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### Authors

Borges, Guilherme

Benjet, Corina

Orozco, Ricardo

et al.

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# Alcohol, cannabis and other drugs and subsequent suicide ideation and attempt among young Mexicans



Guilherme Borges <sup>a,\*</sup>, Corina Benjet <sup>a</sup>, Ricardo Orozco <sup>a</sup>, Maria-Elena Medina-Mora <sup>a</sup>, David Menendez <sup>b</sup>

<sup>a</sup> Nacional Institute of Psychiatry, de Psiquiatría, Tlalpan, Mexico City, Mexico

<sup>b</sup> University of Wisconsin- Madison, Department of Psychology, WI, USA

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## ABSTRACT

**Objective:** To report results from a follow-up study of alcohol, cannabis and other drugs on suicidal behavior.

**Method:** We estimated prospective associations of substance use as a risk factor for incident suicide ideation and attempt, from a follow-up conducted in 2013 (n = 1071) of the original Mexican Adolescent Mental Health Survey conducted in 2005.

**Results:** Cannabis use before age 15 (ideation risk ratio (RR) = 3.97; 95% confidence interval (CI) = 1.43–11.03; attempt RR = 5.23; 95% CI = 1.17–23.32), early onset of DSM-IV drug use disorder (DUD) among cannabis users (ideation RR = 3.30; 95% CI = 1.11–9.84; attempt RR = 4.14; 95% CI = 1.28–13.36), high frequency of cannabis use (RR for attempts = 4.60; 1.03–20.60) and recent DSM-IV-DUD among cannabis users (RR for attempts = 4.74; 1.09–20.57) increased the RR. For “other drug use”, significant results were found among those with high frequency use of other drugs such that they had a higher RR of suicide attempt (5.04; 1.03–24.64). For alcohol, only those who initiated alcohol before age 15 had higher RRs of suicide attempt (1.79; 1.00–3.20).

**Discussion:** Those who used cannabis at an early age, early onset of DSM-IV-DUD, and those with heavy cannabis use and recent DSM-IV-DUD among cannabis users in the last 12-months had increased risk of suicide ideation and attempt. Drugs other than cannabis showed some of these associations, but to a lesser degree. Prevention of substance use and treatment of those already engaged in drug use, by decreasing suicide ideation and attempt, may help to prevent suicide in Mexico.

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## 1. Introduction

According to a recent WHO report, in Mexico the number of suicides between the years 2000 and 2012 increased by 10.6% and the suicide death rate increased by 17.1%, while at the international level the suicide death rate decreased by 26% (World Health Organization, 2014a). Evidence-based actions need to be implemented to stop the increasing trend of suicides in Mexico. However, because suicide is a rare outcome, few analytical studies on death by suicide exist in Mexico to provide the empirical evidence needed (Chávez-Hernández and Macías-García, 2016). Nevertheless, a key

risk factor for death by suicide is suicidal ideation and attempts (World Health Organization, 2014a; Nock et al., 2008), also a matter of great psychological distress by themselves and more readily available for study (Borges et al., 2009).

Mental disorders, including alcohol use disorders (World Health Organization, 2014b) and drug use disorders (Borges et al., 2000) are one of the main risk factors for death by suicide and suicide attempts. Alcohol dependence was responsible for the second largest proportion (13.25%) of the suicide disability-adjusted life years (DALY) that were attributable to mental and substance use disorders in 2010, only behind major depressive disorder (Ferrari et al., 2014). The attributable fraction of alcohol on suicide in 2012 was estimated to be 20% of all DALYS ((World Health Organization, 2014a), Fig. 14). These same sources also point to the impact of other substances on suicide, especially opioid, amphetamine and cocaine dependence (Ferrari et al., 2014). New

\* Corresponding author. National Institute of Psychiatry, Ramon de la Fuente, Calzada Mexico Xochimilco 101, Col. San Lorenzo Huipulco, Mexico City CP14370, Mexico.

E-mail address: [guibor@imp.edu.mx](mailto:guibor@imp.edu.mx) (G. Borges).

evidence is also emerging on the possible role of cannabis use on suicidal behavior (Agrawal and Lynskey, 2014; Borges et al., 2016; Shalit et al., 2016), a matter of great relevance because of the large prevalence of cannabis use in several countries, including Mexico (United Nations Office on Drugs and Crime, 2015).

There is variation in the magnitude and consistency of the association between alcohol and drug use with suicide, suicide ideation and suicide attempts (suicidal behavior). Research is more abundant and consistent for the use of alcohol, as reviewed others (Berglund and Ojehagen, 1998; Conner et al., 2008; Norström and Rossow, 2016). Recent meta-analyses have showed elevated risk for these outcomes attributed to alcohol use disorders (Darvishi et al., 2015; Roerecke and Rehm, 2014). On the other hand, there is an emerging consensus that the use of drugs (illicit drugs, specifically cocaine, amphetamines and opioids), increases the risk of suicidal behavior (Schneider, 2009). The evidence for the relation between illicit drug use and suicidal behavior is nevertheless limited in that most of the studies are cross-sectional (Borges et al., 2000; Miller et al., 2011; Wong et al., 2013), with few case-control (Petronis et al., 1990) or follow-up studies (Westman et al., 2015; Hjorthøj et al., 2015). Longitudinal research on the topic is even more limited among adolescents and young adults, two groups especially at risk for both substance use and suicidal behavior (World Health Organization, 2014a; Nock et al., 2008; World Health Organization, 2014b). Results among adolescents are inconsistent, with some positive findings (Wilcox and Anthony, 2004; Andrews and Lewinsohn, 1992; Fergusson and Lynskey, 1995; Newcomb et al., 1993; Reinherz et al., 1995; Seo and Lee, 2013; Rossow and Norström, 2014) but also some reports of no-association for both alcohol and drug use and onset of suicide ideation and attempts (Wilcox and Anthony, 2004; Strandheim et al., 2014; Cluver et al., 2015; Thompson et al., 2007; Thompson and Light, 2011; Werbeloff et al., 2016). When available, most of the evidence on substance use are of “any use” and often does not differentiate early users and heavy users, or users of alcohol and specific illicit drugs. Among the latter, cannabis use is of particular relevance because it is the drug of preference in most countries (including Mexico), changes in legislation for cannabis use are seen everywhere and its association with suicidal behavior has been a matter of considerable debate. Also, most research on the topic is from high income countries, but low and middle income countries also share a heavy burden of substance use and suicide, and the importance of particular substances varies across countries, with alcohol use usually showing a larger burden in low and middle income countries.

Because of the lack of longitudinal data for suicide ideation and attempt in Mexico, we investigated the role of alcohol, cannabis and other drug use as potential risk factors for the incidence of suicide ideation and attempt among a group of respondents living in the Mexico City Metropolitan Area, aged 12–17 when first assessed in 2005 and 19–26 years of age when assessed at follow-up (Benjet et al., 2016). In our study, by focusing on substance use and substance use disorders, we aim to narrow the impact of other variables that may play a role when studying the incidence of suicidal ideation and attempt.

## 2. Material and methods

### 2.1. Dataset

This is a prospective cohort study that uses data from a recent follow-up conducted in 2013 (Benjet et al., 2016) of the original Mexican Adolescent Mental Health Survey conducted in 2005 (Benjet et al., 2009). The Mexican Adolescent Mental Health Survey was a stratified multistage area probability survey, designed to be

representative of the 1,834,661 adolescents aged 12 to 17 who were permanent residents of the Mexico City Metropolitan Area at the time of the survey and who were not institutionalized. Participants were administered the computer-assisted adolescent version of the World Mental Health Composite International Diagnostic Interview (WMH-CIDI (Kessler and Üstün, 2004; Merikangas et al., 2009);) by trained lay interviewers in their homes. A verbal and written explanation of the study was given to both parents and adolescents. Interviews were administered only to those participants for whom a signed informed consent from a parent and/or legal guardian and the assent of the adolescent were obtained. The wave I sample included 3005 adolescents, with a 71% response rate. The ethics committee of the National Institute of Psychiatry approved the recruitment, consent and field procedures. The data were subsequently weighted to adjust for differential probabilities of selection and nonresponse. Post-stratification to the total Mexico City Metropolitan Area adolescent population according to the year 2000 Census in the target age and sex range was also performed (Benjet et al., 2009). Eight years later, in 2013 when the participants were 19–26 years old, we searched for all original participants for a follow-up interview. We were able to locate and re-interview 1071 respondents from the baseline Mexican Adolescent Mental Health Survey, representing a response rate of 62.0% of located and eligible participants, though this was only 35.6% of the wave I sample. Because of possible attrition bias in the follow-up,  $\chi^2$  tests were performed which tested differences in socio-demographic and mental health characteristics of those participants that were re-interviewed versus those that were not, which found no differences in baseline lifetime DSM-IV disorders for wave I vs. wave II respondents. The variables that showed bias (i.e., sex, being a student, living with both parents and income) were used to calculate weights using the WTADJUST procedures in SUDAAN software (Research Triangle Institute, 2012) to ensure that wave II participants represented the initial wave I sample (Benjet et al., 2016). The 1071 individuals re-interviewed in 2013 are the sample of this report.

### 2.2. Variables

*Suicide ideation and suicide attempt.* Wave I and wave II surveys used the same diagnostic instrument, the WMH-CIDI and are fully comparable. For this report we are interested in comparing the incidence of two outcomes, suicide ideation and suicide attempts (suicidal behavior), during the eight-year period. Lifetime and 12-month prevalence and risk factors for suicidal behaviors in the wave I survey have been extensively reported before (Borges et al., 2007, 2008; Nock et al., 2012). In 2005 the respondents were asked about lifetime experiences of suicidal ideation (“Have you ever seriously thought about committing suicide?”), and suicide attempts (“Have you ever attempted suicide?”). Those positive for suicide ideation and suicide attempt in 2005 (prevalent cases) were excluded from this report. Those free of suicide ideation and suicide attempt were then asked about the same experiences in 2013 and those reporting suicide ideation and suicide attempt at any time during the eight-year interval are the incident cases. Because self-administered surveys have been shown to yield higher rates of reporting of embarrassing behaviors than interviewer-administered surveys (Turner et al., 1998), these experiences were listed in a self-administered booklet and referred to by letter (Events “A” and “C”) for respondents who were able to read.

*Substance use (alcohol, cannabis and other drugs).* Alcohol use data include lifetime use of any alcoholic beverage, and illicit drug use data include cannabis, cocaine, tranquilizers or stimulants used without a medical prescription, and other illegal substances including heroine, inhalants, LSD, etc. Because most of our sample

used mainly cannabis and there is a recent interest in the role of cannabis on suicidal behavior, we present information for cannabis use separately. Among those who used drugs other than cannabis, the most common drugs were tranquilizers or stimulants followed by cocaine and other illegal substances.

Consistent with the approach taken in other studies participating in the World Mental Health Surveys, we used what has been termed a “gated approach” for assessing alcohol and drug use disorders (Degenhardt et al., 2007, 2008; Grant et al., 2007) when using the Diagnostic and Statistical Manual of Mental Disorders, fourth edition (DSM-IV). Accordingly, our alcohol and drug use disorder categories included four diagnoses: alcohol abuse, alcohol dependence with abuse, illicit drug abuse, and illicit drug dependence with abuse.

Our exposure variables are hierarchical (i.e., scalar). Thus, for the category of lifetime alcohol exposure, our reference is (1) never having had an alcoholic beverage and our positive alcohol exposure categories are (2) lifetime use but not before age 15 and (3) lifetime use before age 15; for 12 month alcohol use our reference is (1) never having had any alcoholic beverage/never in the last 12 months and our positive alcohol exposure categories are (2) drank in the last 12 months but less than once a month and (3) drank in the last 12 months at least 1–3 times per month. For lifetime DSM-IV Alcohol Use Disorders (AUD), our reference is (1) No AUD, (2) any AUD at age 15 or later and (3) AUD before age 15; for 12 month the reference is (1) no AUD, (2) any lifetime AUD but not in the 12 months prior to baseline and (3) 12 month AUD at baseline. Parallel scalar definitions of exposure were used for cannabis and for other drugs use.

*Other variables used for control of confounding.* Baseline DSM-IV mental disorders. The diagnostic assessment included measurement of DSM-IV mood (major depressive disorder, dysthymia, and bipolar disorder), anxiety (panic disorder, agoraphobia without panic disorder, specific phobia, social phobia, generalized anxiety disorder, posttraumatic stress disorder), impulse-control (oppositional-defiant disorder, conduct disorder, and attention deficit/hyperactivity disorder), and eating disorders (bulimia and binge disorder).

Baseline sociodemographic factors previously shown to be related to suicidal behavior (Nock et al., 2008), such as sex, age/cohort, years of education (in three categories: 0–6, 7–9 and 10–12), occupation (student or not), were used to adjust the incidence reported for suicidal behavior within the eight-year period.

### 2.3. Analysis

We estimated the eight-year incidence of suicide ideation and suicide attempt by cross-tabulations. To estimate prospective associations of substance use as risk factors for incident suicide ideation and attempt, risk ratios (RR) were calculated as functions of average marginal predictions from fitted logistic regression models (Graubard and Korn, 1999). Average marginal predictions allow comparisons of predictive outcomes, risk between groups of people in the population, after controlling for differences in covariate distributions between the groups. We preferred to estimate the RR directly instead of using odds ratios (OR), which is now feasible with standard software (Bieler et al., 2010). We used RRs for the eight-year period instead of hazard rates from time-to-event (survival) analysis because we lack exact knowledge of the time of event occurrence. We used the SUDAAN 11.0.1 software package to obtain point estimates, standard errors, confidence intervals, and p values for the parameters and contrasts of interest using the Taylor series method (Wolter, 1985). Multivariate significance was evaluated using Wald  $\chi^2$  tests and 0.05 as the probability level.

To assess possible study attrition bias,  $\chi^2$  tests were performed

which tested differences in socio-demographic and mental health characteristics of those participants that were re-interviewed versus those that were not. The variables that showed bias were used to calculate weights using the WTADJUST procedures in SUDAAN software to ensure that wave II participants represented the initial wave I sample.

### 3. Results

Table 1 shows the distribution of respondents free of suicide ideation at wave I (2005) ( $n = 960$ ) and those free of suicide attempt in 2005 ( $n = 1041$ ) by basic sociodemographic characteristics at wave II (2013). The distributions are similar for both outcomes. Gender and age distribution was very even, in part due to the generation of weights. One third of the sample was still attending school, and most had attained a high-school level education. Almost half of sample was still living with their parents, but about a third was married/cohabiting and about a third had already a child.

Table 2 shows the distribution and the crude risk estimates of lifetime substance use and the eight-year incidence of suicide ideation and attempt (top panel) and the estimates for 12-month substance use and suicide ideation and attempt (bottom panel). While the incidence of both suicide ideation ( $n = 212$ , an eight-year incidence risk of 13.4% for suicide ideation) and suicide attempt ( $n = 61$ , an eight-year incidence risk of 5.9% for suicide attempt) tends to be higher among those that used all substances before 15 years of age and among those who used more frequently in the last 12 months, overall  $\chi^2$  tests for the differences between the

**Table 1**  
Sociodemographic characteristics at wave II (year 2013) of cohort free of suicide ideation and attempt at wave I (year 2005). Mexican Adolescent Mental Health Survey follow-up, 2005–2013.

	Suicidal ideation free cohort		Suicidal attempt free cohort	
	(n = 960)		(n = 1041)	
	n	% (S.E.)	n	% (S.E.)
Sex				
Male	435	52.1 (2.1)	455	50.6 (2.0)
Female	525	47.9 (2.1)	586	49.4 (2.0)
Age (years)				
19	33	3.1 (0.6)	38	3.3 (0.6)
20	198	17.1 (1.7)	210	16.8 (1.7)
21	198	17.5 (1.6)	207	17.2 (1.4)
22	171	14.8 (1.5)	184	14.5 (1.5)
23	143	17.8 (1.5)	153	17.6 (1.4)
24	126	16.6 (1.5)	148	17.5 (1.5)
25	90	12.9 (1.1)	100	12.9 (1.0)
26	1	0.1 (0.1)	1	0.1 (0.1)
Currently at school				
No	619	66.7 (1.6)	673	66.9 (1.5)
Yes	341	33.3 (1.6)	368	33.1 (1.5)
Highest education				
None/primary	34	4.4 (0.6)	36	4.2 (0.6)
Secondary (7–9 years)	318	33.9 (1.6)	344	33.8 (1.7)
High school (10–12)	404	40.4 (2.0)	440	40.7 (2.0)
College (13+)	204	21.4 (1.4)	221	21.3 (1.5)
Married/cohabiting				
No	649	66.2 (1.6)	695	65.5 (1.5)
Yes	311	33.8 (1.6)	346	34.5 (1.5)
Has at least one child				
No	636	65.4 (1.7)	677	64.3 (1.6)
Yes	324	34.6 (1.7)	364	35.7 (1.6)
Living with both parents				
No	456	50.2 (2.4)	506	51.3 (2.1)
Yes	504	49.8 (2.4)	535	48.7 (2.1)

Unweighted n's; weighted %; S.E. - Standard Error.

**Table 2**

Eight year cumulative incidence of suicidal behaviors (at wave II) by baseline substance use and disorders (alcohol or drugs).

	Suicidal ideation at wave II					Suicidal attempt at wave II				
	N	n	Risk (S.E.)	X <sup>2</sup> (d.f.)	p-value	N	n	Risk (S.E.)	X <sup>2</sup> (d.f.)	p-value
<b>Total</b>	<b>960</b>	<b>121</b>	<b>13.4 (1.3)</b>	-	-	<b>1041</b>	<b>61</b>	<b>5.9 (0.8)</b>	-	-
<b>Lifetime substance use at baseline (onset)</b>										
<b>Alcohol use<sup>a</sup></b>			2.24 (2)	0.124				3.04 (2)	0.062	
Never	425	46	11.0 (1.6)			448	19	4.3 (1.0)		
At 15 or older	116	11	9.7 (3.3)			126	5	3.7 (2.1)		
Before 15 y	397	60	17.0 (2.4)			445	36	8.3 (1.5)		
<b>Cannabis use</b>			1.34 (2)	0.277				1.75 (2)	0.191	
Never	941	114	12.6 (1.5)			1015	57	5.5 (1.0)		
At 15 or older	12	3	19.9 (12)			17	1	6.3 (6.8)		
Before 15 y	7	4	71.0 (19)			9	3	34.1 (17)		
<b>Other drug use<sup>b</sup></b>			1.15 (2)	0.329				3.80 (2)	0.033	
Never	937	116	13.0 (1.3)			1011	59	5.9 (0.8)		
At 15 or older	9	1	8.0 (7.9)			11	0	0.0 (0.0)		
Before 15 y	14	4	37.9 (14)			19	2	10.8 (8.1)		
<b>DSM-IV AUD<sup>c</sup></b>			0.09 (2)	0.917				8.89 (2)	<0.001	
No AUD	938	118	13.4 (1.3)			1015	61	6.0 (0.8)		
At 15 or older	11	2	13.7 (9.8)			13	0	0.0 (0.0)		
Before 15 y	11	1	10.5 (8.0)			13	0	0.0 (0.0)		
<b>DSM-IV DUD among cannabis users<sup>d</sup></b>			3.93 (2)	0.030				3.58 (2)	0.040	
No DUD	951	118	13.1 (1.4)			1029	59	5.7 (0.8)		
At 15 or older	3	0	0.0 (0.0)			4	0	0.0 (0.0)		
Before 15 y	6	3	58.5 (22)			8	2	30.2 (16)		
<b>DSM-IV DUD among other drug users<sup>b</sup></b>			2.17 (2)	0.131				1.86 (2)	0.173	
No DUD	953	119	13.2 (1.3)			1029	60	5.8 (0.8)		
At 15 or older	3	0	0.0 (0.0)			4	0	0.0 (0.0)		
Before 15 y	4	2	59.1 (25)			8	1	18.4 (16)		
<b>12-month substance use at baseline</b>										
<b>Alcohol use frequency</b>			0.77 (2)	0.472				0.02 (2)	0.982	
Never/not in past 12 m	842	100	12.6 (1.3)			903	51	5.9 (0.8)		
Less than once a month	62	11	16.3 (4.4)			72	6	6.1 (2.7)		
At least 1–3 times per month	56	10	19.4 (6.3)			66	4	5.4 (3.0)		
<b>Cannabis use frequency</b>			0.68 (2)	0.515				0.46 (2)	0.635	
Never/not in past 12 m	949	118	13.1 (1.4)			1027	59	5.7 (0.8)		
Less than once a month	7	1	14.5 (18)			10	1	10.6 (13)		
At least 1–3 times per month	4	2	50.7 (26)			4	1	32.0 (25)		
<b>Other drug use frequency</b>			0.60 (2)	0.553				0.42 (2)	0.661	
Never/not in past 12 m	951	119	13.3 (1.3)			1030	59	5.7 (0.8)		
Less than once a month	7	1	7.6 (7.6)			8	1	6.3 (6.3)		
At least 1–3 times per month	2	1	53.2 (35)			3	1	40.3 (30)		
<b>DSM-IV AUD</b>			0.02 (2)	0.982				8.76 (2)	<0.001	
No AUD	938	118	13.4 (1.3)			1015	61	6.0 (0.8)		
Lifetime disorder but not 12 month	6	1	12.1 (12)			9	0	0.0 (0.0)		
12 month disorder	16	2	12.3 (7.4)			17	0	0.0 (0.0)		
<b>DSM-IV DUD among cannabis users</b>			1.72 (2)	0.195				2.55 (2)	0.094	
No DUD	951	118	13.1 (1.4)			1029	59	5.7 (0.8)		
Lifetime disorder but not 12 month	2	0	0.0 (0.0)			5	0	0.0 (0.0)		
12 month disorder	7	3	42.6 (25)			7	2	31.2 (23)		
<b>DSM-IV DUD among other drug users</b>			1.49 (2)	0.241				2.58 (2)	0.092	
No DUD	953	119	13.2 (1.3)			1029	60	5.8 (0.8)		
Lifetime disorder but not 12 month	2	0	0.0 (0.0)			7	0	0.0 (0.0)		
12 month disorder	5	2	38.7 (25)			5	1	24.4 (22)		

S.E. - Standard Error; d.f. - Degrees of Freedom; AUD - Alcohol Use Disorder; DUD - Drug Use Disorder; Unweighted frequencies, weighted risks.

<sup>a</sup> 22 missing values.<sup>b</sup> Other drugs include: cocaine, medical prescription drugs not taken as prescribed or without prescription and other drugs, like LSD, peyote, etc.<sup>c</sup> AUD include DSM-IV alcohol abuse and alcohol dependence.<sup>d</sup> DUD include DSM-IV drug abuse and drug dependence.

distributions of substance use across lifetime and 12-month use and disorders were found mostly for cannabis use. Very few differences are seen for alcohol use.

Table 3 shows the relative risk estimates of suicide ideation and attempt adjusted by our set of demographics and mental disorders, by lifetime use (top panel) and by 12-month substance use (bottom panel). Here it is more apparent the differences in risk estimates by levels of substance use involvement. For lifetime use (top panel), those that initiated use of alcohol, cannabis and other drugs before age 15 have a tendency to show increased RRs of suicide ideation and suicide attempt (except for other drug use and suicide attempt). In the same vein, for 12-month (bottom panel) alcohol,

cannabis and other drug use, those who used more frequently had higher RRs for ideation and attempt (except for high frequency of past year alcohol use and suicide attempt). More specifically, for the relation between alcohol use and suicide ideation and attempts, we only found that those who used alcohol before age 15 had an increased risk of suicide attempt (RR = 1.79; 95%CI = 1.00–3.20). For other drugs, while their use increased the RRs in almost all instances, only those who used more frequently in the last 12 months had an increased and statistically significant RR for suicide attempt (RR = 5.04; 1.03–20.60). On the other hand, every variable of exposure to cannabis use produced increased RRs of suicide ideation and attempt, a handful with only borderline significance;

**Table 3**  
Adjusted risk ratios of suicidal behaviors (at wave II) by baseline substance use and disorders (alcohol or drugs).

	Suicidal ideation at wave II		Suicidal attempt at wave II	
	aRR <sup>a</sup>	95% CI	aRR <sup>a</sup>	95% CI
<b>Lifetime substance use at baseline (onset)</b>				
<b>Alcohol use</b>				
Never	1.00	(ref.)	1.00	(ref.)
At 15 or older	0.61	(0.31–1.18)	0.87	(0.22–3.38)
Before 15 y	1.25	(0.75–2.09)	<b>1.79</b>	<b>(1.00–3.20)</b>
<b>Cannabis use</b>				
Never	1.00	(ref.)	1.00	(ref.)
At 15 or older	1.36	(0.33–5.62)	1.11	(0.11–11.44)
Before 15 y	<b>3.97</b>	<b>(1.43–11.03)</b>	<b>5.23</b>	<b>(1.17–23.32)</b>
<b>Other drug use</b>				
Never	1.00	(ref.)	1.00	(ref.)
At 15 or older	0.51	(0.05–5.21)	N/E	N/E
Before 15 y	1.96	(0.97–3.97)	0.98	(0.19–5.09)
<b>DSM-IV AUD</b>				
No AUD	1.00	(ref.)	1.00	(ref.)
At 15 or older	0.68	(0.09–4.91)	N/E	N/E
Before 15 y	0.49	(0.11–2.11)	N/E	N/E
<b>DSM-IV DUD among cannabis users</b>				
No DUD	1.00	(ref.)	1.00	(ref.)
At 15 or older	N/E	N/E	N/E	N/E
Before 15 y	<b>3.30</b>	<b>(1.11–9.84)</b>	<b>4.14</b>	<b>(1.28–13.36)</b>
<b>DSM-IV DUD among other drug users</b>				
No DUD	1.00	(ref.)	1.00	(ref.)
At 15 or older	N/E	N/E	N/E	N/E
Before 15 y	3.37	(0.89–12.72)	1.79	(0.18–17.77)
<b>12-month substance use at baseline</b>				
<b>Alcohol use frequency</b>				
Never/not in past 12 m	1.00	(ref.)	1.00	(ref.)
Less than once a month	0.97	(0.56–1.67)	0.91	(0.35–2.39)
At least 1–3 times per month	1.07	(0.41–2.76)	0.80	(0.19–3.24)
<b>Cannabis use frequency</b>				
Never/not in past 12 m	1.00	(ref.)	1.00	(ref.)
Less than once a month	0.83	(0.08–8.36)	1.64	(0.17–16.08)
At least 1–3 times per month	3.18	(0.99–10.21)	<b>4.60</b>	<b>(1.03–20.60)</b>
<b>Other drug use frequency</b>				
Never/not in past 12 m	1.00	(ref.)	1.00	(ref.)
Less than once a month	0.71	(0.11–4.42)	1.09	(0.17–7.04)
At least 1–3 times per month	2.42	(0.55–10.59)	<b>5.04</b>	<b>(1.03–24.64)</b>
<b>DSM-IV AUD</b>				
No AUD	1.00	(ref.)	1.00	(ref.)
Lifetime disorder but not 12 month	0.65	(0.08–5.50)	N/E	N/E
12 month disorder	0.56	(0.12–2.60)	N/E	N/E
<b>DSM-IV DUD among cannabis users</b>				
No DUD	1.00	(ref.)	1.00	(ref.)
Lifetime disorder but not 12 month	N/E	N/E	N/E	N/E
12 month disorder	2.51	(0.68–9.27)	<b>4.74</b>	<b>(1.09–20.57)</b>
<b>DSM-IV DUD among other drug users</b>				
No DUD	1.00	(ref.)	1.00	(ref.)
Lifetime disorder but not 12 month	N/E	N/E	N/E	N/E
12 month disorder	2.34	(0.56–9.66)	3.96	(0.78–20.10)

aRR - Adjusted Risk Ratio; CI - Confidence Interval; ref. - Reference category; N/E - cannot estimate parameter due to zero cell.

Bold numbers are estimates significant at  $p \leq 0.05$ .

<sup>a</sup> Risk ratios adjusted by sex and baseline characteristics: age/cohort, education, attending school, any DSM-IV anxiety disorders, any DSM-IV mood disorders, any DSM-IV impulse disorders and any DSM-IV eating disorders.

we found that cannabis use before age 15 (ideation RR = 3.97; 95% CI = 1.43–11.03; attempt RR = 5.23; 95% CI = 1.17–23.32), DSM-IV-DUD among cannabis users before age 15 (ideation RR = 3.30; 95% CI = 1.11–9.84; attempt RR = 4.14; 95% CI = 1.28–13.36), high frequency of cannabis use (RR for attempts = 5.04; 1.03–24.64) and recent DSM-IV-DUD among cannabis users (RR and attempts = 4.74; 1.09–20.57) increased the RR.

#### 4. Discussion

In this prospective eight-year follow-up study of 1071 adolescents as they became young adults living in the Mexico City metropolitan area, we found that cannabis use and disorders before

age 15 and high frequency of use and recent cannabis use disorders increased the RR of both suicide ideation and attempt. Those who used other drugs more frequently had an increased RR of suicide attempt. The relation of alcohol with suicide ideation and attempt was more limited, with only those who used alcohol before age 15 showing increased risk of suicide attempt.

Our findings of no associations between alcohol use and suicide ideation is similar to many other longitudinal studies (Strandheim et al., 2014; McGee et al., 2005; Tekin and Markowitz, 2008; Juon and Ensminger, 1997; Seo and Lee, 2013; Wilcox and Anthony, 2004; Thompson et al., 2007), but not to all (Reinherz et al., 1995); on the other hand, our reported association between alcohol use before age 15 showing increased risk of suicide attempt

is similar to positive findings from some (Borowsky et al., 2001; Andrews and Lewinsohn, 1992) but not others (Thompson and Light, 2011; Juon and Ensminger, 1997; Thompson et al., 2007; Wilcox and Anthony, 2004). This lack of longitudinal associations for alcohol and suicidal ideation and attempt among adolescents is in marked contrast with the general positive findings for adults (Darvishi et al., 2015; Roerecke and Rehm, 2014) and is a matter for future inquiry. In particular, developmental perspectives in which associations could be shown for different age groups/cohorts are needed.

Our results showing a tendency for associations between other drugs and suicide ideation (Zhang and Wu, 2014; Rasic et al., 2013; Reinherz et al., 1995; Fergusson and Lynskey, 1995) and attempts (Wilcox and Anthony, 2004; Rasic et al., 2013; Reinherz et al., 1995; Fergusson and Lynskey, 1995; Borowsky et al., 2001; Andrews and Lewinsohn, 1992), are reported in the literature, sometimes more marked for women than men (Wilcox and Anthony, 2004; Andrews and Lewinsohn, 1992), and usually with very large confidence intervals that may include the null value. We found only two studies for cocaine use and suicide ideation (both positive (Tekin and Markowitz, 2008; Juon and Ensminger, 1997), and only one for suicide attempt and cocaine use (Juon and Ensminger, 1997). Studies with larger samples and adolescents at risk of using hard drugs (other than cannabis) are sorely needed.

Most of our positive findings were for cannabis use and suicide ideation and attempt. While at a first glance these findings may be considered unexpected and controversial, our study contributes to a growing body of evidence showing the presence of this association (Seo and Lee, 2013; Clarke et al., 2014; Zhang and Wu, 2014; Van Ours et al., 2013; Silins et al., 2014; Shalit et al., 2016); for a review see (Agrawal and Lynskey, 2014; Borges et al., 2016). Some of these studies and ours, have in common a more detailed assessment of cannabis use, that includes not just “any cannabis use” but scalar variables that are able to differentiate between early users, low, infrequent, and non-current users from those that are high, frequent, and currently users of cannabis. A summary of longitudinal research providing either estimates of ORs or RRs for cannabis use and suicide ideation and attempt among adolescents are shown on Fig. 1. For both suicide ideation (top) and suicide attempt (bottom) it is apparent that most research shows increased ORs or RRs (the right side of the figure) and that studies that include measures of high frequency, early use, recent use and disorders (Pedersen, 2008; Van Ours et al., 2013; Rasic et al., 2013; Silins et al., 2014) tend to show higher estimates than studies relaying on “any cannabis use” (Borowsky et al., 2001; Wilcox and Anthony, 2004; McGee et al., 2005; Tekin and Markowitz, 2008; Seo and Lee, 2013; Zhang and Wu, 2014; Thompson and Light, 2011; Clarke et al., 2014), but exceptions exist for both (Juon and Ensminger, 1997; Rasic et al., 2013; Clarke et al., 2014). While our results are in tandem with current research in this area, we added a wider number of cannabis variables, covering lifetime and 12-month, high frequency and disorders. Our longitudinal, incidence based models, also included a comprehensive list of psychopathology, two matters of constant discussion and uncertainty in the literature (Hall and Degenhardt, 2014). Mechanisms of action to explain the effect of cannabis on both suicide ideation and attempt at the moment are speculative at the least and tentative at most (Agrawal and Lynskey, 2014; Borges et al., 2016) and several pathways are possible. These pathways can be separated into the short-term effects and the long-term effects of cannabis use (World Health Organization, 2016). While short-term effects of cannabis can be important for several mental disorders and health related outcomes, there is currently no evidence that acute use of cannabis is associated with suicide ideation and attempts, but the work in this area is quite limited (Borges et al., 2016). On the other hand, chronic

effects of cannabis among youth could be related to suicide ideation and attempts by influencing new onset of mental disorders and contributing to negative events such as low grades, academic failure and family discord. Higher frequency of cannabis use, early cannabis use and early cannabis use disorders are particularly deleterious by possibly affecting brain development (memory and cognition) and has been associated with use of other drugs and juvenile offending (World Health Organization, 2016). Formulating, and testing, specific mechanisms of action for chronic cannabis use to affect suicide ideation and attempts is an urgent next step (Borges et al., 2016).

#### 4.1. Limitations

This study has limitations worth noting. While it is true that our number of cases of suicide ideation and especially suicide attempt were few, they were not beyond the usual sample size for studies in this area of research. Nevertheless, the low incidence reported here prevented us from carrying out any subgroup analyses, for instance by gender, a matter of relevance as shown above in some of the estimates in our graph. Interestingly, it was for the exposure variable with the largest prevalence in 2005 (alcohol use) that we found most of our null results. Our sample is representative of the largest metropolitan area in Mexico, but it does not include other cities and other age groups that may differ in risk factors. We adjusted our findings by some key psychiatric disorders, such as major depression and conduct disorder, but psychological traits such as impulsivity, or the presence of hopelessness may have played a part in our results. While these limitations suggest caution in the interpretation of these findings, we know of no other study similar to ours in Mexico or in other low or middle-income countries.

#### 4.2. Conclusion

Because of the longitudinal nature of our research, we can discard two important threats to validity in these relations: first, as we studied incident cases, by study design it is not possible that reverse causality (suicide ideation and attempt causing substance use) played a role in this finding. Also, because of extensive control of psychiatric disorders, including mood disorders, these results are not likely to be exclusively caused by prior psychopathology (such as depression). Policy makers in the country could use our results, together with other studies on this topic reviewed above, to formulate policy programs that, finally, address a modifiable risk factor for suicide prevention.

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#### Contributors

Authors Borges and Benjet and Medina-Mora designed and wrote the protocol, collected data and obtained funds (Benjet, PI). Authors Borges and Benjet discussed the report plan, managed the

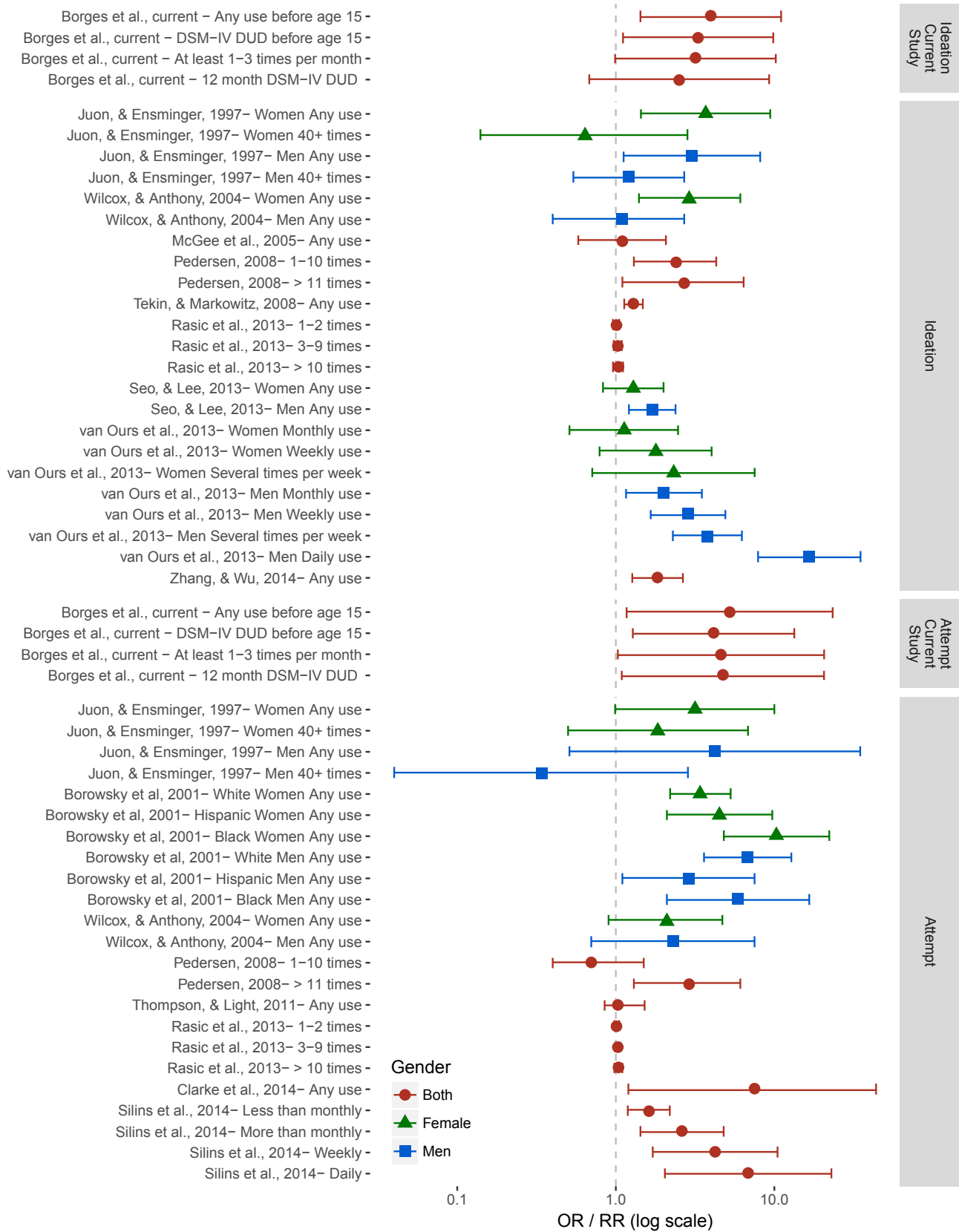


Fig. 1. Summary of longitudinal studies on cannabis and suicide ideation and attempt among adolescents.

literature searches and analyses. Authors Menendez and Orozco performed coding and data analyses, review and summarized the

literature. Author Borges wrote the first draft of the manuscript and subsequent versions with inputs from authors Benjet, Medina-



Mora and all others. All authors contributed to and have approved the final manuscript.

### Conflict of interest

No authors reported any conflict of interest.

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