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Young-adult compared to adolescent onset of regular cannabis use: A 20-year prospective cohort study of later consequences

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Abstract

Introduction. *This paper compares consequences of cannabis use initiated after high school with those of cannabis initiation in adolescence, with estimates of the proportion of adverse consequences accounted for by adult-onset and adolescent-onset cannabis users.* ***Methods.*** *A state-representative sample in Victoria, Australia (*n *= 1792) participated in a 10-wave longitudinal study and was followed from age 15 to 35 years.* Exposure variable: *Patterns of cannabis use across 20 years.* Outcomes at age 35*: Alcohol use, smoking, illicit drug use, relationship status, financial hardship, depression, anxiety and employment status.* ***Results.*** *Substantially more participants (13.6%) initiated regular use after high school (young-adult onset) than in adolescence (7.7%, adolescent onset). By the mid-30s, both young-adult and adolescent-onset regular users were more likely than minimal/non-users (63.5%) to have used other illicit drugs (odds ratio [OR] > 20.4), be a high-risk alcohol drinker (OR > 3.7), smoked daily (OR > 7.2) and less likely to be in relationships (OR < 0.4). As the prevalence of the young-adult-onset group was nearly double of the adolescent-onset group, it accounted for a higher proportion of adverse consequences than the adolescent-onset group.* ***Discussion and Conclusions.*** *Cannabis users who began regular use in their teens had poorer later life outcomes than non-using peers. The larger group who began regular cannabis use after leaving high school accounted for most cannabis-related harms in adulthood. Given the legalisation of cannabis use in an increasing number of jurisdictions, we should increasingly expect harms from cannabis use to lie in those commencing use in young adulthood.* [Chan GCK, Becker D, Butterworth P, Hines L, Coffey C, Hall W, Patton G. Young-adult compared to adolescent onset of regular cannabis use: A 20-year prospective cohort study of later consequences. *Drug Alcohol Rev* 2021]

Key words: cannabis, adult onset, adolescent onset, regular cannabis use.

Introduction

Cannabis has been a widely-used recreational drug around the world for over half a century [1]. The Single Convention on Narcotic Drugs [2] ratified by most countries banned its recreational use but in recent years 11 US states, Canada and Uruguay have made it legal for young adults to purchase and use cannabis. For example, young adults aged 21 years and older can legally purchase recreational cannabis in California while the age of legal purchase is 18 years in some Canadian provinces. These legislative changes have been accompanied by a steady decrease in the perceived risk of using cannabis among young people [3], a decline in price and an increase in cannabis potency [4,5], all of which may increase harmful effects of use [6].

There are well-documented associations between adverse health outcomes and daily use of cannabis that begins in adolescence and continues into young adulthood [7]. Daily use is associated with impaired respiratory function, cannabis dependence, depression, anxiety and psychotic disorders [8]. One view is that adolescents are more vulnerable to the effects of regular cannabis use because of rapid neurodevelopment that occurs in the teenage years [9]. Daily use in adolescence is associated with cognitive impairment [10] and early exposure to cannabis may also increase the

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reward sensitivity to other substances and heighten risks for later abuse of, and dependence on, drugs other than cannabis [11].

The risks from later-onset cannabis use in young adults are less well understood. Most previous work has focused on regular users who first used in early to mid-adolescence but some work has suggested that a relatively small but substantial proportion of users begin regular cannabis use in early adulthood [12–14]. For example, Zhang *et al.* [13] found that 7% of their sample in the USA started using cannabis several times a month in their early 20s and their consumption progressed to weekly use in their 30s. Given the shifts in legislation in many jurisdictions, it is possible that the prevalence of late-onset initiation of cannabis use will increase among young adults over the minimum legal purchase age. This raises an important question: will later initiation of regular cannabis use in young adulthood have adverse psychosocial consequences? As the majority of previous studies have followed up adolescents only into their mid-20s, the consequences of later-onset regular cannabis use are unclear.

The aims of this study were to compare the psychosocial sequelae at age 35 of the onset of regular cannabis use in adolescence compared with young adulthood. First, we characterise longitudinal patterns of cannabis use from adolescence to mid-30s with the expectation that at least three patterns would be identified: minimal use, early adolescent onset and young adult onset [12]. Secondly, we examined the long-term sequelae in adulthood of these adolescent and young-adult patterns of initiating cannabis use; namely, other substance use, relationship status, employment or educational status, financial circumstance and mental health. Regular cannabis use has adverse effects on neurocognition and brain structure [15,16], and was associated with a range of short and long term adverse psychosocial outcomes [8]. Its impact is likely to be strongest among those who initiated regular use during adolescence, as the adolescent brain was undergoing rapid development. The existing literature shows that regular cannabis use during adolescence predicts long-term adverse psychosocial adjustment, such as dropping out of school, cognitive impairment and poor mental health in adulthood [7,8]. We thus hypothesized that adolescent onset of regular cannabis use (weekly or more frequently) would be associated with the worst psychosocial outcomes at age 35, followed by young-adult-onset and then minimal cannabis users. We also estimated the proportion of adverse outcomes in the population, accounted for by individuals who started using cannabis in mid-adolescence and in young adulthood. The latter analysis controlled for antecedent risk factors for the different patterns of cannabis use frequency (e.g. alcohol and tobacco use, depressive symptoms, antisocial behaviour and peer use) [17,18]. The analyses were complemented by thorough sensitivity analyses that evaluated the plausibility of a causal interpretation of these associations.

Methods

Participants were from the Victorian Adolescent Health Cohort Study. Between 1992 and 2014, we undertook a 10-wave cohort study of health in young people in the state of Victoria, Australia. At baseline, a representative sample of mid-secondary school adolescents was selected using a two-stage cluster sampling procedure. One classroom from each school entered the cohort in the later part of the ninth school year (Wave 1) and a second classroom 6 months later (Wave 2), early in the 10th school year. The flowchart of study participants was shown in Appendix S1. Further detail on this study design and sample is available elsewhere [19]. Of 2032 eligible students, 1943 participated at least once in the adolescent phase. A further 155 participants were excluded because they had missing data on the cannabis item in more than five waves. The present study was based on the remaining 1792 participants. The data collection protocols were approved by the Human Research Ethics Committee of the Royal Children's Hospital, Australia.

Measures

Cannabis use

From Wave 1 to Wave 6, cannabis use was measured using the item 'How often do you use marijuana?' with the response set: 'Never'; 'Not in past 6 months'; 'A few times a year'; 'Monthly'; 'Weekly' or 'Daily'. These responses were recoded into four levels: 'No use' (Combining 'Never' and 'Not in past 6 months'); 'Less than weekly' (combining 'A few times a year' and 'Monthly); 'Weekly'; and 'Daily'. From Wave 7 to Wave 10, cannabis use was measured using the item 'Thinking about the past 12 months, when you were using marijuana most frequently, about how often did you use it?' with the response set: 'No use, less than once a month'; '1 to 3 days a month'; '1 to 2 days a week'; '3 or 4 days a week'; and 'almost every day'. These responses were recoded into four levels: 'No use'; 'Less than weekly' (combining less than once a month and 1 to 3 days a month); 'Weekly' (combining 1 to 2 days a week and 3 or 4 days a week); and 'Daily'.

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Outcomes at Wave 10 (aged 35 years)

Financial hardship was measured using four items, 'Over the last 12 months, due to a shortage of money, have any of the following happened: You have not been able to pay gas, electricity or telephone bills on time; You could not pay the mortgage or rent on time; You could not afford a night out once a fortnight; or You could not afford a holiday away for at least one week a year'. A positive response to any one of the four items was coded as experiencing financial hardship. Past year *major depressive disorder* and *anxiety disorder* were defined according to International Classification of Diseases, Tenth Revision criteria, with major depressive disorder assessed using the CIDI-Auto [20] and anxiety disorder using the CIDI-Short Form [21]. Participants were classified with anxiety disorder if they were diagnosed with generalised anxiety disorder, social phobia, agoraphobia or panic disorder. *High-risk drinking* was defined as having 5 or more standard drinks (each 10 g alcohol) on at least 1 day in the week prior to data collection. Participants who reported using amphetamine, heroin, cocaine, hallucinogens, LSD or ecstasy in the past 12-months were coded as positive for *illicit drug use. Relationship status* was measured with the item 'How would you describe your current situation?: Not in a relationship; Have a boyfriend or girlfriend; Married or living with a partner'. *Employment status* was coded based on the responses to the item 'What are you doing about work at the moment?: Have a paid job; Unemployed, involved in job search; Unemployed, not involved in job search; Doing voluntary work; Working for payment in kind; None of these'. The first response was coded as 'Had a paid job' and all the others were coded as 'Not having a paid job'. *Smoking* was measured coded into 'Non-smoker', 'Occasional smoker' and 'Daily smoker'.

Potential confounders measured at Wave 2 (aged 15.5 years)

In the subsequent analysis, we compared and adjusted for potential confounders at Wave 2 instead of Wave 1, because Wave 2 was the first wave with the full sample (by design; see Methods and Appendix S1).

Symptoms of depression and anxiety were measured using the revised Clinical Interview Schedule [22]. A score of 11 or above indicated presence of symptoms of clinically significant depression and anxiety.

Antisocial behaviour was dichotomised according to whether there was a positive response to any of the 10 items from the Self Report of Early Delinquency Scale [23] which included behaviours such as property damage, theft and interpersonal violence. Participants who reported involvement in two or more behaviours, or more than once of any one behaviour, were coded as positive for antisocial behaviour.

High-risk drinking was defined as having 5 or more standard drinks (10 g alcohol) on at least 1 day in the week prior to data collection.

Peer cannabis use were measured using the items 'How many of your friends use the following: cannabis' with the response set: 'None'; 'Some'; 'Most or all'.

Analysis

Longitudinal latent class analysis was used to identify longitudinal patterns of cannabis use from adolescence to adulthood. This technique can identify subgroups in the population who show similar patterns of use over the 20-year study period. Unlike other trajectory-based modelling techniques such as growth mixture modelling and latent class growth analysis, longitudinal latent class analysis does not require a priori specification of a growth structure (such as linear or quadratic growth) and so it can better model abrupt changes in trajectory around key transitions, such as finishing high school. In addition, longitudinal latent class analysis can also better handle the small change in the cannabis use measure over the study period (past 6 month use in Wave 1 to 6 and past 12 month use from Wave 7 onwards) as this technique did not require the measure to be the same [24]. Details about model selection criteria were shown in Appendix 1.

We then examined the association between Wave 10 outcomes and longitudinal patterns of cannabis use using regression analyses, with a focus on comparisons between young-adult-onset users, minimal users and adolescent-onset users. Each participant was weighted in the regression analysis using the Bolck–Croon–Hagenaars weights described in Vermunt [25] to account for uncertainty in membership classification. Missing data in the latent class analysis was handled using full information maximum likelihood estimation. In the regression analyses, missing data were imputed in 20 datasets using multiple imputation [26]. Latent class analyses were conducted using Mplus 7.3 and the imputation, profile and regression analyses were conducted in STATA 14.

To evaluate the robustness of our results and the plausibility of a causal interpretation, we conducted sensitivity analyses using *E*-values to evaluate the plausibility of the associations being explained by residual confounding [27]. Although longitudinal analyses can establish the temporal relationship between an

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exposure and outcome, a key threat to causal interpretation is that there may be unmeasured confounders that confounded the association. The *E*-value approach evaluates the plausibility of uncontrolled confounding by quantifying the strength of confounding that is required to completely account for the observed associations. An *E*-value represented the minimum strength of association that an unmeasured set of confounders would need to have with both exposure (cannabis use group) and the outcome (e.g. illicit substance use) to fully explain the association [27]. As such, under a longitudinal design with adjustment for key known confounders (e.g. adolescent substance use, anti-social behaviour and peer's cannabis use), a high *E*-value, in a context of few obvious strong confounders, suggests that an association is at least partially causal.

Results

The prevalence of cannabis use from Wave 1 to Wave 10 was low during high school (<20%), with most participants reporting less than weekly cannabis use (see Appendix S2, Figure 2 for detailed consumption level in the sample). The prevalence of cannabis use increased across adolescence, from 11.3% in Wave 1 (mean age: 14.9 years) to 18.7% in Wave 6 (mean age: 17.4 years). After high school, the prevalence increased markedly to 58.6% in Wave 7 (mean age: 20.7 years) before decreasing steadily to 13.6% by Wave 10 (mean age: 35.1 years).

Longitudinal patterns of cannabis use

The longitudinal latent class analysis identified four patterns of cannabis use: 'Minimal or non-use (n = 1139; 63.5%)'; 'Consistent occasional use (n = 272, 15.2%)'; 'Adolescent onset regular use (n = 138, 7.7%)'; and 'Young-adult onset regular use (n = 243, 13.6%)'. Model fit statistics and detailed model selection processes for the longitudinal latent class analysis are provided in Appendix S3. Figure 1 shows the probabilities of using cannabis at different frequencies for each pattern class. Detailed descriptions of these classes are provided in Appendix S4. It should be noted that the young-adult-onset regular use group, while the probability of weekly or daily use was lower than that for less than weekly use, the probability of using cannabis weekly or more often in at least one adult wave was over 0.75.

Profile of different patterns at Wave 2 (age: 14.9) and at Wave 10 (age: 35.1)

Table 1 (top half) shows the profiles of each class at Wave 2. Occasional users and adolescent-onset regular users reported the larger proportions of high-risk drinking, tobacco smoking, antisocial behaviour during adolescence, peers who smoked and used cannabis, and highest levels of depressive and/or anxiety symptoms. The levels of peer smoking and cannabis use, and personal alcohol and tobacco use, for the young-adult-onset use group were between those of the minimal use group and the other two cannabis using classes. Overall, the profile of young-adult-onset regular use group at Wave 2 was more similar to the minimal use group than the occasional and adolescent-onset regular use group. Detailed results of the regression analysis examining associations between Wave 2 correlates and cannabis use patterns are shown in Appendix S5 because these associations were not the focus of this paper.

Table 1 (bottom half) shows the profiles of each class at Wave 10. The substance use profiles of the young-adult and adolescent-onset regular use group were similar and their levels of use higher than those of occasional and minimal use. For example, less than 1% of the minimal/non-use group and 14% of the occasional use group reported illicit substance use, compared to 49% and 37% in the adolescent and young-adult-onset regular use group. Those in the adolescent-onset regular use group reported higher levels of anxiety and depression than the other three cannabis use groups.

Prediction of Wave 10 outcome

Table 2 (first three columns, from left to right) shows the class prediction of outcomes at Wave 10, relative to minimal use. After adjusting for potential confounders measured at Wave 2 (see footnotes in Table 2), no pattern of cannabis use was significantly associated with financial hardship and anxiety at 35 years. All cannabis use groups reported high-risk alcohol use [adjusted odds ratio (AOR) >1.7] and use of other illicit drugs (AOR >8.6). Both young-adult and adolescent-onset regular use groups were less likely to be in a relationship (AOR 0.3, 95% confidence interval; CI [0.3, 0.7] and AOR 0.3, 95% CI [0.1, 0.6]) than minimal or non-use groups. The adolescent-onset regular user group had a higher risk of depression than the minimal use group (AOR 2.9, 95% CI [1.2, 6.7]).

Table 2, columns 4 and 5, shows the class prediction of outcomes compared to the 'Occasional use'

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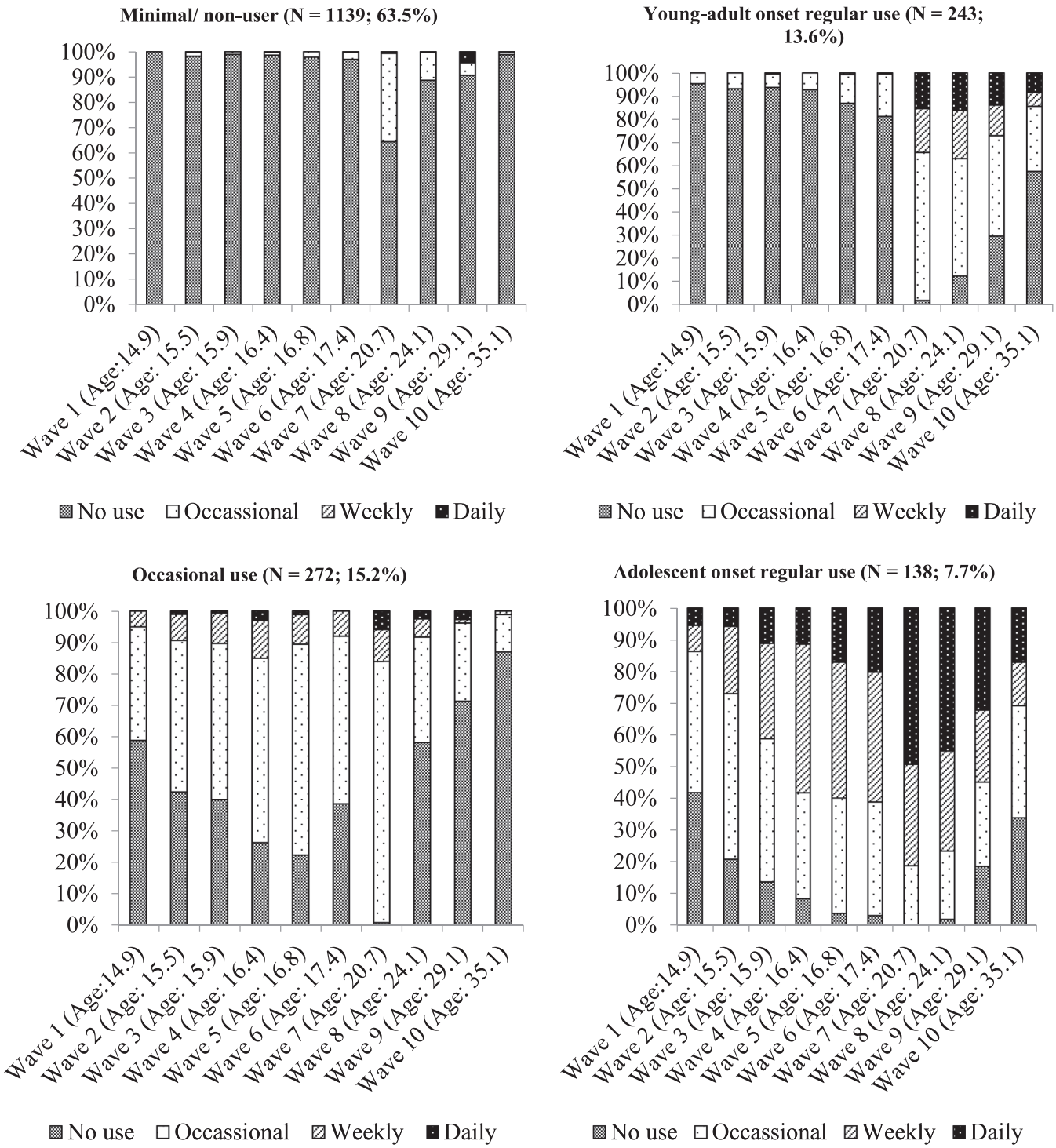

Figure 1. *Longitudinal patterns of cannabis use identified from the latent class analysis.*

group. Overall, both adolescent-onset and young-adult-onset regular use group were at higher risk of high-risk alcohol use, smoking, other illicit drug use and they were less likely to be in a relationship compared to the occasional use group. The adolescent-onset regular group was at heightened risk of depression and was less likely to have a paid job. There was no significant difference in any of the outcomes in the comparison between young-adult-onset and adolescent-onset regular use groups (column 6).

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Table 1. *Psychosocial and substance use profiles of the four groups of cannabis uses at the average ages of 15.5 (Wave 2) and 35 (Wave 10) years*

	Minimal/non-use (n = 1139)		Occasional use (n = 272)		Adolescent-onset regular use (n = 138)		Young-adult-onset regular use (n = 243)	
	%	95% CI	%	95% CI	%	95% CI	%	95% CI
Gender								
Male	40.5	(37.5, 43.5)	44.8	(38.0, 51.5)	69.3	(60.1, 77.8)	68.3	(60.1, 75.8)
Wave 2 (mean age: 15.5 years)								
High depression and/or anxiety symptoms	21.3	(18.6, 23.9)	37.1	(30.3, 43.9)	43.0	(33.7, 52.3)	23.9	(16.4, 31.3)
Antisocial behaviours	32.8	(29.8, 35.8)	74.1	(67.7, 80.4)	82.0	(74.2, 89.9)	51.1	(42.9, 59.3)
High-risk drinking	3.2	(1.9, 4.5)	26.7	(20.4, 33.0)	39.6	(30.5, 48.7)	12.0	(6.5, 17.6)
Smoking status								
Non-smoker	87.4	(85.2, 89.5)	33.6	(26.8, 40.4)	17.8	(10.0, 25.5)	75.8	(68.7, 83.0)
Occasional smoker	9.3	(7.4, 11.3)	36.0	(29.4, 42.6)	37.9	(28.2, 47.6)	17.4	(11.1, 23.6)
Daily smoker	3.3	(2.1, 4.5)	30.4	(23.9, 36.9)	44.3	(34.7, 53.9)	6.8	(2.2, 11.4)
Peers' cannabis use								
None	68.2	(64.9, 71.4)	12.5	(7.4, 17.5)	3.4	(0.0, 7.8)	49.1	(40.1, 58.2)
Some	29.8	(26.5, 33.0)	62.8	(55.8, 69.9)	48.7	(38.9, 58.4)	48.8	(39.7, 57.8)
Most/all	2.1	(1.0, 3.2)	24.7	(18.6, 30.8)	47.9	(38.0, 57.8)	2.1	(0.0, 5.6)
Wave 10 (mean age: 35.1 years)	%	95% CI	%	95% CI	%	95% CI	%	95% CI
High-risk drinking	24.8	(21.7, 27.9)	41.0	(33.7, 48.4)	63.0	(53.0, 73.1)	61.4	(52.3, 70.5)
Not in a relationship	16.9	(14.3, 19.4)	13.0	(7.8, 18.1)	39.7	(29.8, 49.5)	32.2	(24.1, 40.3)
Smoking status								
Non-smoker	90.0	(87.9, 92.2)	73.8	(66.8, 90.7)	32.8	(23.4, 42.1)	51.0	(42.6, 59.4)
Occasional smoker	1.7	(0.6, 2.7)	4.6	(1.3, 7.8)	10.9	(6.0, 1538)	10.4	(4.5, 16.3)
Daily smoker	8.3	(6.3, 10.3)	21.7	(15.1, 28.2)	56.9	(47.3, 66.4)	38.1	(29.9, 46.4)
Past 12-month use of other illicit substances	0.6	(0.0, 1.7)	14.3	(8.4, 20.1)	48.5	(38.0, 59.0)	36.8	(28.0, 45.5)
Study	10.9	(8.8, 13.0)	17.1	(11.5, 22.8)	8.3	(2.3, 14.3)	11.9	(6.1, 17.8)
Had a paid job	83.2	(80.7, 85.7)	88.5	(83.5, 93.4)	80.0	(72.2, 87.7)	90.5	(85.1, 95.9)
Financial hardship	20.7	(17.8, 23.5)	30.3	(23.3, 37.3)	40.2	(29.3, 51.0)	25.3	(16.9, 33.7)
Depression	10.6	(8.4, 12.9)	12.9	(7.7, 18.1)	23.7	(15.1, 32.4)	12.1	(6.3, 17.8)
Anxiety	9.6	(7.4, 11.8)	16.5	(11.1, 22.0)	20.9	(11.9, 29.9)	14.1	(7.2, 20.9)
Peers' cannabis use (daily or almost daily use)								
None	91.9	(89.8, 94.0)	84.3	(77.9, 90.8)	30.1	(20.3, 39.9)	53.0	(44.0, 62.0)
Some/most/all	8.1	(6.0, 10.2)	15.7	(9.2, 22.1)	69.9	(60.1, 79.7)	47.0	(38.0, 56.0)

CI, confidence interval.

Sensitivity analysis using E-*values*

In summary, both adolescent and young-adult-onset regular use was strongly associated with high-risk alcohol use, cigarette smoking, other illicit drug use and not being in a relationship. Table 3 showed the *E*-values of the key comparisons that were statistically significant. The *E*-values for the comparison on smoking and other illicit drug use were very high. For example, in the comparison between adolescent-onset regular use and occasional use, the *E*-value for smoking was 9.47, indicating that the finding could only be explained away by a set of unmeasured confounders that were associated with both adolescent-onset regular use and smoking by a risk ratio of 9.47 each, above and beyond the adjusted covariates; weaker confounding could not do so. Given that several key potential confounders were already adjusted for, we think it unlikely that there would be a large enough unmeasured confounder that could completely explain away our finding. Therefore, at least part of the associations of regular cannabis use with both smoking and other illicit drug use are likely to be causal. The *E*-values for the comparison on high-risk alcohol use and being in a relationship were smaller and moderate in size, leaving open the possibility that they are explained by residual confounding.

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Table 2. *Association between cannabis class membership and outcomes measured in wave 10 (average age 35 years)*

	Reference class: Minimal use (n = 1139)						Reference class: Occasional use				Reference class: Adolescent-onset regular use	
	1. Occasional use (n = 272)		2. Adolescent-onset regular use (n = 138)		3. Young-adult-onset regular use (n = 243)		4. Adolescent-onset regular use		5. Young-adult-onset regular use		6. Young-adult-onset regular use	
Wave 10 outcomes (35 years)	OR[a]	95% CI	OR	95% CI	OR[a]	95% CI	OR[a]	95% CI	OR[a]	95% CI	OR[a]	95% CI
High-risk alcohol use	2.1*	(1.5, 3.0)	5.2*	(3.2, 8.2)	4.8*	(3.1, 7.5)	2.5*	(1.4, 2.2)	2.3*	(1.4, 3.8)	0.9	(0.5, 1.7)
Smoking	3.1*	(2.0, 4.6)	18.6*	(9.0, 22.7)	6.1*	(4.1, 9.1)	5.8*	(3.3, 10.2)	2.7*	(1.7, 4.4)	0.5**	(0.3, 0.8)
Other illicit drug use	9.4*	(4.7, 18.8)	42.3*	(21.8, 82.0)	22.8*	(12.2, 42.7)	5.7*	(2.9, 10.9)	3.5*	(1.9, 6.5)	0.6	(0.4, 1.1)
In a relationship	1.4	(0.8, 2.2)	0.3*	(0.2, 0.5)	0.4*	(0.3, 0.6)	0.2*	(0.1, 0.4)	0.3*	(0.2, 0.6)	1.4	(0.8, 1.4)
Financial hardship	1.7**	(1.2, 2.4)	2.6*	(1.6, 4.2)	1.3	(0.8, 2.1)	1.5	(0.9, 2.6)	0.8	(0.4, 1.4)	0.5**	(0.3, 1.0)
Depression	1.2	(0.7, 2.1)	2.6*	(1.5, 4.5)	1.2	(0.6, 2.1)	2.1	(1.1, 4.1)	0.9	(0.5, 1.9)	0.4**	(0.2, 0.9)
Anxiety	1.9**	(1.2, 3.0)	2.5**	(1.4, 4.5)	1.5	(0.8, 2.9)	1.3	(0.7, 2.6)	0.8	(0.4, 1.6)	0.6	(0.3, 1.3)
Had a paid job	1.6	(0.9, 2.6)	0.8	(0.48, 1.36)	1.9	(1.0, 3.8)	0.5	(0.3, 1.0)	1.2	(0.5, 2.8)	2.4**	(1.1, 5.3)
	AOR[b]	95% CI	AOR	95% CI	AOR[b]	95% CI	AOR[b]	95% CI	AOR[b]	95% CI	AOR[b]	95% CI
High-risk alcohol use	1.7**	(1.1, 2.8)	3.2*	(1.6, 6.3)	3.7*	(2.4, 5.9)	1.9**	(1.0, 3.3)	2.1**	(1.2, 4.0)	1.2	(0.5, 2.5)
Smoking	1.5	(0.9, 2.7)	7.3*	(3.9, 13.8)	7.2*	(4.7, 11.0)	4.9*	(2.7, 8.7)	4.8*	(2.6, 8.8)	1.0	(0.5, 1.9)
Other illicit drug use	8.6*	(4.1, 18.7)	36.8*	(17.0, 80.1)	20.4*	(10.7, 39.1)	5.9*	(2.8, 12.4)	3.2**	(1.5, 6.5)	0.5	(0.2, 1.3)
In a relationship	1.3	(0.7, 2.3)	0.3*	(0.1, 0.6)	0.4*	(0.3, 0.7)	0.1*	(0.1, 0.4)	0.3*	(0.2, 0.7)	1.5	(0.7, 3.2)
Financial hardship	1.1	(0.7, 1.8)	1.8	(0.9, 3.7)	1.3	(0.8, 2.2)	1.6	(0.9, 3.0)	1.2	(0.6, 2.4)	0.7	(0.3, 1.7)
Depression	1.2	(0.6, 2.2)	2.9**	(1.2, 6.7)	1.2	(0.6, 2.3)	2.4**	(1.1, 5.3)	1.0	(0.5, 2.2)	0.4	(0.2, 1.1)
Anxiety	1.4	(0.8, 2.5)	1.9	(0.8, 4.7)	1.6	(0.8, 3.2)	1.4	(0.7, 3.0)	1.2	(0.5, 2.6)	0.8	(0.3, 2.2)
Had a paid job	2.0**	(1.1, 4.0)	0.8	(0.4, 1.6)	1.5	(0.7, 3.1)	0.4**	(0.2, 0.8)	0.7	(0.3, 1.9)	2.0	(0.7, 5.4)

*$P < 0.001$; **$P < 0.05$. [a]Odd ratios from logistic regression models. [b]Adjusted odd ratios from logistic regression models adjusted for all shown measures. Models were adjusted for Wave 2 measures: gender, depression and anxiety symptoms, antisocial behaviours, high-risk alcohol use, tobacco use and peer's cannabis use. CI, confidence interval; OR, odds ratio.

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Table 3. E-*value of adjusted odds ratio in the comparison between minimal use and adolescent and young-adult-onset regular use, and between occasional use and adolescent-onset regular use*

	Reference class: Minimal use		Reference class: Occasional use	
	Adolescent-onset regular use	Young-adult-onset regular use	Adolescent-onset regular use	Young-adult-onset regular use
High-risk alcohol use	2.98	3.26	2.10	2.26
Smoking	14.08	13.88	9.47	9.07
Other illicit drug use	73.10	40.29	9.47	5.85
In a relationship	3.05	2.54	5.78	3.05

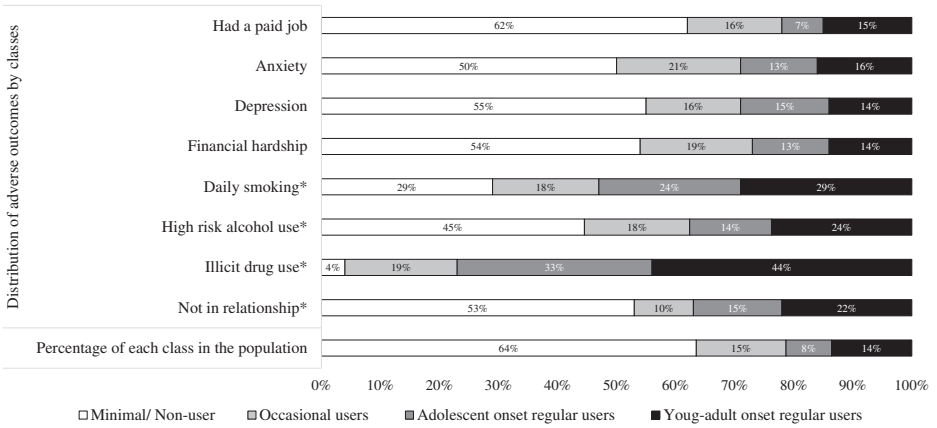

Figure 2. *Distribution of high-risk alcohol use, daily smoking, illicit drug use and not in relationship across the four cannabis using classes. Percentages were estimated based on 20 imputed datasets. These percentages need to be interpreted with respective to the percentage of each class in the population (bottom of the figure). *Variables there were highly significant (*$P < 0.001$*) in the above adjusted logistic regression. The distribution of these variables by classes were substantially different from the percentage of the corresponding class in the population.*

Proportion of Wave 10 outcomes accounted for by each pattern

Results from the logistic regression above demonstrated that both adolescent and young-adult onset regular cannabis use were strongly associated with several adverse outcomes, and that these associations were strongest for adolescent-onset regular cannabis use. Figure 2 shows another perspective of the data. Although the prevalence of young-adult-onset regular use in the sample was only 13.6%, this group accounted for the highest proportion of later illicit drug use and daily smoking, and a much higher proportion of high-risk drinking than the adolescent-onset regular use group (7.7%). The distribution of having a paid job, anxiety, depression and financial hardship were similar to the percentage of each class in the population.

Discussion

In this study, initiation of regular cannabis use predominantly occurred after leaving high school rather than in adolescence. By the mid-30s, participants with a later onset of regular cannabis use had similar substance use and social adjustment profiles compared to those who started regular use in adolescence: a majority of members of both groups engaged in high-risk drinking and daily smoking; the use of other illicit substances was common in both groups; and both groups were less likely to be in a relationship. The main difference in outcomes between these two groups was a higher rate of depression in the adolescent-onset regular use group, a difference no longer significant after adjusting for confounding at study entry. The similarities in outcomes between these two groups were particularly striking (e.g. over 60% of those in the adolescent and young-adult-onset regular groups engaged in high-risk drinking, compared to 25% in the minimal/non-use group and 41% in the occasional use group; see Table 1 for other comparisons), given their very distinct risk profiles in mid-adolescence: adolescent-onset regular users had higher levels of adolescent smoking, antisocial behaviour and cannabis using peers than

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those initiating use after leaving school. Our hypotheses that adolescent onset of regular cannabis use would be associated with the worst psychosocial sequelae at age 35, followed by young-adult-onset and then minimal users, were supported.

We used sensitivity analyses based on recent advances in biostatistics to test the plausibility of causal interpretations [27]. While we cannot totally rule out the possibility of unmeasured residual confounding, sensitivity analyses showed that it would require extreme confounding to explain away the associations between young-adult-onset regular use and illicit drug use and tobacco smoking. A large confounding effect would also be needed to explain the associations between young-adult-onset regular use and high-risk alcohol use and not being in a relationship. Given that we have adjusted for several well-known confounders, it seems unlikely that unmeasured confounders could fully explain the associations, leaving a high likelihood of at least partial causation.

In our analysis, those who begin using cannabis regularly in young adulthood emerged as an important group for intervention. Until now, adolescents were the major focus of drug prevention efforts [28]. Our results point to the importance of discouraging regular use, regardless of timing of onset. The prevalence of young-adult-onset regular use was nearly twice that of adolescent-onset regular use and young-adult-onset group accounted for a larger portion of substance-related and social problems at age 35 years than the adolescent-onset regular cannabis use group (see Figure 2). To reduce adverse cannabis-related consequences, it is thus important to also prevent regular use in the population, not just among adolescents.

Our results may have implications for jurisdictions that have recently legalised recreational use (e.g. some states in the USA, Canada) or are beginning public discussions about cannabis legalisation (e.g. New Zealand). Legalisation increases the availability of cannabis and allows the purchase of cannabis after the age of 19 in Canada and 21 in US states where recreational cannabis is legalised. This policy may increase young-adult-onset regular cannabis use. In the USA, the legalisation of recreational cannabis use has increased the prevalence of cannabis use in adults, but not to date in adolescents [29] suggesting that legalisation increases later initiation of regular use [30,31]. Most prevention efforts have focused on cannabis initiation among students in high school but in the light of our findings, there is also a case for discouraging regular cannabis use in young adults, even where there is little history of adolescent use.

Limitations

Two key study strengths were the use of a statewide-representative sample followed from adolescence (15 years) well into mid-adulthood (35 years), and the use of biostatistical method to assess the likelihood of causal explanation. However, the study had limitations. Because we measured self-reported cannabis use, it is possible that under-reporting of use may have introduced bias into model estimates. Although self-report is commonly used in epidemiological studies such as the Global School-based Student Health Survey [32] and Australia's National Drug Strategy Household Survey [33], the use of single items for measuring some constructs (e.g. peer's substance use) may have introduced bias in estimating the association between exposure and study outcomes. Our results come from a cohort of young Victorians who grew to adulthood when cannabis was an illegal drug. This raises the possibility that some young-adult-onset uses might have under-reported their cannabis use during adolescence. Given that the profile of young-adult-onset use was very similar to minimal use, we believe the rate of such differential under-reporting across the study period was likely to be small and unlikely to negate our findings. Lastly, only frequency of cannabis use was measured and no data on quantity and potency of cannabis products were collected.

Conclusion

Initiation of regular cannabis use after high school strongly predicted smoking and illicit drug use in the mid-30s. This group also accounted for a higher proportion of illicit drug use and smoking in the cohort. Sensitivity analyses suggested that this association was at least partially causal. Given the legalisation of cannabis use in an increasing number of jurisdictions, we should increasingly expect harms from cannabis use to lie in those commencing use in young adulthood.

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Conflict of Interest

The authors have no conflicts of interest.

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Supporting Information

Additional Supporting Information may be found in the online version of this article at the publisher's website:

Appendix S1. Study flowchart.
Appendix S2. Cannabis use from age 14 to age 35 in the study sample.
Appendix S3. Model selection and model fit statistics.
Appendix S4. Description of latent classes.
Appendix S5. Association between Wave 2 correlates and latent classes.

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