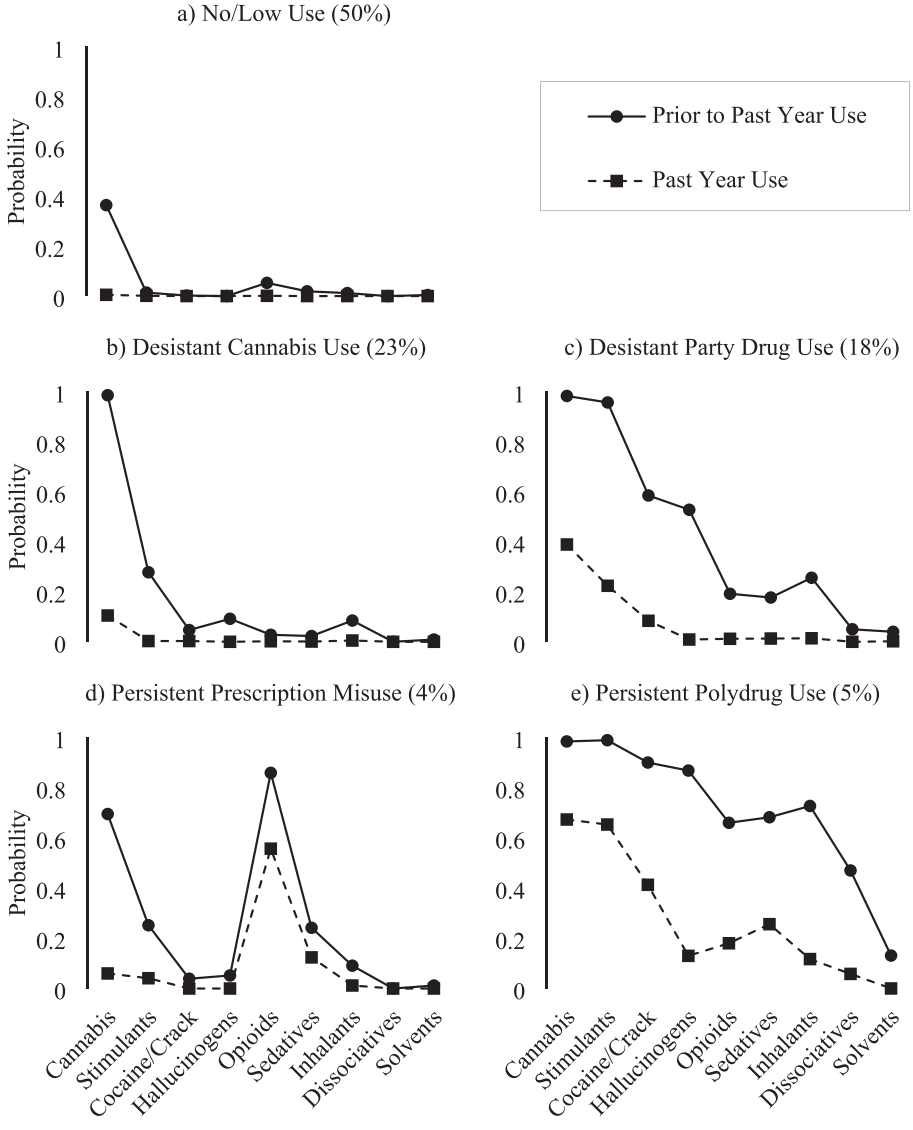


Figure 1 Drug use endorsement probabilities for no/low use (a), desistant cannabis use (b), desistant party drug use (c), persistent prescription misuse (d), and persistent polydrug use (e) classes.

near-zero current use (Fig. 1b), (iii) desistant party drug use (DP; 18%;), with near-universal past cannabis and stimulant use, and elevated probabilities of past cocaine/crack and hallucinogen use that were reduced to zero or near-zero for current use (except cannabis; Fig. 1c), (iv) persistent prescription drug misuse (PRX; 4%), with near-universal past prescription opioid misuse, and elevated probabilities of past cannabis use and current opioid use (Fig. 1d), and (v) persistent polydrug use (PP; 5%), with elevated probabilities of past use for all substances except solvents, and sustained elevated probabilities of current cannabis, stimulant, and, more moderately, cocaine/crack use (Fig. 1e). The validity of the latent classes was supported by their differences across a range of important drug use correlates (Table 2).

Distinguishing prescription misuse and illicit drug use

We examined specific substances within heterogeneous drug categories that included both prescription and illicitly manufactured forms (i.e. opiates, stimulants). This substantiated that prescription misuse, rather than street drug use, characterized PRX: 92% of members had misused prescription opioids whereas only 4% had ever used heroin/opium. Conversely, PP, which also showed elevated probabilities for opioid use, evidenced higher rates of illicit opioid use (41%; $\chi^2(1) = 68.67$, $P < 0.0001$), but lower rates of prescription opioid misuse (55%; $\chi^2(1) = 59.85$, $P < 0.0001$) as compared to PRX. Opioid use disorder was more common among those who used illicit opioids than those who misused prescription opioids ($\chi^2(1) = 52.92$, $P < 0.0001$), explaining higher observed rates of opioid use disorder in PP as compared to PRX despite high rates of opioid use in both classes (Table 2). Similarly, although both DP and PP displayed comparable rates of past stimulant use (96–99%; $\chi^2(1) = 1.45$, $P = 0.23$; Fig. 1c, e), they showed divergent patterns of current use ($\chi^2(1) = 134.90$, $P < 0.0001$). Both classes evidenced high, although significantly different, rates of ecstasy use (DP = 85%, PP = 97%; $\chi^2(1) = 16.55$, $P < 0.0001$) and prescription stimulant misuse (DP = 76%, PP = 96%; $\chi^2(1) = 36.94$, $P < 0.0001$), but five times the proportion of PP members reported use of methamphetamine (DP = 11%, PP = 56%; $\chi^2(1) = 174.04$, $P < 0.0001$). Respondents who used methamphetamine evidenced higher rates of stimulant use disorder than those who used ecstasy ($\chi^2(1) = 123.51$, $P < 0.0001$) or misused prescription stimulants ($\chi^2(1) = 109.05$, $P < 0.0001$). Of relevance, methamphetamine tends to be used more chronically and via routes that increase risk for addiction (e.g. injection), whereas ecstasy is typically used less frequently, restricted to more specific, youth-oriented contexts (e.g. clubs/raves), ingested orally, and has lower addictive potential [30-34].

Twin similarity and contributions of genetic and environmental influences

The validity of the latent classes was supported by the twin similarity for latent class membership (see Supporting information Table S4 for cross-tabulations of twin similarity with concordances and relative risks) [35]. Kappa coefficients were higher among MZ twins (men = 0.30, $P < 0.0001$; women = 0.35, $P < 0.0001$) than among same-sex DZ twins, (men = 0.20, $P = 0.0005$; women = 0.19, $P < .0001$; $\chi^2 = 6.33$, df = 1, $P = 0.01$), providing evidence for a genetic contribution to latent class membership. The estimate for opposite-sex DZ twins was relatively low, although also significant (k = 0.07, $P = 0.02$).

Biometric models (Fig. 2; Supporting information Table S5) applied individually to each of the five latent classes revealed that there were significant genetic influences for DP and PP, with a substantially larger heritability for the more persistent class. Liability for both DC and PRX was primarily explained by unique environmental factors.

Latent class contrasts

Persistent prescription misuse versus desistant cannabis use

PRX and DC evidenced more similarities than might be expected (Table 3). Although female gender decreased odds of DC (adjusted odds ratio [AOR] = 0.14), these classes did not differ on other demographic characteristics or age of first alcohol, nicotine, or cannabis use. Opportunity to use cannabis decreased odds of PRX (AOR = 0.04), as did opportunity to use stimulants (AOR = 0.58); opportunity to use opioids and sedatives increased odds of PRX (AOR = 39.61, 3.35). PRX evidenced fewer drug-using male friends (AOR = 0.37) and lower odds of alcohol use disorder (AOR = 0.68). Depression (AOR = 2.38) and having attempted suicide (AOR = 2.31) increased odds of PRX as compared to DC.

Persistent polydrug use versus desistant party drug use

Compared to DP, PP members were more likely to be male (AOR = 2.07), never married (AOR = 3.48), and less educated (AOR = 0.86; Table 3). Older age of first use of alcohol (AOR = 0.86) and cannabis (AOR = 0.88) decreased odds of PP as compared to DP. Opportunity to use all substances (except stimulants and solvents) increased odds of PP (AOR = 2.34–5.53), as did reporting more male friends and coworkers who use drugs (AOR = 2.78–7.15). PP also evidenced higher odds of all drug use disorders (AOR = 1.62–3.95), ASPD (AOR = 3.27), and suicidal ideation (AOR = 1.98).

Table 2 Characteristics of the five latent classes

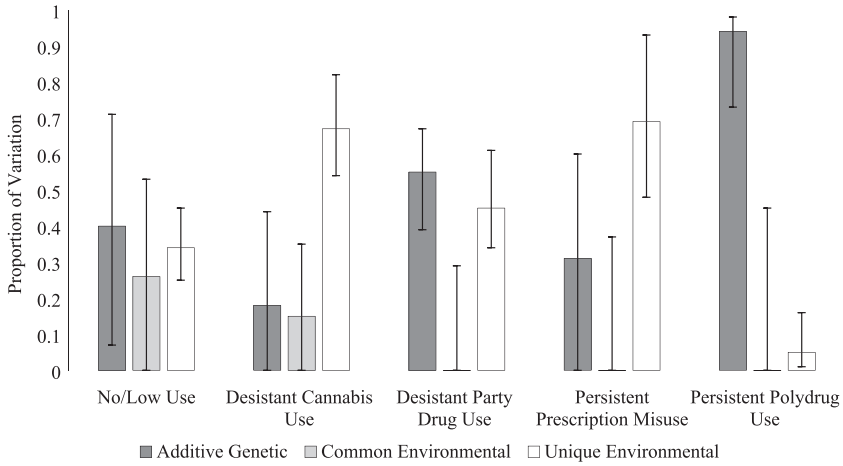
			Desistant classes		Persistent classes		
	Full sample	1. No/low use	2. Desistant cannabis use	3. Desistant party drug use	4. Persistent prescription misuse	5. Persistent polydrug use	Omnibus χ^2
Demographics	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	
Full sample	3785 (100)	1901 (50)	855 (23)	681 (18)	169 (4)	179 (5)	–
Within men	1365 (36)	333 (24)	572 (42)	306 (22)	37 (3)	117 (9)	–
Within women	2420 (64)	1568 (65)	283 (12)	375 (16)	132 (5)	62 (3)	–
% Female	64	82	33	55	78	35	–
	mean (SE)	mean (SE)	mean (SE)	mean (SE)	mean (SE)	mean (SE)	
Age	31.77 (0.05)	32.31 (0.10)^{3}	32.13 (0.15)	31.63 (0.13)^{1}	32.51 (0.28)	31.81 (0.22)	24.60*
Education	13.24 (0.02)	13.40 (0.04)^{5}	13.08 (0.08)	13.23 (0.07)	13.14 (0.14)	12.78 (0.13)^{1}	29.08*
% Married	57	67^{35}	61^{35}	36^{1245}	60^{35}	12^{1234}	414.59*
Lifetime drugs used	mean (SE)	mean (SE)	mean (SE)	mean (SE)	mean (SE)	mean (SE)	
	1.73 (0.03)	0.52 (0.01)^{2345}	1.56 (0.02)^{1345}	3.87 (0.04)^{1245}	2.49 (0.08)^{1235}	6.66 (0.09)^{2345}	5642.66*
Age of first use	mean (SE)	mean (SE)	mean (SE)	mean (SE)	mean (SE)	mean (SE)	
Alcohol	15.85 (0.04)	16.87 (0.08)^{235}	14.98 (0.10)^{145}	14.97 (0.09)^{145}	16.16 (0.24)^{235}	13.94 (0.18)^{1234}	473.3*
Nicotine	14.27 (0.06)	15.09 (0.14)^{235}	13.90 (0.16)^{15}	13.68 (0.16)^{1}	14.59 (0.37)^{5}	12.52 (0.29)^{124}	96.14*
Cannabis	17.91 (0.07)	19.69 (0.33)^{235}	18.15 (0.14)^{135}	16.89 (0.13)^{125}	18.15 (0.41)^{5}	15.64 (0.24)^{1234}	215.28*
Opportunity to use	%	%	%	%	%	%	
Cannabis	89	75^{2345}	100^{134}	99^{1245}	89^{1235}	100^{134}	468.90*
Stimulants	46	10^{2345}	66^{1345}	98^{124}	41^{1235}	99^{124}	4095.32*
Cocaine/crack	27	5^{235}	25^{135}	78^{1245}	14^{35}	95^{1234}	2620.21*
Hallucinogens	27	3^{2345}	30^{1345}	70^{1245}	12^{1235}	95^{1234}	2329.30*
Opioids	24	15^{345}	12^{345}	30^{1245}	95^{123}	82^{123}	840.22*
Sedatives	14	5^{345}	5^{345}	22^{125}	36^{125}	84^{1234}	631.23*
Inhalants	14	0^{235}	17^{135}	30^{1245}	10^{35}	86^{1234}	874.00*
Dissociatives	6	<1^{35}	1^{35}	11^{1245}	0^{35}	68^{1234}	349.47*
Solvents	6	1^{235}	8^{15}	9^{15}	6^{5}	28^{1234}	102.95*
Peer drug use	% of peers	% of peers	% of peers	% of peers	% of peers	% of peers	
Male friends	45	20^{2345}	61^{2345}	74^{1245}	40^{1235}	90^{2345}	1627.87*
Female friends	33	15^{2345}	40^{135}	62^{1245}	29^{135}	76^{2345}	1134.38*
Coworkers	9	6^{35}	9^{35}	14^{12}	9^{5}	23^{124}	131.21*
Lifetime use disorder	%	%	%	%	%	%	
Alcohol	37	15^{2345}	70^{14}	66^{145}	47^{1235}	82^{134}	736.21*
Nicotine	32	15^{2345}	47^{15}	57^{1}	44^{15}	70^{124}	472.00*
Cannabis	16	0^{2345}	18^{135}	45^{1245}	14^{135}	74^{1234}	919.69*

(*Continues*)

Table 2. (Continued)

		Desistant classes			Persistent classes		
	Full sample	1. No/low use	2. Desistant cannabis use	3. Desistant party drug use	4. Persistent prescription misuse	5. Persistent polydrug use	Omnibus χ^2
Stimulants	9	0^{35}	0^{35}	25^{1245}	3^{35}	73^{1234}	589.12*
Cocaine/crack	1	0^{5}	0^{5}	3^{5}	0^{5}	15^{1234}	46.99*
Hallucinogens	2	0^{5}	0^{5}	3^{5}	0^{5}	4^{1234}	79.10*
Opioids	2	0^{5}	0^{5}	3^{5}	3^{5}	19^{1234}	62.92*
Sedatives	1	0^{5}	0^{5}	$<1^{5}$	3^{5}	14^{1234}	41.22*
Inhalants	<1	0	0	0	0	2	6.06
Dissociatives	<1	0	0	0	0	<1	9.35
Solvents	<1	0	0	0	0	<1	2.01
Psychiatric symptoms	%	%	%	%	%	%	
ADHD	4	2^{35}	5	6^{1}	8	11^{1}	33.01*
Conduct disorder	9	$<1^{2345}$	12^{15}	17^{15}	16^{15}	39^{1234}	288.14*
ASPD	3	0^{2345}	3^{15}	4^{15}	8^{1}	23^{123}	96.21*
Depressive episode	25	22^{45}	21^{45}	27^{4}	49^{123}	37^{12}	53.77*
Suicidal ideation	27	19^{345}	27^{45}	32^{15}	45^{12}	55^{123}	115.27*
Suicide attempt	4	3^{3}	2^{5}	8^{1}	12	12^{2}	41.47*

Lifetime drugs used range = 0–9; ADHD = attention deficit/hyperactivity disorder; ASPD = antisocial personality disorder; superscript denotes significant pairwise difference from correspondingly numbered class at Bonferroni-corrected $P < 0.0002$. *$P < 0.0001$.



Note. Error bars represent 95% confidence intervals.

Figure 2 Proportion of variation in latent class membership liability attributable to additive genetic, common environmental, and unique environmental factors.

Persistent polydrug use versus persistent prescription misuse

Despite both evidencing patterns of persistent drug use, PRX and PP differed substantially in their patterns of problems and risk (Table 3). PP members were more likely to be male (AOR = 6.28) and never married (AOR = 7.80), report younger ages of first alcohol (AOR = 0.82) and cannabis use (AOR = 0.83), have more opportunity to use drugs (except opioids and solvents; AOR = 10.66–66.06), and report more peers who use drugs (AOR = 4.66–9.20). PP evidenced higher odds of cannabis and stimulant use disorders (AOR = 6.14–28.01); rates of all illicit drug use disorders (except cannabis) were 5% or lower among PRX members, compared to as high as 72% in the PP class. Of the psychiatric conditions, conduct disorder increased odds of PP (AOR = 2.40), while depression decreased odds of PP compared to PRX (AOR = 0.53).

DISCUSSION

As hypothesized, our quasi-longitudinal LCA identified two classes that represented desistence from previous drug involvement and two classes that represented persistent drug involvement. We also demonstrated that persistent polydrug use is more heritable than desistant drug use. A number of characteristics differentiated people who persisted in their use from those who desisted, and the two persistent typologies from each other. As anticipated, people who reported persistent polydrug use evidenced higher rates of lifetime SUD than did those who ultimately desisted in their drug use. Younger age of first alcohol and cannabis use emerged as a factor increasing odds of persistent polydrug use, even compared to respondents who ultimately desisted but reported a history of multi-drug use. The differences between the two persistent use classes highlight that prescription opioid availability fosters risk for misuse even in the face of numerous protective factors, such as older age of first substance use, limited opportunity to use substances, and few drug-using peers [36,37]. Conversely, the patterns characteristic of the PP class reinforce repeated findings that show younger age of first use, opportunity to use drugs, and having many drug-using peers to be associated with high-risk drug use and substance-related problems.

Psychiatric symptoms appear to be important risk factors for both forms of persistent use, specifically, antisociality (conduct disorder, ASPD) for polydrug use and depressive symptoms for prescription drug misuse. The rates of conduct disorder and ASPD were far lower among PRX members than PP members, linking antisociality more specifically to polydrug use, which itself confers risk for persistence via increased risk of SUD. Individuals with conduct disorder tend to initiate substance use at younger ages [38], which incurs risk for continued use; regular use in the teens and early 20s dramatically increases risk of substance use into mid-adulthood [2,39]. ASPD is by definition a persistent disorder that itself is robustly associated with drug use [40,41]; as such, the persistence of ASPD may partially explain the persistence of polydrug use [42,43]. With respect to PRX, the high rates of depression and suicidality are notable given bidirectional evidence that individuals with depressive symptoms are more likely to misuse prescribed opioid analgesics [44] and that use of opioid analgesics increases risk for depression [45]. As such, screening for history of depression may be an important component of evaluating candidacy for opioid-based pain management approaches to minimize risk of prescription misuse.

Table 3 Latent class contrasts

	Contrast		
	Persistent Rx misuse vs. desistant cannabis use	Persistent polydrug use vs. desistant party drug use	Persistent polydrug use vs. persistent Rx misuse
Reference category	*desistant cannabis use*	*desistant party drug use*	*persistent Rx misuse*
Demographics	adjusted OR (95% CI)	adjusted OR (95% CI)	adjusted OR (95% CI)
Sex	**0.14 (0.09–0.20)**	**2.07 (1.45–2.97)**	**6.28 (3.61–10.91)**
Marital status	0.98 (0.68–1.43)	**3.48 (2.20–5.50)**	**7.80 (4.34–14.04)**
Education	0.98 (0.86–1.11)	**0.86 (0.76–0.97)***	0.86 (0.72–1.02)
Lifetime drugs used	adjusted OR (95% CI)	adjusted OR (95% CI)	adjusted OR (95% CI)
	5.06 (3.84–6.66)	**7.34 (5.44–9.90)**	**14.30 (6.95–29.43)**
Age of first use	adjusted OR (95% CI)	adjusted OR (95% CI)	adjusted OR (95% CI)
Alcohol	1.01 (0.91–1.13)	**0.86 (0.78–0.95)****	**0.82 (0.71–0.95)***
Nicotine	0.99 (0.93–1.05)	0.97 (0.87–1.03)	0.99 (0.91–1.06)
Cannabis	0.99 (0.93–1.06)	**0.88 (0.82–0.96)****	**0.83 (0.75–0.92)****
Opportunity to use	adjusted OR (95% CI)	adjusted OR (95% CI)	adjusted OR (95% CI)
Cannabis	**0.04 (0.01–0.16)**	–	–
Stimulants	**0.58 (0.36–0.94)***	2.46 (0.51–11.93)	**16.28 (1.58–168.02)***
Cocaine/crack	0.66 (0.37–1.17)	**2.54 (1.26–5.14)***	**66.06 (13.54–322.19)**
Hallucinogens	**0.34 (0.19–0.60)*****	**2.34 (1.17–4.67)***	**34.51 (8.26–144.27)**
Opioids	**39.61 (23.29–67.39)**	**3.08 (1.86–5.10)**	**0.24 (0.06–0.98)***
Sedatives	**3.35 (1.86–6.01)**	**4.26 (2.64–6.88)**	**10.66 (2.59–43.84)****
Inhalants	0.55 (0.28–1.07)	**4.29 (2.65–6.95)**	**22.48 (6.13–82.45)**
Dissociatives	0.29 (0.06–1.57)	**5.53 (3.43–8.89)**	–
Solvents	0.47 (0.20–1.12)	1.54 (0.85–2.77)	1.69 (0.37–7.61)
Perceived peer drug use	adjusted OR (95% CI)	adjusted OR (95% CI)	adjusted OR (95% CI)
Male friends	**0.37 (0.19–0.72)****	**7.15 (2.84–18.01)**	**9.20 (6.98–57.31)**
Female friends	1.45 (0.69–3.03)	3.94 (2.30–6.75)	**4.66 (1.82–11.96)*****
Coworkers	1.97 (0.64–6.03)	**2.78 (1.37–5.58)****	**6.68 (1.50–28.83)***
Lifetime use disorder	adjusted OR (95% CI)	adjusted OR (95% CI)	adjusted OR (95% CI)
Alcohol	**0.68 (0.49–0.95)***	1.15 (0.73–1.81)	1.73 (0.89–3.38)
Nicotine	1.16 (0.83–1.64)	1.04 (0.69–1.57)	1.21 (0.63–2.31)
Cannabis	1.04 (0.65–1.66)	**1.62 (1.05–2.48)***	**6.14 (23.13–12.07)**
Stimulants	–	**3.95 (2.64–5.89)**	**28.01 (11.82–66.37)**
Cocaine/crack	–	**2.78 (1.37–5.61)****	–
Hallucinogens	–	**2.51 (1.37–4.60)****	–
Opioids	–	**2.55 (1.22–5.31)***	2.96 (0.71–12.32)
Sedatives	–	**3.18 (1.27–7.97)***	1.06 (0.22–5.23)
Psychiatric symptoms	adjusted OR (95% CI)	adjusted OR (95% CI)	adjusted OR (95% CI)
ADHD	0.80 (0.38–1.70)	1.00 (0.53–1.89)	1.06 (0.46–2.44)
Conduct disorder	1.08 (0.60–1.92)	1.50 (0.95–2.37)	**2.40 (1.25–4.62)****
ASPD	1.85 (0.77–4.47)	**3.27 (1.76–6.10)*****	1.75 (0.74–4.12)
Depressive episode	**2.38 (1.62–3.48)**	0.99 (0.66–1.49)	**0.53 (0.32–0.87)***
Suicidal ideation	1.30 (0.87–1.94)	**1.98 (1.34–2.91)****	1.60 (0.96–2.66)
Suicide attempt	**2.31 (1.13–4.75)***	0.78 (0.42–1.45)	0.80 (0.37–1.74)

Predictor reference categories: sex = female, marital status = married, opportunity to use = no, use disorder = not present; psychiatric symptoms = not present; ADHD = attention deficit/hyperactivity disorder; ASPD = antisocial personality disorder; dash (–) indicates at least one cell N being too low to accurately estimate contrast (N = 0–5); Bonferroni-corrected $P = 0.0002$; bold indicates significance, $P \leq 0.0001$ unless noted. $^{***}P < 0.05$. $^{**}P \leq 0.005$. $^{*}P \leq 0.0005$.

The PRX class evidenced unique characteristics. It was the only class for which cannabis did not have the highest use probability as compared to the other drugs, its breadth of use was relatively small, and it appeared quite similar to the lower-using classes with respect to gender composition, use probability for non-prescription substances, risk factors for substance-related problems, and SUD prevalence. As has been observed over the years of the opioid epidemic, individuals who are non-drug seeking and/or drug naïve not infrequently receive legitimate opioid prescriptions and subsequently misuse opiods [13,46]. Most adults receive more opioid medication than is needed to manage their pain and keeps the surplus at home, creating easy opportunity for misuse [47]; a majority of adults who misuse

prescription medication source the substance from their own prescription [48]. This pattern is in line with findings that most individuals who initiate drug use in their mid- to late-20s use psychoactive prescription medications [2]. This is particularly important in light of the ongoing opioid epidemic in the United States. Although it cannot fully explain the surge in heroin use and overdose deaths, opioid prescribing and misuse has been implicated in these increases; most people who use heroin initiated opioid use with prescription analgesics (although it should be noted that most people who misuse prescription opioids do not transition to heroin use) [37]. Trends in opioid use over the past century capture a pattern of prescription misuse impacting groups historically not involved in opioid use, demonstrating that these drugs reach individuals who do not fit the "typical" profile of drug use risk [36]. That is, opioid prescribing opens a door to opioid misuse to otherwise seemingly low-risk individuals who are not typically presented with opportunities to use drugs.

The PRX class was also predominately female, despite men generally engaging in drug use at higher rates than women [49]. This is in line with findings that women are disproportionately represented in mid-20s prescription "downer" initiates [2,50]. Further, there is evidence that women misuse pain medication more than men and are more likely to become dependent on nonmedically used prescription medications, such as opioid analgesics [49,51,52], and men are more likely to abuse prescription stimulants than prescription opioids [53]. The latter finding may explain men's disproportional representation in the DP and PP classes and their relative absence in the PRX class. It is notable that rates of opioid use disorder were relatively low in the PRX class, potentially reflecting findings that women most often misuse prescription opioids in a "rule abiding" manner (e.g. misusing medication from one's own prescription, ingesting via the intended route of administration, using at prescribed doses) [54–56]. These patterns point toward a gender effect that should be pursued in future research.

Limitations

There are limitations of this study to note. First, it is unclear how these results from a sample of Australian adults will generalize to other countries. Laws surrounding the regulation of opioid analgesics have also changed since the time of data collection, potentially altering accessibility. Additionally, the "past use" time point represents a wider window than does the "current use" time point, and these data were retrospective, cross-sectional self-reports rather than truly longitudinal data. As such, it was not possible to use a longitudinally-oriented analytic approach, such as latent transition analysis [57]. Regardless, as we sought to define our latent classes by behavior over time rather than observe changes in latent class over time, LCA provided an appropriate method. Despite these limitations, the present study leveraged multiple time points and twin data to provide a novel approach to understanding trajectories of illicit drug use among adults, laying a foundation for future longitudinal work in this area.

CONCLUSIONS

This study presents a successful replication of a past model of subtypes of drug users and its effective extension to a quasi-longitudinal analysis examining temporal patterns of drug use. The results presented here reflect that (i) there are distinct, heritable types of drug use with unique substance preferences and temporal characteristics, (ii) specific substances are more strongly associated with persistent use and SUD than other drugs in the same drug class, (iii) exposure to prescription opioids among seemingly low-risk individuals may set in motion a pattern of persistent drug use despite the presence of protective factors, and (iv) subtypes of drug users evidence differential levels of antisocial behavior that could represent a predisposition to or manifestation of their pattern of drug use. These findings illuminate factors associated with divergent trajectories of individuals who initiate drug use; that is, risks that contribute to some "desisting" while others persist in their use. Although much can be learned from a genetically informative quasi-longitudinal study of polysubstance use, we look forward to future truly longitudinal, genetically informed multivariate studies that can examine the initiation, persistence, and desistence of the full spectrum of illicit drugs [58].

Declaration of interests

None.

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Author contributions

Genevieve Dash: Conceptualization; formal analysis; investigation; methodology; validation; visualization. **Nicholas Martin:** Data curation; project administration; resources. **Arpana Agrawal:** Data curation; funding acquisition; project administration; resources. **Michael Lynskey:** Data curation; funding acquisition; project administration; resources. **Wendy Slutske:** Conceptualization; formal analysis; investigation; methodology; resources; supervision; validation; visualization.

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Supporting Information

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Table S1. Model fit for class solutions of replication model
Table S2. Odds ratios for prior to past year and past year drug use
Table S3. Use probabilities by latent class
Table S4. Twin similarity for latent class membership
Table S5. Variation in latent class propensity attributable to additive genetic (a^2), common environmental (c^2), and unique environmental (e^2) factors