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RESEARCH REPORT

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Adolescent substance use and high school noncompletion: exploring the nature of the relationship using a discordant twin design

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Abstract

Background and Aims: Previous studies have demonstrated associations between substance use and reduced educational attainment; however, many were unable to account for potential confounding factors like genetics and the rearing environment. In the few studies that controlled for these factors, the substances assessed were limited to alcohol, cannabis, and tobacco. To address these limitations, we examined the relationship between adolescent use of seven kinds of substances, the number of additional substances used, and high school noncompletion within a large sample of Australian twins.

Design: A series of two-level generalized mixed effects logistic regressions were conducted to examine associations between adolescent substance use and high school noncompletion.

Setting: Australia.

Participants: A total of 9579 adult Australian twins from two cohorts of the Australian Twin Registry.

Measurements: Assessments of high school completion, childhood major depression, conduct disorder symptoms, substance use initiation, demographics, and parental educational attainment using the Australian version of the Semi-Structured Assessment for the Genetics of Alcoholism.

Findings: There were unique within-twin-pair effects of use of sedatives (odds ratio [OR] = 22.39 [95% confidence interval (CI) = 1.18–423.48]) and inhalants/solvents (OR = 10.46 [95% CI = 1.30–84.16]) on high school noncompletion. The number of substances used in adolescence was strongly associated with high school noncompletion across all discordant twin models (ORs from 1.50–2.32, *Ps* < 0.03).

Conclusions: In Australia, adolescent substance use appears to be associated with early school dropout, with the effects of any given substance largely because of the confounding factors of parental education, childhood conduct disorder symptoms, and use of other substances. Sedatives and inhalants/solvents have effects on high school noncompletion that cannot be explained by polysubstance use or familial factors.

KEYWORDS
Discordant twin design, educational attainment, inhalant use, polysubstance use, sedative use, solvent use, substance use adolescence, substance use

INTRODUCTION

Late adolescence is a developmental period characterized by experimentation with substance use. By the end of high school, 66% of Australians have used alcohol, 14% have used tobacco, 36% have used cannabis, and 10% have used an illicit drug other than cannabis [1, 2]. At the same time, adolescents face critical life junctures, including choices about continuing/discontinuing education [3]. Adolescents who use substances may have reduced educational attainment. In a world in which education has significant impacts on economic prospects [4], as well as health and wellbeing [5, 6], this is a substantial disadvantage.

The association between substance use and educational attainment has been well-established [7–11]; however, the nature of the association has been widely debated. Theories can be broken into two broad camps: those suggesting adolescent substance use serves as an indicator of broader risk for educational noncompletion (i.e. a shared etiological model) and those suggesting adolescent substance use causally contributes to reduced educational attainment (i.e. a causal model). There is some evidence that the relationship is because of a complex combination of the two, whereby adolescent substance use is a marker of risk, as well as a causal mechanism leading to reduced education [9].

Studies of twin pairs are uniquely well-suited for examining the nature of this relationship [12]. Because of their ability to control for genetic and shared environmental factors, twin studies account for many confounding factors that may otherwise lead to the appearance of a causal association. However, the link between substance use and educational attainment has been relatively understudied within twin samples, with only four to date [13–16]. Three studies examined adolescent alcohol use as a predictor of educational attainment and found that substance-using twins were more likely than their non-substance using co-twins to not complete both high school and college [13–15], although there were slight inconsistencies, in that Waldron *et al.* [15] found that effects for early first intoxication and early first drink were present in monozygotic (MZ), but not dizygotic (DZ) twins. The one study that examined tobacco use as a predictor of college completion found a similar effect for lifetime daily smoking, but not lifetime nicotine dependence [13]. Nonetheless, predictors were lifetime, rather than adolescent tobacco use, leaving questions about whether the pattern of use was established before college noncompletion.

Other studies failed to find differences in education between substance-using twins and their non-substance using co-twins. The relationship between adolescent cannabis use and educational attainment was evaluated in two studies, with both demonstrating that a twin's exposure to cannabis was not associated with reduced education after accounting for genetics and the shared environment [13, 16]. The one study [13] examining effects of a lifetime diagnosis of illicit drug dependence on the odds of college completion came to a similar conclusion.

In summary, discordant twin studies have been consistent in demonstrating that adolescent use of alcohol is associated with reduced education even after controlling for familial factors, but other substances have either not been the focus of a discordant twin study or have been the focus of a single study [13–15]. Importantly, these studies failed to account for co-use of other substances, despite the fact that many adolescents engage in polysubstance use [17, 18]. Therefore, it remains unclear whether individual substances confer unique risk or if substance use in general is a risk factor for educational noncompletion.

In the present study, we examined associations between the use of seven classes of psychoactive substances before age 18 and high school noncompletion using a discordant twin design. The discordant twin design can be used to tease apart drug exposure effects from confounding effects of genes and shared environments [12]. In a series of models, we controlled for demographic factors, history of psychiatric disorder, parental education, and co-occurring substance use to assess unique risks associated with adolescent use of specific substances. Based on the limited extant research, we anticipated an overall individual-level effect of adolescent use on high school noncompletion for all substances. We also expected that alcohol-using twins would be less likely to complete high school than their non-alcohol using co-twins. For other substances, we had no hypotheses about whether the effect would be because of drug exposure itself or accounted for by shared familial factors. However, we did expect that associations between all specific substances and high school noncompletion would diminish once co-occurring substance use was covaried. This analysis was not pre-registered, and results should be considered exploratory.

METHOD

Participants

Data were drawn from two cohorts of the Australian Twin Registry (ATR), a nationally representative registry of adult Australian twins. The resulting combined sample size was 9579 twins, of which 58.63% were female (biological sex was assessed rather than gender). See Table 1 for detailed sample characteristics.

Australian twin registry cohort 2 (ATR-II)

Twins age 23 to 39 years old (mean [M] = 29.94, SD = 2.47; born 1964–1971) completed telephone interviews between 1996 and 2000; 6265 twins participated, 55.27% were female. There were 1450 MZ female twins, 1087 MZ male twins, 1158 DZ female twins, 962 DZ male twins, and 1524 DZ opposite sex twins; 84 twins were missing zygosity information.

Australian twin registry cohort 3 (ATR-III)

Twins age 27 to 40 years old (M = 31.84, SD = 2.48; born 1972–1979) completed computer-assisted telephone interviews between 2005 and 2009; 3314 twins participated, 64.98% were female. There were 972 MZ female twins, 479 MZ male twins, 734 DZ female twins,

TABLE 1 Sample characteristics

	Full sample		*ATR-II cohort*		*ATR-III cohort*	
	%	*n*	*%*	*n*	*%*	*n*
Female	58.63	5614	55.27	3462	64.98	2152
Monozygotic	42.11	3988	41.05	2537	44.10	1451
Childhood major depression	4.15	397	3.10	194	6.13	203
Conduct disorder diagnosis	13.24	1262	15.48	963	9.03	299
Personal educational attainment						
Less than high school	18.26	1749	22.36	1401	10.51	348
Completed high school	33.07	3167	43.24	2709	13.83	458
Completed technical/teachers' college	15.34	1469	8.59	538	28.11	931
Completed undergraduate degree	20.47	1960	16.65	1043	27.69	917
Completed postgraduate degree	12.86	1232	9.16	574	19.87	658
Father's educational attainment						
Less than high school	55.65	5330	59.23	3711	48.88	1619
Completed high school	16.79	1608	19.89	1246	10.93	362
Completed technical/teachers' college	10.65	1020	6.50	407	18.51	613
Completed undergraduate degree	9.72	931	8.95	561	11.17	370
Completed postgraduate degree	7.18	688	5.43	340	10.51	348
Mother's educational attainment						
Less than high school	54.44	5214	57.29	3589	49.06	1625
Completed high school	22.36	2141	25.86	1620	15.73	521
Completed technical/teachers' college	10.47	1003	8.57	537	14.07	466
Completed undergraduate degree	7.87	754	5.24	328	12.86	426
Completed postgraduate degree	4.86	465	3.05	191	8.27	274
	Mean	SD	Mean	SD	Mean	SD
Age	30.59	2.63	29.94	2.47	31.83	2.47
Conduct disorder symptoms	1.02	1.46	1.12	1.52	0.84	1.32
No. substances used in lifetime	3.37	1.74	3.15	1.66	3.80	1.81
No. substances used in adolescence	2.02	1.15	1.92	1.10	2.21	1.24

ATR = Australian Twin Registry

368 DZ male twins, and 739 DZ opposite-sex twins; 22 participants were missing zygosity information.

Measures

Interviews were based on the Australian version of the Semi-Structured Assessment for the Genetics of Alcoholism [19]. The present study used the assessments of personal educational attainment, childhood major depression, conduct disorder (CD) symptoms, substance use initiation, demographics, and parental educational attainment.

Adolescent substance use

Participants were asked about lifetime use or misuse (in the case of prescription drugs and common household items) of 11 types of substances (alcohol, tobacco, cannabis, stimulants, hallucinogens, cocaine, inhalants, opiates, sedatives, solvents, and phencyclidine [PCP]). Given that solvents are a form of inhalants [20], we combined these two substance types into a single variable reflecting use of either. Individuals who endorsed having used a substance in their lifetime were asked their age at first use. If an individual used the substance before age 18, adolescent use for that substance was coded "1"; otherwise, use was coded "0." We calculated 4-year test–retest reliabilities for the adolescent substance use variables among a subset of participants from ATR-II who were re-contacted after their initial interview; up to 215 participants had data for both time points. Test–retest reliabilities ranged from 0.62 (95% CI = 0.50–0.71 for tobacco) to 0.87 (95% CI = 0.56–0.96 for opiates). Supporting information Table S1 provides all the test–retest reliabilities.

A count of the 11 adolescent substance use variables represented the total number of substances used in adolescence. Among a subset of 217 participants from ATR-II, the 4-year test–retest reliability was excellent for the number of substances used variable (intraclass correlation coefficient = 0.91 [0.88–0.93]). When including this variable as a covariate in analyses, a leave-one-out approach was taken, whereby

the total number of substances used was calculated excluding the substance being used as a predictor.

High school completion/noncompletion

Educational attainment was assessed with the question, "What is the highest educational level you have completed?" Response options differed across cohorts, with ATR-II including five possible responses and ATR-III including 10. Responses were harmonized across cohorts [21]. The resulting variable ranged from not completing primary school to obtaining a post-graduate degree (scores of "1" indicated that a participant did not complete high school, "2" indicated completion of high school, "3" indicated completion of technical college [community college], "4" indicated obtaining an undergraduate degree, and "5" indicated obtaining post-graduate education). For the current study, we created a binary variable indicating high school completion/non-completion. We focused on this milestone because the relation between substance use and educational attainment differed across levels of education (violating the proportional odds assumption) and three of the four previous discordant twin studies used high school noncompletion as the outcome [14–16].

Parental educational attainment

Maternal and paternal education were both assessed as 5-level ordinal variables ranging from not completing high school to completing post-graduate education. We did not dichotomize parental education because we did personal educational attainment because the proportional odds assumption only applies to outcome variables and not covariates; therefore, we chose to retain all available information on parental education. There was substantial agreement within twin pairs for parental education (maternal: k = 0.63 [0.61–0.65]; paternal: k = 0.66 [0.64–0.68]).

Childhood major depression episode

Participants reported their experiences with depression throughout their lifetime. Each diagnostic criterion for depression was assessed [22]; participants were asked whether there was a period of at least 2 weeks in which five or more depression symptoms occurred together nearly every day. Those who endorsed five or more symptoms reported their age at the most severe episode and the earliest episode, if different from the most severe. Individuals who reported a depression episode beginning before age 18 were coded as having a childhood major depression episode ("1"); others were coded "0."

Conduct disorder symptoms

The Diagnostic and Statistical Manual of Mental Disorders (DSM)-IV-TR [22] criteria for CD were assessed. Participants were instructed to consider behaviors that occurred before age 18. Although the DSM-IV-TR requires that two criteria ("often stays out at night" and "often truant from school") occur before age 13, these age requirements were not imposed within the current interview. The 15 CD symptoms were summed (internal consistency reliabilities [Cronbach's α]: ATR-II = 0.67, ATR-III = 0.64). The 4-year test–retest reliability of CD symptoms among a subset of 217 participants from the ATR-II was good (ICC = 0.84 [0.79–0.88]).

Data analysis

Two sets of multiple-step analyses were conducted within SAS v9.4 [23] to examine effects of adolescent use of individual substances on high school noncompletion. Additional analyses examining adolescent substance use as a predictor of college completion can be found in the Supporting information. Cocaine, opiate, and PCP use were excluded because of the small number of pairs that were discordant ($n \leq 90$) for use of these substances (Table 2); analyses of these substances would have been underpowered. Two-level generalized mixed effects logistic regressions were conducted using PROC GLIMMIX. Mixed effects logistic regressions were used because the outcome variable was binary [24]. Mixed effects models were selected because of clustering inherent in twin data wherein individual twins (level 1) are nested within twin pairs (level 2). Level 1 and 2 variances were estimated, along with a random intercept. Model estimated coefficients were exponentiated to produce odds ratios (ORs), representing the change in the odds of not completing schooling.

Analyses began with individual level models that accounted for the non-independence of twin data. These models approximate analyses among unrelated individuals and examine evidence for an overall effect of the predictor. In the first step, a binary variable indicating use/no use of the substance was entered as the sole predictor. Next, partially adjusted models were fit including zygosity, sex, cohort, CD symptoms, childhood major depression, and parental educational attainment as covariates. In the final step for the individual level models, another covariate was included to control for the number of additional substances used during adolescence. This fully adjusted model was fit to determine whether an observed association with high school noncompletion was because of use of the specific substance or better explained by general substance use.

Individual level analyses were followed by discordant twin analyses that control for potential sources of familial confounding that may contribute to the overall effect observed in the individual level models [12]. All discordant twin models included a random intercept to account for non-independent twin data. If either twin within a complete pair (n = 3977 complete twin pairs) was missing data on adolescent use of a particular substance, the twins were excluded from discordant twin analyses for that substance (see Table 2 for the number of twin pairs with complete data for each substance). Analyses modeled the environmental exposure of interest as a within-

TABLE 2 Number of discordant and concordant twin pairs for adolescent use of individual substances and rates of adolescent use

Substance	*Concordant for no use*	*Discordant*	*Concordant for use*	*Adolescent use (%)*
Cannabis	2266	1003	695	31.99
Alcohol	403	892	2678	78.59
Tobacco	473	880	2621	77.51
Cocaine*	**3940**	**24**	**1**	0.39
Stimulants	3782	162	20	2.76
Opiates*	**3870**	**90**	**5**	1.41
Sedatives	3830	118	16	1.75
Hallucinogens	3777	152	22	2.77
PCP*	**3958**	**7**	**0**	0.07
Inhalants/solvents	3727	203	34	3.56

PCP = phencyclidine

* indicates substances that were not included in discordant twin analyses because of small sample sizes (<100 of discordant twin pairs.

twin-pair coefficient and between-twin-pair coefficient. The within-twin-pair coefficient represents the difference between an individual twin's substance use and the twin pair's average, reflecting variation among individual twins that is consistent with an exposure effect of substance use on high school noncompletion [12]. Within discordant twin pairs, the within-twin-pair component would be 0.5 for the twin who used the substance and −0.5 for the twin who did not. If a within-twin-pair effect is significant, this suggests the environmental exposure contributes to early school dropout even after accounting for genetics and the shared environment. Among DZ twins, a significant within-twin pair effect may also be because of genetic influences; therefore, we formally evaluated whether this effect differed for DZ and MZ twins (i.e. genetic confounding).

The between-twin-pair coefficient is the pair average for substance use and reflects variation shared among twins. The between-twin-pair component would be 0 if both twins did not use the substance, 0.5 if one used the substance, and 1 if both used the substance. When the between-twin-pair effect is significant, this suggests that genetics or the familial environment partially account for the effect on school noncompletion.

In the first step of the discordant twin models, only the within- and between-twin-pair components were included as predictors. To assess potential genetic confounding, a within-twin-pair-by-zygosity interaction was tested. When genetic confounding is present, this means genetic influences account for part of the observed association between a predictor and the outcome. Next, partially adjusted models were fit including zygosity, sex, cohort, CD symptoms, childhood major depression, and parental educational attainment as covariates. Finally, a fully adjusted model was fit controlling for the number of additional substances used.

RESULTS

As expected, the substances most used in adolescence were alcohol (78.59%), tobacco (77.51%), and cannabis (31.99%). Few adolescents used the remaining substances (see Table 2). In general, adolescent use of any given substance was significantly (at $P < 0.01$) positively correlated with use of other substances (see Table 3). Among men, only alcohol, cocaine, and PCP were not significantly negatively correlated with high school completion. Among women, alcohol, opiates, and PCP were not significantly negatively correlated with high school completion. Several correlations were significantly different for men and women (stimulants: Fisher's $Z = 2.54$, $P < 0.01$; sedatives: Fisher's $Z = 2.35$, $P < 0.01$; hallucinogens: Fisher's $Z = 3.40$, $P < 0.01$).

Individual level models

In unadjusted models, adolescent use of all substances except alcohol was significantly associated with high school noncompletion (see Table S2 for full results). In partially adjusted models, tobacco (OR = 3.54 [1.24–10.10]), sedatives (OR = 9.98 [1.40–71.19]), and inhalants/solvents (OR = 4.81 [1.41–16.35]) remained significantly associated with high school noncompletion, whereas effects of cannabis, stimulant, and hallucinogen use became nonsignificant (see Table S2). Finally, across the fully adjusted models (see Table S3 for full results), the number of additional substances used in adolescence was strongly associated with high school noncompletion, whereas only tobacco (OR = 2.95 [1.02–8.52]) and inhalants/solvents (OR = 3.59 [1.02–12.58]) remained independently and significantly associated (see Figure 1).

Discordant twin models

In the unadjusted model, there were significant within-twin-pair effects on high-school noncompletion for cannabis (OR = 2.66 [1.78–3.97]), tobacco (OR = 2.13 [1.31–3.47]), stimulants (OR = 5.16 [1.99–13.40]), sedatives (OR = 15.92 [4.70–53.89]), hallucinogens (OR = 8.25 [3.01–22.60]), and inhalants/solvents (OR = 4.24 [1.79–10.05]). Between-twin-pair effects were seen for adolescent use of tobacco

TABLE 3 Correlations among adolescent substance use and high school completion

	1.	2.	3.	4.	5.	6.	7.	8.	9.	10.	11.
1. Cannabis use	–	0.26*	0.23*	0.09*	0.18*	0.09*	0.10*	0.22*	0.03	0.18*	−0.05*
2. Alcohol use	0.24*	–	0.32*	0.03	0.07*	0.02	0.05*	0.07*	0.01	0.09*	0.00
3. Tobacco use	0.23*	0.30*	–	0.03	0.07*	0.04*	0.06*	0.07*	0.01	0.07*	−0.08*
4. Cocaine use	0.08*	0.02	0.03	–	0.22*	0.13*	0.14*	0.14*	0.16*	0.09*	−0.04*
5. Stimulant use	0.19*	0.06*	0.07*	0.30*	–	0.18*	0.23*	0.25*	0.11*	0.15*	−0.05*
6. Opiate use	0.11*	0.01	0.03	0.20*	0.23*	–	0.15*	0.11*	0.08*	0.07*	−0.02
7. Sedative use	0.15*	0.05*	0.06*	0.23*	0.28*	0.29*	–	0.14*	0.07*	0.16*	−0.06*
8. Hallucinogen use	0.23*	0.08*	0.07*	0.19*	0.40*	0.22*	0.28*	–	0.13*	0.19*	−0.04*
9. PCP use	0.05*	0.02	0.02	0.21*	0.08*	0.17*	0.15*	0.11*	–	0.12*	−0.02
10. Inhalant/solvent use	0.22*	0.08*	0.08*	0.16*	0.28*	0.17*	0.22*	0.29*	0.09*	–	−0.07*
11. High school completion	−0.06*	−0.03	−0.09*	−0.04	−0.10*	−0.06*	−0.11*	−0.11*	−0.02	−0.07*	–

Correlations for women are above the diagonal, correlations for men are below the diagonal. *Indicates $P < 0.01$. All correlations are φ coefficients.

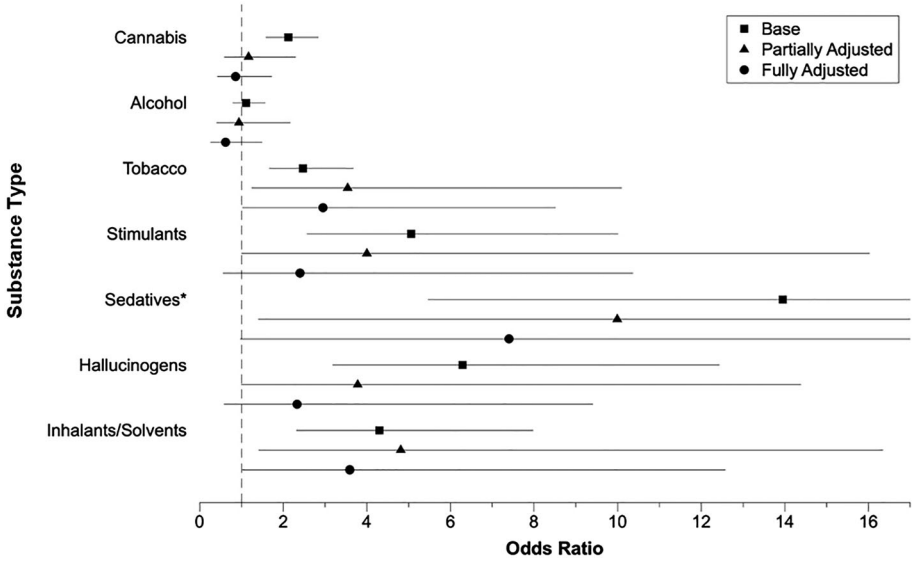

FIGURE 1 Results of the individual level models predicting high school noncompletion from adolescent substance use. *Indicates that the upper bounds of the 95% CI for model estimates are not displayed on the chart (base model upper bound = 35.61; partially adjusted model upper bound = 71.19; fully adjusted model upper bound = 56.54)

(OR = 3.19 [1.79–5.68]), sedatives (OR = 27.38 [1.97–379.78]), hallucinogens (OR = 6.44 [1.19–34.97]), and inhalants/solvents (OR = 6.74 [1.66–27.42]). There was evidence for genetic confounding in the effects of adolescent stimulant (interaction OR = 0.04 [0.005–0.29]) and sedative (interaction OR = 0.03 [0.003–0.30]) use, such that within-twin-pair effects were greater among DZ compared to MZ twins.

In partially adjusted models, significant within-twin-pair effects remained for tobacco (OR = 3.93 [1.14–13.52]), sedatives (OR = 30.52 [1.86–501.25]), and inhalants/solvents (OR = 16.07 [2.03–127.29]) whereas all between-twin-pair effects became nonsignificant (Table 4). Once co-occurring substance use was accounted for, the only substances for which within-twin-pair effects remained significant were sedatives (OR = 22.39 [1.18–423.48]) and inhalants/solvents (OR = 10.46 [1.30–84.16]) (Table 5).

DISCUSSION

Within this sample of adult Australian twins, adolescent use of all psychoactive substance types (except alcohol) was associated with not completing high school. However, when covariates were included and a genetically informative approach was taken, associations seemed largely because of confounding factors, such as parental education, childhood behavior problems, and co-occurring polysubstance use. After accounting for confounding factors, sedatives and inhalants/solvents were the only two substances for which a substance-using twin had significantly higher odds of not completing high school compared to their non-substance-using co-twin. Given that there were no significant within-twin-pair effects of adolescent substance use on college completion (see Supporting information), effects of sedatives

TABLE 4 Results of the partially adjusted discordant twin models predicting high school noncompletion from adolescent use of each type of substance

	Cannabis OR (95% CI)	*Alcohol* OR (95% CI)	*Tobacco* OR (95% CI)	*Stimulants* OR (95% CI)	*Sedatives* OR (95% CI)	*Hallucinogens* OR (95% CI)	*Inhalants/solvents* OR (95% CI)
Between-twin-pair effect	1.57 (0.53–4.62)	1.19 (0.32–4.47)	3.61 (0.79–16.58)	1.51 (0.08–27.02)	23.12 (0.12–4404.14)	2.67 (0.16–43.82)	1.76 (0.11–27.94)
Within-twin-pair effect	0.94 (0.38–2.30)	0.90 (0.29–2.76)	**3.93 (1.14–13.52)**	6.23 (0.76–51.13)	**30.52 (1.86–501.25)**	5.55 (0.74–41.86)	**16.07 (2.03–127.29)**
Sex (reference = male)	0.84 (0.40–1.77)	0.83 (0.39–1.76)	0.80 (0.38–1.70)	0.86 (0.41–1.83)	0.76 (0.36–1.60)	0.86 (0.41–1.83)	0.90 (0.42–1.92)
Zygosity (reference = DZ)	0.87 (0.38–2.01)	0.86 (0.37–2.00)	0.91 (0.39–2.10)	0.84 (0.36–1.95)	0.85 (0.37–1.97)	0.85 (0.37–1.97)	0.86 (0.37–2.00)
Cohort (reference = ATR2)	0.42 (0.16–1.06)	0.47 (0.20–1.13)	0.48 (0.20–1.16)	0.46 (0.19–1.09)	0.45 (0.19–1.07)	0.46 (0.19–1.10)	0.46 (0.19–1.10)
Conduct disorder symptoms	**1.85 (1.46–2.34)**	**1.89 (1.50–2.37)**	**1.79 (1.42–2.25)**	**1.84 (1.46–2.31)**	**1.79 (1.43–2.26)**	**1.84 (1.47–2.31)**	**1.84 (1.46–2.33)**
Childhood major depression	1.74 (0.68–4.46)	1.76 (0.69–4.51)	1.72 (0.67–4.44)	1.67 (0.65–4.31)	1.53 (0.59–4.02)	1.67 (0.65–4.32)	1.70 (0.65–4.44)
Mother's education	0.69 (0.47–1.03)	0.70 (0.47–1.04)	0.70 (0.47–1.04)	0.69 (0.47–1.03)	0.70 (0.47–1.04)	0.69 (0.46–1.02)	0.69 (0.46–1.03)
Father's education	**0.50 (0.34–0.74)**	**0.50 (0.34–0.74)**	**0.51 (0.34–0.75)**	**0.50 (0.34–0.73)**	**0.49 (0.33–0.73)**	**0.47 (0.35–0.76)**	**0.49 (0.33–0.72)**

DZ = dizygotic, OR = odds ratio, CI = confidence interval.
Bold indicates significance at $P < 0.05$.

TABLE 5 Results of the fully adjusted discordant twin models predicting high school noncompletion from adolescent use of each type of substance

	Cannabis OR (95% CI)	*Alcohol* OR (95% CI)	*Tobacco* OR (95% CI)	*Stimulants* OR (95% CI)	*Sedatives* OR (95% CI)	*Hallucinogens* OR (95% CI)	*Inhalants/Solvents* OR (95% CI)
Between-twin-pair effect	0.97 (0.32–2.97)	0.64 (0.17–2.46)	2.60 (0.56–11.97)	0.61 (0.02–12.37)	29.80 (0.05–16307.80)	1.40 (0.08–26.06)	1.44 (0.09–23.39)
Within-twin-pair effect	0.71 (0.29–1.79)	0.63 (0.20–2.00)	3.42 (1.00–11.72)	3.77 (0.43–32.89)	**22.39 (1.18–423.48)**	3.06 (0.40–23.46)	**10.46 (1.30–84.16)**
Sex (reference = male)	0.88 (0.41–1.88)	0.86 (0.40–1.83)	0.87 (0.41–1.86)	0.94 (0.44–2.00)	0.83 (0.39–1.77)	0.92 (0.43–1.95)	0.94 (0.44–2.00)
Zygosity (reference = DZ)	0.87 (0.37–2.05)	0.89 (0.38–2.07)	0.91 (0.39–2.12)	0.89 (0.39–2.07)	0.88 (0.38–2.04)	0.89 (0.38–2.06)	0.89 (0.38–2.07)
Cohort (reference = ATR2)	0.43 (0.17–1.10)	**0.34 (0.14–0.82)**	**0.38 (0.16–0.93)**	**0.36 (0.15–0.88)**	**0.37 (0.15–0.90)**	**0.37 (0.15–0.89)**	**0.38 (0.16–0.94)**
Conduct disorder symptoms	**1.64 (1.29–2.10)**	**1.60 (1.26–2.03)**	**1.63 (1.28–2.07)**	**1.63 (1.29–2.08)**	**1.62 (1.27–2.06)**	**1.64 (1.29–2.08)**	**1.66 (1.30–2.13)**
Childhood major depression	1.49 (0.56–3.96)	1.47 (0.56–3.86)	1.49 (0.57–3.92)	1.48 (0.56–3.89)	1.41 (0.53–3.74)	1.48 (0.56–3.88)	1.54 (0.58–4.07)
Mother's education	0.67 (0.45–1.00)	**0.66 (0.44–0.98)**	0.68 (0.45–1.01)	0.67 (0.45–1.00)	**0.67 (0.45–0.99)**	0.67 (0.45–1.00)	0.67 (0.45–1.00)
Father's education	**0.49 (0.33–0.73)**	**0.51 (0.35–0.75)**	**0.51 (0.35–0.74)**	**0.51 (0.35–0.74)**	**0.49 (0.33–0.72)**	**0.51 (0.35–0.75)**	**0.49 (0.33–0.73)**
No. of additional substances used	**2.32 (1.48–3.65)**	**2.14 (1.45–3.15)**	**1.54 (1.08–2.20)**	**1.69 (1.20–2.39)**	**1.56 (1.12–2.18)**	**1.65 (1.17–2.34)**	**1.50 (1.06–2.12)**

DZ = dizygotic, CI = confidence interval, OR = odds ratio.

and inhalants/solvents may be temporally limited and specific to the high school completion milestone.

Adolescent sedative use in the sample primarily involved use of diazepam (Valium; 44.89% of users), temazepam (Restoril; 43.59% of users in ATR-III; not assessed in ATR-II), oxazepam (Serepax; 40.90% of users), and flunitrazepam (Rohypnol; 23.86% of users). These drugs (also known as benzodiazepines) are commonly misused in conjunction with other substances, particularly alcohol and opiates [25]. Consistent with this, 93.45% of participants who used sedatives in adolescence also endorsed using alcohol and 20.24% reported using opiates (compared to an overall sample prevalence of 1.41%). Effects of benzodiazepines on cognition have been a controversial area of research [26], but reviews of chronic use have tended to conclude that there are potentially long-term effects on both implicit and explicit memory [26, 27]. However, it is unclear to what extent these effects may be present among adolescents who do not yet have a history of chronic use.

Another possibility is that high rates of opiate use among adolescents who use sedatives (more than 14 times the rate in the overall sample) may explain the observed association with high school noncompletion. Opiate use could not be examined directly as a predictor because of low prevalence rates within the sample, but sedatives were the substance most strongly correlated with adolescent opiate use (r = 0.21). However, when we re-ran the fully adjusted model covarying adolescent opiate use to evaluate this possibility, the change in the within-twin-pair effect of sedative use was negligible (from OR = 22.39 to OR = 21.64). Future research should more directly explore effects of opiate use on education and investigate the role of co-occurring sedative use.

For sedatives, it is important to mention that there was evidence of significant genetic confounding. Therefore, shared genetic factors likely account for part of the observed association between the use of sedatives in adolescence and high school noncompletion. Follow-up analyses revealed that adolescent sedative use and high school noncompletion had a perfect to near-perfect genetic correlation (r_g = 1.00 [1.00 to 0.69]). Therefore, genes that confer risk for adolescent sedative use may also confer risk for early school dropout. This is consistent with studies of measured genes, which have found that educational attainment is negatively genetically correlated with substance use phenotypes [28], although there are exceptions to this pattern for certain alcohol use phenotypes [29, 30].

The effect of inhalants/solvents on high school noncompletion could not be accounted for by confounding factors. Within the current sample, the most used inhalants/solvents during adolescence were nitrous oxide (laughing gas; 53.73%), amyl nitrate (poppers; 42.29%), glue (34.41%), petrol (23.66%), and lighter fluid (23.12%). Unlike sedatives, where the drugs' potential effects on cognition have been controversial and somewhat unclear, the cognitively impairing effects of inhalant use are known and acknowledged [31–33]. Animal models suggest adolescent users may be at especially high risk for neurotoxic effects [34], in part because of adolescents showing reduced sensitivity to initial effects of toluene (one of the primary chemicals responsible for the drug's high) while at the same time being more vulnerable to experiencing neurological impairments given maturational processes occurring during this developmental period [34–36]. Cognitive impairments appear to persist even after a period of abstinence [31]. Given that inhalants are often one of the first substances used by adolescents [37, 38] and are widely available, systematic prevention and intervention approaches that include families and schools [39,40] are needed to prevent the substantial cognitive and behavioral outcomes of inhalant use, including possible increases in early school dropout.

Unexpectedly, unlike previous studies [13–15], we did not find effects for adolescent alcohol use. This may be in part because of differences in our measurement of alcohol use. For example, Rose and colleagues [14] examined twin pairs discordant for drinking problems [41], and Waldron and colleagues [15] used a drinking index comprised of measures of early first drink, early first intoxication, and alcohol consumption (the number of lifetime intoxications, past year frequency of drinking, average drinks per occasion, and max drinks). Although one of the measures used by Grant and colleagues [13] was the same as our own (i.e. using alcohol before age 18), they also examined twins discordant for lifetime alcohol dependence and found stronger effects on college noncompletion for that measure than for any use, although both were significant. Therefore, it may be that heavy drinking or experiencing alcohol problems in adolescence is more predictive of early school dropout than any use.

These results highlight the role of polysubstance use in educational noncompletion. Co-occurring substance use was significantly associated with high school noncompletion, and its inclusion in models diminished the effect of adolescent use of any substance, with the effect becoming non-significant in most instances. These findings are consistent with a previous study that found polysubstance use increased the risk of high school noncompletion beyond the risk because of use of a single substance [42]. As the wide-ranging hazards of polysubstance use become well-recognized [17,43–46], further examination of the role of polysubstance use in educational attainment is warranted.

Limitations

Despite several strengths, there were limitations to the current study. First, data on adolescent substance use were collected retrospectively (~12–13 years later), which may have led to inaccurate or biased recall [47, 48]. Based on a subset of participants, 4-year test–retest reliabilities (ICCs) for self-reports of adolescent substance use ranged from 0.62 for tobacco to 0.87 for opiates, with an average reliability across substances of 0.74. This level of reliability is close to the standard guideline of 0.75, which is indicative of good reliability when true changes on a measure are viewed as negligible [49], and it is higher than average levels of 1-year test–retest reliability observed in another nationally representative study [48]. Regardless, future research could benefit from using prospective measures of adolescent substance use to predict later educational attainment.

A second concern is related to power to detect effects for certain substances. For the least powered of the discordant twin analyses (i.e. sedatives), the smallest OR that we were well-powered to detect was 2.36. ORs >2 were required for adequate power to detect effects of stimulant and hallucinogen use. The consequence of low power can be seen in imprecision of the estimates obtained for these substances. Although this is certainly a limitation, it must be recognized that these substances have low prevalence rates in adolescence, and we were only able to conduct these analyses by combining two large cohorts of the Australian Twin Registry.

CONCLUSION

Adolescent substance use is associated with early school dropout, with the effects of any given substance largely because of the confounding factors of parental education, childhood conduct disorder symptoms, and use of other substances. Two exceptions to this were sedatives and inhalants/solvents. These substances had effects on high school noncompletion that could not be explained by polysubstance use or familial factors. There may be specific mechanisms by which these substances produce changes that lead to impairments and reduced education. These mechanisms are less clear for sedatives, but for inhalants/solvents, severe neurotoxic effects may be to blame.

More generally, these results show polysubstance use should be considered when attempting to evaluate the effects of specific substances. Its exclusion may lead to incorrect conclusions about the harms of any specific substance; for example, before controlling for use of other substances, it appeared there were significant within-twin-pair effects of adolescent tobacco use, but this effect became non-significant once other substance use was accounted for. By continuing to evaluate the effects of specific substances, along with more general effects of polysubstance use, we may develop a clearer understanding of the role of substance use in educational attainment and other important life outcomes.

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DECLARATION OF INTERESTS

None to declare.

AUTHOR CONTRIBUTIONS

Ian R. Gizer: Supervision. **Michael T. Lynskey:** Funding acquisition; project administration. **Dixie J. Statham:** Project administration. **Andrew C. Heath:** Project administration. **Nicholas G. Martin:** Project administration; resources. **Wendy S. Slutske:** Resources; software; supervision.

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