RESEARCH REPORT

ADDICTION

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Does recreational cannabis legalization change cannabis use patterns? Evidence from secondary school students in Uruguay

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Funding information

National Institute on Drug Abuse, Grant/ Award Number: R01DA040924-01; ANID-Millenium Science Initiative Program, Grant/Award Number: NCS2021003

Abstract

Background and Aims: In 2013, Uruguay became the first country to legalize and regulate the production and distribution of cannabis for recreational use. We measured whether Uruguay's non-commercial model of recreational cannabis legalization was associated with changes in the prevalence of risky and frequent cannabis use among secondary school students.

Design: We used data from repeated cross-sectional surveys of secondary students in Uruguay and Chile (2007–2018). Using a difference-in-difference approach, we evaluated changes in the prevalence of past-year, past-month, any risky and frequent cannabis use following enactment (2014) and implementation (2016) of cannabis legalization among the full sample of secondary students and among students who reported past-year/month use. We examined changes separately for students ages 12 to 17, and students for whom cannabis became legally accessible, ages 18 to 21.

Setting: Uruguay and Chile (2007-2018).

Participants: Secondary school students in 8th, 10th and 12th grade (n = 204 730).

Measurements: Past-year and past-month cannabis use; any risky cannabis use measured with the Cannabis Abuse Screening Test (CAST); and frequent cannabis use (10-+ days in the past-month).

Findings: We found a decrease in past-year and past-month use following enactment or implementation. Among students ages 18 to 21, post-enactment, we observed a transitory increase in 2014 that decreased thereafter for: any risky use among those who reported past-year use (prevalence difference [PD] = 13.5%; 95% CI: 2.0, 24.9), frequent use in the full sample (PD = 4.5%; 95% CI: 1.0, 8.1), and frequent use among those who reported past-month use (PD = 16.8%; 95% CI: 1.9, 31.8).

Conclusion: The legalization of recreational cannabis in Uruguay was not associated with overall increases in either past-year/past-month cannabis use or with multi-year changes in any risky and frequent cannabis use among young people.

KEYWORDS

Adolescent, cannabis, frequent cannabis use, legalization, risky cannabis use, youth

INTRODUCTION

The regulatory landscape of cannabis has shifted significantly over the past two decades. More states and countries are legalizing or considering the legalization of cannabis for adult use. In December 2013, Uruguay became the first country to legalize the cultivation, production, sale and consumption of cannabis. Although cannabis use had been decriminalized since 1974, there was no legal source to obtain cannabis in the country [1]. The new regulation introduced three mutually exclusive ways for legally accessing recreational cannabis: citizens above 18 can either register to purchase cannabis in pharmacies, register to become a home grower or join a cannabis club. Although companies are able to obtain a license to cultivate cannabis to sell in pharmacies, the government controls production, sets the price at which cannabis can be sold and only allows sales of flowers. The regulation also imposes limitations on the quantity a registered user can purchase (maximum 10 grams per week) and the quality of the product and on the potency of cannabis (currently up to 9% of tetrahydrocannabinol [THC] and at least 3% of cannabidiol [CBD]) [2, 3]. Cannabis clubs can have between 15 and 45 members and produce up to 480 annual grams per member. Self-growers are allowed to have up to 6 plants and produce a maximum of 480 grams per year [4, 5]. The regulation does not allow any advertisement or events that promote cannabis use and requires plain packaging containing warning labels [6, 7]. To deter cannabis tourism, only Uruguayan citizens and permanent residents are able to register for any of the means of access. For minors, the legal status of cannabis did not change. Cannabis use was decriminalized since the 1970s, and continues to be decriminalized. Estimates from the Uruguayan Drug Observatory suggest that in 2018, the regulated market of cannabis had reached \sim 30% of the people who reported past-year cannabis use [8].

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Among youth, cannabis remains the most commonly used controlled substance [9]. One of the main concerns surrounding legalization is that harms associated with cannabis use at an early age, including altered brain development, cognitive impairment, increased risk of psychotic disorders and poor educational outcomes, could increase because of recreational cannabis legalization [10–12]. Amid cannabis policy changes worldwide, it is important to understand how these changes may affect cannabis use patterns among adolescents.

Studies examining the impact of recreational cannabis legalization, have mostly taken place in the United States (US) [13–18], with emerging evidence from Canada [19, 20]. These studies have focused mainly on the overall prevalence of use as an outcome, evaluating different types of market-oriented models of legalization from already established medical cannabis markets [13–21].

In the United States, although early studies suggested small increases in use in Washington, but not in Colorado [13–15], most recent studies have not found increases in the overall prevalence of use among adolescents following enactment of recreational cannabis legalization [16–18]. In Canada, results from an early study examining cannabis use patterns found a small increase in youth cannabis use since the beginning of the federal discourse around legalization [19].

However, in a subsequent study, Zuckermann *et al.* [20] did not find significant changes in youth cannabis use post-legalization.

Few studies have looked at changes in cannabis use patterns following recreational cannabis legalization. Cerdá *et al.* [18] found that among states that legalized recreational cannabis in the United States, adolescent cannabis use disorder increased slightly following legalization, and the increase was higher among those who reported pastyear use. However, the authors found no changes in the frequency of cannabis use in the overall sample of adolescents or among those reporting past-year use. Similarly, among young people ages 18 to 25, there was no difference in cannabis use disorder and frequency of use before and after the enactment of recreational cannabis [18]. In a cohort study in California of young adults, ages 18 to 24, results indicated no significant changes on frequency of cannabis use postlegalization [22].

Uruguay presents an opportunity to evaluate the consequences associated with a national non-commercial model of legalization of recreational cannabis use, where the state controls production, sales and advertising [23]. The consequences of a commercial recreational cannabis legalization model may not replicate to the case of a highly regulated recreational cannabis model, and as governments consider how to legalize cannabis, it is important to examine the consequences associated with this alternative approach. Although past-year and past-month prevalence of cannabis use among adolescents has increased in Uruguay in the past 10 years [24, 25], Lagueur et al. [26] found no meaningful differences in past-year and past-month cannabis use or frequent use (10 days or more) among secondary school students following the enactment of the law. It is possible, however, that examining changes in use across adolescents regardless of age obscures important differences associated with legal access to cannabis. Legalization may have had a different impact on young people ages 18+, who gained legal access to cannabis following legalization, compared to younger adolescents.

In the present study, we evaluated whether cannabis legalization increased past-year, past-month, risky and frequent (i.e. 10 days or more in the past-month) cannabis use, differentiating between youth who became legally able to access cannabis (ages 18+) and those who did not (ages 12–17). To identify whether cannabis legalization may have had distinct associations on students with a prior history of cannabis use, we examined changes in risky and frequent cannabis use among the full sample and among those who reported past-year/past-month use. We compared Uruguay with Chile, where recreational cannabis has not been legalized.

METHODS

Data

We used data from repeated cross-sectional surveys of students enrolled in 8th, 10th, and 12th grade (typically ages 13–18, although with students ranging from ages 12–21) in urban areas in Uruguay (10 000 + inhabitants) and Chile (30 000 + inhabitants) for years 2007–2018. The drug observatories in each country, whose objective is to develop an information and research system on consumption and supply of drugs to inform drug policies, coordinate the data collection [27, 28].

Secondary school enrolment is relatively high in Uruguay and Chile and compared to other Latin American countries, with rates between 84% to 89% and 68% to 88%, respectively, during the study period [29]. These surveys use a common standardized research protocol [30], similar to the Monitoring the Future Surveys in the United States [31]. The surveys are conducted on average every 2 years and are self-administered. Survey years by country are presented in Supporting information Table S1. Students are informed that participation in the survey is confidential and voluntary. In both Uruguay and Chile, the school cooperation rate ranged between 76% and 86%. In both countries, the schools and classrooms were selected via clustered. multi-stage random sampling design. In Uruguay, the sampling strata were school type (e.g. public, private) by region (e.g. Montevideo and Interior), and primary sampling units were the schools. In Chile, the sampling strata were school type by grade, and primary sampling units were classrooms. Further methodological details of the survey, the questionnaires and main results are available at the Uruguayan National Drug Observatory [32] and the Chilean Drug Observatory [33].

Uruguay's drug observatory manually cleans survey data before making it available for researchers. Observations are removed if respondents responded positively to a question about having used a fictional drug 'relevón', if respondents left 50% or more of the questionnaire blank, or responded more than four inconsistencies in reporting age of initiation of use, past-month, past-year and lifetime use of cannabis. Because of this process, ~0.5% of the respondents were excluded from the database. For comparability, we followed a similar approach in Chile, resulting in a deletion of 5% respondents of the sample. Reasons explaining the larger percentage of poor-quality data in the Chilean survey has been explored in prior research [34].

The research protocol for this study was reviewed by University of California Davis's and New York University's Institutional Review Board and was not considered human subjects research. The research question and analysis plan were not pre-registered. Therefore, results should be considered exploratory.

Measures

Outcomes

Our outcomes are past-year and past-month cannabis use, any risky cannabis use and frequent cannabis use. To identify students with any risky use, we used the binary version of the Cannabis Abuse Screening Test (CAST) [35, 36]. The CAST is a 6-item scale designed by the French Monitoring Center for Drug and Drug addictions to identify problematic patterns of cannabis use [35]. The test's reference period is past-year cannabis use and includes questions on the frequency of use before midday, memory problems associated with use, being encouraged by friends or family members to reduce or

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stop using cannabis, whether the student had unsuccessful attempts to quit or had any problems linked to cannabis consumption [37]. The CAST has been widely used in epidemiologic studies, showing good psychometric properties [38, 39]. In Uruguay and Chile, the CAST scale has been included in adolescent drug use surveys since 2009, showing adequate consistency and internal reliability. Uruguay's Cronbach's α ranged from 0.72 to 0.75, and in Chile from 0.82 to 0.88, depending on the survey year. Further information about the CAST scale and scoring process was included in Supporting information Tables S2–S3.

We defined the frequent use indicator as 1 if the student reported cannabis use 10 days or more in the past-month (reference period for this measure) and 0 otherwise. Ten days or more has been used in previous studies to classify frequent use among adolescents because this would represent consumption beyond only weekends [26, 40, 41].

Analytic approach

We estimated the association of cannabis legalization on past-year, pastmonth, risky and frequent cannabis use in two ways: (i) on average for the period post-legalization, and (ii) for each year following legalization. For risky and frequent cannabis use, we examined changes among the full sample and among those who reported past-year or past-month use, depending on the reference period of the measure. We used a difference-in-difference approach comparing adolescents in Uruguay and Chile pre- and post-intervention, adjusting for sex and type of school (public vs private or subsidized schools, which is a proxy of socioeconomic status). We also ran unadjusted models that are included in Supporting information Tables S5-S6). We chose Chile as the comparison country because of the epidemiological, social, economic and cultural similarities of these Southern Cone countries. Compared to the rest of Latin America, Uruguay and Chile have higher life expectancy, highest Human Development Index, higher standard of living, lowest rates of violence, high participation in the global markets, similar age and sex structure [42-44].

We implemented a linear probability model (i.e. a linear regression model with a binary outcome) [45], commonly used in the econometric policy evaluation literature. We opted for a linear probability model because the coefficients represent the changes in marginal probabilities, and the difference-in-difference estimator can be directly interpreted as the prevalence difference (PD). A more detailed description of the statistical model is included in the Supporting information. As a sensitivity analysis, we ran logit models, results are also presented in Supporting information Tables S7–S8.

Because the legal age to access cannabis is 18, we estimated separate models for those secondary school students who were old enough to legally access recreational cannabis (ages 18–21) following legalization, and those who were not (ages 12–17). All analyses were done using the survey package in Stata MP/15.1 to account for the clustering and stratification in the sample and incorporate survey weights [46].

Legalization occurred in December 2013, the registry for selfgrowers and cannabis clubs opened in 2014, and pharmacy access

was available in 2017. Because legalization was implemented in stages, we examined changes in past-year, past-month, risky and frequent cannabis use with two sets of models: (i) treating 2014 as the first post-intervention year (enactment), and (ii) treating 2016 as the first post-intervention year (implementation: two of the three modes of access were available). The survey year 2018 was the only year when the three modes of access were available.

Sensitivity analysis

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We conducted several sensitivity analyses. First, to evaluate results under different assumptions of missing responses to the outcome measures, we replicated the analyses after Multiple Imputation by Chained Equations. A table showing missing data by survey and year for each outcome is presented in Supporting information Table S3. We performed five imputations with auxiliary variables common across countries within each analytic sample and accounted for the complex sampling design by including design variables in the imputation models [47–49]. Second, although CAST is not a measure of cannabis use disorder, previous research indicates that scoring values of 2 to 3 in the risk level measure may be a good predictor of cannabis use disorder [35, 37]. Therefore, we looked at low risky use (1-2 points) separate from moderate and high risky use (3 points or more). Results from multiple imputed models and alternative specifications of risky use of cannabis are presented in Supporting information Tables S9–S12 and Supporting information Figures S1-S2.

RESULTS

Table 1 presents the characteristics of the sample by country and age group. The median size of the sample between survey years 2007 and 2018 was 5528 adolescents in Uruguay, and 29 371 adolescents in Chile. Differences in sample sizes were because of differences in each country's population size. The majority of the sample included adolescents between ages 12 and 17 (86.1%, for both countries combined). On average, among students ages 12 to 17, 46.8% were male in Uruguay and 48.7% in Chile; and among students ages 18 to 21, 45.8% were male in Uruguay and 48.9% were male in Chile. A larger fraction of students in Uruguay attended public schools (between 81.4%-84.6% in Uruguay and between 33.6%-35.4% in Chile). In both countries, the average age in the 12 to 17 age group was 15 years and in the 18 to 21 age group the average age was 18 years. For both age groups, a smaller proportion of students in Uruguay than in Chile report parents with secondary education or more. Overall, the prevalence of past-year use, past-month use and any risky use was lower in Uruguay than in Chile. Frequent use among those who reported past-month use was higher in Uruguay than in Chile.

Figure 1 shows the observed weighted prevalence over time of past-year cannabis use (2007–2018), and past-month cannabis use (2007–2018). Figure 2 and Figure 3 show the observed weighted prevalence over time of risky cannabis use (2009–2018) and frequent

cannabis use (2007–2018) among the full sample and among those who reported cannabis use in the past-year (for risky use) and in the past-month (for frequent use) by age group. Past-year and past-month cannabis use increased in both countries and both age groups. Risky use increased in the two countries for ages 18 to 21.

The association of cannabis legalization on the six outcomes by age group is shown in Table 2 and Table 3. Table 2 shows the PD treating 2014 as the first-year post-intervention, and Table 3 presents the difference in outcomes treating 2016 as the first post-intervention year. PD can be interpreted as the additional number of adolescents per 100 who reported cannabis use, any risky or frequent use of cannabis, in Uruguay compared to Chile, post versus pre-legalization. We present the average results overall for the period post-legalization and for each year post-legalization.

The difference in prevalence in the pre- versus post-legalization period among adolescents ages 12 to 17 was lower in Uruguay than in Chile: PD = -7.7 (95% CI: -9.6, -5.8) for past-year use and PD = -5.5 (95% CI: -6.9, -4.2) for past-month use. Equally, for youth ages 18 to 21, the difference in prevalence between the pre- and post-legalization period was lower in Uruguay than in Chile: PD = -5.8 (95% CI: -10.3, -1.2) for past-year use and PD = -4.9 (95% CI: -8.7, -1.1) for past-month use.

For adolescents between ages 12 and 17, who do not have legal access, the change in prevalence pre- versus post-legalization of risky cannabis use (PD = -5.0; 95% Cl: -6.2, -3.8) and frequent cannabis use (PD = -1.8; 95% Cl: -2.4, -1.2) was lower in Uruguay than in Chile. Similarly, among those ages 18 to 21, who are allowed to access legally, the change in prevalence pre- and post-legalization for any risky use was lower in Uruguay than in Chile (PD = -3.5; 95% Cl: -6.8, -0.2), and there was no meaningful difference in frequent use pre- versus post-legalization (PD = -0.6; 95% Cl: -2.5, 1.4).

Once we looked at changes for each year post-legalization, we found a transitory higher increase in 2014, in any risky use among students ages 18 to 21 who reported past-year use in Uruguay (compared to Chile) (PD = 13.5; 95% Cl: 2.0, 24.9) that decreased afterward. Further, among 18 to 21 years, we also observed a transitory increase in 2014 in frequent use in the full sample (PD = 4.5; 95% Cl: 1.0, 8.1) and among those who reported past-month use (PD = 16.8; 95% Cl: 1.9, 31.8). Figures 4–6 show the predicted trends for the prevalence for each of the outcomes.

As shown in Table 3, the majority of results remained robust to treating 2016 as the first post-legalization year. Nevertheless, we observed an increase in any risky use among those who reported past-year use among ages 12 to 17 in 2018, once self-cultivation and cannabis club registrations had been implemented. Overall, results remained consistent in the unadjusted models (Supporting information Tables S5–S6), using logit models (Supporting information Tables S7–S8), and after imputing missing data (Supporting information Tables S7–S10). When we examined the low and moderate/high categories separately, we only observed an increase in the low-risk category among ages 12 to 17 when treating 2016 as the first post-intervention year (Supporting information Tables S11–S12, and Supporting information Figures S1–S2).

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TABLE 1Characteristics of secondary students in Uruguay and Chile (2007–2018) by age group

	Uruguay			Chile			
	2007-2011	2014-2018	Full sample	2007-2011	2014-2018	Full sample	
Age 12-17 y							
Past-year cannabis use (%)	11.2	16.9	14.6	14.9	28.4	21.6	
Past-month cannabis use (%)	6.6	9.5	8.3	8.1	16.6	12.3	
Risky use ^a (%, full sample)	5.6	8.2	7.2	6.3	13.8	10.8	
Risky use ^a (%, students who reported past-year use)	56.5	53.4	54.3	60.2	58.0	58.5	
Heavy use (%, full sample)	2.0	2.9	2.5	2.3	4.9	3.6	
Heavy use (%, students who reported past-month use)	32.9	35.2	34.4	26.2	29.5	28.5	
Male (%)	46.2	47.3	46.8	48.2	49.1	48.7	
Attending public school (%)	80.9	81.8	81.4	38.0	32.7	35.4	
Maternal education (% secondary schooling completed)	42.9	52.4	48.4	63.5	70.6	67.0	
Paternal education (% secondary schooling completed)	42.1	52.0	47.7	62.6	68.2	65.3	
Age (mean), y	14.9	14.9	14.9	15.0	15.0	15.0	
Detailed age (%), y							
12	0.01	0.2	0.1	0.1	0.1	0.1	
13	21.1	23.3	22.4	21.0	18.8	19.9	
14	23.5	17.3	19.8	17.4	19.0	18.2	
15	22.5	23.5	23.1	22.9	21.5	22.2	
16	17.3	16.7	17.0	18.1	20.2	19.1	
17	15.6	18.9	17.6	20.6	20.4	20.5	
N (unweighted)	14 034	19 011	33 045	63 767	79 420	143 187	
Ages 18-21 y							
Past-year cannabis use (%)	22.5	36.0	30.5	25.9	45.3	36.7	
Past-month cannabis use (%)	13.0	23.2	19.0	13.3	28.4	21.7	
Risky use ^a (%, full sample)	9.6	18.7	15.0	10.2	22.6	18.4	
Risky use ^a (%, students who reported past-year use)	44.9	54.3	51.6	56.0	57.4	57.1	
Heavy use (%, full sample)	4.3	8.5	6.8	4.9	9.8	7.7	
Heavy use (%, students who reported past-month use)	34.4	39.3	37.9	31.7	33.7	33.1	
Male (%)	42.3	48.3	45.8	49.0	48.9	48.9	
Attending public school (%)	83.7	85.3	84.6	34.1	33.2	33.6	
Maternal education (% secondary schooling completed)	48.6	55.6	52.7	60.8	66.5	64.0	
Paternal education (% secondary schooling completed)	45.0	58.3	52.6	60.7	65.5	63.4	
Age (mean), y	18.5	18.4	18.4	18.2	18.2	18.2	
Detailed age (%), y							
18	69.5	73.1	71.6	83.8	81.7	82.6	
19	19.3	17.8	18.4	13.9	15.8	15.0	
20	7.7	7.1	7.4	2.0	2.2	2.1	
21	3.5	2.0	2.6	0.3	0.3	0.3	
N (unweighted)	2412	2338	4750	9395	14 353	23 748	

Percentages are weighted, 2014 corresponds to the first-year post-legalization year.

^aAny risky marijuana use only available for 2009–2018.

DISCUSSION

In the present study, we examined whether national legalization of cannabis cultivation, production, sale and adult use in Uruguay

affected the levels of risky and frequent use of cannabis among school-based adolescents and youth ages 12 to 17 and 18 to 21. This is the first study to assess the impact of a national recreational cannabis legalization policy on risky cannabis use and to distinguish

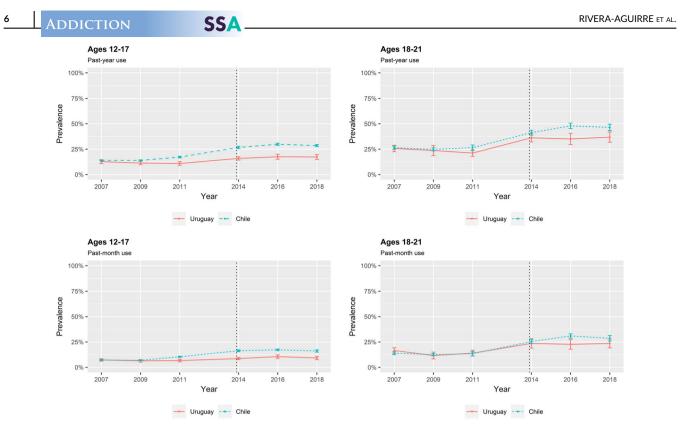


FIGURE 1 Observed prevalence of past-year and past-month cannabis use (2007–2018) among secondary students ages 12–17 and 18–21

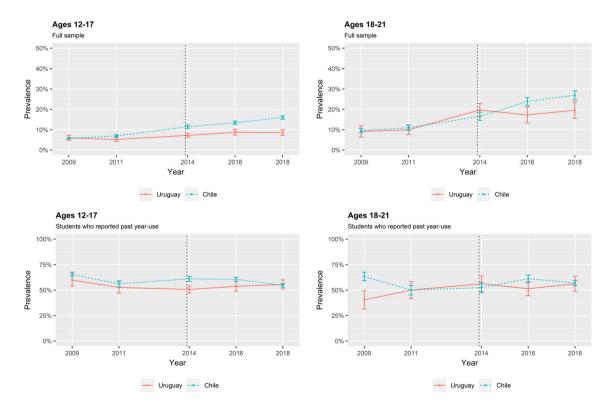
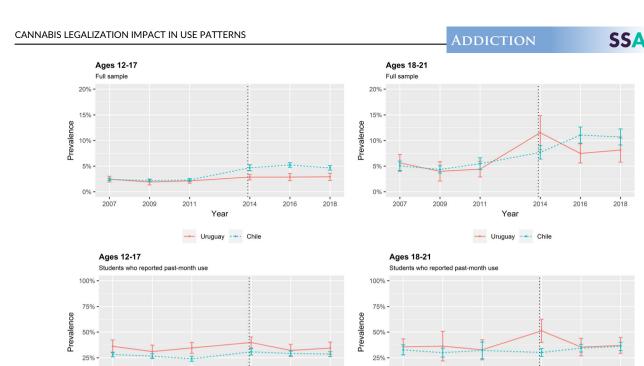


FIGURE 2 Observed prevalence of any risky cannabis use (2009–2018) among secondary students ages 12–17 and 18–21 in the full sample and among those who reported past-year use



2016

2014

Year

--- Uruguay ---- Chile

0%

2007

and among those who reported past-month use

2009

2011

7

2018

TABLE 2 Estimated PD of past-year and past-month use, any risky use and frequent use after versus before legalization in Uruguay compared to Chile by age group

2018

FIGURE 3 Observed prevalence of frequent cannabis use (2007-2018) among secondary students ages 12-17 and 18-21 in the full sample

0%

2007

2009

2011

2014

Year

--- Uruguay ---- Chile

2016

	Ages 2	12-17			Ages 18-21				
	PD	(95% CI)	PD	(95% CI)	PD	(95% CI)	PD	(95% CI)	
Outcome	Past-year		Past-month		Past-year		Past-month		
Cannabis use	i				÷				
Average	-7.7	(-9.6, -5.8)	-5.5	(-6.9,-4.2)	-5.8	(-10.3, -1.2)	-4.9	(-8.7,-1.1)	
2014	-6.7	(-9.0, -4.3)	-6.0	(-7.6, -4.3)	-2.0	(-7.7, 3.7)	-2.1	(-7.7, 3.6)	
2016	-8.2	(-11.1, -5.3)	-5.0	(-7.1, -2.9)	-9.4	(-16.2, -2.6)	-8.0	(-13.7, -2.3)	
2018	-7.2	(-10.0, -4.3)	-5.2	(-7.4, -3.1)	-6.2	(-12.8, 0.5)	-4.6	(-10.2, 1.0)	
	Full sample		Students who reported past-year use		Full sample		Students who reported past-year use		
Any risky use									
Average	-5.0	(-6.2, -3.8)	-1.7	(-7.1, 3.6)	-3.5	(-6.8, -0.2)	7.4	(-1.2, 16.1)	
2014	-3.7	(-5.2, -2.2)	-6.3	(-12.5, -0.2)	3.0	(-1.2, 7.1)	13.5	(2.0, 24.9)	
2016	-4.1	(-6.0, -2.3)	-3.0	(-9.9, 3.8)	-6.0	(-10.7, -1.2)	1.6	(-9.0, 12.2)	
2018	-6.9	(-8.7, -5.1)	4.4	(-2.1, 11.0)	-6.6	(-11.6, -1.6)	10.3	(-0.3, 20.9)	
	Full sample		Students who reported past-month use		Full sample		Students who reported past-month use		
Frequent use									
Average	-1.8	(-2.4, -1.2)	-1.6	(-7.1, 3.9)	-0.6	(-2.5, 1.4)	2.3	(-7.9, 12.5)	
2014	-1.7	(-2.5, -0.8)	1.6	(-5.9, 9.0)	4.5	(1.0, 8.1)	16.8	(1.9, 31.8)	
2016	-2.3	(-3.1, -1.4)	-5.0	(-12.7, 2.6)	-2.7	(-5.3, -0.1)	-2.1	(-14.8, 10.5)	
2018	-1.7	(-2.6, -0.8)	-2.7	(-10.4, 4.9)	-1.6	(-4.7, 1.4)	-2.6	(-15.0, 9.8)	

PD = prevalence difference, additional number of adolescents per 100 who reported past-year, past-month, any risky or frequent use.

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TABLE 3 Estimated PD of past-year and past-month use, any risky use and frequent use after versus before implementation of legalization in Uruguay compared to Chile by age group

	Ages 12-17					Ages 18-21				
	PD	(95% CI)	PD	(95% CI)	PD	(95% CI)	PD	(95% CI)		
Outcome	Past-year		Past-month		Past-year		Past-month			
Cannabis use										
Average	-6.8	(-8.9, -4.7)	-4.0	(-5.5, -2.5)	-6.2	(-11.1, -1.2)	-5.0	(-9.2, -0.8)		
2016	-6.7	(-9.5, -3.9)	-3.8	(-5.8, -1.8)	-9.0	(-15.6, -2.4)	-7.7	(-13.3, -2.0)		
2018	-5.7	(-8.4, -3.0)	-4.1	(-6.1, -2.0)	-5.8	(-12.3, 0.7)	-4.3	(-9.8, 1.2)		
	Full sample		Students who reported past-year use		Full sample		Students who reported past-year use			
Any risky use										
Average	-4.4	(-5.8, -3.1)	3.5	(-1.3, 8.3)	-5.9	(-9.6, -2.3)	0.7	(-7.3, 8.8)		
2016	-3.3	(-5.1, -1.6)	-0.3	(-6.4, 5.8)	-6.5	(-11.2, -1.8)	-3.1	(-12.7, 6.6)		
2018	-6.1	(-7.9, -4.3)	7.2	(1.4, 12.9)	-7.1	(-12.0, -2.2)	5.7	(-4.0, 15.3)		
Full sample		mple	Students who reported past-month use		Full sample		Students who reported past-month use			
Frequent use										
Average	-1.6	(-2.3, -1.0)	-3.9	(-9.6, 1.9)	-3.1	(-5.3, -0.9)	-8.1	(-17.6, 1.3)		
2016	-2.0	(-2.9, -1.1)	-5.6	(-12.9, 1.7)	-3.4	(-6.0, -0.7)	-8.2	(-19.8, 3.3)		
2018	-1.4	(-2.3, -0.6)	-3.3	(-10.6, 4.0)	-2.3	(-5.4, 0.8)	-8.7	(-20.0, 2.5)		

PD = prevalence difference, additional number of adolescents per 100 who reported past-year, past-month, any risky or frequent use.

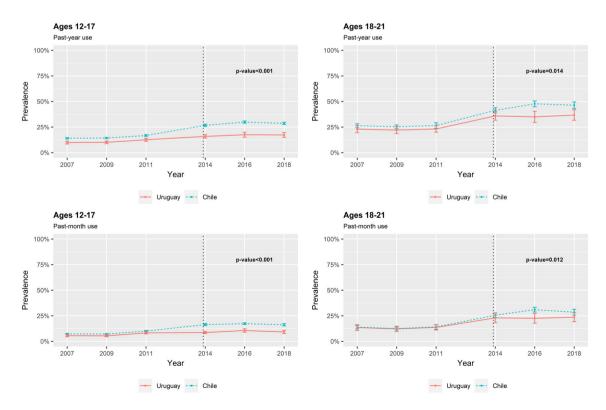
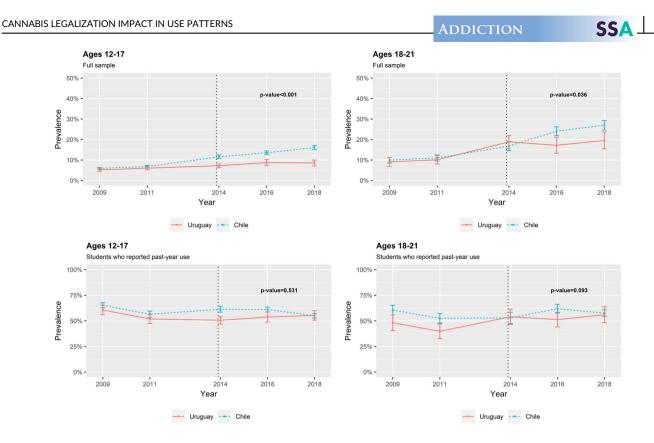


FIGURE 4 Estimated prevalence of past-year cannabis use and past-month cannabis use (2007–2018) among secondary students ages 12–17 and 18–21. *Note*: The *P* value corresponds to the two tailed average difference pre/post enactment of cannabis legalization between Uruguay and Chile



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FIGURE 5 Estimated prevalence of any risky cannabis use (2009–2018) among secondary students ages 12–17 and 18–21 in the full sample and among those who reported past-year use. *Note:* The *P* value corresponds to the two tailed average difference pre/post enactment of cannabis legalization between Uruguay and Chile

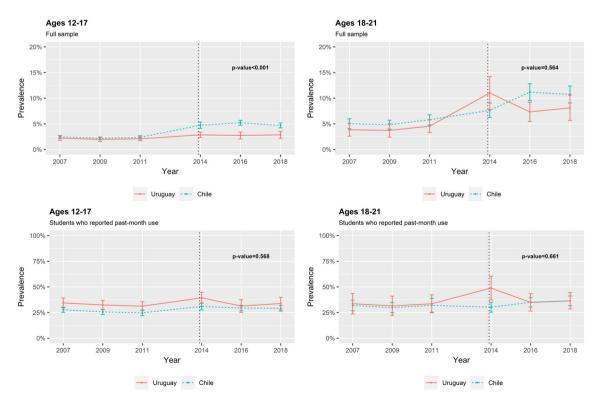


FIGURE 6 Estimated prevalence of frequent cannabis use (2007–2018) among secondary students ages 12–17 and 18–21 in the full sample and among those who reported past-month use. *Note:* The *P* value corresponds to the two tailed average difference pre/post enactment of cannabis legalization between Uruguay and Chile

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between age groups who may have responded differently to legalization [14, 15, 50]. We hypothesized that we would see a larger change in the prevalence of use, any risky and frequent cannabis use among secondary students ages 18 to 21 whose legal access to cannabis changed.

Our results build on existing evidence that suggests legalization in Uruguay was not associated with increases in cannabis use [26]. However, we find some evidence to support the hypothesis of a differential association between those above the legal age to access (18 years of age or more) and those below (under 18 years of age). Contrary to Laqueur *et al.* [26], who did not examine changes separately by age groups, we found some indication of a temporary increase in 2014 in frequent use and in risky use, but only among adolescents ages 18 to 21. The increase occurred before fully implemented legalization, suggesting that in the short term, cannabis use may be sensitive to changes in social norms (2014 as the first post-legalization year).

Our findings differ from studies that evaluated the impact of recreational cannabis legalization on adolescents in the United States and used Monitoring the Future surveys, a similar sample of secondary students to those used in our study. In the United States, small increases in cannabis use among adolescents were found in Washington following enactment of recreational cannabis legalization [15]. However, our findings are similar to recent studies evaluating recreational cannabis legalization among adolescents including a larger number of states, where states that legalized cannabis found small decreases or no changes in adolescent cannabis use following legalization [16, 18]. Regarding risky cannabis use, our findings contrast with those of Cerdá *et al.* [18], who found that recreational cannabis legalization in the United States was associated with small increases in cannabis use disorder among adolescents ages 12 to 17 and among users, but not among young people ages 18 to 25.

By 2018, 62% of students reported cannabis flowers as the main source of cannabis used, which according to the Uruguayan Drug Observatory comes from local production and mainly from selfgrowers [25]. In contrast, reports from using pressed cannabis, which corresponds to the cannabis found in the black market has decreased from 24% in 2016 to 15% in 2018 [25]. Differences between findings across studies evaluating the effect of legalization on patterns of cannabis use may be attributable to differences between the Uruguayan model and the regulatory approaches currently adopted in US states. In Uruguay, the state controls production and sales of cannabis, prohibits marketing, imposes THC limits, and only sales of cannabis flowers are allowed, whereas in the United States, states that have legalized recreational cannabis have followed a more for-profit commercial approach [51]. Although these results should be interpreted with caution mainly because 2018 is the first data point available where sales in pharmacies had begun in Uruguay, and because we are not studying the source of the cannabis consumed by adolescents, these short-term findings may suggest that a highly regulated market may mitigate harms among adolescents and youth, in contrast to commercial approaches. Additionally, although on average we do not see any increase in cannabis use among secondary students, cannabis

diversion from self-growers and cannabis clubs, which may have a higher THC concentration than the cannabis sold in pharmacies, may pose concerns as the legal cannabis market grows [25].

Limitations

The results should be considered in light of several limitations. First, the surveys were conducted in secondary schools and among adolescents attending school in urban areas. Therefore, our study does not include adolescents who may have dropped secondary education or were absent at the time of the survey. Arguably, adolescents and youth who dropped out of the school system could be involved in riskier cannabis use behaviours than their peers attending school. Furthermore, in the older cohort (ages 18-21) particularly for ages 20 to 21, results may not be generalizable because it is expected the majority of youth in this age group have graduated from secondary school. Similarly, our study does not include students attending schools in areas with <10 000 inhabitants. Therefore, these results may not be generalizable to the rural population. Second, self-report surveys may be subject to recall and social desirability biases, which may affect the quality of the data. In particular, legalization could affect response patterns. However, because cannabis use in Uruguay has been decriminalized since the 1970s, we did not expect changes in reporting because of legalization [52]. Additionally, we examined rates of missing substance use report over time to test for the possibility that legalization affected the accuracy of reporting and we did not find any substantive changes in student reporting following legalization. Third, cannabis legalization was not fully implemented until 2017, when pharmacies started to sell cannabis. Our study period may be too short to detect changes in risky cannabis use and frequent use among adolescents. Fourth, for outcomes where the levels between Uruguay and Chile pre-legalization differ, we assume the difference in the level between Chile and Uruguay have remained the same in the absence of legalization. However, this is a strong assumption that may not be warranted. Last, previous research shows that CAST has strong power to screen for cannabis dependence and cannabis use disorder as defined by the Diagnostic, and Statistic Manual of Mental Disorders (DSM)-5 [39]. However, it has not been clinically validated [39], particularly for low risk levels and for Uruguay and Chile. As countries depart from a prohibitionist model of regulation, continuous use of screening scales could help to identify at-risk individuals to prevent cannabis-related problems before they appear. Nevertheless, clinical validation research should evaluate the relevance of current available measures for cannabis use disorder and risky cannabis use in the context of legalization, as noted by other studies [53, 54].

CONCLUSION

Our results suggest that legalization of recreational cannabis in Uruguay was not associated with increases in past-year and past-

month cannabis use, and with changes in any risky and frequent cannabis use. Any risky and frequent cannabis use temporarily increased in 2014 (before cannabis legalization was fully implemented) among youth 18 to 21 attending secondary education, but subsequently decreased, suggesting Uruguay's regulatory approach has not led to overall changes in risky and frequent cannabis use in adolescents and youth 18 to 21. A future evaluation of the long-term impact of national recreational cannabis legalization on adolescents and youth 18 to 21 is still needed.

ACKNOWLEDGEMENTS

We are thankful to the Observatorio Uruguayo de Drogas and the Observatorio Chileno de Drogas for facilitating the databases and technical assistance. This work was supported by the National Institute on Drug Abuse, R01DA040924-01 (Cerdá). AC and RQ received funding from ANID-Millenium Science Initiative Program, NCS2021003.

DECLARATION OF INTERESTS

None.

AUTHOR CONTRIBUTIONS

Ariadne Rivera-Aguirre: Conceptualization; data curation; formal analysis; investigation; methodology; project administration; resources; software; supervision; validation; visualization. Alvaro Castillo-Carniglia: Conceptualization; data curation; formal analysis; methodology; resources; software. Hannah Laqueur: Conceptualization; methodology. Kara Rudolph: Conceptualization; methodology. Silvia Martins: Conceptualization; funding acquisition. Jessica Ramírez: Investigation; resources. Rosario Queirolo: Investigation. Magdalena Cerda: Conceptualization; funding acquisition; methodology; project administration; supervision.

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How to cite this article: Rivera-Aguirre A, Castillo-Carniglia A, Laqueur HS, Rudolph KE, Martins SS, Ramírez J, et al. Does recreational cannabis legalization change cannabis use patterns? Evidence from secondary school students in Uruguay. Addiction. 2022;1–12. <u>https://doi.org/10.1111/add.</u> 15913