Can Psychopathology Predict Adolescent Drug Use or Moderate the Effect of a Schoool-Based Drug Use Prevention Program?

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Abstract
Although psychiatric symptoms and drug use are commonly associated with adolescence, the causal relationship has not been fully established. In this study, we sought to identify baseline predictors of adolescent drug use focused on psychopathology and participation in the school-based prevention program #Tamojunto 2.0. We also aimed to assess the moderating effect of mental health in reducing adolescent drug use, which is the primary outcome of the #Tamojunto 2.0 program. A cluster randomized controlled trial with two parallel arms was conducted in 73 Brazilian public schools (37 in the intervention group and 36 in the control group). Baseline and 9-month follow-up measures of 5208 students in the 8th grade—mean age of 13.2 years (SD = 0.8) and equal gender ratio—were assessed. The main outcome variable of the study was adolescents' past-month drug use at 9-month follow-up. The explanatory variables were past-month drug use, the RCT group, psychopathology, and sociodemographic items (gender, age, and socioeconomic status) at baseline. Findings indicated that besides females, older age, an abnormal score of mental health symptoms, and previous drug use were the most significant predictors of adolescent drug consumption. We found no evidence of a moderating effect of mental health symptoms in reducing drug use because of intervention. These results suggest that strategies for drug use prevention among adolescents should consider abnormal mental health as a predictor of drug use, but not in the case of #Tamojunto 2.0, as a moderator of the intervention effect. Brazilian Register of Clinical Trials: RBR-8cnkwq (http://www.ensaiosclinicos.gov.br/rg/RBR-8cnkwq/).

Keywords Adolescents · Mental health · Drugs · Prevention · Randomized controlled trial

Adolescence is a period of great risk for the development of psychiatric disorders, given the many psychological changes typical of this age group (Braga & Dell'Aglio, 2013). This often happens in close association with the consumption of alcohol and drugs (Fidalgo, 2016; Rivera-Rivera et al., 2015). The co-occurrence of mental and substance use disorders

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is a complex phenomenon with important clinical and social impacts, including poorer outcomes/prognosis (Najt et al., 2011). Although the evidence of the coexistence of alcohol and drug use problems and mental health issues among adolescents is strong, the causality direction of this relationship is still uncertain and calls for well-designed longitudinal studies (Skogen et al., 2014).

Reliable evidence shows variations in the temporal order of the onset of mental illness and substance abuse, depending on the psychiatric diagnosis (Jané-Llops & Matytsina, 2006). For example, attention deficit hyperactivity disorder appears as one of the predictors of early alcohol use among children (Gudjonsson et al., 2012; Sibley et al., 2014), anxiety usually precedes substance use disorders (Kessler, 2004), psychotic episodes are indicated as potential consequences of marijuana use in adolescence (Arsenault et al., 2004), and depression has both directions documented (Gratzer et al., 2004; Kessler et al., 2003). By contrast, the literature also suggests that early experimentation of alcohol and other drugs is considered an important predictor of certain mental ailments, such as depression, suicidal ideation and attempts, and substance use disorders (Liang & Chikritzhs, 2015; Rasic et al., 2013).

Considering the several mechanisms involved in this pathway, some drug use prevention programs often have protective effects on other adolescent risk behaviors (Griffin & Evidence-Based, 2010). Recent evidence demonstrates that universal prevention programs could enhance students' life skills (self-knowledge, assertiveness, decision-making ability), improve their mental health, including reducing their anxiety and distress, and reduce the levels of alcohol and tobacco use (O'Neill et al., 2011; Skeen et al., 2019; Trudeau et al., 2015; Velasco et al., 2017). Additionally, combined prevention for substance use and mental health in adolescence has presented promising results (Teesson et al., 2020), particularly for selective programs that target these disorders' shared underlying vulnerabilities—for instance, the prevention program *Preventure*, which is offered to adolescents with personality risk factors (Kelly et al., 2021; Newton et al., 2016).

Another important aspect to be considered is that student programs for preventing drug use among adolescents depend on their cognitive and interpersonal skills, besides their interest and motivation during the activities developed. Therefore, the presence of mental health symptoms in students may interfere with the effects that these programs have on them, as they would not be able to adequately perform the program's activities (Skeen et al., 2019; Spaeth et al., 2010). In this regard, mental health symptomatology may be an important moderator of life skills training prevention programs, being responsible for differential effects by subgroups.

In Brazil, prevalence rates of adolescent psychiatric disorders are high, ranging from 7 to 16% (Almeida et al., 2018; Anselmi et al., 2010; Paula et al., 2015). The available data on reported adolescent drug use is concerning as well: 55.5% for alcohol consumption and 9.0% for illicit drug use (IBGE, 2016). As Brazil is a middle-income country with inadequate health resources and even more restricted availability of mental health services for children and adolescents, these data further demonstrate the importance of adopting efficient prevention strategies.

The Brazilian Ministry of Health has made certain endeavors in the past years toward this direction: a national government drug use prevention program for Brazilian adolescents—adapted from the European evidence-based school program *Unplugged* and called #Tamojunto 2.0—was implemented in 2019 with its effectiveness being tested before it was adopted as a public policy (Sanchez et al., 2020).

Given the interplay between psychopathology and drug use among adolescents, in this study, we hypothesize that having a higher number of mental health symptoms can predict

future drug use by adolescents, as well as modify the positive effects of the student prevention program #Tamojunto 2.0. Therefore, our main objective was to identify the baseline predictors of adolescent drug use focused on psychopathology and participation in the school-based prevention program #Tamojunto 2.0. We also aimed to assess the moderating effect of mental health in the impact of #Tamojunto 2.0 in reducing adolescent drug use.

Methods

Study Design

This study is a secondary analysis from a cluster randomized controlled trial (RCT) performed on 5208 adolescents, aiming to assess the effect of the prevention program #Tamojunto 2.0 among students from 73 Brazilian public schools in 3 different cities (São Paulo, Fortaleza, and Eusébio). According to the RCT protocol (Sanchez et al., 2019) and the primary outcomes published (Sanchez et al., 2020), participants were divided into two groups: control arm (usual curricula, no intervention) and intervention arm (in which the prevention program #Tamojunto 2.0 was added to the 8th-grade curricula).

Baseline data were collected in February and March 2019, before the program implementation, and follow-up data were collected 9 months later, in November and December 2019, respectively. This time interval between the two waves of data collection was defined considering the school year in Brazil. Control and intervention schools were assessed simultaneously.

The #Tamojunto 2.0 RCT was registered in the Brazilian official registry of clinical trials—Registro Brasileiro de Ensaios Clínicos under protocol number RBR-8cnkwq. The study was approved by the Ethics Committee of the Universidade Federal de São Paulo (protocol 2.806.30). The consent form was signed by the schools' directors, teachers, and students.

Randomization

Randomization was conducted considering schools as a reference, and the random procedure was executed using a national educational list (that includes all schools from each city). The schools included were all public schools with 8th-grade classes and from the cities that the federal government indicated and had not participated in the previous #Tamojunto RCT. The selected schools then went through a second randomization process to determine which schools were allocated to the control and the intervention groups (preserving an allocation ratio of 1:1 per city).

Sample

The sample size was calculated using the software PASS 15.0. Considering a power of 82% in identifying the difference between groups of 2.5% in the prevalence of binge drinking in the past month, an initial prevalence of 10%, a significance level of 5%, and an intraclass correlation of 0.005, would entail a total sample of 6300 adolescents (3150 in each group, distributed among 35 clusters/schools and with at least 90 participants in each arm).

From 78 schools initially invited, 73 (93.6%) accepted to be included in the study. Considering the classes' registrations, 6993 students were expected, but only 5371 were present

in the baseline data collection. Eventually, the baseline included 5208 valid questionnaires, after excluding those who refused (2.2%), returned blank, and responded positively to a fictional drug. The 9-month follow-up assessment sample included 3898 respondents. The above information is depicted in the flowchart of the #Tamojunto 2.0 RCT (Fig. 1).

Intervention

#Tamojunto 2.0 is a Brazilian adapted version of a European school-based program for the prevention of adolescent drug use called *Unplugged*. It contains 12 weekly classes providing information about drugs and imparting personal, social, and interpersonal skills. The lessons are offered to the students by trained teachers and guided by interactive manuals (Faggiano et al., 2008).

For this study, in the schools receiving the intervention, one teacher per class received #Tamojunto 2.0 training (16 h) and all 8th-grade students were invited to participate in the #Tamojunto 2.0 prevention program. To guarantee the quality of the program delivered, teachers were also supervised by a team from the Brazilian Ministry of Health, which was responsible for the program implementation. As this was a part of an effectiveness study of a government program, teachers could interrupt the program. Finally, 67% of the enrolled classes completed 12 lessons, with a mean rate of 8 lessons per class.
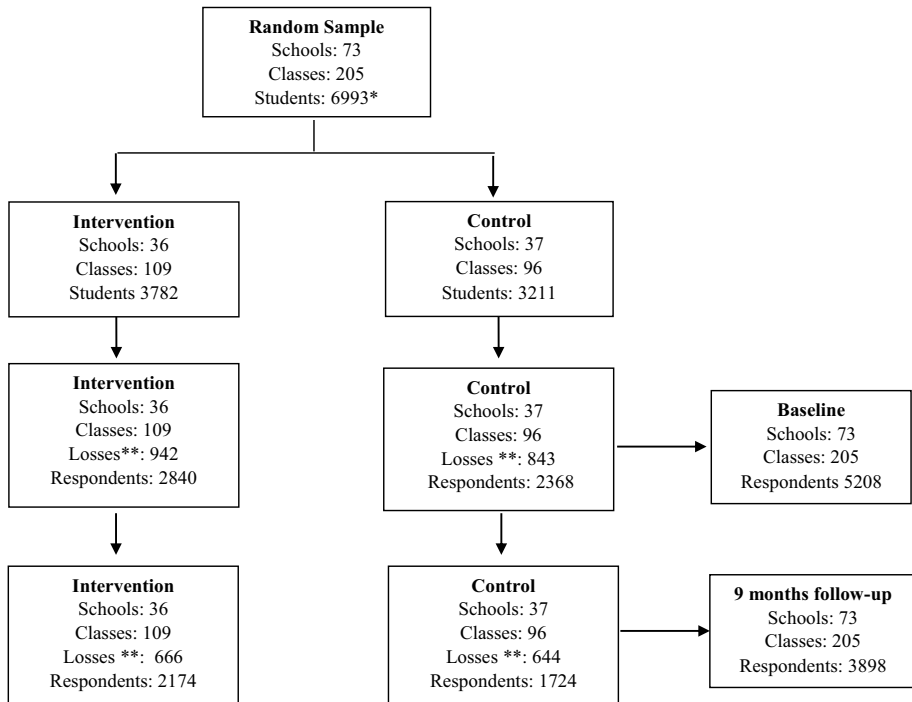
Fig. 1 Flowchart of the randomized controlled trial of the Prevention Program #Tamojunto2.0. One asterisk (*) enrolled in schools in 2019; two asterisks (**) due to absence in the day of collection, refusal to participate, and blank questionnaires

Instrument and Variables

Data were collected through an anonymous instrument applied to the students in their classroom by our research team, in the absence of teachers. The instrument was adapted from the European Drug Addiction Prevention Trial (EU-DAP) questionnaire (Prado et al., 2016). It also included some questions from the VI Brazilian Survey of Drug Use among Students, the Brazilian National School Health Survey (Carlini et al., 2010), and the Strengths and Difficulties Questionnaire (SDQ)—a screening mental health questionnaire (Fleitlich-Bilyk et al., 2000; Goodman et al., 1998).

The outcome variable of this study was adolescents' past-month drug use at 9-month follow-up. Adolescents answered a dichotomous (yes/no) question about engaging in an episode of binge drinking and using tobacco, marijuana, and inhalants, during the last 30 days. Explanatory variables were assessed at baseline and comprised past-month drug use, participation in the control or intervention group of the RCT, dichotomous result (positive/negative) of SDQ, and sociodemographic data (gender, age, and socioeconomic status according to the Brazilian scale from the Associação Brasileira das Empresas de Pesquisa (ABEP), which considers ownership of some consumer goods and parental education and ranges from 1 to 100, with a higher score implying a higher status). The ABEP score is also divided into five bands, related to the total points: A (45–100); B (29–44); C (17–28); and D/E (1–16) (Brasileira & de Empresas de Pesquisa - ABEP, 2016).

SDQ is a brief behavioral screening tool composed of 25 items on psychological attributes (skills and troubles); its self-completion version is suitable for adolescents aged 11–16 years. The items are divided into five subscales (five items in each): emotional symptoms, conduct problems, hyperactivity/inattention, peer relationship problems, and prosocial behavior. Each item has three possible scores (0, 1, and 2) and the sum of these points equals the subscale score. SDQ total difficulties score comprises four subscales (emotional, conduct, hyperactivity, and peer relationship). Following the authors' recommendations and considering our low-risk sample (Goodman et al., 2003), the cutoff point adopted to consider the participant with an SDQ total difficulties score in the abnormal range was ≥ 20. Results for this scale were considered if at least 12 of the 20 corresponding items were completed.

To prevent false drug use responses, participants that answered positively for lifetime use of a fictional drug were excluded from the analysis (35 at baseline and 37 at follow-up).

Statistical Analysis

Descriptive statistics analysis was performed using Stata 16.0 and contained information on the distribution of adolescents at baseline, according to their sociodemographic features, past-month drug use, and mental health status (SDQ), and the distribution of adolescents' past-month drug use at follow-up, according to baseline variables.

We used the intention-to-treat to analyze the effect of #Tamojunto 2.0 on past-month drug use at follow-up. For missing data in the second assessment, multiple imputations were performed to include all randomized subjects in the analysis, as the CONSORT recommends. For that, we used the Bayes estimation of an unrestricted variance–covariance model, assuming all variables in the dataset as a dependent. Variables imputed were gender, age, ABEP, total difficulties subscale of SDQ, and baseline and follow-up past-month drug use. Fifty imputation data sets were created and then used in the analysis by applying

the maximum likelihood estimator. These analyses were performed in the program Mplus version 8.5 (Muthén & Muthén, 2017).

The estimator used was the maximum likelihood with robust standard errors, in which the standard error was computed dealing with the non-independence of the observation (i.e., adolescents nested in schools) via Mplus command TYPE = Complex, as suggested by Asparouhov and Muthén (2009). Considering past-month drug use, four logistic regressions were estimated, one for each drug. The significance level was established at 5%.

Results

Both groups (intervention and control) were homogenous regarding sex, age, and socioeconomic status, based on the ABEP scale. The mean age of participants was 13.23 years (SD = 0.85), and 45.57% of the participants in the sample were from São Paulo. Sociodemographic characteristics of adolescents who participated at baseline, as well as their baseline descriptive analysis regarding past-month drug use and mental health symptoms, are presented in Table 1.

Table 2 illustrates the distribution of the sample according to adolescents' past-month drug use at 9-month follow-up concerning baseline variables. Girls displayed a higher prevalence of binge drinking episodes and use of tobacco and inhalants compared to boys. The differences between the age groups were significant for binge drinking, tobacco, and marijuana use—although 8.5% of the sample were in the older age group, they correspond to up to 19% marijuana users. Socioeconomic status (ABEP classification) and allocation in the intervention or control group were not statistically significant. For all drugs analyzed (binge drinking, tobacco, inhalants, and marijuana), the prevalence of baseline mental health symptoms (SDQ positive) among those who reported use at follow-up was almost twice as high compared to abstainers (e.g., for binge drinking: 39.91% of binge drinkers had a previous SDQ positive against 21.71% among those who denied an episode of binge drinking). Baseline drug use rates were several times higher in the group of users at follow-up (e.g., four times higher for binge drinking and fifteen times for marijuana).

Regarding the univariate analysis of the predictors of adolescent drug use at 9-month follow-up (Table 3), statistically significant baseline variables were as follows: abnormal range of SDQ total difficulties score, being a girl (except for marijuana), being older (except for inhalants), and all baseline drug use (binge drinking, tobacco, inhalants, marijuana). The evidence of the effect of the intervention on all outcomes was found lacking (e.g., for binge drinking: cOR 0.86, 95% CI 0.70–1.05; $p = 0.141$).

Through multivariate analysis (Table 3), the predictors of drug use at follow-up were as follows: abnormal range of SDQ total difficulties score (for binge drinking, tobacco, and marijuana), being a girl (for binge drinking, tobacco, and inhalants), older ages (for binge drinking, tobacco, and marijuana), binge drinking (for all drugs), tobacco (for tobacco and marijuana), inhalants (only for inhalants), and marijuana (for binge drinking and marijuana). Regarding the values of these predictions, we realized that the previous use of the drug represents a significantly higher risk than other factors, including psychopathology—for example, binge drinking: aOR 4.55, 95% CI 3.57–5.82; $p < 0.001$ (previous binge drinking) × aOR 1.66, 95% CI 1.32–2.08; $p < 0.001$ (SDQ abnormal).

Lack of evidence of a moderating effect of abnormal SDQ total difficulties score was found in the response to the prevention program #Tamojunto 2.0, according to past-month drug use at 9-month follow-up (Table 4).

Table 1 Distribution of adolescents in the randomized controlled trial of the Prevention Program #Tamojunto2.0 (2019) at baseline, according to sociodemographic, past month drug use, and mental health symptoms (N=5208)

	Total (N=5208)		Control group (N=2368)		Intervention group (N=2840)	
	N	%	N	%	N	%
City						
São Paulo	2373	45.57	926	39.10	1.447	50.95
Fortaleza	2051	39.38	1022	43.16	1.029	36.23
Eusébio	784	15.05	420	17.74	364	12.82
Gender						
Boys	2576	50.06	1140	48.63	1.436	50.06
Girls	2570	49.94	1024	51.37	1.366	49.94
Age (years)						
12–14	4645	91.44	2.081	90.16	2.564	92.50
15–17	435	8.56	227	9.84	208	7.5
Mean age (SD)	13.23 ± 0.85		13.28 ± 0.89		13.19 ± 0.81	
ABEP*						
A (45–100)	179	3.48	71	3.08	108	3.86
B (29–44)	1279	24.84	522	22.21	757	27.05
C (17–28)	2809	54.55	1.304	55.49	1.505	53.77
D/E (1–16)	882	17.13	453	19.28	429	15.33
Mean score (SD)	24.75 ± 9.19		24.16 ± 9.15		25.25 ± 9.19	
Past month drug use						
Alcohol	1.129	21.88	540	22.96	589	20.98
Binge drinking	786	15.19	386	16.38	400	14.19
Tobacco	155	3.01	82	3.48	73	2.62
Inhalants	210	4.09	108	4.60	102	3.66
Marijuana	167	3.26	95	4.06	72	2.58
Any substance	1162	23.31	561	24.54	601	22.28
Mental health symptoms						
SDQ positive**	962	26.78	472	27.43	490	26.19

*Socioeconomic status; **Dichotomous (total difficulties subscale ≥ 20)

Discussion

Predictors of drug use among Brazilian adolescents and the moderating effect of psychopathology on the response to the prevention program #Tamojunto 2.0 were investigated in this study. We found that being a girl, older age, previous drug use, and a higher presence of mental health symptoms were the major predictors of drug consumption at follow-up. However, evidence of a moderating effect of mental health symptoms in reducing drug use because of the intervention was not found.

Concerning poorer mental health status as a predictor of drug use among Brazilian adolescents, our findings agree with those in other studies that identified an association between psychiatric symptoms and adolescent alcohol and drug use (Schwinn et al., 2010;

Table 2 Distribution of adolescent past month drug use at 9-month follow-up, according to baseline variables

Predictors (baseline)	Binge drinking (N=3875)			Tobacco (N=3883)			Inhalants (N=3889)			Marijuana (N=3862)		
	No (%)	Yes (%)	p	No (%)	Yes (%)	p	No (%)	Yes (%)	p	No (%)	Yes (%)	p
SDQ total difficulties score												
Abnormal*	**21.71**	**39.91**	**<0.001**	**23.58**	**44.17**	**<0.001**	**23.10**	**48.98**	**<0.001**	**23.82**	**39.84**	**<0.001**
Gender			**<0.001**			**0.010**			**<0.001**			0.211
Boys	**52.66**	**37.54**		**50.76**	**40.37**		**51.08**	**36.45**		50.40	45.70	
Girls	**47.34**	**62.46**		**49.24**	**59.63**		**48.92**	**63.55**		49.60	54.30	
Age			**<0.001**			**<0.001**			0.223			**<0.001**
12–14 years old	**94.92**	**88.43**		**94.34**	**83.75**		94.01	91.88		**94.55**	**80.77**	
15–17 years old	**5.08**	**11.57**		**5.66**	**16.25**		5.99	8.12		**5.45**	**19.23**	
ABEP**			0.842			0.853			0.369			0.855
A (45–100)	3.30	3.58		3.29	4.35		3.27	4.46		3.30	3.83	
B (29–44)	25.31	26.18		25.50	23.60		25.25	28.71		25.41	23.50	
C (17–28)	55.44	53.50		55.14	55.28		55.46	49.50		55.13	54.64	
D/E (1–16)	15.95	16.75		16.07	16.77		16.03	17.33		16.17	18.03	
Group			0.294			0.130			0.910			0.787
Control	43.79	46.07		43.97	50.00		44.25	43.84		44.15	45.16	
Intervention	56.21	53.93		56.03	50.00		55.75	56.16		55.85	54.84	
Drug use												
Binge drinking	**8.06**	**36.41**	**<0.001**	**11.21**	**44.10**	**<0.001**	**11.62**	**30.69**	**<0.001**	**10.79**	**47.78**	**<0.001**
Tobacco	**1.09**	**7.29**	**<0.001**	**1.36**	**18.63**	**<0.001**	**1.81**	**7.00**	**<0.001**	**1.24**	**18.82**	**<0.001**
Inhalants	**2.83**	**8.46**	**<0.001**	**3.32**	**13.84**	**<0.001**	**2.72**	**22.61**	**<0.001**	**3.14**	**16.39**	**<0.001**
Marijuana	**1.31**	**7.95**	**<0.001**	**1.77**	**16.25**	**<0.001**	**2.03**	**8.50**	**<0.001**	**1.41**	**21.31**	**<0.001**

*Dichotomus (abnormal = scores ≥ 20); **Socioeconomic status; Data in bold indicate statistically significant differences.

Table 3 Univariate and multivariate analysis of predictors of adolescent drug use at follow-up ($N=5208$)

Univariate analysis	Binge drinking at follow-up			Tobacco at follow-up			Inhalants at follow-up			Marijuana at follow-up		
	cOR	95% CI	p	cOR	95% CI	p	cOR	95% CI	p	cOR	95% CI	p
SDQ total difficulties score (abnormal)*	**2.40**	**1.97–2.92**	**<0.001**	**2.79**	**1.99–3.92**	**<0.001**	**3.17**	**2.42–4.17**	**<0.001**	**2.46**	**1.74–3.48**	**<0.001**
Gender (girls)	**1.82**	**1.50–2.20**	**<0.001**	**1.50**	**1.08–2.09**	**0.016**	**1.78**	**1.39–2.27**	**<0.001**	1.22	0.93–1.60	0.153
Age (years)	**1.51**	**1.37–1.67**	**<0.001**	**1.61**	**1.38–1.88**	**<0.001**	1.08	0.91–1.28	0.384	**1.77**	**1.52–2.05**	**<0.001**
ABEP score**	1.01	1.00–1.02	0.244	1.00	0.98–1.01	0.575	1.01	0.99–1.03	0.291	1.00	0.98–1.02	0.912
Group (intervention)	0.86	0.70–1.05	0.141	0.74	0.52–1.05	0.091	0.96	0.72–1.29	0.802	0.88	0.64–1.21	0.435
Drug use (baseline)												
Binge drinking	**6.72**	**5.38–8.39**	**<0.001**	**6.37**	**4.51–9.02**	**<0.001**	**3.25**	**2.39–4.43**	**<0.001**	**7.48**	**5.52–10.13**	**<0.001**
Tobacco	**7.55**	**4.86–11.73**	**<0.001**	**16.07**	**9.73–26.54**	**<0.001**	**3.57**	**1.98–6.44**	**<0.001**	**16.31**	**9.57–27.80**	**<0.001**
Inhalants	**3.08**	**2.21–4.30**	**<0.001**	**4.84**	**2.95–7.94**	**<0.001**	**9.79**	**6.82–14.04**	**<0.001**	**5.71**	**3.72–8.78**	**<0.001**
Marijuana	**7.04**	**4.74–10.46**	**<0.001**	**11.17**	**6.71–18.59**	**<0.001**	**3.52**	**2.01–6.17**	**<0.001**	**18.54**	**11.79–29.16**	**<0.001**

Multivariate analysis	Binge drinking at follow-up			Tobacco at follow-up			Inhalants at follow-up			Marijuana at follow-up		
	aOR	95% CI	p	aOR	95% CI	p	aOR	95% CI	p	aOR	95% CI	p
SDQ total difficulties score (abnormal)*	**1.66**	**1.32–2.08**	**<0.001**	**1.78**	**1.21–2.62**	**0.003**	**2.32**	**1.71–3.15**	**<0.001**	1.47	0.97–2.24	0.069
Gender (girls)	**1.79**	**1.45–2.21**	**<0.001**	**1.44**	**1.00–2.07**	**0.049**	**1.46**	**1.13–1.88**	**0.004**	1.78	0.85–1.63	0.317
Age (years)	**1.34**	**1.20–1.50**	**<0.001**	**1.31**	**1.08–1.57**	**0.005**	0.93	0.77–1.13	0.462	**1.44**	**1.21–1.73**	**<0.001**
ABEP score**	1.01	1.00–1.02	0.310	0.99	0.97–1.01	0.282	1.00	0.99–1.02	0.626	0.99	0.97–1.01	0.354
Group (intervention)	0.94	0.78–1.14	0.546	0.85	0.59–1.23	0.397	1.02	0.76–1.38	0.892	1.08	0.76–1.51	0.680
Drug use (baseline)												
Binge drinking	**4.55**	**3.57–5.82**	**<0.001**	**3.08**	**1.99–4.76**	**<0.001**	**2.13**	**1.46–3.12**	**<0.001**	**3.61**	**2.53–5.16**	**<0.001**
Tobacco	1.76	0.94–3.32	0.080	**4.51**	**2.11–9.65**	**<0.001**	0.79	0.33–1.89	0.600	**2.30**	**1.01–5.25**	**0.047**
Inhalants	1.12	0.68–1.84	0.653	1.21	0.57–2.57	0.627	**6.81**	**4.45–10.42**	**<0.001**	1.46	0.76–2.80	0.254
Marijuana	**1.88**	**1.07–3.32**	**0.029**	1.80	0.75–4.36	0.192	1.00	0.46–2.17	1.000	**4.53**	**2.25–9.11**	**<0.001**

*Dichotomus (abnormal = scores ≥ 20); **Socioeconomic status; Data in bold indicate statistically significant differences.

Table 4 The interaction model considering the moderator from baseline (analysis controlled by age, sex, socioeconomic status, group, and baseline measure)—$N = 5208$

Int (SDQ total difficulties score* X group)		
	Odds ratio (95% CI)	p
Binge drinking	1.00 (0.69;1.45)	0.998
Tobacco	1.17 (0.62;2.19)	0.633
Inhalants	1.17 (0.65;2.13)	0.601
Marijuana	1.06 (0.57;1.98)	0.852

*Dichotomus (abnormal = scores ≥ 20)

Skogen et al., 2014; Wittchen et al., 2007). However, instead of investigating specific symptoms of some psychiatric disorders, in our study, we chose the SDQ total difficulties score as a mental health marker because it is a widely used instrument to detect mental disorders in populations aged under 18 years (Deighton et al., 2014). In addition, we reinforced the importance of devoting more attention to the mental health of adolescents in the school environment, which has been a promising target for public health strategies focusing on risky behaviors.

In line with other studies that demonstrate that adolescent drinking and smoking have been associated with later alcohol and polysubstance use (Salom et al., 2015), our study identified binge drinking at baseline predicting all other drug use at follow-up. This reinforces the theory that prior consumption of legal drugs can lead to the use of illicit drugs (Schilling et al., 2017) and draws attention to adolescents with potential risk to polysubstance use, and consequently, to worst health outcomes (Morley et al., 2015).

Regarding the prediction of female gender on adolescent drug use, previous findings in Brazilian surveys have shown a trend of increasing rates of alcohol and other drug use by girls in the last 6 years (IBGE, 2016; Wolle et al., 2011). This might be explained by recent changes in women's role in society and the increasing acceptance of drinking by women (Almeida et al., 2020). Added to the fact that female adolescents may be biologically more susceptible to the negative consequences of substance abuse (Medina et al., 2008), this finding indicates that public health strategies must consider this current shift in gender differences and direct a special focus on girls' social norms and attitudes toward alcohol and drug use.

Despite our findings indicating that older ages predict drug use (except for inhalants), the extant literature highlights that early onset of substance use implicates more risk for negative consequences in the future (Poudel & Gautam, 2017). Possible explanations for this finding are related to the fact that this is an older group in the same school year, which may imply previous school failure, and also possible association with behavior problems, not accounted by the SDQ instrument. Nonetheless, we understand that prevention strategies should direct actions toward this population at risk at the earliest.

Although #Tamojunto 2.0 has succeeded in preventing the initiation of drug use (Sanchez et al., 2020), we did not find a significant association between receiving #Tamojunto 2.0 and lower rates of binge drinking, tobacco, inhalants, and marijuana use at 9-month follow-up. We believe that a possible explanation for this unexpected finding is that a longer intervention would be necessary to evidence such impact.

For not finding any moderating effect of psychopathology in the response to the program, we assume that #Tamojunto 2.0 did not affect the adolescents' drug use at follow-up, regardless of their previous mental health status. Considering that the program could have had a selective effect, we believe that it would be relevant to test this hypothesis. Thus, further

research needs to be conducted to clarify the influence of adolescent mental health on the outcomes of drug use prevention programs.

Indeed, this study stands out for its longitudinal methodology and a large population-based sample of adolescents. As the evidence base is mostly from high-income countries (Barry et al., 2013; Teesson et al., 2020), we also highlight the importance of producing valid information about this public health issue in a middle-income country, where resources are limited and cultural adaptation is essential for appropriate prevention strategies.

Some limitations of this study should be mentioned. The first is that our measures were all self-reported, and thus, our data may contain misinterpretation of the investigated problems. Besides, we faced many absent students in baseline collection, which is frequent in Brazilian public schools (IBGE, 2013). We also had important missing data at follow-up, a common limitation of longitudinal studies. For that, missing data techniques were used to preserve its significance.

We conclude that psychopathology does not moderate the effect of the #Tamojunto 2.0 intervention but can predict drug among Brazilian adolescents. Moreover, as the strongest predictor of drug use in the follow-up was mental health symptoms and previous use of several drugs, developing prevention strategies based on an active search for mental health difficulties and report of drug use is highly recommended to reduce drug use rates.

Author Contribution All authors contributed to the study conception, design, and analysis. They read and approved the final manuscript.

Data Availability Data are available on request.

Code Availability Not applicable.

Declarations

Ethics Approval This study was approved by the Ethics in Research Committee at the Universidade Federal de São Paulo (protocol 2.806.30).

Consent to Participate Consent to participate was obtained from the schools' directors, students, and parents.

Consent for Publication The authors provide their consent to Springer to publish this work.

Conflict of Interest The authors declare that they have no conflict of interest.

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