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PRESS RELEASE

Cannabis and progression to other substance use in young adults: findings from a 13-year prospective population-based study

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ABSTRACT

Background Adolescent cannabis use predicts the onset of later illicit drug use. In contrast, little is known about whether cannabis in young adulthood also predicts subsequent progression or cessation of licit or illicit drug use.

Methods 13-year longitudinal cohort study with recruitment in secondary school students in Victoria, Australia. There were six waves of adolescent data collection (mean age 14.9—17.4 years) followed by three in young adulthood (mean age 20.7, 24.1 and 29.0 years). Discrete-time proportional hazards models were used to assess predictive associations between cannabis use frequency (occasional (<weekly), weekly to less than daily and daily) in 1756 participants in earlier young adult waves and subsequent cigarette smoking, high-risk alcohol use and amphetamine, ecstasy and cocaine use, including incident use (uptake) and cessation in later young adult waves.

Results Compared with continuing occasional cannabis use: (1) never use provided the strongest protection from uptake of all drugs; (2) quitting cannabis lowered rates of illicit drug use uptake; (3) weekly+cannabis users had two to three times the rates of illicit drug use uptake, while daily users had six times the rate of uptake of cigarette smoking; and (4) never use of cannabis was associated with higher rates of cessation from licit drug use, while daily cannabis predicted lower cessation rates for all drugs except cocaine.

Conclusions This study provides compelling evidence of the continuing association between cannabis, licit and other illicit drug use well into young adulthood. Preventing cannabis use uptake and use escalation remain crucial health aims given the burden associated with cigarette, alcohol and illicit drug use.

BACKGROUND

Adolescence brings shifts in lifestyle and social roles that coincide with experimentation with cannabis and other drugs. The relationship between adolescent cannabis use and a variety of adverse health and life outcomes has been an important recent research focus. In addition to increasing the risk of future problematic cannabis use,[1–3] educational failure[4] and poor social adjustment in young adulthood,[5 6] regular cannabis use has been found to increase the risk of subsequent use of other illicit drugs, such as amphetamine and cocaine.[7–10]

The 'gateway' theory of drug use posited a central positioning of cannabis in a sequence of drug involvement commencing with tobacco and alcohol use, with cannabis use preceding initiation into use of other illicit drugs and increasing the likelihood of their use.[11] There remains uncertainty about whether the association between cannabis and subsequent illicit drug use reflects characteristics of people who use cannabis, the effects of the drug itself or other uncontrolled confounders in the available studies.[12–15]

Cannabis use is believed to peak in early adulthood, with a decline from the mid-20s, perhaps due to new roles and responsibilities.[16–18] Few studies have examined the question of whether cannabis use may affect the natural history of other illicit drug use in young adulthood—for example, patterns of progression, cessation and relapse—as well as the initiation of use. This is particularly relevant in more recent birth cohorts in which there has been a notable rise in the prevalence of cannabis use and the use of amphetamines and ecstasy among young adults, coupled with a decrease in the age of initiation of drug use.[19 20]

The effect of cannabis use on the natural history of alcohol and tobacco use has also received little attention. This is of substantial public health importance given the enormous preventable health burden associated with the latter substances. Tobacco and alcohol are typically initiated prior to cannabis use, and the prevalence of their use across the lifespan is higher. Regular adult cigarette smoking patterns are commonly established during adolescence,[21] and adolescent tobacco smoking increases the odds of problematic cannabis use in young adulthood, even after adjusting for frequency of adolescent cannabis use.[3] There is a growing body of data suggesting that cannabis use may predict transitions into, and maintenance of, tobacco use.[22–24] There is some evidence that adolescents may select into early distinct cannabis and alcohol use trajectories, but whether cannabis use affects later uptake and persistence of alcohol use is uncertain.[8 25]

In this paper, we extend previous work on the relationships between cannabis and other drug use in young adulthood by investigating the:

1. cross-sectional relationships between cannabis use frequency and cigarette smoking, high-risk alcohol use and amphetamine, cocaine and ecstasy use over time; and
2. prospective associations between patterns of earlier cannabis use and incident use and cessation of licit and illicit drug use, after controlling for potential confounding factors.

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METHODS

Sample

Between August 1992 and January 2008, we conducted a nine-wave cohort study of health in adolescents and young adults in Victoria, Australia. The cohort was a representative sample of Victorian mid-secondary school adolescents in 1992, defined in a two-stage cluster sample. The first phase of sampling was by school and the second by classroom, with two classes selected at random from a state-wide sample of 44 schools, one class entering the study in the latter part of the ninth school year (wave 1) and the second class 6 months later (wave 2). School retention rates to year 9 in the year of sampling were 98%. Potential participants absent at the time of surveying in waves 1 and 2 were invited to take part in subsequent waves, but still in the same year level as other cohort participants. Thus, variation within wave in the adolescent phase was consistent with the variation you would find in any classroom. Participants were interviewed at four 6-month intervals during the teens (waves 3–6) with three follow-up waves in young adulthood, aged 20–21 years (wave 7), 24–25 years (wave 8) and 29 years (wave 9). In waves 1–6, participants self-administered the questionnaire on laptop computers with telephone follow-up of those absent from school. From a total sample of 2032 students, 1943 (95.6%) participated at least once during the first six (adolescent) waves (figure 1). The seventh to ninth waves were undertaken using computer-assisted telephone interviews,[26] with 1756 (53% female) participating in at least one of these waves and known to be alive at the time of the wave 9 survey. Of these, 1282 completed all three young adult waves, 293 completed two and 181 completed one only. Wave 9 interviews were completed by January 2008, at which time, 15 cohort members were known to have died, 108 were lost to follow-up and 319 refused to participate.

Measures

Background measures included sex, school location at study inception (metropolitan Melbourne or rural), parental education (not tertiary, tertiary), parental smoking status and parental divorce/separation during the participant's adolescence.

Cannabis use: Participants reported their frequency of cannabis use. We identified non-use, less than weekly use ('occasional'), weekly but less than daily use ('weekly') or almost daily use ('daily'). In the prospective analysis of incidence and cessation of other drugs at waves 8 and 9, cannabis non-users at the previous waves (7 and 8, respectively) were reclassified as previous users (not currently using but reported using in at least one earlier wave) and non-users.

Cigarette smoking: Participants who reported smoking any cigarettes in the past month were classified as cigarette smokers.

Alcohol use was assessed using a beverage- and quantity-specific 1-week diary.[27] *Long-term high-risk alcohol use* was calculated according to Australian guidelines[28] from the total alcohol consumed during the week prior to survey and defined as exceeding 14 standard drinks (1 standard drink=10 g alcohol) in the week prior to survey.

Illicit substance use other than cannabis use was defined as use in the past year of ecstasy/designer drugs and cocaine at waves 7–9 and amphetamines for waves 2–9.

Incident (new) cigarette smoking and high-risk alcohol use was identified at waves 8 and 9 in participants who had not previously reported this, including in adolescence. Incident cocaine and ecstasy use was identified at waves 8 and 9 in participants who had not reported use at a previous adult wave. Participants who used amphetamines in adolescence were deemed ineligible for incident uptake at waves 8 or 9.

Cessation was defined at waves 8 and 9 as a report of not using cigarettes, amphetamine, cocaine or ecstasy or as drinking alcohol below the high-risk threshold among those who reported use in the previous wave.

Analysis

The prevalence of licit and illicit drug use in the adult waves (7–9) and cross-sectional associations between frequency of cannabis use and other concurrent drug use were estimated. Associations between background factors and cigarette smoking, high-risk alcohol use, cannabis use and any other illicit drug use at waves 7–9 were assessed using logistic regression models fitted using generalised estimating equations to allow for repeated measures within individuals. Discrete-time proportional hazards models, using robust SEs, were used to model associations between both incidence of other drug use and cessation of other drug use, and the frequency of cannabis use at the previous wave. As the young adult survey periods were longer than those in the adolescent phase, resulting in a larger spread of ages, we adjusted for age in these analyses (table 1).

While there was little missingness on individual measures for each survey completed, we used multiple imputation to address potential bias and loss of information arising from respondents' missing waves.[29] Of the 59 outcome, background and auxiliary variables included in the multiple imputation model, 4 variables were completely observed, 12 had <10% missing, 32 had 10% to <20% missing and 11 had >20% missing. No variable was missing for >25% of participants. We imputed 20 complete data sets under a multivariate normal model using adaptive rounding for binary measures.[30] The analysis included only those participants who had been seen at least once in adolescence (waves 2–6) and at least once in adulthood (waves 7–9); wave 1 was omitted as it contained observations from only 46% of the cohort, and participants with no adult phase observations were omitted as they contained too little information. Thirty-three participants had responded to one or more adult waves but were only seen once in adolescence at wave 1, and we included these individuals by bringing forward their wave 1 observations to wave 2. Thus, the analysis data set was defined by participation in at least one of the young adult waves (waves 7–9) and known to be alive at the time of the wave 9 survey (n=1756).

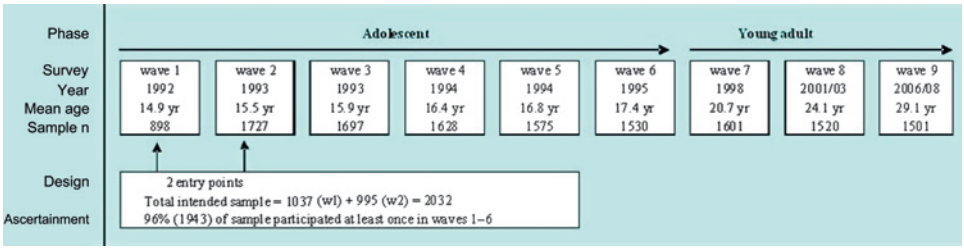

Figure 1 Sampling and ascertainment in the Victorian Adolescent Health Cohort, 1992–2008.

Table 1 Cannabis use as a predictor of incident uptake and cessation from licit or illicit drug use at 24 and 28 years (waves 8 and 9) in 1756 cohort participants, adjusted for possible background confounders

Outcome transition exposure	Cigarettes HR* (95% CI)	High-risk alcohol HR (95% CI)	Amphetamine HR* (95% CI)	Cocaine HR (95% CI)	Ecstasy HR (95% CI)
Incident uptake	n=106†	n=274	n=212	n=208	n=352
Cannabis use in the previous wave					
Never user	0.44 (0.25 to 0.76)	0.45 (0.33 to 0.62)	0.23 (0.14 to 0.40)	0.15 (0.08 to 0.28)	0.18 (0.12 to 0.27)
Past user‡	0.52 (0.21 to 1.3)	0.72 (0.43 to 1.2)	0.52 (0.31 to 0.88)	0.53 (0.30 to 0.93)	0.37 (0.24 to 0.58)
Occasional	1	1	1	1	1
Weekly	1.4 (0.36 to 5.2)	1.3 (0.74 to 2.4)	2.6 (1.7 to 4.1)	2.3 (1.5 to 3.5)	2.1 (1.5 to 3.0)
Daily	6.1 (2.7 to 13)	1.5 (0.83 to 2.8)	2.9 (1.7 to 4.8)	1.9 (1.2 to 3.2)	2.8 (2.0 to 4.0)
Cessation	n=352	n=427	n=173	n=110	n=221
Cannabis use in the previous wave					
Never user	1.6 (1.1 to 2.3)	1.5 (1.1 to 2.1)	1.2 (0.37 to 3.6)	7.0 (0.42 to 117)	1.4 (0.57 to 3.4)
Past user	1.3 (0.97 to 1.8)	0.94 (0.68 to 1.3)	0.67 (0.35 to 1.3)	1.1 (0.48 to 2.3)	1.5 (0.93 to 2.3)
Occasional	1	1	1	1	1
Weekly	0.90 (0.60 to 1.4)	0.81 (0.56 to 1.2)	0.67 (0.42 to 1.1)	0.75 (0.40 to 1.4)	0.73 (0.49 to 1.1)
Daily	0.59 (0.37 to 0.93)	0.66 (0.42 to 1.0)	0.57 (0.36 to 0.91)	0.79 (0.45 to 1.4)	0.65 (0.42 to 1.0)

*HRs from multivariable discrete-time proportional hazards models, adjusted for sex, age, school location at study inception, parental divorce/separation, parental smoking status and parental tertiary education, using robust SEs to allow for repeated measures within individuals.
†'n' denotes the number of events across both waves 8 and 9.
‡Reported cannabis use at a wave prior to the at-risk interval for incident transition or cessation, that is, participants who reported using any cannabis in adolescence (waves 2–6) were identified, and this information was used to determine whether non-users in wave 7 were actually 'past users' (they had used prior to the index wave). Similarly, wave 8 non-users were deemed 'past users' if they reported adolescent use or use in wave 7.

Low prevalence of amphetamine use in waves 2–6 precluded imputation, so amphetamine use was assumed to be absent in these waves when not completed. All frequencies and ORs were obtained by averaging results across the imputed data sets with inferences under multiple imputation obtained using Rubin's rules.[29 31] All analysis was undertaken using Stata 11.[32]

RESULTS

There was a decrease in the prevalence of cigarette smoking from 24 to 29 years, while high-risk alcohol use remained fairly stable (table 2). A decreased prevalence of any 12-month cannabis use was largely driven by decreased occasional use, resulting in an *increase* in the relative frequency of regular (weekly+) use among all users: 20 years: 24% (95% CI 22 to 27); 24 years: 36% (95% CI 32 to 40); 29 years: 39% (95% CI 35 to 44). In comparison, the overall 12-month prevalence of other illicit drug use increased markedly, albeit from much lower levels. By 29 years, one in five participants reported using amphetamine, ecstasy or cocaine in the past 12 months compared with one in four who used cannabis.

From ages 20–29 years, the prevalence of 12-month cigarette smoking and high-risk alcohol use was consistently higher among those reporting at least weekly (although not necessarily daily) cannabis use (figure 2). Twelve-month amphetamine, cocaine or ecstasy use was virtually non-existent among non-users of cannabis. While use of these drugs was more likely among more regular cannabis users at 20 and 24 years, by 29 years, the association between cannabis use frequency and other illicit drug use was less clear, particularly for cocaine.

Table 3 describes the associations between background factors and cannabis, high-risk alcohol, cigarette and other illicit drug use in young adulthood. Age, male sex, attending a metropolitan school and parental tertiary education, divorce/separation and cigarette smoking were associated with use of at least one type of substance during the young adult phase (table 3). We therefore adjusted for these potential confounders in all models.

Other drug use uptake

Table 1 displays the associations between young adult cannabis use (ages 20 years_wave 7 and 24 years_wave 8) and rates of incident uptake and cessation of cigarette smoking, high-risk alcohol consumption and amphetamine, cocaine and ecstasy use at the subsequent wave (ages 24 years_wave 8 and 29 years_wave 9, respectively). Compared with those who reported

Table 2 Prevalence of drug use in the past 12 months at ages 20 years, 24 years and 29 years in 1756 cohort participants

Substance use in past 12 months	20 years (wave 7) % (95%CI)	24 years (wave 8) % (95% CI)	29 years (wave 9) % (95% CI)
Any cigarette smoking	40.9 (38.5 to 43.3)	39.6 (37.1 to 42.0)	34.0 (31.6 to 36.3)
High-risk alcohol use	24.5 (22.4 to 26.6)	29.2 (26.9 to 31.4)	26.4 (24.1 to 28.7)
Any cannabis use	58.4 (56.1 to 60.8)	34.1 (31.8 to 36.4)	27.7 (25.4 to 30.0)
Maximum frequency of cannabis use			
Occasional	44.1 (41.7 to 46.5)	21.8 (19.7 to 23.9)	16.8 (14.8 to 18.7)
Weekly	7.3 (6.0 to 8.5)	6.5 (5.2 to 7.7)	4.1 (3.1 to 5.2)
Daily	7.1 (5.8 to 8.3)	5.8 (4.7 to 6.9)	6.8 (5.6 to 8.0)
Any of amphetamines, cocaine, ecstasy	11.0 (9.4 to 12.5)	21.2 (19.1 to 23.3)	21.2 (19.1 to 23.4)
Amphetamines	7.7 (6.4 to 9.0)	11.1 (9.5 to 12.7)	12.5 (10.6 to 14.4)
Cocaine	3.0 (2.2 to 3.8)	8.4 (7.0 to 9.7)	8.8 (7.3 to 10.3)
Ecstasy	7.7 (6.4 to 9.0)	18.3 (16.4 to 20.2)	15.8 (14.0 to 17.7)

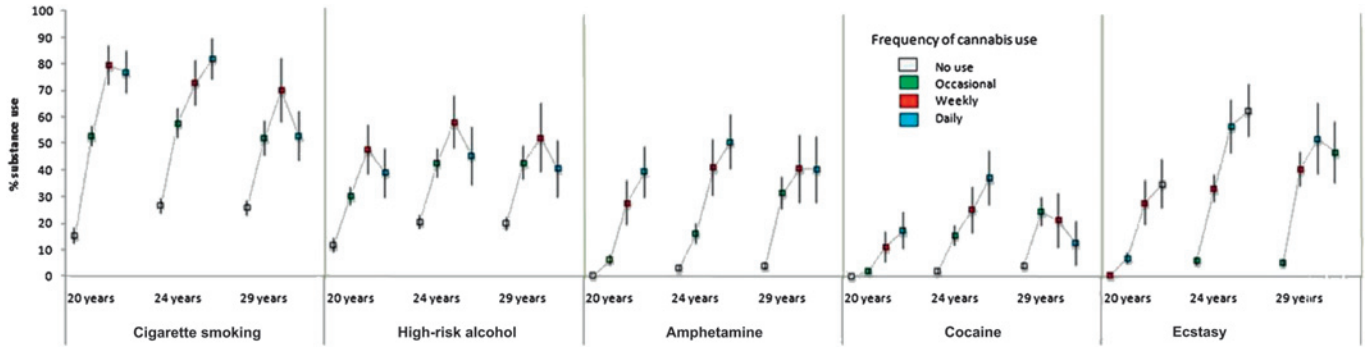

Figure 2 Prevalence of substance use at 20 years (wave 7), 24 years (wave 8) and 29 years (wave 9) in 1756 cohort participants, stratified by concurrent cannabis use at each wave. Per cents are shown with 95% CIs.

occasional cannabis use in the previous wave, never-users were clearly at reduced risk of incident use of all other drugs. Past (or 'lapsed') users had lower rates of incident use of all illicit drugs. The relatively small proportion of incident transitions (7% of never smokers) into smoking means these estimates were less precise. Participants reporting daily cannabis use had started smoking cigarettes by the next wave at six times the rate of occasional cannabis users, but there was only weak evidence that daily cannabis users were at greater risk of incident high-risk alcohol consumption. In those reporting weekly and daily cannabis use rates of subsequent incident amphetamine, cocaine and ecstasy use were consistently about two to three times the rate of those reporting occasional use.

Cessation of other drug use

Cessation of cigarette smoking and high-risk alcohol use was somewhat more likely among those who had never used cannabis compared with those reporting occasional cannabis use in the previous wave. Conversely, those using cannabis daily were less likely than occasional users to quit cigarette, high-risk alcohol, amphetamine or ecstasy use. Additional adjustment for high-risk alcohol use and cigarette smoking in the previous wave had a negligible impact on the associations between cannabis use and incidence and cessation of other illicit drug use.

CONCLUSIONS

The prevalence of cannabis use declined sharply as this cohort aged, with regular users comprising an increasing proportion of ongoing users; concomitantly, prevalence of other illicit drug use increased, consistent with Australian population data.[33] Cannabis use appeared intimately connected with the course of both licit and illicit drug use in these years beyond adolescence. We confirmed the links between adolescent cannabis use and subsequent illicit drug use[7–10] as well as its 'reverse gateway' effect on smoking uptake.[22–24 33] We found that frequent cannabis use in young adulthood was associated with increased rates of *progression* in both cigarette smoking and other illicit drug use. Never having used cannabis predicted substantially reduced rates of uptake of all other drugs. So too, quitting cannabis predicted a reduced uptake of drug use, particularly of illicit drugs.

Ongoing regular cannabis use (particularly daily use) predicted the maintenance of other drug use, markedly reducing rates of cessation of high-risk alcohol use and use of all other drugs excluding cocaine. This latter may partly reflect differing population patterns of illicit drug use in Australia during this period, with lower cocaine prevalence rates (5% reporting past year use) than amphetamine (7%) and ecstasy (11%), and more sporadic patterns of use, compared with these other drugs.[34]

Table 3 Associations between background factors and drug use from 21 to 28 years in 1756 cohort participants

Background factor	N	Cannabis use OR* (95% CI)	High-risk alcohol OR (95% CI)	Cigarette smoking OR (95% CI)	Any of amphetamine, cocaine, ecstasy OR (95% CI)
Age at wave (years)		0.9 (0.85 to 0.88)	1.01 (1.00 to 1.03)	1 (0.96 to 0.98)	1.08 (1.06 to 1.10)
Sex					
Female	931	1	1	1	1
Male	825	1.9 (1.6 to 2.2)	4.3 (3.6 to 5.1)	1.3 (1.1 to 1.6)	2.0 (1.6 to 2.4)
School at study inception					
Metropolitan	1299	1	1	1	1
Rural	457	0.9 (0.74 to 1.0)	1.3 (1.1 to 1.5)	0.9 (0.76 to 1.1)	0.7 (0.56 to 0.90)
Parental education					
Not tertiary	1183	1	1	1	1
Tertiary	573	1.3 (1.1 to 1.5)	1.2 (1.0 to 1.4)	0.9 (0.72 to 1.0)	1.4 (1.1 to 1.7)
Parental divorce/separation					
No	1369	1	1	1	1
Yes	387	1.6 (1.3 to 1.9)	1.2 (0.94 to 1.4)	1.6 (1.3 to 1.9)	1.3 (1.1 to 1.7)
Parental smoking					
No	1066	1	1	1	1
Yes	690	1.3 (1.1 to 1.5)	1.1 (0.95 to 1.3)	1.9 (1.6 to 2.3)	1.2 (0.97 to 1.5)

*ORs from univariate logistic regression models, with robust SEs allowing for repeated measures within individuals.

Despite being protective in the uptake of other drugs, cannabis quitting had no clear effect on cessation of other drug use.

Given the differential association between cannabis use frequency and uptake versus cessation of different drug classes, it is likely that various mechanisms might underpin these associations. Cannabis affects dopaminergic reward systems implicated in the rewarding and reinforcing properties of several drugs, including alcohol, opioids and MDMA (ecstasy).[35–38] Recent evidence suggests that both repeated administration of tetrahydrocannabinol (THC, the main psychoactive cannabinoid in cannabis) and cannabis withdrawal may exert long-lasting functional and structural changes to this system.[39–41] Our findings on increased uptake and persistence of other substance use in regular cannabis users may also reflect psychosocial processes. Various indices of social marginalisation, such as poorer educational outcomes, unemployment and welfare dependence, as well as greater exposure to availability of drugs and more permissive attitudes towards other drug use that may be associated with regular cannabis use, might provide a conducive context and lower the barriers for engaging in other substance use.[14 42] Our data on smoking uptake and cessation suggest a reciprocal relationship between cannabis use and cigarette smoking that varies according to age and stage of drug involvement,[43] and which may be changing due to earlier initiation to cannabis use and decreasing approval of cigarette smoking. In addition to the mechanisms described above, our data on an increased likelihood of smoking among regular cannabis users may also reflect reduced barriers to smoking due to shared route of administration.[43 44] Given the sparse literature on the natural history of cannabis and other drug use in young adulthood, a better understanding of possible mechanisms underpinning these associations is an important direction for research.[45]

Kandel and colleagues' seminal longitudinal work on cannabis cessation in adulthood[42] found that, among other factors, adult social role participation, particularly marriage and parenthood, were important in shortening a cannabis use career. Our findings suggest that promoting the transitions out of cannabis use in young adulthood may also bring benefits in reducing use of other substances. However, as the likelihood of cessation also depends on earlier levels of cannabis use, delaying onset and reducing early escalation in cannabis use will also remain important.

Strengths and limitations

The main strengths of this study include the population-based sample, the high participation rates and the frequent drug use and other measures over 13 years. By definition, we can only speculate on the possible effects of non-participation at waves 7–9 on outcome patterns compared with those seen in the participants, but given the relatively high cohort retention (78% of adolescent participants), we believe that it is unlikely to have caused major biases in our results. All data were based on self-report that was not externally validated, but this has been accepted as an appropriate way in which to gain information about population behaviours.[46–48] As ecstasy and cocaine use were not measured during adolescence, it is possible that some cases of illicit drug use incidence were overstated. However, given the low population prevalence of use of these drugs among adolescents (1%–4%) and an average age of initiation of at least 20 years,[34] it is unlikely this had a notable effect on estimates. Furthermore, Australian national guidelines used to define high-risk alcohol consumption did not distinguish between binge drinking and long-term harm. As the threshold for harm is 14 standard drinks per week, this should encompass serious binge drinking. There is also potential for misclassification of drinking status as alcohol consumption was based on diary data collected for the week prior to survey. Finally, confounding by unmeasured genetic or other background factors cannot be excluded, although controlling for several important contextual factors made little difference to the estimates.

The generalisability of these data beyond Australia is supported by a general comparability between rates of cannabis use among Australian adults and adolescents in other Western countries such as New Zealand, the USA, Canada and the UK.[49] Nevertheless, it is worth considering recent research across 17 countries that revealed a strong influence of the background national prevalence of drug use on patterns of drug use initiation and progression.[15]

What is already known on this subject

- There is good evidence that adolescent cannabis use increases the subsequent risk for onset of other illicit drug use.
- In contrast, we know little about the extent to which cannabis use in young adulthood may predict subsequent escalation or maintenance of licit and illicit drug use.

What this study adds

- Continued cannabis use into young adulthood predicted greater uptake and maintenance of both licit and illicit drug use in this period.
- In contrast, quitting cannabis use predicted lower rates of progression to other illicit drug use.
- Efforts to reduce progression to higher levels of cannabis use and the promotion of cannabis quitting have the potential to reduce the disease burden associated with other drugs.

Implications

Ongoing regular cannabis use in young adulthood predicts the uptake and maintenance of licit and illicit drug use throughout this period. Whether cannabis use is a marker for other risk processes remains debatable but promotion of reduced use of cannabis in young adulthood including cannabis quitting may be a valuable and potentially cost-effective public health strategy in reducing the burden of disease associated with licit and illicit drugs.

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Competing interests None.

Ethics approval This study was conducted with the approval of the Royal Children's Hospital's Ethics in Human Research Committee and the University of New South Wales Human Research Ethics Committee.

Provenance and peer review Not commissioned; externally peer reviewed.

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