



Full length article

Sex differences in nonmedical prescription tranquilizer and stimulant use trends among secondary school students in Argentina, Chile, and Uruguay



Alexander S. Perlmutter^{a,b,*}, Ariadne E. Rivera-Aguirre^{c,d}, Pia M. Mauro^a,
 Alvaro Castillo-Carniglia^{d,e,1}, Nicolás Rodríguez^f, Nora Cadenas^g, Magdalena Cerdá^{c,d},
 Silvia S. Martins^a

^a Columbia University Mailman School of Public Health, 722 W 168th St, New York, NY, 10032, USA

^b Université Paris Descartes UMR1153, Hôpital Hôtel-Dieu, 1 Place du Parvis Notre-Dame, Paris, 75004, France

^c Center for Opioid Epidemiology and Policy, Department of Population Health, New York University School of Medicine, 180 Madison Avenue, New York, NY, 10016, USA

^d Department of Population Health, New York University School of Medicine, 180 Madison Avenue, New York, NY, 10016, USA

^e Society and Health Research Center, Facultad de Humanidades, Universidad Mayor, Badajoz 30, Santiago, Chile

^f Research Department, National Service for Prevention and Rehabilitation of Drug and Alcohol Use (SENDA), Agustinas 1235, 9th floor, Santiago, Chile

^g Dirección de Epidemiología, Observatorio Argentino de Drogas, Calle Sarmiento 546, Ciudad Autónoma de Buenos Aires, C1041AAL, Argentina

ARTICLE INFO

Keywords:

Nonmedical prescription drug use
 Nonmedical prescription tranquilizer use
 Nonmedical prescription stimulant use
 Adolescents
 Trends
 Epidemiology

ABSTRACT

Background: Little is known about recent nonmedical prescription tranquilizer and stimulant use trends in Latin America. We tested whether recent trends among students in three South American countries differed by sex over time.

Methods: Three countries independently collected National School Students Survey on Drugs. Students in 8th, 10th, and 12th grades were sampled in Argentina (2007–2014, N = 328,202), Chile (2007–2015, N = 136,379), and Uruguay (2007–2016, N = 32,371). Weighted linear regression models predicted the prevalences and trends over time of past-year nonmedical tranquilizer and stimulant use by country, and tested whether trends differed by sex, adjusting for school type and grade.

Results: In Argentina from 2007 to 2014, past-year nonmedical prescription tranquilizer (girls: 2.8 to 2.6%, boys: 2.5 to 2.3%) and stimulant (girls: 1.7 to 1.3%, boys: 1.9 to 1.5%) use trends did not differ by sex. In Chile from 2007 to 2015, nonmedical prescription tranquilizer use trends significantly differed comparing girls (3.9 to 10%) with boys (3.2 to 6.9%); stimulant use trends did not differ comparing girls (1.6 to 2.0%) with boys (2.0 to 1.3%). In Uruguay from 2007 to 2014 and 2014–2016, past-year nonmedical prescription tranquilizer (girls: 5.1 to 6.6%; boys: 2.8 to 4.2%) and stimulant (girls: 1.8 to 0.7%; boys: 1.8 to 0.7%) use trends did not differ by sex.

Conclusions: Trends of nonmedical prescription tranquilizer use recently increased in Chile and Uruguay, widening by sex over time in Chile only. The drivers of increasing tranquilizer use among girls in Chile and Uruguay merit further investigation.

1. Introduction

The adverse health outcomes associated with adolescent non-medical prescription tranquilizer and stimulant use are extensive (Boyd et al., 2015; McCabe et al., 2016, 2017a; McCabe and West, 2013, 2014; Perlmutter et al., 2018; Schepis et al., 2016; Striley et al., 2017; Wang et al., 2015). In particular, threats to psychosocial health associated with misusing these drugs in adolescence may continue into adulthood (Chen et al., 2018; McCabe et al., 2017a, b; McCabe and West, 2013). Most evidence on adolescent nonmedical drug use and adverse health

correlates originates from the United States (US), Canada, Europe, and Australia (Perlmutter et al., 2018). Less is known about adolescent nonmedical drug use in Latin America. Argentina, Chile, and Uruguay have comparable social, economic and epidemiologic characteristics (Jones and Lluch, 2015; Rofman et al., 2016), and may be more similar in some respects (i.e., marijuana legalization/decriminalization) (Mendiburo-Seguel et al., 2017) to the US, Canada, Europe, and Australia than to other Latin American countries; thus, they may also have similar patterns of adolescent drug use.

In Latin America, prescription drug use (tranquilizers and

* Corresponding author at: 722 West 168th St. Room 720.10 New York, NY, 10032, USA.

E-mail address: asp2183@cumc.columbia.edu (A.S. Perlmutter).

¹ Present address and School of public Health, Universidad Mayor. José Toribio Medina 38, Santiago, Chile.

stimulants) presents serious potential public health threats, even drawing concerns of a potential US-type drug epidemic with high mortality and economic cost if prevalence increases (Hynes et al., 2019). Prevalence of nonmedical prescription tranquilizer use among adolescents in Argentina, Chile, and Uruguay is higher than in many other Latin American countries (range: 1.1% to 9.3%) (Observatorio Chileno de Drogas, 2014 (OCD); OCD, 2016; Hynes et al., 2015); the average is around 3% in the US (Miech et al., 2018). One report documented past-year adolescent nonmedical tranquilizer use prevalence as 2.4% in Argentina (2011), 9.3% in Chile (2013), and 3.1% in Uruguay (2014) (Hynes et al., 2015). In Chile, adolescent nonmedical tranquilizer use increased from 4.6% in 2007 to 9.5% in 2015 (OCD, 2014, 2016). Additionally, stimulant use control in Latin America has been weak (Faraone and Bianchi, 2018; Larrobla, 2016), providing opportunity for nonmedical use to spread. Argentina, Chile, and Uruguay had considerably low past-year adolescent nonmedical stimulant use prevalences in the first half of the 2010s (< 2%), lower than prevalences reported in much of the Americas (Hynes et al., 2015); however, much remains unknown about how quickly nonmedical use of these drugs has changed over time in these countries.

No prior studies on trends in adolescent nonmedical prescription drug use over time and on how trends differ by sex in Latin America exist (Martins and Ghandour, 2017). US data showed that girls have a greater prevalence of nonmedical tranquilizer use in early adolescence than boys (Miech et al., 2016), but earlier evidence was mixed (Young et al., 2012). Canadian data showed no differences in nonmedical tranquilizer use by sex, but that boys had greater nonmedical prescription stimulant use compared with girls (Becker et al., 2007). Studies of adolescents and adults in Brazil documented higher nonmedical prescription stimulant use among females than males (Nappo et al., 2002; O'Dea and Cinelli, 2016). Though there is some indication that sex differences are present in Argentina, Chile, and Uruguay (OCD, 2014, 2016; Hynes et al., 2015), these have not yet been consistently examined across the three countries over time. Knowing whether girls are consistently more likely than boys to use these drugs without a prescription would generate knowledge on sex differences concerning nonmedical prescription drug use outside the US context, and allow for hypotheses concerning the sources of any sex disparities in nonmedical prescription drug use. Such knowledge will be useful to these countries when developing their substance use policies.

To address this gap, we conducted an analysis of secondary school students' survey data from the national drug observatories in Argentina, Chile, and Uruguay from 2007 to 2014, 2015, and 2016, respectively. The objectives of the current study were to: 1) estimate the sex-specific yearly prevalences of nonmedical prescription tranquilizer and stimulant use, and 2) test whether girls' and boys' trends of nonmedical prescription tranquilizer and stimulant use differed over time among 8th, 10th, and 12th grade students in Argentina, Chile, and Uruguay. We hypothesized that girls would have greater and increasing nonmedical prescription tranquilizer and stimulant use relative to boys over time in Argentina, Chile, and Uruguay.

2. Methods

2.1. Data source

Individual-level data from adolescents in Argentina, Chile, and Uruguay were obtained from the National School Students Survey on Drugs (Observatorio Argentino de Drogas (OAD), 2016; OCD, 2014; Observatorio Uruguayo de Drogas (OUD), 2009), the same source of data used in the 2015 Report on Drug Use in the Americas² (Hynes et al., 2015). These cross-sectional surveys have been conducted every

two to three calendar years since 2001, and collect information that helps identify trends in characteristics and correlates of substance use among students. The survey instruments are similar to those used in the Monitoring the Future (MTF) surveys in the US (Miech et al., 2016) and the European School Survey Project on Alcohol and Other Drugs (Kraus and Nociar, 2016), and were implemented comparably, but not identically, in Argentina, Chile, and Uruguay. Surveys were self-report and administered confidentially in students' classrooms. Further details about how surveys were administered in the different countries are available in each survey report and/or national drug observatory webpage.

The sampling design included 8th, 10th, and 12th grades students aged 11–20 years (mostly 13–18) in public, private (in all three countries) or subsidized private (only in Chile) schools in geographical areas exceeding 80,000 inhabitants in Argentina, 30,000 in Chile, and 10,000 in Uruguay. Each country's schools and classrooms were selected via clustered, multi-stage random sampling. In Argentina and Uruguay, sampling strata were school types within urban areas³ by region due to the costs of surveying rural areas; primary sampling units were schools followed by classrooms which were randomly selected. In Chile, strata were school type by grade within mostly urban areas^b because 10th and 12th grade students must attend urban schools. Primary sampling units were classrooms. School principals were contacted about the survey when their school was selected, and if schools cooperated, trained interviewers explained to students the objectives of the study, the structure of the questionnaire, and that it was voluntary, confidential, and anonymous (Castillo-Carniglia et al., 2017). The school cooperation rate was greater than 75% for Argentina's, Uruguay's and Chile's most recent survey (OCD, 2016; UNODC, 2017). The final sample was representative of the secondary school student populations in each country. This study was determined to be not human subjects research by the Institutional Review Boards of New York University and Columbia University. Further information on the multi-stage sampling design is available upon request.

2.2. Study population

We restricted the study sample using listwise deletion based on the criteria used in Uruguay to remove individuals with poor quality data before data entry, and to maintain comparability between the three countries. We removed individuals that reported any past month use of five or more illicit substances such as ecstasy, cocaine, and heroin. It is unlikely that adolescents attending school would use all of these drugs at the same time, especially considering some of these substances are widely unavailable in the region (Castillo-Carniglia et al., 2017). Second, we removed lifetime users of a fictional drug "relevo", and inconsistent responders reporting age of initiation of use, past month, past year, and lifetime use of marijuana. In Argentina and Chile, 2684 (0.66%) and 6484 (2.58%) were removed. No additional student from the Uruguay sample was removed, as these changes had been made to the data during the original survey data cleaning phase. After validation, the sample of students included in the data set consisted of N = 405,166 students in Argentina, N = 244,364 students in Chile, and N = 50,648 students in Uruguay.

We used the survey years for which past-year nonmedical prescription tranquilizer and stimulant use were available. In Argentina, these variables were available in 2007, 2009, 2011, and 2014 when assessing past-year nonmedical tranquilizer use. Argentina's 2011 survey's question about past-year nonmedical stimulant use gave examples of antidepressants and stimulants (Supplemental Table), so we did not use that data. In Uruguay, data were available in the same years as Argentina (for tranquilizer use) and 2016. In Chile, they were available

² Inter-American Drug Abuse Control Commission (CICAD) published this report.

³ The 2017 urban population in Argentina was 91.7%, while in Chile it was 87.5% and 95.2% in Uruguay (United Nations Population Division, 2018)

in 2007, 2009, 2011, 2013 and 2015. We also restricted ages to 11–20 years old to exclude unrealistic ages (e.g., 3 or 36 years old) and to be consistent with the age ranges used in a previous study examining drug use response methodology among Chilean students in 8th–12th grades (Castillo-Carniglia et al., 2017). After restriction to non-missing data, our final sample consisted of $N = 328,202$ students in Argentina, $N = 136,379$ students in Chile, and $N = 32,371$ students in Uruguay. A total of 12,280 (3.5%), 1979 (1.5%), 1317 (4.7%) observations with no values for past-year nonmedical tranquilizer use and 19,141 (5.7%), and 6603 (4.4%), 1366 (4.4%) with no values for past-year nonmedical stimulant use were dropped from the adjusted analysis in which we modeled those outcomes for Argentina, Chile, and Uruguay, respectively. Additionally, observations missing any of the measures (section 2.3) were excluded from the main analysis.

2.3. Measures

2.3.1. Outcome Variable

1) past-year nonmedical prescription tranquilizer use, and 2) past-year nonmedical prescription stimulant use. For each question, a response option indicating past-year use was present in the surveys that students completed in Argentina and Uruguay. For Chile, we combined the responses “in the past 30 days” and “more than a month and less than a year ago” to create the past-year use variable for each substance.

2.3.2. Independent variables

Self-reported sex (boy, girl), survey year, school type (public and private in all countries, subsidized schools in Chile only), and school grade (8th, 10th, and 12th) were the independent variables.

2.4. Statistical analyses

2.4.1. Sample characteristics and descriptives

Analyses were conducted separately in each country. We computed the sample characteristics and descriptive statistics of the independent variables by the two outcome variables. Percentages were survey-weighted to match the population distribution of secondary school students. To account for the complex survey design, variance estimates were obtained through Taylor linearization series using STATA/SE 15.1 (Stata Corp, 2016).

2.4.2. Adjusted prevalence model

Prevalences Of Use Over Time. To estimate the prevalence of past-year nonmedical prescription tranquilizer use by sex in every year, we regressed the outcome on a categorical year variable, other independent variables including sex, and a cross-product term for statistical interaction between sex and year, using weighted linear regression. If the Wald chi-squared test for statistical interaction between sex and year was not significant ($p > 0.05$), we removed the cross-product term from the model for parsimony.

Regression coefficients for the year variable indicated the average prevalence difference in past-year nonmedical prescription tranquilizer use comparing each dummy variable for year (e.g., 2009) with the reference group for year (2007). Prevalence differences were transformed to prevalences as model-based predicted probabilities using the ‘margins’ command in STATA/SE 15.1 (Stata Corp, 2016). This process was done for each country separately and repeated for past-year nonmedical prescription stimulant use.

2.4.3. Diagnosing trends visually for potential splines

We visually examined the graphical output from the prevalence models to determine where, if at all, the slope of the prevalences may have changed from year to year for either sex in order to create piecewise linear spline variables (Toms and Lesperance, 2003). Spline variables are continuous terms for year that take the same value for year before the hypothesized change point (i.e., knot) and then increase

from the knot. For instance, if there were a knot in 2013 based upon our visual diagnosis, then the years before 2013 would have the same value for continuous year (e.g., 0: 2007, 2009, 2011; 1: 2013, 2: 2015). Each segment of time (e.g., 2007–2011 and 2013–2015) would be considered two different splines. There were $k + 1$ splines for every k knot.

2.4.4. Adjusted trend model

Trends Of Use Over Time. To estimate the trend of past-year non-medical prescription tranquilizer use by sex across time, we regressed the outcome on a continuous year variable (or splines if applicable), other independent variables including sex, and a cross-product term for statistical interaction between sex and continuous year (or splines if applicable) using weighted linear regression. As in section 2.4.2., we removed cross-product terms from the model when the Wald chi-squared test for statistical interaction was not statistically significant.

The trend model estimated the yearly average change in prevalence over time (i.e., slope or trend) indicated by the continuous year variable. Trend was significant when the t -test for year was $p < 0.05$. A significant cross-product term for statistical interaction between sex and pre-knot spline meant trends differed by sex before a specified knot, or, in the absence of a knot, across the entire time period. A significant cross-product term for statistical interaction between sex and post-knot spline meant trends differed by sex after a specified knot. We reported whether trends differed by sex for different segments of time—otherwise, over the entire study period. We also overlaid boys’ and girls’ trendlines on the prevalence graph. This process was done for each country separately and repeated for past-year nonmedical prescription stimulant use.

3. Results

3.1. Argentina (2007–2014)

The average age in Argentina was 15.1 years old (SD: 1.8). Over half of Argentina’s student population was girls (Table 1). More students were in 8th versus 10th and 12th grades, and public (62%) versus private schools. Average unadjusted past-year nonmedical prescription tranquilizer and stimulant use prevalences were 2.5% and 1.5%, respectively.

The average prevalences of past-year nonmedical prescription tranquilizer and stimulant use were greater among 12th and 10th graders than 8th graders, and among 10th graders than 12th and 8th graders, respectively (Table 1).

The average unadjusted prevalence of past-year nonmedical prescription tranquilizer use was greater for girls than boys (2.6% vs. 2.2%, Table 1). Adjusted trends did not differ by sex (Fig. 1a).

The average unadjusted prevalence of past-year nonmedical prescription stimulant use was also greater for girls than boys (1.6% vs. 1.5%, Table 1). Adjusted trends of nonmedical tranquilizer use also did not differ by sex ($p = 0.228$) (Fig. 1b).

3.2. Chile (2007–2015)

The average age in Chile was 15.5 (SD: 1.7). Chile’s student population was split evenly by sex (Table 2). More students were in 8th and 10th versus 12th grades, and subsidized schools (54%) versus public (36%) and private schools (10%). Average unadjusted past-year non-medical prescription tranquilizer and stimulant use prevalences were 6.2% and 1.4%, respectively.

Average past-year nonmedical tranquilizer and stimulant use prevalences were greater among 10th and 12th graders than 8th graders (Table 2).

The average unadjusted prevalence of past-year nonmedical tranquilizer use was greater for girls than boys (7.4% vs. 5.1%, Table 2). We modeled trends from 2007 to 2015 for boys and girls with a cross-product term between year and sex because there was no significant

Table 1
Sample and descriptive characteristics by past-year nonmedical prescription tranquilizer and stimulant use of secondary school[§] students aged 11–20 years in Argentina (2007–2014) from the National School Students Survey.

	Overall sample characteristics		Past-year nonmedical prescription tranquilizer use		Past-year nonmedical prescription stimulant use	
	% [95% CI]	N	% [95% CI]	N	% [95% CI]	N
Total		328,202	2.47 [2.35, 2.60]	7,734	1.54 [1.44, 1.63]	3,830
Sex						
Boys	45.78 [45.10, 46.46]	149,655	2.28 [2.12, 2.45]	3,099	1.63 [1.50, 1.77]	1,735
Girls	54.22 [53.54, 54.90]	178,547	2.63 [2.49, 2.78]	4,635	1.46 [1.35, 1.58]	2,095
Current school grade						
8th	43.19 [42.15, 44.24]	125,692	1.86 [1.71, 2.03]	2,188	1.27 [1.13, 1.43]	1,159
Boys	45.20 [44.10, 46.31]	59,808	1.61 [1.42, 1.83]	888	1.14 [0.98, 1.32]	509
Girls	41.49 [40.39, 42.60]	65,884	2.09 [1.89, 2.32]	1,230	1.40 [1.20, 1.62]	650
10th	33.83 [33.11, 34.56]	114,275	2.93 [2.74, 3.13]	3,160	1.89 [1.73, 2.07]	1,613
Boys	33.68 [32.86, 34.51]	51,801	2.71 [2.44, 3.00]	1,227	2.11 [1.86, 2.39]	729
Girls	33.96 [33.19, 34.74]	62,474	3.12 [2.88, 3.37]	1,933	1.71 [1.53, 1.91]	884
12th	22.98 [22.37, 23.60]	88,235	2.91 [2.68, 3.17]	2,456	1.51 [1.35, 1.69]	1,058
Boys	21.12 [20.42, 21.81]	38,046	3.00 [2.63, 3.44]	984	1.92 [1.63, 2.26]	497
Girls	24.55 [23.87, 25.24]	50,189	2.85 [2.59, 3.14]	1,472	1.21 [1.05, 1.39]	561
Current school type						
Public	62.25 [60.56, 63.91]	218,729	2.45 [2.32, 2.60]	5,108	1.48 [1.38, 1.60]	2,486
Boys	64.88 [63.12, 66.60]	102,052	2.28 [2.11, 2.47]	2,191	1.54 [1.39, 1.70]	1,157
Girls	60.03 [58.17, 61.87]	116,677	2.61 [2.43, 2.80]	2,917	1.44 [1.30, 1.58]	1,329
Private	37.75 [36.09, 39.44]	109,473	2.50 [2.29, 2.73]	2,626	1.64 [1.47, 1.82]	1,344
Boys	35.12 [33.40, 36.88]	47,603	2.28 [1.97, 2.64]	908	1.83 [1.58, 2.12]	578
Girls	39.97 [38.13, 41.83]	61,870	2.66 [2.43, 2.92]	1,718	1.49 [1.30, 1.71]	766

Abbreviations: Confidence Interval (CI), Frequency (N): [§] secondary school varies by country but refers to grades 8–12 in Argentina.; Missing values for past-year nonmedical prescription tranquilizer (N = 12,280) and stimulant use (N = 19,141).;

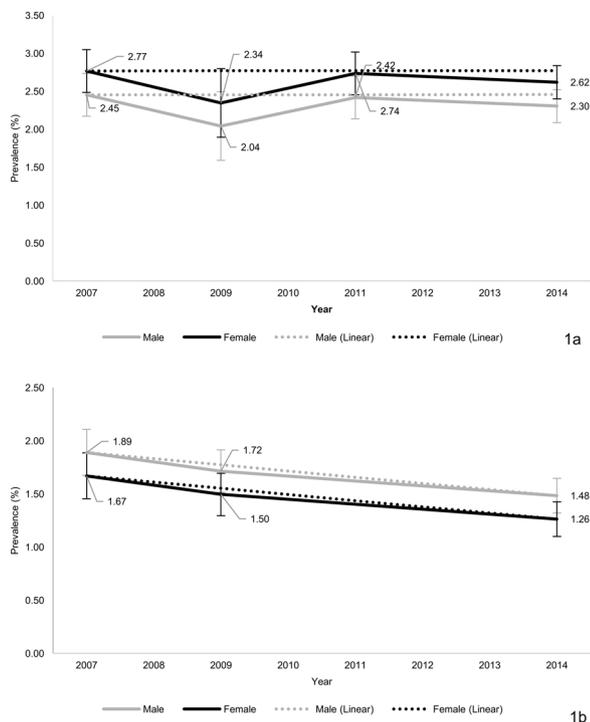


Fig. 1. (a) Past-year nonmedical prescription tranquilizer use prevalence and trend among secondary school 11–20-year-old students in Argentina by sex from 2007 to 2014 (N = 315,922). (b) Past-year nonmedical prescription stimulant use prevalence and trend among secondary school 11–20-year-old students in Argentina by sex from 2007 to 2014 (N = 242,677)

Note: All estimates presented in figures were adjusted for school grade and school type. Annotations. Fig. 1a: Girls’ and boys’ trends are no different and no evidence of change from 2007 to 2014. Fig. 1b: Girls’ and boys’ trends are no different and decrease at a rate of 0.058 percentage points per year from 2007 to 2014. Fig. 2a: Girls’ and boys’ trends increase at rates of 0.912 and 0.572 percentage points per year, respectively, from 2007 to 2015.

change in the time trends in 2009, as tested using linear splines. The rate of past-year nonmedical tranquilizer use increased for girls (3.9% to 10.0%) faster than for boys (3.2% to 6.9%) in Chile (Fig. 2a).

The average unadjusted prevalence of past-year nonmedical stimulant use was not different by sex (1.4% vs. 1.5%, Table 2). Adjusted trends increased for girls (1.6%–2.0%) and decreased for boys (2.0%–1.3%), intersecting in 2010 (Fig. 2b).

3.3. Uruguay (2007–2016)

The average age in Uruguay was 15.3 (SD: 1.4). Over half of Uruguay’s student population was girls (Table 3). More students were in 8th versus 10th and 12th grades, and public (81%) versus private schools. Average unadjusted past-year nonmedical prescription tranquilizer and stimulant use prevalences were 4.0% and 0.9%, respectively.

Average past-year nonmedical tranquilizer and stimulant use prevalences were greater among 12th graders versus 10th graders and 8th graders, and among 10th and 12th graders versus 8th graders, respectively (Table 3).

The average unadjusted prevalence of past-year nonmedical tranquilizer use was greater for girls than boys (5.4% vs. 2.9%, Table 3). We modeled trends from 2007 to 2014 and 2014–2016 because a spline term with a knot in 2014 was statistically significant. Adjusted trends did not differ (p = 0.101) by sex from 2007 to 2014. They also did not differ (p = 0.818) from 2014 to 2016 (Fig. 3a).

The unadjusted prevalences of past-year nonmedical stimulant use in Uruguay were not different by sex (Table 3). Adjusted trends did not differ (p = 0.789) for girls (1.8% to 0.7%) and boys (1.8% to 0.7%) (Fig. 3b).

4. Discussion

Our study used the National School Students Surveys on Drugs to examine the overall and sex-specific trends over time in past-year nonmedical prescription tranquilizer and stimulant use in Argentina (2007–2014), Chile (2007–2015), and Uruguay (2007–2016). To the best of our knowledge, this study was the first to model trends over time

Table 2
Sample and descriptive characteristics by past-year nonmedical prescription tranquilizer and stimulant use of secondary school[§] students aged 11–20 years in Chile (2007–2015) from the National School Students Survey.

	Overall sample characteristics		Past-year nonmedical prescription tranquilizer use		Past-year nonmedical prescription stimulant use	
	% [95% CI]	N	% [95% CI]	N	% [95% CI]	N
Total		136,379	6.21 [6.01, 6.41]	8996	1.43 [1.34, 1.54]	3025
Sex						
Boys	48.79 [48.05, 49.54]	66,661	5.11 [4.86, 5.38]	3818	1.37 [1.28, 1.48]	1626
Girls	51.21 [50.46, 51.95]	69,718	7.44 [7.16, 7.73]	5178	1.48 [1.36, 1.60]	1399
Current school grade						
8th	36.39 [35.92, 36.86]	51,357	5.01 [4.71, 5.33]	2778	1.26 [1.12, 1.41]	1026
Boys	37.12 [36.32, 35.59]	25,407	3.82 [3.49, 4.19]	1,121	1.12 [0.95, 1.32]	511
Girls	35.69 [34.88, 36.51]	25,950	6.18 [5.72, 6.67]	1,657	1.39 [1.22, 1.58]	515
10th	36.20 [35.72, 36.68]	49,637	7.05 [6.67, 7.46]	3581	1.64 [1.51, 1.79]	1199
Boys	36.47 [35.59, 37.35]	24,354	5.53 [5.08, 6.01]	1,502	1.48 [1.32, 1.65]	628
Girls	35.95 [35.05, 36.87]	25,283	8.53 [8.00, 9.08]	2,079	1.80 [1.61, 2.02]	571
12th	27.41 [26.95, 27.88]	35,385	7.04 [6.07, 7.40]	2637	1.60 [1.43, 1.80]	800
Boys	26.42 [25.63, 27.22]	16,900	6.35 [5.81, 6.93]	1,195	1.85 [1.65, 2.09]	487
Girls	28.36 [27.52, 29.21]	18,485	7.65 [7.24, 8.07]	1,442	1.38 [1.14, 1.67]	313
Current school type						
Public	35.98 [35.50, 36.46]	52,479	6.13 [5.82, 6.46]	3622	1.58 [1.43, 1.74]	1314
Boys	35.56 [34.72, 36.41]	25,349	5.08 [4.71, 5.47]	1,553	1.51 [1.33, 1.72]	707
Girls	36.37 [35.51, 37.25]	27,130	7.11 [6.69, 7.57]	2,069	1.64 [1.45, 1.85]	607
Private	10.19 [9.96, 10.43]	21,033	4.85 [4.37, 5.38]	1217	1.36 [1.21, 1.52]	405
Boys	10.68 [10.20, 11.19]	10,634	3.80 [3.36, 4.29]	526	1.59 [1.37, 1.85]	231
Girls	9.72 [9.31, 10.16]	10,399	5.95 [5.14, 6.88]	691	1.12 [0.92, 1.36]	174
Subsidized	53.83 [53.34, 54.32]	62,867	6.70 [6.10, 6.51]	4157	1.46 [1.34, 1.59]	1306
Boys	53.75 [52.88, 54.63]	30,678	5.40 [5.01, 5.81]	1,739	1.37 [1.34, 1.56]	688
Girls	53.90 [53.00, 54.80]	32,189	7.93 [7.53, 8.34]	2,418	1.54 [1.37, 1.74]	618

Abbreviations: Confidence Interval (CI), Frequency (N).

§ secondary school varies by country, but refers to grades 8 but refers to grades 8–12 in Chile.

Missing values for past-year nonmedical prescription tranquilizer (N = 1,979) and stimulant use (N = 6,603)

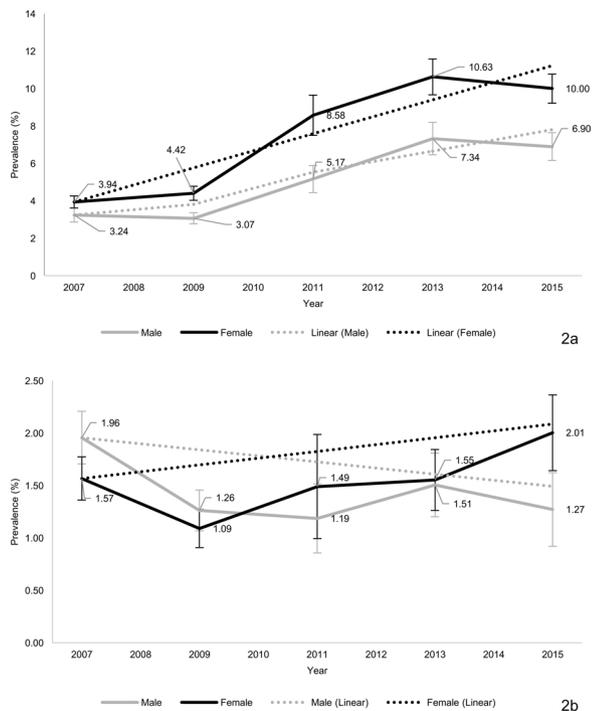


Fig. 2. Past-year nonmedical prescription tranquilizer use prevalence and trend among secondary school 11–20-year-old students in Chile by sex from 2007 to 2015 (N = 134,192).

(b) Past-year nonmedical prescription stimulant use prevalence and trend among secondary school 11–20-year-old students in Chile by sex from 2007 to 2015 (N = 129,769)

Note: All estimates presented in figures were adjusted for school grade and school type. Annotations. Fig. 2b: Girls’ and boys’ trends increased and decreased at rates of 0.065 and 0.058 percentage points per year, respectively, from 2007 to 2015.

in nonmedical tranquilizer and stimulant use in these South American countries and quantify differences in trends for girls and boys. Our study corroborated earlier findings (Bejarano et al., 2011; OCD, 2014; Hynes et al., 2015) indicating that in each country, secondary school girls had a higher prevalence of nonmedical tranquilizer use compared with boys. In Chile, we observed larger increases in nonmedical tranquilizer use prevalence for girls than boys from 2007 to 2015. In Uruguay, nonmedical tranquilizer use was more prevalent for girls than boys from 2007 to 2016; both sexes’ use trended down from 2007 to 2014 then up until 2016. This trend is very similar to the corresponding trend observed among US high school students over the same period (Miech et al., 2018). Lastly, nonmedical stimulant use was low and trended down equally for both boys and girls in Argentina and Uruguay and boys in Chile. These trends largely mimic those seen among US high school students (Miech et al., 2018). We are unable to compare or contrast our results with trends in other Latin American countries due to a lack of reporting.

The first major finding of this paper was that nonmedical prescription tranquilizer use prevalences were higher for girls than boys in each country over time. A primary reason for high prevalence of non-medical tranquilizer use among adolescent girls may be high levels of indicated use for affective and sleeping disorders in the general population of adolescent girls and women, in part because these disorders are diagnosed more in girls (Bouscoulet et al., 2008; Grant et al., 2005; McCabe et al., 2017a; Schepis and Hakes, 2013; Stein et al., 2017; Vicente et al., 2012). A study on sleeping disorders among adults aged 40 years and older in Latin American cities (Bouscoulet et al., 2008) found that sedative use was much greater among women than men in Montevideo, Uruguay (27% vs. 13%) and Santiago, Chile (31% vs. 11%). High sedative use among adult women may influence adolescent girls’ use patterns through increasing availability. For instance, in Argentina, 67% of women and 21% of men obtained prescription tranquilizers for nonmedical use from a friend (Secretaría de Programación para la Prevención de la Drogadicción y la Lucha contra el Narcotráfico, 2017). In Chile, 50% of past-year nonmedical tranquilizer users

Table 3

Sample and descriptive characteristics by past-year nonmedical prescription tranquilizer and stimulant use of secondary school[§] students aged 11–20 years in Uruguay (2007–2016) from the National School Students Survey.

	Overall sample characteristics		Past-year nonmedical prescription tranquilizer use		Past-year nonmedical prescription stimulant use	
	% [95% CI]	N	% [95% CI]	N	% [95% CI]	N
Total		32,371	4.04 [3.74, 4.35]	1265	0.91 [0.78, 1.06]	315
Sex						
Boys	46.33 [45.26, 47.40]	14,808	2.92 [2.57, 3.32]	385	0.91 [0.74, 1.13]	142
Girls	53.67 [52.60, 54.74]	17,563	5.36 [4.92, 5.85]	880	0.98 [0.80, 1.21]	173
Current school grade						
8th	45.39 [41.83, 49.40]	13,838	2.68 [2.33, 3.08]	336	0.75 [0.60, 0.93]	104
Boys	47.51 [43.46, 51.59]	6,713	1.86 [1.45, 2.38]	114	0.71 [0.50, 0.99]	46
Girls	43.55 [39.45, 47.75]	7,125	3.44 [2.92, 4.05]	222	0.79 [0.58, 1.07]	58
10th	34.71 [31.96, 37.56]	11,761	4.91 [4.35, 5.54]	523	1.17 [0.93, 1.48]	136
Boys	34.85 [31.90, 37.92]	5,374	3.41 [2.80, 4.14]	148	1.07 [0.77, 1.47]	64
Girls	34.58 [31.72, 37.56]	6,387	6.23 [5.40, 7.18]	375	1.27 [0.92, 1.74]	72
12th	19.90 [17.88, 22.10]	6772	6.57 [5.85, 7.38]	406	1.00 [0.72, 1.41]	75
Boys	17.64 [15.65, 19.82]	2,721	4.79 [3.88, 5.90]	123	1.15 [0.68, 1.92]	32
Girls	21.86 [19.60, 24.30]	4,051	7.82 [6.81, 8.97]	283	0.91 [0.59, 1.40]	43
Current school type						
Public	81.08 [79.72, 82.36]	25,470	4.48 [4.12, 4.87]	1023	0.94 [0.80, 1.12]	242
Boys	80.05 [78.50, 81.51]	11,495	3.10 [2.69, 3.57]	306	0.90 [0.70, 1.16]	101
Girls	81.97 [80.36, 83.47]	13,975	5.64 [5.13, 6.21]	717	0.98 [0.77, 1.24]	141
Private	18.92 [17.64, 20.28]	6901	3.10 [2.71, 3.75]	242	0.97 [0.68, 1.37]	73
Boys	19.95 [18.49, 21.50]	3,313	2.23 [1.65, 2.99]	79	0.96 [0.63, 1.46]	41
Girls	18.03 [16.53, 19.64]	3,588	4.11 [3.40, 4.95]	163	0.97 [0.65, 1.47]	32

Abbreviations: Confidence Interval (CI), Frequency (N).

§ secondary school varies by country, but refers to grades 8 but refers to grades 8–12 in Uruguay.

Missing values for past-year nonmedical prescription tranquilizer (N = 1,317) and stimulant use (N = 1,366).

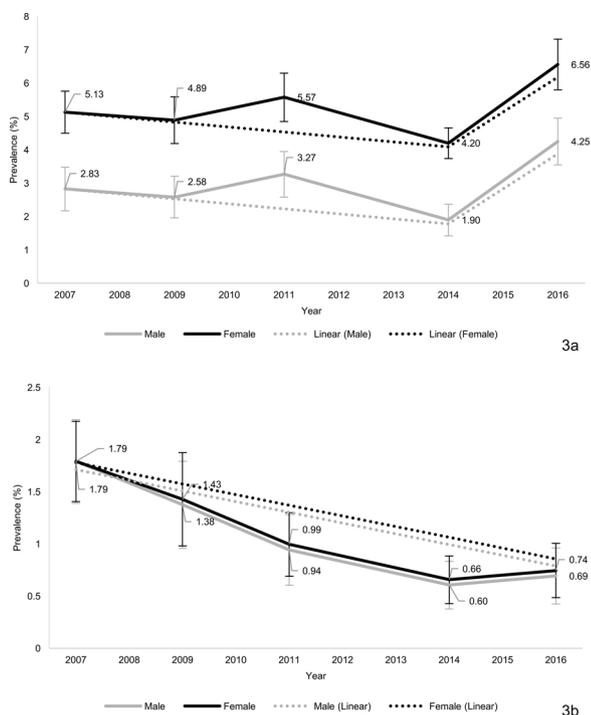


Fig. 3. (a) Past-year nonprescription tranquilizer use prevalence and trend among secondary school 11–20-year-old students in Uruguay by sex from 2007 to 2016 (N = 31,054).

(b) Past-year nonprescription stimulant use prevalence and trend among secondary school 11–20-year-old students in Uruguay by sex from 2007 to 2016 (N = 31,005)

Note: All estimates presented in figures were adjusted for school grade and school type. Annotations Fig. 3a: Girls’ and boys’ trends decreased from 2007 to 2014 at 0.150 percentage points per year, then increased from 2014 to 2016 at 1.199 percentage points per year. Fig. 3b: Girls’ and boys’ trends decreased at 0.103 percentage points per year from 2007 to 2016.

primarily received the medication through a partner, relative, or friend, higher than all other means (OCD, 2017). As observed in many samples, high within-home availability is a common factor in adolescents having access to their parents’ prescription medications for misuse (Chen et al., 2018; Perlmutter et al., 2018). Higher availability in homes may help decrease adolescent girls’ perceived risk of nonmedical use of tranquilizers. For instance, in Uruguay, adolescents were five times more likely to consume tranquilizers without a prescription if someone in their home used them (OUD, 2016). In Brazilian capital cities, lifetime adolescent tranquilizer/sedative use was higher for adolescent girls whose family members were tranquilizer/sedative users, and for adolescents who perceived low risk of use (Opaleye et al., 2013). In contrast, Bejarano et al. (2011) found that South American adolescent⁴ girls had greater perceived risk of frequent nonmedical tranquilizer use than boys. If captured in future surveys, measuring girls’ and boys’ perceived risk and availability of nonmedical tranquilizer use could help illuminate why girls have greater and increasing use rates than boys. Previous research on our study’s population found that perceived risk and availability’s relationship with marijuana use varies from country to country (Schleimer et al., 2019); therefore, variation in perceived risk and availability of nonmedical prescription drug use (data not available in our study) might explain differences in use trends not only between Argentina, Chile, and Uruguay but also these countries and the US, Canada, Europe, and Australia.

Our second major findings were that trends in past-year nonmedical prescription tranquilizer use 1) increased for both boys and girls in Chile from 2007 to 2015, but faster for the latter, and 2) that a sudden spike occurred in Uruguay from 2014 to 2016 for boys and girls. In both contexts, a higher proportion of girls used prescription tranquilizers nonmedically than boys. Explanations for these large increases are needed. In the US in the 1970s, 12th grade nonmedical barbiturate and tranquilizer use was its highest on record—over 10% (Miech et al., 2016)—when prescriptions for anxiolytics peaked nationwide (Lader, 1991). A similar pattern among US adults is currently transpiring with opioids (Kolodny et al., 2015). More evidence is needed on tranquilizer

⁴ Argentina, Ecuador, Uruguay (2005 data), and Bolivia (2004 data)

prescription practices and regional distribution and sales in the Southern Cone.

Our last major finding was that nonmedical prescription stimulant was low and did not differ by sex across time in any of the three countries. Policy changes based upon intra-country events may be driving these trends. For instance, after an ADHD diagnosis increase in the 1990s in Argentina, a 2005 statement by more than 200 prominent experts on the issue criticized the spread of ADHD diagnosis, and suggested four main actions: 1) only expert field professionals to assess children, 2) medication as a last resort only, 3) child's family and social context taken into account, and 4) restricting media broadcasting of ADHD information (Faraone and Bianchi, 2018). This statement led to regulatory changes in packaging, and new information about warnings and contraindications in the country (Faraone and Bianchi, 2018). Meanwhile, after high use in the early years of our study in Uruguay, the United Nations cautioned the Ministry of Health in 2010 concerning high stimulant use (Larrobla, 2016). Concerning Chile, literature on the epidemiology of ADHD and stimulant treatment is still scarce, so it is difficult to establish how the indication of prescription stimulants is related to nonmedical use let alone sex differences (Navarro et al., 2018). Nevertheless, it is known that Chile's second most procured legal drug is methylphenidate and that the country was one of the top 10 worldwide consumers of the drug in 2013 (INCB, 2014). This should stimulate the investigation of the relationship between the observed trends, ADHD diagnosis, and indicated prescription stimulant consumption among adolescents. In sum, health system, cultural, and political factors may be driving trends in nonmedical use of stimulants in Argentina and Uruguay while less is known about the situation in Chile.

Our study has numerous strengths. First, our sample was nationally representative of each country's adolescent student population in each survey year. Second, students recorded answers confidentially in their classrooms, limiting the social desirability bias that would be introduced by an interviewer. Third, since our samples overlapped and succeeded those in other reports and studies (Bejarano et al., 2011; OCD, 2014; Hynes et al., 2015), we were able to compare our results within countries. Because we reproduced or found consistencies with others' results, our study appeared to exhibit internal and external validity. Finally, concerning external validity, each of the countries that we examined have important differences, such as the types of schools that children attend and distributions of class sizes, which could serve as a potential indicator of dropouts. Highlighting these factors and perceived risk and availability (Schleimer et al., 2019; Bejarano et al., 2011) in future studies can help us better understand differences in trends between these countries and with the US, Canada, Europe, and Australia.

Limitations are noted. First, self-reported measures may be affected by recall bias concerning the timing or type of substance use behaviors. Second, within-country differences in survey questions were observed for outcomes in Uruguay from 2007-2009. It was possible that our categorization of nonmedical use overestimated prevalences in those years; however, our 2007 results were in accordance with Uruguay's previously reported 2005 prevalences (Bejarano et al., 2011), increasing confidence in the current findings. Third, no country had variables available in all years on perceived risk and availability, limiting our ability to assess correlates of the observed substance use trends. These measures could be added in future studies to more comprehensively understand the trends and sex differences in adolescent nonmedical tranquilizer and stimulant use. Fourth, our validation of the survey did not assess the validity of the questions; nevertheless, the surveys were designed based on those asked in the MTF annual survey of adolescents (Miech et al., 2016). Fifth, survey administration methodology varied by country; specifically, Chile used separate answer sheets while Argentina and Uruguay used a questionnaire booklet to record responses. A study on Chile's questionnaire methodology found that use of separate answer sheets relative to responding in the questionnaire booklet significantly increased the time taken to respond to

the survey, the number of inconsistencies, and reports of using a fake drug (Castillo-Carniglia et al., 2017). Although our validation of the survey corrected for differences in the number of inconsistencies and other potential sources of measurement error, the effect on the results in Chile may not be fully corrected. Our analyses were stratified by country to account for such differences, so we could not make direct statistical comparisons in trends across countries. Lastly, we were unable to identify any timely social or economic policy shifts that may have led to the observed changes in nonmedical prescription tranquilizer and stimulant use, suggesting a non-policy-related mechanism.

5. Conclusion

In this study, we conducted three repeated cross-sectional descriptive analyses of sex-specific trends of past-year nonmedical prescription tranquilizer and stimulant use in three South American countries. Nonmedical stimulant use appears to be a decreasing threat to adolescents in Argentina and Uruguay, and boys in Chile, while nonmedical tranquilizer use appears to be an increasing concern in recent years, primarily among youth in Chile and Uruguay. Assessing overprescribing and indicated use of tranquilizers among women in future research may be the next steps towards comprehensively understanding nonmedical tranquilizer use among adolescents in these countries. The actions taken by Argentina's and Uruguay's governments to reduce adolescent nonmedical stimulant use may not be applicable to reducing nonmedical tranquilizer use because these trends may have different drivers.

Role of funding

This work was supported by the US National Institutes of Health, National Institute on Drug Abuse [grant numbers T32DA031099 (PI: Hasin), 1R01DA040924-01A1 (PI: Cerdá), and K01DA045224 (PI: Mauro)]. Funders had no role in the study design; in the collection, analysis or interpretation of data; in the writing of the report; or in the decision to submit the article for publication.

Contributors

Mr. Perlmutter and Dr. Martins designed the study. Ms. Rivera-Aguirre and Dr. Cerdá managed the data. Mr. Perlmutter, Ms. Rivera Aguirre, Dr. Mauro, Dr. Castillo-Carniglia, and Dr. Martins conducted the literature review and data analysis. Mr. Rodriguez, Ms. Cadenas, and Dr. Cerdá contributed to the literature review. All authors read and approved the final manuscript.

Declaration of Competing Interest

No conflict declared.

Acknowledgements

Thank you, Susie Hoffman, Lam-Ha Dang, Paul Reeping, Diana Garofolo, Hillary Samples, Luis Segura, Julian Santaella-Tenorio for your excellent feedback and patience.

Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:<https://doi.org/10.1016/j.drugalcdep.2019.107607>.

References

Becker, W.C., Fiellin, D.A., Desai, R.A., 2007. Non-medical use, abuse and dependence on sedatives and tranquilizers among US adults: psychiatric and socio-demographic

- correlates. *Drug Alcohol Depend.* 90, 280–287. <https://doi.org/10.1016/j.drugalcdep.2007.04.009>.
- Bejarano, B., Ahumada, G., Sánchez, G., Cadenas, N., de Marco, M., Hynes, M., Cumsille, F., 2011. Perception of risk and drug use: an exploratory analysis of explanatory factors in six Latin American countries. *J. Int. Drug Alcohol Tobacco Res.* 1, 9–17.
- Bouscoulet, L.T., Vázquez-García, J.C., Muiño, A., Márquez, M., López, M.V., de Oca, M.M., Talamo, C., Valdivia, G., Pertuze, J., Menezes, A.M.B., Pérez-Padilla, R., 2008. Prevalence of sleep related symptoms in four latin American cities. *J. Clin. Sleep Med.* 4, 579–585.
- Boyd, C.J., Austic, E., Epstein-Ngo, Q., Veliz, P.T., McCabe, S.E., 2015. A prospective study of adolescents' nonmedical use of anxiolytic and sleep medication. *Psychol. Addict. Behav.* 29, 184–191. <https://doi.org/10.1037/adb0000026>.
- Castillo-Carniglia, A., Pizarro, E., Marín, J.D., Rodríguez, N., Casas-Cordero, C., Cerdá, M., 2017. The effects of using answer sheets on reported drug use and data quality in a classroom survey: a cluster-randomized study. *Drug Alcohol Depend.* 178, 194–200. <https://doi.org/10.1016/j.drugalcdep.2017.05.012>.
- Chen, L.-Y., Perlmutter, A.S., Segura, L., Santaella, J., Schleimer, J., Mendez, M., Ghandour, L., Cerda, M., Martins, S.S., 2018. Nonmedical prescription drug use in adolescents and young adults. In: Schepis, T.S. (Ed.), *The Prescription Drug Abuse Epidemic: Incidence, Treatment, Prevention, and Policy*. ABC-CLIO, Santa Barbara.
- Faraone, S.A., Bianchi, E., 2018. *The Journey of ADHD in Argentina: From the Increase in Methylphenidate Use to Tensions among Health Professionals. Global Perspectives on ADHD: Social Dimensions of Diagnosis and Treatment in Sixteen Countries*. Johns Hopkins University Press.
- Grant, B.F., Hasin, D.S., Stinson, F.S., Dawson, D.A., June Ruan, W., Goldstein, R.B., Smith, S.M., Saha, T.D., Huang, B., 2005. Prevalence, correlates, co-morbidity, and comparative disability of DSM-IV generalized anxiety disorder in the USA: results from the National Epidemiologic Survey on Alcohol and Related Conditions. *Psychol. Med.* 35, 1747–1759. <https://doi.org/10.1017/S0033291705006069>.
- Hynes, M., Clarke, P., Ahumada, G., Cumsille, F., Demarco, M., Lemos, A.M., Araneda, J.C., Keuroglan, L., 2015. Report on Drug Use in the Americas. Inter-American Drug Abuse Control Commission, Washington, DC.
- Hynes, M., Clarke, P., Ahumada, G., Cumsille, F., Lemos, A.M., Barry, T., Araneda, J.C., 2019. Report on Drug Use in the Americas. Inter-American Drug Abuse Control Commission, Washington, DC.
- International Narcotics Control Board, 2014. Report of the International Narcotics Control Board 2013. Vienna, Austria.
- Jones, G., Lluch, A., 2015. *The Impact of Globalization on Argentina and Chile: Business Enterprises and Entrepreneurship*. Edward Elgar Publishing, Incorporated.
- Kolodny, A., Courtwright, D.T., Hwang, C.S., Kreiner, P., Eadie, J.L., Clark, T.W., Alexander, G.C., 2015. The prescription opioid and heroin crisis: a public health approach to an epidemic of addiction. *Annu. Rev. Public Health* 36, 559–574. <https://doi.org/10.1146/annurev-publhealth-031914-122957>.
- Kraus, L., Nociar, A., 2016. ESPAD Report 2015: Results From The European School Survey Project On Alcohol And Other Drugs. European Monitoring Centre for Drugs and Drug Addiction.
- Lader, M., 1991. History of benzodiazepine dependence. *J. Subst. Abuse Treat.* 8, 53–59.
- Larrobla, E., 2016. *El TDAH y El Uso de La Ritalina Para Su Tratamiento*, Facultad de Psicología. Universidad de la República Uruguay, Montevideo, Uruguay.
- Martins, S.S., Ghandour, L.A., 2017. Nonmedical use of prescription drugs in adolescents and young adults: not just a Western phenomenon. *World Psychiatry* 16, 102–104. <https://doi.org/10.1002/wps.20350>.
- McCabe, S.E., Veliz, P., Boyd, C.J., 2016. Early exposure to stimulant medications and substance-related problems: the role of medical and nonmedical contexts. *Drug Alcohol Depend.* 163, 55–63. <https://doi.org/10.1016/j.drugalcdep.2016.03.019>.
- McCabe, S.E., Veliz, P., Boyd, C.J., Schulenberg, J.E., 2017a. Medical and nonmedical use of prescription sedatives and anxiolytics: adolescents' use and substance use disorder symptoms in adulthood. *Addict. Behav.* 65, 296–301. <https://doi.org/10.1016/j.addbeh.2016.08.021>.
- McCabe, S.E., Veliz, P., Wilens, T.E., Schulenberg, J.E., 2017b. Adolescents' prescription stimulant use and adult functional outcomes: a national prospective study. *J. Am. Acad. Child Adolesc. Psychiatry* 56, 226–233. <https://doi.org/10.1016/j.jaac.2016.12.008>. e224.
- McCabe, S.E., West, B.T., 2013. Medical and nonmedical use of prescription stimulants: results from a national multicohort study. *J. Am. Acad. Child Adolesc. Psychiatry* 52, 1272–1280. <https://doi.org/10.1016/j.jaac.2013.09.005>.
- McCabe, S.E., West, B.T., 2014. Medical and nonmedical use of prescription benzodiazepine anxiolytics among U.S. High school seniors. *Addict. Behav.* 39, 959–964. <https://doi.org/10.1016/j.addbeh.2014.01.009>.
- Mendiburo-Seguel, A., Vargas, S., Oyanedel, J.C., Torres, F., Vergara, E., Hough, M., 2017. Attitudes towards drug policies in Latin America: results from a Latin-American Survey. *Int. J. Drug Policy* 41, 8–13. <https://doi.org/10.1016/j.drugpo.2016.10.001>.
- Miech, R.A., Johnston, L.D., O'Malley, P.M., Bachman, J.G., Schulenberg, J.E., Patrick, M.E., 2018. Monitoring the Future National Survey Results on Drug Use, 1975–2017: Volume I, Secondary School Students.
- Miech, R.A., Johnston, L.D., O'Malley, P.M., Bachman, J.G., Schulenberg, J.E., 2016. *Monitoring the Future National Survey Results on Drug Use, 1975–2015: Volume I, Secondary School Students*. Drug Use, 1975–2015: Volume I, Secondary School Students.
- Nappo, S.A., Tabach, R., Noto, A.R., Galduróz, J.C.F., Carlini, E.A., 2002. Use of anorectic amphetamine-like drugs by Brazilian women. *Eat. Behav.* 3, 153–165. [https://doi.org/10.1016/S1471-0153\(01\)00054-X](https://doi.org/10.1016/S1471-0153(01)00054-X).
- Navarro, S.R., Rojas, P., Ochoa, M.P., 2018. From problematic children to problematic diagnosis: the paradoxical trajectories of child and adolescent ADHD in Chile. In: Bergey, M.R., Filipe, A.M., Conrad, P., Singh, I. (Eds.), *Global Perspectives on ADHD: Social Dimensions of Diagnosis and Treatment in Sixteen Countries*. Johns Hopkins University Press.
- O'Dea, J., Cinelli, R.L., 2016. Use of Drugs to Change Appearance in Girls and Female Adolescents, Chemically Modified Bodies. Springer, pp. 51–76. https://doi.org/10.1057/978-1-137-53535-1_4.
- Observatorio Argentino de Drogas, 2016. *Manual de Epidemiología Guía para Observatorios Provinciales de Drogas*. Buenos Aires, Argentina.
- Observatorio Chileno de Drogas, 2014. *Décimo estudio nacional de drogas en población escolar: principales resultados nacionales, 2013*. Santiago de Chile, Chile.
- Observatorio Chileno de Drogas, 2016. *Décimo primer estudio nacional de drogas en población escolar: principales resultados nacionales, 2015*. Santiago de Chile, Chile.
- Observatorio Chileno de Drogas, 2017. *Décimo segundo estudio nacional de drogas en población general de Chile: principales resultados nacionales, 2016*. Santiago de Chile, Chile.
- Observatorio Uruguayo de Drogas y Junta Nacional de Drogas, 2009. *Encuesta Nacional sobre Consumo de Drogas en Enseñanza Media 2009*. Presidencia de la República Uruguay.
- Observatorio Uruguayo de Drogas y Junta Nacional de Drogas, 2016. *VII Encuesta Nacional Sobre Consumo de Drogas en Estudiantes de Enseñanza Media*. pp. 2016.
- Opaleye, E.S., Noto, A.R., Sanchez, Z.M., Amato, T.C., Locatelli, D.P., Gossop, M., Ferris, C.P., 2013. Nonprescribed use of tranquilizers or sedatives by adolescents: a Brazilian national survey. *BMC Public Health* 13, 499. <https://doi.org/10.1186/1471-2458-13-499>.
- Perlmutter, A.S., Bauman, M., Mantha, S., Segura, L.E., Ghandour, L., Martins, S.S., 2018. Nonmedical prescription drug use among adolescents: global epidemiological evidence for prevention, assessment, diagnosis, and treatment. *Curr. Addict. Rep.* 5, 120–127. <https://doi.org/10.1007/s40429-018-0194-y>.
- Rofman, R., Amarante, V., Apella, I., 2016. *Demographic Change in Uruguay: Economic Opportunities and Challenges*. World Bank Publications.
- Schepis, T.S., Hakes, J.K., 2013. Dose-related effects for the precipitation of psychopathology by opioid or tranquilizer/sedative nonmedical prescription use: results from the National Epidemiologic Survey on Alcohol and Related Conditions. *J. Addict. Med.* 7, 39–44. <https://doi.org/10.1097/ADM.0b013e318277e9e5>.
- Schepis, T.S., West, B.T., Teter, C.J., McCabe, S.E., 2016. Prevalence and correlates of co-ingestion of prescription tranquilizers and other psychoactive substances by U.S. High school seniors: results from a national survey. *Addict. Behav.* 52, 8–12. <https://doi.org/10.1016/j.addbeh.2015.08.002>.
- Schleimer, J.P., Rivera-Aguirre, A.E., Castillo-Carniglia, A., et al., 2019. Investigating how perceived risk and availability of marijuana relate to marijuana use among adolescents in Argentina, Chile, and Uruguay over time. *Drug Alcohol Depend.* 201, 115–126. <https://doi.org/10.1016/j.drugalcdep.2019.03.029>.
- Secretaría de Programación para la Prevención de la Drogadicción y la Lucha contra el Narcotráfico, 2017. *Sexto Estudio Nacional en población de 12 a 65 años, sobre consumo de sustancias psicoactivas*. Argentina. Buenos Aires, Argentina.
- Stein, D.J., Lim, C.C.W., Roest, A.M., de Jonge, P., Aguilar-Gaxiola, S., Al-Hamzawi, A., Alonso, J., Benjet, C., Bromet, E.J., Bruffaerts, R., de Girolamo, G., Florescu, S., Gureje, O., Haro, J.M., Harris, M.G., He, Y., Hinkov, H., Horiguchi, I., Hu, C., Karam, A., Karam, E.G., Lee, S., Lepine, J.-P., Navarro-Mateu, F., Pennell, B.-E., Piazza, M., Posada-Villa, J., ten Have, M., Torres, Y., Viana, M.C., Wojtyniak, B., Xavier, M., Kessler, R.C., Scott, K.M., 2017. The cross-national epidemiology of social anxiety disorder: data from the World Mental Health Survey Initiative. *BMC Med.* 15, 143. <https://doi.org/10.1186/s12916-017-0889-2>.
- Striley, C.W., Kelso-Chichetto, N.E., Cottler, L.B., 2017. Nonmedical prescription stimulant use among girls 10–18 years of age: associations with other risky behavior. *J. Adolesc. Health* 60, 328–332. <https://doi.org/10.1016/j.jadohealth.2016.10.013>.
- Toms, J.D., Lesperance, M.L., 2003. Piecewise regression: a tool for identifying ecological thresholds. *Ecology* 84, 2034–2041. <https://doi.org/10.1890/02-0472>.
- Vicente, B., Saldivia, S., Melipillán, R., Valdivia, M., Kohn, R., 2012. Prevalence of psychiatric disorders among Chilean children and adolescents. *Rev. Med. Chil.* 140, 447–457. <https://doi.org/10.1111/j.1469-7610.2012.02566.x>.
- Wang, Y., Cottler, L.B., Striley, C.W., 2015. Differentiating patterns of prescription stimulant medical and nonmedical use among youth 10–18 years of age. *Drug Alcohol Depend.* 157, 83–89. <https://doi.org/10.1016/j.drugalcdep.2015.10.006>.
- Young, A.M., Glover, N., Havens, J.R., 2012. Nonmedical use of prescription medications among adolescents in the United States: a systematic review. *J. Adolesc. Health* 51, 6–17. <https://doi.org/10.1016/j.jadohealth.2012.01.011>.
- United Nations Office on Drugs and Crime, 2017. *World Drug Report 2016*. Vienna, Austria.