Research paper

Effectiveness of a school-based substance use prevention program taught by police officers in Brazil: Two cluster randomized controlled trials of the PROERD

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ABSTRACT

Background: The Drug and Violence Resistance Educational Program (PROERD) is widely disseminated and implemented as a public policy in Brazil. PROERD's current curricula are the translation of the North American program DARE-Keepin'it REAL, based on the theories of socio-emotional learning and resistance training. The present study aims to evaluate the effectiveness of PROERD in the prevention of drug use.

Method: Two PROERD curricula were analyzed through two cluster randomized controlled trials conducted with 4030 students (1727 5th graders and 2303 7th graders) in 30 public schools in São Paulo. The intervention group received ten PROERD classes delivered by trained police officers, and the control group received no intervention. Data collection was performed using self-administered questionnaires on smartphones at two points in time (baseline pre-intervention and nine months follow-up). The outcomes evaluated were initiation and recent drug use. Two different paradigms were used in a multilevel analysis: an analysis of complete cases (CC) and an intention to treat missing data through full information maximum likelihood and selection model.

Results: We found no evidence of the effectiveness of PROERD as an intervention for the prevention of drug use. For the conditional transition analysis, we found that 7th graders in the PROERD group who were already binge drinking at baseline had a significantly higher chance of maintaining this consumption pattern when compared to the control group.

Conclusion: The lack of preventive effects found here suggests that a process evaluation may address concrete implementation and cultural adaptation issues.

Introduction

Considering the growing body of literature reporting that harm that is causally related to substance use in young people (Degenhardt et al., 2016; Hall et al., 2016), implementing effective prevention interventions for this age group remains an important goal to reduce the public health impact (Whiteford et al., 2013). School-based prevention programs have shown the potential to reduce drug use among adolescents (Strøm et al., 2014). Interactive programs based on a social influence approach that foster the development of interpersonal and intrapersonal skills are more likely to be more effective than those based on other models (Cuijpers, 2002; Faggiano et al., 2008; Tobler et al., 2000). Al-

though school-based drug use prevention programs have been widely implemented and tested mainly in the USA and some European countries, there is a lack of information related to prevention approaches in low-and middle-income countries (Foxcroft & Tsertsvadze, 2012).

In Brazil, as in other parts of the world, alcohol and drug use are the most important risk behaviors among adolescents. The results of the most recent national epidemiological survey revealed that Brazilian adolescents aged 13–15 years had already consumed alcohol (55.5%) and illicit drugs (9.0%) at least once in their lifetime, with marijuana use, the most prevalent illicit drug, reported by 4% of students. Moreover, lifetime drunkenness was reported by 22% of the 9th grade students (IBGE, 2016). Even though in Brazil the first experience of alcohol consumption occurs very early, at an average of 13 years of age

(Carlini et al., 2010), very few evidence-based prevention programs have been implemented and proven efficacious in Brazilian schools (Pereira et al., 2016; Sanchez et al., 2021).

The Drug and Violence Resistance Educational Program (Programa Educacional de Resistência às Drogas e à Violência – PROERD) is the most widely implemented school-based prevention curriculum in Brazil (Pereira & Sanchez, 2020). It is implemented by trained police officers in all Brazilian states. Since late 2019, this implementation has been a public policy in the State of São Paulo (State Law 17, 171/2019). However, no effectiveness studies have been conducted to assess its effect on reducing drug consumption among Brazilian adolescents.

The present two curricula of PROERD are a translation of the North American program DARE-Keepin'it REAL (DARE-kiR) (Day et al., 2017), renamed in Brazil as "PROERD-Caindo na Real". DARE-kiR is an adapted version of the kiR curriculum disseminated by Drug Abuse Resistance Education (D.A.R.E.) and implemented by police officers in the United States. No data on the effectiveness of the DARE-kiR program on drug use have been published until now (Caputi & Thomas McLellan, 2017). The only published paper reporting findings from DARE-kiR is a quasi-experimental matched group study that analyzed only secondary outcomes among elementary students. The results showed promising effects on resisting peer pressure, confidence in explaining reasons for refusal of cigarettes, and decision making skills (Day et al., 2017). The original version of kiR was previously tested and presented mixed results. Evaluations of the program showed largely favorable results for the 7th grade curriculum in the Latin population, although some differences were observed in other curricula (Marsiglia & Hecht, 2005).

Other versions of the kiR program (Marsiglia & Hecht, 2005), not the version translated and implemented by PROERD (DARE-kiR), were previously tested in US schools. These versions presented contradictory results, which were most favorable to the program, especially among the Latin population. Among 7th grade students, kiR showed a reduction in the report of lifetime alcohol use (Gosin et al., 2003), discontinuity of alcohol use (Kulis et al., 2007, reduction in the number of doses and days of alcohol use (Warren et al., 2006), and a higher rate of discontinuity of alcohol use in the intervention group compared to the control group (Kulis et al., 2007. Subsequently, the 5th grade kiR curriculum showed a significant increase in the prevalence of substance use over 3 years when compared to students in the control condition (Elek et al., 2010). The program was also tested in Guatemala, in its linguistically adapted version, where a small effect was found in reducing the use of cigarettes and marijuana (Kulis et al., 2019).

Considering that prevention programs imported from diverse cultures can promote ineffective or even harmful effects in a different country (Moos, 2005; Sanchez et al., 2017), it is critical to evaluate whether the two curricula of PROERD had similar effects in Brazil as those observed in the US. The present study aims to evaluate the effectiveness of the school-based prevention program PROERD/"Caindo na Real" in delaying the first use of drugs (e.g., alcohol, tobacco, inhalants, and marijuana) and binge drinking, and to decrease the recent prevalence of use among 5th and 7th grade students.

Methods

Considering that PROERD has two different curricula designed for different grades (i.e., 5th and 7th grade), the effectiveness of the two PROERD curricula was evaluated through two cluster randomized controlled trials (cRCT) in parallel, with two arms each, and conducted with 1727 5th grade students and 2303 7th grade students across 30 public schools in the city of São Paulo, Brazil. In 2019, both intervention groups (5th and 7th grade) received 10 PROERD classes by trained police officers, while the control group received no intervention.

A baseline assessment was conducted before the implementation of the program during February and March 2019, and follow-up data

were collected nine months after (in November and December 2019). The school year period in Brazil is between February and December. Data were collected simultaneously from the control and intervention schools.

All procedures in the present study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The study was registered in the Brazilian Ministry of Health Register of Clinical Trials (REBEC) under protocol number 6q23nk. The study protocol was approved by the Research Ethics Committee of the Federal University of São Paulo (number:1327/2018). Consent to participate in the study was written and obtained from the schools' directors before randomization and from the students after randomization occurred.

Sampling

We calculated two different sample sizes for the evaluation of the PROERD effect, considering that PROERD has two different curricula designed for different grades (5th and 7th grade).

The necessary sample size calculated for 5th grade was 1820 participants (70 students per group) for a power of 80%, a significance level of 5%, a 0.3 effect size, and a 0.02 interclass correlation (Ahn et al., 2014). Concerning the 7th grade, the minimum sample size necessary (Donner & Klar, 2010) was calculated to be 1608 participants (67 per group) for a power of 80%, a significance level of 5%, a difference of proportions of 7%, and 0.02 interclass correlation. The parameters used were based on the results of a study by kiR USA (Marsiglia et al., 2011).

Randomization

The selection process of the schools took place in three stages: 1) identification of the universe of state schools in the municipality of São Paulo that offered 5th and 7th grades, extracted from the list of national schools registered by the National Institute of Studies and Research Education Anísio Teixeira (INEP) ($n = 155$); 2) exclusion of schools that received PROERD in the last three years, based on data provided by the Military Police (96 schools were excluded and 59 were maintained); 3) randomization of the 59 schools to the control or intervention condition. The first 30 schools on the randomized list were considered the sample of the study and the following 29 schools were included as potential reserve schools, in the case of refusal. The participation of the schools in this process was authorized by the State Secretariat of Education.

A random drawing (implemented using PASS software version 22) was conducted by a collaborator (HCM), who was not involved in the data collection. Randomization to the intervention or the control group was conducted using Efron's biased coin, which allows the maintenance of a balanced sample (1:1 allocation ratio). Efron's strategy tends to balance the experiment, but at the same time is not overly vulnerable to various common forms of experimental bias. The primary application is used in clinical trials where the balance in the numbers randomly assigned to two treatment groups is desirable regarding power considerations (Efron, 1971). Within the intervention schools, all 5th and 7th grade students participated in the PROERD program. Different from what was registered on the INEP list, two of the 30 schools offered only 7th grade in 2019. For this reason, the sample of 5th grade schools included 28 schools while the sample of 7th grade schools included 30 schools.

Intervention

The PROERD "Caindo na Real" program consists of 10 weekly classes with an average duration of 50 min. The program is taught by trained police officers through the use of a student and teacher manual. Each lesson has one to three activities that address drug prevention. The

teacher's handbook provides information about each lesson's procedures, objectives, required materials, activities to be performed, and tips. The police officers who deliver the program were trained in an 80-h training session offered by the Military Police, under the guidance of American developers (D.A.R.E. America).

The Military Police of the State of São Paulo was responsible for implementing the program. No information regarding the cultural adaptation process was provided or published by the institution. A comparison of the manuals of DARE-kiR and PROERD depicts that the only difference is that the program has been translated into a different language. Therefore, it appears that the program may be missing a proper cultural adaptation of the situations discussed in each lesson. An evaluation of the program's effectiveness was carried out by an independent team from the university that did not hold a role in the implementation process.

Instruments and measures

We used a self-reported audio-guided questionnaire which was completed anonymously by the students through the use of smartphones. The questionnaire was administered by the researchers in the classroom, without the teacher present.

The questionnaire used for data collection has been used in previous studies to evaluate school drug prevention programs in Brazil. Further, it was designed based on the European Drug Addiction Prevention Trial questionnaire (Faggiano et al., 2010), and translated and adapted into Brazilian Portuguese (Cainelli de Oliveira Prado et al., 2016). We also added a few questions from the World Health Organization questionnaire, used in the VI Brazilian Survey of Drug Use Among Students (Carlini et al., 2010), and the Brazilian National Survey of School Health (PENSE) questionnaire, which is used by the Brazilian Ministry of Health (IBGE, 2016). Socioeconomic status (SES) was assessed using the Socioeconomic Scale from the Associação Brasileira de Empresas de Pesquisa (Abep, 2016).

The outcomes analyzed included the time of first drug use and binge drinking as well as recent drug use and binge drinking, both evaluated as "yes/no". Case of recent use was considered at baseline as drug use occurring over the past year (i.e., past 12 months) and at follow-up, defined as drug use occurring within the past 6-months. This was done since the follow-up data were collected after nine months, and we wanted to guarantee no overlap. Case of first drug use was defined as the students who self-reported no lifetime use of drugs at the baseline, but then changed to lifetime use at the follow-up time point (no to yes).

For the 5th grade students, the drugs investigated were alcohol, tobacco, and marijuana. For the 7th-grade students, we also included questions on inhalants and cocaine. For this assessment, questions such as "In the past 6 months have you drunk alcoholic beverages?" and "Have you ever tried marijuana?' were used. The pattern of binge drinking was also investigated in both grades and was defined as the consumption of five or more alcoholic drinks on one occasion.

In each assessment, students provided a code generated from letters and numbers from their personal information, as previously used in drug prevention program evaluations (Valente et al., 2018). This code allowed the researchers to match individual questionnaires from different evaluation time points while providing anonymity and confidentiality of the participants, which is essential for a study on illicit behavior (Galanti et al., 2007). The datasets of the two time point assessments were integrated by matching a secret code using the Levenshtein algorithm, which can identify similarities between a set of characteristics (Levenshtein, 1965).

To avoid over-reporting of drug use, data from students who reported lifetime use of a fictional drug (named Holoten and Carpinol) were excluded from the analysis at each time point. We excluded from the analysis 14 and 12 questionnaires at baseline and 11 and eight questionnaires at follow-up, for 5th and 7th grades, respectively.

Statistical analysis

The data were initially run as descriptive analysis, that is, the categorical variables were summarized by number and percentage and the continuous variables, by means and standard deviations. All descriptive analyses were performed using the program STATA 16.

Two different paradigms were used to analyze the effects of the PROERD program on the recent use and initiation of drugs: complete case (CC) and intention-to-treat analysis (ITT). The CC analysis used logit changes through repeated measures. In this analysis, only observations with completed data from baseline and follow-up were considered; therefore, cases with missing values were excluded. For the ITT, two statistical methods were used to deal with the missing data and, concomitantly, the effect was estimated among all participants, without considering the extent to which they complied with the treatment requirements or if they were present at the follow-up evaluation. The multivariate analyses were adjusted for sex, age, SES, and baseline drug use, and considered the multilevel structure of the study design which is described in the Methods section.

Conditional transition within-subject analyses were also performed to calculate the effect of the program for each profile of adolescents, according to their report of drug use at baseline. Different from the previous analysis, conditional patterns consider the comparison of the same person over time in four patterns: 1) who was a user at baseline and maintained the use at follow up (yes-yes); 2) who was a user at baseline and stopped at follow-up (yes-no); 3) who was a non-user at baseline and maintained the non-use at follow-up (no-no); 4) who was a non-user at baseline and changed to use at follow-up (no-yes).

Missing data

In the ITT analysis, two methods were used to handle the missing data: full information maximum likelihood (FIML) and Selection Model (SM). FIML considers that each parameter is estimated directly for each individual based on the observed variables that are present in the dataset, using all available data. FIML assumes that the missing data mechanism is random (Missing at Random - MAR) when the probability of missing data on a variable is related to some other measured variable in the model, but not to the value of the variable with missing values itself (Enders, 2001). The SM method assumes that the pattern of data loss occurs in a non-random manner (Missing Not at Random - MNAR), that is, when the missing values of a variable are related to an unobserved variable, meaning that the probability of attrition is directly related to the outcome (Li et al., 2017). Considering that testing empirically for the true patterns of missing values is not currently possible, we decided to perform an intention-to-treat analysis considering both MAR and MNAR, using FMIL and SM, respectively (Mcpherson et al., 2014). In addition, with the use of FIML and SM, the effect of the program can be estimated for all students who started the study regardless of the loss of follow-up over time, following the guidelines of the ITT paradigm. The SM and FMIL estimation to handle missing data was run on MPLUS 7.4 because STATA 16 is not prepared to perform these analyses for a multilevel structure.

Multilevel structure

All inferential analyses were performed in Mplus version 8.4 (Muthén & Muthén, 2017), in which the estimator used for all the analyses was the maximum likelihood with robust standard errors (MLR). The MLR accounts for the non-independence of the observation (i.e., adolescents nested in schools), and the standard error was computed by considering the multilevel structure by a command in Mplus called TYPE = Complex, as proposed by Asparouhov (Asparouhov, 2005), us-
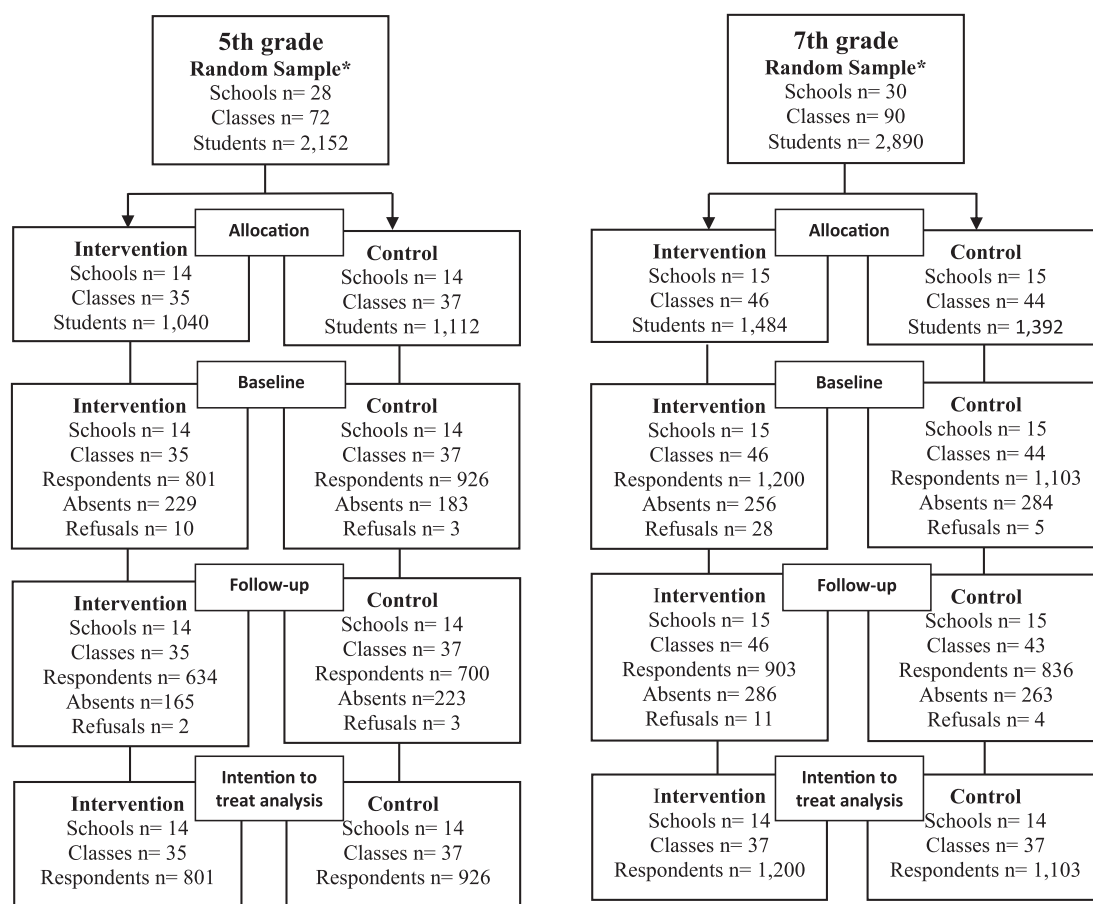
Fig. 1. Flowchart of the randomized controlled trial to assess the effect of the drug use prevention program PROERD, among 5th and 7th grade students.

ing a sandwich estimator (Asparouhov, 2006). Thus, a logistic regression analysis was performed at a significance level of 5%.

For the attrition analysis, we compared students whose data from the two time points were matched with students who answered only the baseline questionnaire.

Results

Among the 2152 5th grade students enrolled in the 72 classes from the 28 schools randomized in the study, 1727 students answered the baseline questionnaire, and 1334 students answered the follow-up questionnaire nine months after baseline (77.24%). Among the 2890 7th grade students enrolled in the 90 classes from the 30 schools randomized in the study, 2303students answered the baseline questionnaire, and 1739 students answered the follow-up questionnaire nine months after baseline (75.51%), as presented in Fig. 1.

Table 1 presents the characteristics of the 5th and 7th grade students who participated in the baseline assessment of the PROERD RCT. The intervention and control groups were homogenous at baseline with respect to all variables, except sex (included as an adjustment in all multivariate analyses). Alcohol was the most commonly used drug in both grades at both time points (i.e., baseline and follow-up).

Table 2 and 3 show the descriptive statistics for the complete case analysis with inferential statistics for both inter-and intragroup changes over time. According to Table 2, the prevalence of lifetime use of tobacco, marijuana, and the pattern of binge drinking among 7th-grade students was higher at follow-up than at the initial assessment in both groups. Among the 5th grade students, we did not identify this increase in the prevalence of drug use initiation at follow-up compared to the initial assessment (Table 3).

Table 4 depicts the effects of the PROERD program based on the intention to treat the paradigm using two different missing data estimations (FMIL and SM) on drug consumption among 5th and 7th year students. No statistically significant difference was found between the groups over time.

Table 5 shows the results of the drug use at baseline using a transitional conditional analysis to evaluate the past 6 months of drug use. A potential negative effect was found in one of the patterns of the conditional analyses, suggesting that 7th-grade students who attended the program and already practiced binge drinking before baseline had a higher chance of maintaining this behavior in comparison to the control group (OR = 3.38, 95%CI 1.27–9.05, $p = 0.015$). However, we must consider this negative finding with caution since the absolute number of cases with a pattern of binge drinking at baseline was small [pattern binge at baseline and follow-up (yes-yes) = 36 cases; pattern binge at baseline and non-binge at follow-up (yes-no) = 39 cases].

Adolescents lost in the nine-month follow-up were 22.76% among the 5th graders and 24.49% among the 7th graders. In the attrition analysis, as expected, students who missed the nine-month follow-up showed a significantly higher prevalence of the use of certain substances at baseline, especially among the 7th grade students. For example, among the 5th grade students, while the prevalence of past-year binge drinking was 0.83% among the followed students, it was 2.3% among the lost students ($p = 0.017$). Among the 7th grade students, the prevalence of alcohol use was 35.41% among the followed students and 44.74% among the lost students ($p < 0.001$). However, when attrition was compared between groups (i.e., intervention and control), no significant difference was found. Age also differed between the followed and lost students, but no difference in sex was found (**Tables S1 and S2, supplementary file**).

Table 1

Distribution of 5th and 7th grade students according to sociodemographic, drug use (alcohol, binge drinking, tobacco and marijuana) and allocation group in the cluster randomized controlled trial of the PROERD program, at baseline. Brazil, 2019 (N = 4030; 1727 5th and 2303 7th graders).

	Total		Intervention		Control		
	N	%	*N*	%	N	%	*p*-value
5th grade students	(N = 1727)		(N = 801)		(N = 926)		
Gender							0.027
Male	882	51.07	432	53.93	450	48.60	
Female	845	48.93	369	46.07	476	51.40	
Age (mean ± SD)	10.12 ± 0.65	10.10 ± 0.68	10.14 ± 0.61	0.257			
SES*							0.156
A	117	9.00	49	7.94	68	9.96	
B	447	34.38	224	36.30	223	32.65	
C	646	49.69	309	50.08	337	49.34	
D-E	90	6.92	35	5.67	55	8.05	
Alcohol							
Lifetime Use	303	17.54	148	18.48	155	16.74	0.344
Past year Use	161	9.36	82	10.30	82	8.86	0.312
Binge drinking[a]							
Lifetime Use	33	1.92	15	1.88	18	1.95	0.924
Past year Use	20	1.16	9	1.13	11	1.19	0.910
Tobacco							
Lifetime Use	31	1.80	16	2.01	15	1.62	0.553
Past year Use	12	0.70	6	0.75	6	0.65	0.799
Marijuana							
Lifetime Use	10	0.58	3	0.38	7	0.76	0.298
Past year Use	4	0.23	1	0.13	3	0.33	0.391
7th grade students	(N = 2303)		(N = 1200)		(N = 1103)		
Gender							0.835
Male	1187	51.54	621	51.75	566	51.31	
Female	1116	48.46	579	48.25	537	48.69	
Age (mean ± SD)	12.28 ± 0.72	12.28 ± 0.74	12.27 ± 0.71	0.751			
SES*							0.061
A	130	5.71	74	6.25	56	5.12	
B	773	33.93	416	35.14	357	32.63	
C	1222	53.64	629	53.13	593	54.20	
D-E	153	6.72	65	5.49	88	8.04	
Alcohol							
Life Use	866	37.68	439	36.64	427	38.82	0.283
Past year Use	458	19.96	237	19.82	221	20.11	0.861
Binge drinking[a]							
Lifetime Use	229	9.97	127	10.61	102	9.28	0.289
Past year Use	132	5.77	71	5.95	61	5.58	0.695
Tobacco							
Lifetime Use	112	4.88	51	4.26	61	5.55	0.155
Past year Use	36	1.57	20	1.67	16	1.46	0.677
Marijuana							
Lifetime Use	78	3.40	41	3.43	37	3.37	0.935
Past year Use	41	1.79	22	1.84	19	1.73	0.842
Inhalants							
Lifetime Use	239	10.43	126	10.55	113	10.29	0.838
Past year Use	57	2.49	31	2.60	26	2.37	0.726
Cocaine							
Lifetime Use	9	0.39	4	0.34	5	0.46	0.645
Past year Use	2	0.09	0	-	2	0.18	0.140

[a] Binge drinking was considered the consumption of five or more drinks of alcohol on one occasion.

* Socioeconomic classification according to ABEP, information collected in follow-up (N = 1300). Data on inhalants and cocaine were not collected from the 5th grade.

Discussion

This study evaluated the effectiveness of the PROERD school-based drug prevention program that is widely disseminated in Brazilian schools, implemented through two curricula: 5th and 7th grade, both adapted from the North American program Keepin' it REAL. The PROERD program was not effective as a universal program in delaying or reducing the consumption of any drug after nine months, regardless of the paradigm used in the analysis. A negative effect was found in the conditional analyses, considering only a within-subjects change, and suggesting that 7th grade students who attended the program and already practiced binge drinking before baseline had significantly higher chances of maintaining this behavior in comparison to the control group.

However, these results came from a small number of subjects who reported binge drinking at baseline.

The present study advances the knowledge of prevention science by reporting the first effectiveness trial of the Brazilian version of Keepin' it REAL, (PROERD/"Caindo na Real"), the most widespread school prevention program in Brazilian schools. It is noteworthy that a significant portion of school prevention programs are not evaluated or show little success in reducing drug use or delaying the initiation of consumption among adolescents (Foxcroft & Tsertsvadze, 2011; Kulis et al., 2019; Marsiglia et al., 2019; Strøm et al., 2014). Moreover, negative effects in prevention programs are more frequent than might be expected (Elek et al., 2010; Werch & Owen, 2002). A systematic review of the evaluation of preventive interventions found iatrogenic effects for 43

Table 2

Intragroup comparison over time on <u>first use</u> of alcohol and other drugs among 5th and 7th year students participating in the cluster randomized controlled trial of the PROERD program. Complete Cases.

	Intervention Group							Control Group						
	First Use[1] (Baseline)		First Use[2] (Follow-up)		Change intragroup over time[3]			First Use[1] (Baseline)		First Use[2] (Follow-up)		Change intragroup over time[3]		
5th Grade[#]	N	%	N	%	OR	95%CI	p	N	%	N	%	OR	95%CI	p
Alcohol	114/633	18.00	103/633	16.27	0.87	[0.64; 1.19]	0.392	121/699	17.31	114/699	16.31	0.92	[0.69; 1.24]	0.601
Binge drinking[a]	10/630	1.59	9/630	1.43	0.89	[0.35; 2.25]	0.814	12/698	1.72	10/698	1.43	0.82	[0.35; 1.95]	0.662
Tobacco	13/632	2.06	13/632	2.06	1.00	[0.46; 2.17]	1.000	9/697	1.29	20/697	2.87	2.26	[1.02; 4.99]	0.044
Marijuana	1/632	0.16	4/632	0.63	n.e[4]	-	-	3/697	0.43	5/697	0.72	n.e[4]	-	-
7th Grade	N	%	N	%	OR	IC95%	p	N	%	N	%	OR	IC95%	p
Alcohol	322/901	35.74	356/901	39.51	1.22	[0.99; 1.52]	0.064	291/833	34.93	314/833	37.70	1.16	[0.93; 1.45]	0.189
Binge drinking[a]	85/900	9.44	118/900	13.11	1.64	[1.16; 2.32]	0.005	58/830	6.99	98/830	11.81	2.11	[1.43; 3.12]	<0.001
Tobacco	32/901	3.55	82/901	9.10	3.03	[1.93; 4.74]	<0.001	36/833	4.32	61/833	7.32	1.85	[1.18; 2.89]	0.007
Marijuana	18/901	2.00	34/901	3.77	2.34	[1.20; 4.56]	0.013	15/832	1.80	31/832	3.73	2.64	[1.28; 5.44]	0.008
Inhalants	87/896	9.71	78/896	8.71	0.88	[0.64; 1.22]	0.457	79/829	9.53	73/829	8.81	0.91	[0.65; 1.28]	0.606
Cocaine	3/896	0.33	6/896	0.67	n.e[4]	-	-	4/829	0.48	5/829	0.60	n.e[4]	-	-

[1] Lifetime drug use at any time before baseline assessment.
[2] Lifetime drug use at any time during 9 month-follow up.
[3] Logit changes for repeated measures - intragroup.
[4] n.e. = not estimate (less than 10 cases at the follow-up).
[#] Data on inhalants and cocaine were not collected from the 5th grade.
[a] Binge drinking was considered the consumption of five or more drinks of alcohol on one occasion.

Table 3

Intragroup comparison over time on <u>recent use</u> of alcohol and other drugs among 5th and 7th year students participating in the cluster randomized controlled trial of the PROERD program. Complete Cases.

	Intervention Group							Control Group						
	Past-year Use[1] (Baseline)		Recent Use[2] (Follow-up)		Change intragroup over time[3]			Past-year Use[1] (Baseline)		Recent Use[2] (Follow-up)		Change intragroup over time[3]		
5th Grade[#]	N	%	N	%	OR	95%CI	p	N	%	N	%	OR	95%CI	p
Alcohol	58/628	9.24	47/628	7.48	0.73	[0.46; 1.17]	0.196	63/697	9.04	55/697	7.89	0.82	[0.53; 1.27]	0.378
Binge drinking[a]	4/627	0.64	2/627	0.32	n.e[4]	-	-	7/697	1.00	4/697	0.57	n.e[4]	-	-
Tobacco	6/632	0.95	2/632	0.32	n.e[4]	-	-	3/697	0.43	8/697	1.15	n.e[4]	-	-
Marijuana	1/632	0.16	1/632	0.16	n.e[4]	-	-	1/697	0.14	1/697	0.14	n.e[4]	-	-
7th Grade	N	%	N	%	OR	IC95%	p	N	%	N	%	OR	IC95%	p
Alcohol	171/899	19.02	246/899	27.36	2.39	[1.75; 3.27]	<0.001	148/830	17.83	216/830	26.02	2.42	[1.74; 3.35]	<0.001
Binge drinking[a]	40/900	4.44	82/900	9.11	3.34	[1.97; 5.65]	<0.001	35/830	4.22	58/830	6.99	2.21	[1.29; 3.80]	0.004
Tobacco	9/901	1.00	27/901	3.00	4.19	[1.73; 10.16]	0.002	8/832	0.96	22/832	2.64	3.66	[1.44; 9.29]	0.006
Marijuana	9/901	1.00	17/901	1.89	2.54	[0.94; 6.82]	0.065	8/832	0.96	17/832	2.04	3.19	[1.10; 9.27]	0.033
Inhalants	17/896	1.90	28/896	3.13	1.88	[0.95; 3.70]	0.070	21/829	2.53	29/829	3.50	1.52	[0.80; 2.88]	0.202
Cocaine	0/896	0.00	1/896	0.11	n.e[4]	-	-	1/829	0.12	3/829	0.36	n.e[4]	-	-

[1] Use in the past 12 months prior to baseline assessment.
[2] Use in the past 6 months prior to follow-up assessment.
[3] Logit changes for repeated measures - intragroup.
[4] n.e. = not estimated (less than 10 cases per group at the follow-up).
[#] Data on inhalants and cocaine were not collected from the 5th grade.
[a] Binge drinking was considered the consumption of five or more drinks of alcohol on one occasion.

outcomes reported in 17 studies (Werch & Owen, 2002). Previous evaluations carried out in the US also found iatrogenic effects for alcohol and cigarette use, as reported in the Take Charge of Your Life (TCYL) study (Sloboda et al., 2009), and null effects for drug use, as reported in the DARE study (Lynam et al., 1999). In Brazil, an evaluation of the adaptation of the Unplugged program also found an iatrogenic effect for alcohol initiation (Sanchez et al., 2017). This finding shows the importance of evaluating prevention programs to determine the sustainability of a public prevention policy and its potential long-term effects on society (Catalano et al., 2012; Gottfredson et al., 2015).

The possible negative and null effects regarding the prevention of drug use found in this study conflict with the majority of positive results reported for the kiR program in North American studies, which showed a reduction in adolescent alcohol use (Gosin et al., 2003; Kulis et al., 2007; Warren et al., 2006) and the consumption of marijuana and tobacco (Hecht et al., 2018; Kulis et al., 2007; Kulis et al., 2019; Warren et al., 2006). Consequently, we must say that producing a meaningful effect on drug use behavior only through school programs is known to be difficult (Marsiglia et al., 2019; Strøm et al., 2014), and the null and negative results from this study corroborate those found by Elek (2010),

Table 4

Multilevel adjusted analysis of the effect of the program on recent use and first use among 5th and 7th year students participating in the PROERD cluster randomized controlled trial, according to two different paradigms: Complete Cases (CC) and Intention to treat (ITT).

		PROERD Effect at Recent Use[1] Last Months				PROERD Effect at First Use Initiation			
		N	OR*	95%CI	p	N	OR*	95%CI	p
5th Grade[#]									
CC	Alcohol	1284	0.92	[0.54; 1.59]	0.777	1290	1.01	[0.71; 1.44]	0.962
	Binge drinking[a]	1281	n.e.	-	-	1285	1.14	[0.54; 2.39]	0.733
	Tobacco	1289	n.e.	-	-	1289	0.74	[0.36; 1.54]	0.423
	Marijuana	-	n.e.	-	-	-	n.e.	-	-
ITT-FMIL	Alcohol	1727	0.95	[0.56; 1.62]	0.851	1727	1.01	[0.73; 1.41]	0.935
	Binge drinking[a]	1727	n.e.	-	-	1727	1.03	[0.50; 2.11]	0.943
	Tobacco	1727	n.e.	-	-	1727	0.72	[0.37; 1.40]	0.332
	Marijuana	-	n.e.	-	-	-	n.e.	-	-
ITT-SM	Alcohol	1727	0.83	[0.47; 1.48]	0.534	1727	0.90	[0.62; 1.30]	0.580
	Binge drinking[a]	1727	n.e.	-	-	1727	0.73	[0.35; 1.50]	0.393
	Tobacco	1727	n.e.	-	-	1727	0.66	[0.33; 1.33]	0.246
	Marijuana	-	n.e.	-	-	-	n.e.	-	-
7th Grade									
CC	Alcohol	1716	1.04	[0.86; 1.25]	0.705	1721	1.07	[0.88; 1.30]	0.487
	Binge drinking[a]	1717	1.32	[0.87; 2.01]	0.192	1717	1.04	[0.81; 1.35]	0.748
	Tobacco	1722	1.12	[0.63; 1.96]	0.703	1722	1.27	[0.84; 1.90]	0.255
	Marijuana	1722	0.86	[0.44; 1.69]	0.664	1722	0.97	[0.58; 1.62]	0.904
	Inhalants	1716	0.91	[0.47; 1.77]	0.789	1716	0.98	[0.64; 1.49]	0.915
	Cocaine	-		n.e.	-	-	n.e.	-	-
ITT-FMIL	Alcohol	2303	1.02	[0.85; 1.22]	0.842	2303	1.05	[0.87; 1.28]	0.589
	Binge drinking[a]	2303	1.34	[0.89; 2.04]	0.163	2303	1.04	[0.81; 1.33]	0.765
	Tobacco	2303	1.15	[0.67; 1.99]	0.612	2303	1.27	[0.85; 1.91]	0.236
	Marijuana	2303	0.92	[0.49; 1.74]	0.805	2303	0.99	[0.58; 1.69]	0.986
	Inhalants	2303	0.91	[0.47; 1.77]	0.777	2303	0.97	[0.63; 1.48]	0.888
	Cocaine	-	-	n.e.	-	-	n.e.	-	-
ITT- SM	Alcohol	2303	1.01	[0.83; 1.22]	0.895	2303	1.07	[0.88; 1.29]	0.511
	Binge drinking[a]	2303	1.16	[0.82; 1.628]	0.399	2303	1.02	[0.80; 1.31]	0.863
	Tobacco	2303	1.03	[0.72; 1.49]	0.865	2303	1.11	[0.84; 1.46]	0.457
	Marijuana	2303	0.98	[0.60; 1.62]	0.949	2303	1.01	[0.70; 1.44]	0.972
	Inhalants	2303	0.97	[0.68; 1.39]	0.875	2303	1.00	[0.79; 1.26]	0.996
	Cocaine	-	-	n.e.	-	-	n.e.	-	-

* Analyzes adjusted for sex, age, socioeconomic status and baseline drug use.

[1] Use in the past 12 months prior to baseline assessment *versus* use in the past 6 months prior to follow-up assessment.

CC = Complete CasesITT-FMIL= Intention to Treat with Full information maximum likelihood estimationITT-SM=Intention to Treat with Selection Model.n.e. = not estimated (less than 10 cases per group at the follow-up); Cocaine models did not converge.

[#] Data on inhalants and cocaine were not collected from the 5th grade.

[a] Binge drinking was considered the consumption of five or more drinks of alcohol on one occasion.

Hecht (2008) and colleagues. Thus, the ideal prevention strategy would be a combination of school curricular programs and family and community strategies (Marsiglia et al., 2019; UNODC, 2018), in addition to a comprehensive review of public alcohol policies, from the control of advertisements to the truly controlled restriction of sales to minors (Babor, 2010).

We have raised several hypotheses to try to understand the negative and null results: 1) differences in the educational system among 5th and 7th grade students in Brazil in the slum areas of São Paulo, when compared to students of better SES in the USA; 2) poor cultural adaptation of the program; and 3) lack of implementation fidelity.

Data from the Program for International Student Assessment (PISA, 2016) showed that student performance in Brazil was below average on the reading competency test when compared to students from the other 35 member countries of the Organization for Economic Co-operation and Development (OECD, 2020). Thus, the poor literacy and writing proficiency of Brazilian students may have threatened the understanding of the content of the lessons in the program activities. Considering this, it is crucial for a cultural adaptation that takes into account the educational reality of students who will be exposed to the program. Cultural adaptation must ensure that programs respond to the cultural and contextual needs of the community where they are being implemented (Castro et al., 2004), to integrate the main cultural values of the target population with the core elements of the program's curricu-

lum (Hecht et al., 2018; Marsiglia et al., 2009). Moreover, this study did not evaluate the fidelity of the implementation, which is considered a determining factor for obtaining good results (Pettigrew et al., 2014), and the greater the fidelity of program implementation, the better the results for the studied outcomes (Flay et al., 2005; Khoury, Mcintosh, & Hoselton, 2019).

Regarding the negative results for binge drinking for those who were already binge drinking before the intervention, we hypothesize that it is related to the lack of adequate cultural adaptation of the Brazilian version of the program. For instance, all lessons addressed drug use. The situations presented in the lessons of the PROERD 7th grade curriculum do not match the reality of Brazilian adolescents; they are closer to the American reality. Inviting friends to watch football at home, going shopping, or playing basketball are not common situations among young Brazilians. Even the situations that occur at school end up not being applicable due to the difference in school culture and space organization. For example, in Brazil, it is not common for students to form groups at tables during breaks. For example, the cafeteria usually has long tables to accommodate a large number of students who sit next to each other. Further, schools do not have individual lockers for student use. Even drinks that appear in some situations are not commonly consumed by Brazilian youths. For example, in Lesson 4 of the 5th grade curriculum, "friends are planning to bring wine to the game" even though wine is not common among adolescents in Brazil, while liquor, such as vodka

Table 5

Transitional analysis conditioned on the initial status of recent drug use[1] in the cluster randomized controlled trial among 5th and 7th grade students.

Baseline	Baseline Status	Group	Total Students /within schools	Follow-up Yes N	Yes %	No N	No %	OR[*][#]	95%CI	p
5th Grade										
Alcohol	No	Intervention	570/14 Schools	27	4.74	543	95.26	0.70	[0.37; 1.32]	0.266
		Control	634/14 Schools	41	6.47	593	93.53	1		
	Yes	Intervention	58/14 Schools	20	34.48	38	65.52	1.86	[0.72; 4.78]	0.198
		Control	63/14 Schools	14	22.22	49	77.78	1		
Binge drinking[a]	No	Intervention	623/14 Schools	2	0.32	621	99.68	ne	-	-
		Control	690/14 Schools	3	0.43	687	99.57			
	Yes	Intervention	4/14 Schools	0	0.00	4	100.0	ne	-	-
		Control	7/14 Schools	1	14.29	6	85.71			
Tobacco	No	Intervention	626/14 Schools	2	0.32	624	99.68	ne	-	-
		Control	694/14 Schools	8	1.15	686	98.85			
	Yes	Intervention	6/14 Schools	0	00.00	6	100.00	ne	-	-
		Control	3/14 Schools	0	00.00	3	100.00			
Marijuana	No	Intervention	631/14 Schools	1	0.16	630	99.84	ne	-	-
		Control	696/14 Schools	1	0.14	695	99.86			
	Yes	Intervention	1/14 Schools	0	00.00	1	100.00	ne	-	-
		Control	1/14 Schools	0	00.00	1	100.00			
7th Grade										
Alcohol	No	Intervention	728/15 Schools	130	17.86	598	82.14	1.03	[0.78; 1.36]	0.830
		Control	688/15 Schools	118	17.30	564	82.70	1		
	Yes	Intervention	171/15 Schools	116	67.84	55	32.16	1.07	[0.66; 1.73]	0.781
		Control	148/15 Schools	98	66.22	50	33.78	1		
Binge drinking[a]	No	Intervention	860/15 Schools	58	6.74	802	93.26	1.12	[0.75; 1.68]	0.587
		Control	795/15 Schools	46	5.79	749	94.21	1		
	Yes	Intervention	40/15 Schools	24	60.00	16	40.00	**3.38**	**[1.27; 9.05]**	**0.015**
		Control	35/15 Schools	12	34.29	23	65.71	1		
Tobacco	No	Intervention	892/15 Schools	23	2.58	869	97.42	1.07	[0.60; 1.99]	0.826
		Control	824/15 Schools	19	2.31	805	97.69	1		
	Yes	Intervention	9/15 Schools	4	44.44	5	55.56	ne	-	-
		Control	8/15 Schools	3	37.50	5	62.50			
Marijuana	No	Intervention	892/15 Schools	13	1.46	879	98.54	1.06	[0.47; 2.39]	0.887
		Control	824/15 Schools	11	1.33	813	98.67	1		
	Yes	Intervention	9/15 Schools	4	44.44	5	55.56	ne	-	-
		Control	8/15 Schools	6	75.00	2	25.00			
Inhalants	No	Intervention	879/15 Schools	24	2.73	855	97.27	0.96	[0.48; 1.91]	0.903
		Control	808/15 Schools	23	2.85	785	97.15	1		
	Yes	Intervention	17/15 Schools	4	23.53	13	76.47	ne	-	-
		Control	21/15 Schools	6	28.57	15	71.43			
Cocaine	No	Intervention	896/15 Schools	1	0.11	895	99.89	ne	-	-
		Control	828/15 Schools	2	0.24	826	99.76			
	Yes	Intervention	0/15 Schools	0	0	0	0	ne	-	-
		Control	1/15 Schools	1	100	0	0			

[1] Use in the past 12 months prior to baseline assessment *versus* use in the past 6 months prior to follow-up assessment.

[*] PROERD effect in conditional analysis. Within subject analysis: who was a user at baseline and maintained the use at the follow up (yes-yes); who was a user at baseline and stopped at the follow up (yes-no); who was a non-user at baseline and maintained the non-use at the follow up (no-no); who was a non-user at baseline and changed to use at the follow up (no-yes).n.e. = not estimated (less than 10 cases per group).

[#] Small number of subjects can overestimate the odds ratio.

[a] Binge drinking was considered the consumption of five or more drinks of alcohol on one occasion.

and rum, are more commonly consumed (Coutinho et al., 2016). This gap between the examples (suggested by the original manual) does not match the reality of Brazilian adolescents and may leave an open space for the instructor to report situations they experience as police officers related to drug use repression. We already know from studies that a repressive approach, as well as a speech that only emphasizes the negative consequences of drug use, can stimulate consumption, especially among those who have already started consuming (UNODC, 2018).

Previous kiR studies corroborate the importance of creating a curriculum adapted to the different realities that coexist in the country and large urban centers (Kulis et al., 2005; Kulis et al., 2017), such as São Paulo. As an example of this importance, Hecht et al. (2018) compared the rural (adapted) and original (urban) versions of the kiR curriculum applied to students from rural areas in two American states, and found that only the adapted version was effective in reducing drug use in that population; these results are limited only to the effect on cigarette use.

It is important to point out that in the literature, most of the kiR evaluation studies were carried out with the program being applied by

teachers from the school who were previously trained (Hecht et al., 2018; Kulis et al., 2019; Marsiglia et al., 2011, 2015, 2019). In our study, the program was applied by police officers trained to become PROERD instructors. This has been happening since 2014 when military police adopted the kiR curriculum in their prevention program. Therefore, in addition to being the first RCT to evaluate the program in Brazil, it is also one of the first in the literature to evaluate the program applied by police officers.

The main lessons of kiR focus on developing drug resistance strategies (Refuse, Explain, Avoid, and Leave—the REAL of the program title) through students' narratives of resisting offers of substance, based on the principle of cultural grounding (Hecht et al., 2008). However, most effective programs emphasize the general training of social and emotional skills (UNODC, 2018). One example is the Positive Action Program with several lessons per year (80–140), with most of them focused on socio-emotional learning, life skills, and school climate (Beets et al., 2009). Another example is the Life Skills Training (LST), which offers several lessons per year; a majority of the training involves skills such as effec-

tive communication, self-image, decision making, and, similar to kiR, resistance training (Trudeau et al., 2003).

This study had some limitations that must be pointed out. The main concern was selection bias. The data cannot be generalized since the sample universe was taken from schools that did not receive the evaluated program in the three years before our study, and these may not represent all schools in São Paulo. We must consider that the schools selected to participate in this trial were incidentally located in peripheral regions of the city that represent low-income areas and, consequently, more exposed to drug use (Daniel et al., 2009), which may hinder the effectiveness of the program. Thus, we do not know what the effects of the program are when administered in other regions, with children different from those who participated in our study. Additionally, it is important to note that we found a large number of students absent from the classroom during the baseline data collection, considering the number of students provided in the INEP list. However, this loss was already expected because similar studies have been conducted in Brazilian public schools (Sanchez et al., 2017, 2018), where approximately 20% of students are regularly absent from public schools (Penna, 2010). Losses during follow-up are also a common limitation in longitudinal studies (Ariza et al., 2013; Newton et al., 2010; Sanchez et al., 2017) and sophisticated statistical methods have attempted to deal with these losses to estimate the values   lost over time. Finally, the lower prevalence of drug use among Brazilian students might limit the analysis, and we suggest further investigation with a longer follow-up to assess older adolescents in which the drug use prevalence is higher.

Considering that PROERD is the school prevention program most widely disseminated in Brazilian schools, the government should pay attention to these results. Therefore, the recommendation would be a clear assessment of the components of the program that may be misinterpreted by teachers and students and, therefore, need to be removed from the original model or adapted to a Brazilian population to achieve the expected outcomes. The findings of this study suggest that the implementation and adaptation of the program should be evaluated to allow identification of the reasons why the program's effects were inconsistent with previous Keepin it REAL studies.

Ethics

All procedures in the present study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The study was registered in the Brazilian Ministry of Health Register of Clinical Trials (REBEC), under protocol number 6q23nk. The study protocol was approved by the Universidade Federal de São Paulo's Research Ethics Committee (n:1327/2018). Consent to participate in the study was written and obtained from the schools' directors before randomization and from students after randomization.

Declarations of Interest

None.

Acknowledgments

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.drugpo.2021.103413.

References

Abep (2016). *Critério de classificação econômica, Brasil.*

Ahn, C., Heo, M., & Zhang, S. (2014). *Sample size calculations for clustered and longitudinal outcomes in clinical research.* Chapman and Hall/CRC. 10.1201/b17822.

Ariza, C., Pérez, A., Sánchez-Martínez, F., Diéguez, M., Espelt, A., Pasarín, M. I., Suelves, J. M., De la Torre, R., & Nebot, M. (2013). Evaluation of the effectiveness of a school-based cannabis prevention program. *Drug and Alcohol Dependence, 132*(1–2), 257–264. 10.1016/j.drugalcdep.2013.02.012.

Asparouhov, T. (2005). Sampling weights in latent variable modeling. *Structural Equation Modeling: A Multidisciplinary Journal, 12*(3), 411–434. 10.1207/s15328007sem1203_4.

Asparouhov, T. (2006). General multi-level modeling with sampling weights. *Communications in Statistics—Theory and Methods, 35*(3), 439–460. 10.1080/03610920500476598.

Babor, T. F. (2010). *Alcohol: no ordinary commodity.* Research and Public Policy. (Oxford & U. Press. (eds.); 2°). Oxford University Press.

Beets, M. W., Flay, B. R., Vuchinich, S., Snyder, F. J., Acock, A., Li, K., & Burns, K. (2009). Use of a social and character development program to prevent substance use, violent behaviors, and sexual activity among elementary-school students in Hawaii. *American Journal of Public Health, 99*(8), 1438–1445. 10.2105/AJPH.2008.142919.

Cainelli de Oliveira Prado, M., Schneider, D. R., Sañudo, A., Pereira, A. P. D., Horr, J. F., & Sanchez, Z. M (2016). Transcultural adaptation of questionnaire to evaluate drug use among students: The use of the EU-Dap European questionnaire in Brazil. *Substance Use & Misuse, 51*(4), 449–458. 10.3109/10826084.2015.1117101.

Caputi, T. L., & Thomas McLellan, A. (2017). Truth and D.A.R.E.: Is D.A.R.E.'s new Keepin' it REAL curriculum suitable for American nationwide implementation? *Drugs: Education, Prevention and Policy, 24*(1), 49–57. 10.1080/09687637.2016.1208731.

Carlini, E. L., de, A., Noto, A. R., Sanchez, Z., van der, M., Carlini, C. M. A., Locatelli, D. P., Abeid, L. R., Amato, T. C., Opaleye, E. S., Tondowski, C. S., & de. Moura, Y. G. (2010). VI Levantamento Nacional sobre o Consumo de Drogas Psicotrópicas entre Estudantes do Ensino Fundamental e Médio das Redes Pública e Privadade Ensino nas 27 Capitais Brasileiras –2010 *(Vol. 1).* CEBRID - Centro Brasileiro de Informações sobre Drogas Psicotrópicas.

Castro, F. G., Barrera, M., & Martinez, C. R. (2004). The cultural adaptation of prevention interventions: Resolving tensions between fidelity and fit. *Prevention Science, 5*(1), 41–45. http://www.ncbi.nlm.nih.gov/pubmed/15058911.

Catalano, R. F., Fagan, A. A., Gavin, L. E., Greenberg, M. T., Irwin, C. E., Ross, D. A., & Shek, D. T. (2012). Worldwide application of prevention science in adolescent health. *Lancet, 379*(9826), 1653–1664. 10.1016/S0140-6736(12)60238-4.

Coutinho, E. S. F., França-Santos, D., Magliano, E., da, S., Bloch, K. V., Barufaldi, L. A., … Szklo, M. (2016). ERICA: Padrões de consumo de bebidas alcoólicas em adolescentes brasileiros. *Revista de Saúde Pública, 50,* 8s.

Cuijpers, P. (2002). Effective ingredients of school-based drug prevention programs. *Addictive Behaviors, 27*(6), 1009–1023. 10.1016/S0306-4603(02)00295-2.

Daniel, J. Z., Hickman, M., Macleod, J., Wiles, N., Lingford-Hughes, A., Farrell, M., Araya, R., Skapinakis, P., Haynes, J., & Lewis, G. (2009). Is socioeconomic status in early life associated with drug use? A systematic review of the evidence. *Drug and Alcohol Review, 28*(2), 142–153. 10.1111/j.1465-3362.2008.00042.x.

Day, L. E., Miller-Day, M., Hecht, M. L., & Fehmie, D. (2017). Coming to the new D.A.R.E.: A preliminary test of the officer-taught elementary Keepin' it REAL curriculum. *Addictive Behaviors, 74*(May), 67–73. 10.1016/j.addbeh.2017.05.025.

Degenhardt, L., Stockings, E., Patton, G., Hall, W. D., & Lynskey, M. (2016). The increasing global health priority of substance use in young people. *Lancet Psychiatry, 3*(3), 251–264. 10.1016/S2215-0366(15)00508-8.

Donner, A., & Klar, N. (2010). *Design and analysis of cluster randomization trials in health research* (1st ed.). Wiley.

Efron, B. (1971). Forcing a sequential experiment to be balanced. *Biometrika, 58.*

Elek, E., Wagstaff, D. A., & Hecht, M. L. (2010). Effects of the 5th and 7th grade enhanced versions of the Keepin' it real substance use prevention curriculum. *Journal of Drug Education, 40*(1), 61–79. 10.2190/DE.40.1.e.

Enders, C. K. (2001). A primer on maximum likelihood algorithms available for use with missing data. *Structural Equation Modeling: A Multidisciplinary Journal, 8*(1), 128–141. 10.1207/S15328007SEM0801_7.

Faggiano, F., Vigna-Taglianti, F., Burkhart, G., Bohrn, K., Cuomo, L., Gregori, D., Panella, M., Scatigna, M., Siliquini, R., Varona, L., van der Kreeft, P., Vassara, M., Wiborg, G., & Galanti, M. R. (2010). The effectiveness of a school-based substance abuse prevention program: 18-Month follow-up of the EU-Dap cluster randomized controlled trial. *Drug and Alcohol Dependence, 108*(1–2), 56–64. 10.1016/j.drugalcdep.2009.11.018.

Faggiano, F., Vigna-Taglianti, F. D., Versino, E., Zambon, A., Borraccino, A., & Lemma, P. (2008). School-based prevention for illicit drugs use: A systematic review. *Preventive Medicine, 46*(5), 385–396. 10.1016/j.ypmed.2007.11.012.

Flay, B. R., Biglan, A., Boruch, R. F., Castro, F. G., Gottfredson, D., Kellam, S., Mościcki, E. K., Schinke, S., Valentine, J. C., & Ji, P. (2005). Standards of evidence: Criteria for efficacy, effectiveness and dissemination. *Prevention Science, 6*(3), 151–175. 10.1007/s11121-005-5553-y.

Foxcroft, D. R., & Tsertsvadze, A. (2011). Universal multi-component prevention programs for alcohol misuse in young people. In D. R. Foxcroft (Ed.), *Cochrane Database of Systematic Reviews.* John Wiley & Sons, Ltd (Issue 9). 10.1002/14651858.CD009307.

Foxcroft, D. R., & Tsertsvadze, A. (2012). Universal alcohol misuse prevention programmes for children and adolescents: Cochrane systematic reviews. *Perspectives in Public Health, 132*(3), 128–134. 10.1177/1757913912443487.

Galanti, M. R., Siliquini, R., Cuomo, L., Melero, J. C., Panella, M., & Faggiano, F. (2007). Testing anonymous link procedures for follow-up of adolescents

in a school-based trial: The EU-DAP pilot study. *Preventive Medicine, 44*(2), 174–177. 10.1016/j.ypmed.2006.07.019.

Gosin, M., Marsiglia, F. F., & Hecht, M. L. (2003). Keepin' it R.E.A.L. : A drug resistance curriculum tailored to the strengths and needs of pre-adolescents of the southwest. *Journal of Drug Education, 33*(2), 119–142. 10.2190/DXB9-1V2P-C27J-V69V.

Gottfredson, D. C., Cook, T. D., Gardner, F. E. M., Gorman-Smith, D., Howe, G. W., Sandler, I. N., & Zafft, K. M. (2015). Standards of evidence for efficacy, effectiveness, and scale-up research in prevention science: Next generation. *Prevention Science, 16*(7), 893–926. 10.1007/s11121-015-0555-x.

Hall, W. D., Patton, G., Stockings, E., Weier, M., Lynskey, M., Morley, K. I., & Degenhardt, L. (2016). Why young people's substance use matters for global health. *Lancet Psychiatry, 3*(3), 265–279. 10.1016/S2215-0366(16)00013-4.

Hecht, M. L., Shin, Y., Pettigrew, J., Miller-Day, M., & Krieger, J. L. (2018). Designed cultural adaptation and delivery quality in rural substance use prevention: An effectiveness trial for the Keepin' it REAL curriculum. *Prevention Science, 19*(8), 1008–1018. 10.1007/s11121-018-0937-y.

Hecht, M. L., Warren, J. R., Wagstaff, D. A., & Elek, E. (2008). Substance use, resistance skills, decision making, and refusal efficacy among Mexican and Mexican American preadolescents. *Health Communication, 23*(4), 349–357. 10.1080/10410230802229720.

IBGE. (2016). *Pesquisa Nacional de Saúde do Escolar 2015*. IBGE, Coordenação de População e Indicadores Sociais.

Khoury, C. R., Mcintosh, K., & Hoselton, R. (2019). An investigation of concurrent validity of fidelity of implementation measures at initial years of implementation. *Remedial and Special Education, 40*(1), 23–31. https://doi.org/10.1177/0741932518795639.

Kulis, S., Marsiglia, F. F., Elek, E., Dustman, P., Wagstaff, D. A., & Hecht, M. L. (2005). Mexican/Mexican American adolescents and Keepin' it REAL: An evidence-based substance use prevention program. *Children & Schools, 27*(3), 133–145. 10.1093/cs/27.3.133.

Kulis, S. S., Ayers, S. L., & Harthun, M. L. (2017). Substance use prevention for urban American Indian youth: A efficacy trial of the culturally adapted living in 2 worlds program. *Journal of Primary Prevention, 38*(1–2), 137–158. 10.1007/s10935-016-0461-4.

Kulis, S. S., Marsiglia, F. F., Porta, M., Arévalo Avalos, M. R., & Ayers, S. L. (2019). Testing the Keepin' it REAL substance use prevention curriculum among early adolescents in Guatemala City. *Prevention Science, 20*(4), 532–543. 10.1007/s11121-018-0956-8.

Kulis, S., Nieri, T., Yabiku, S., Stromwall, L. K., & Marsiglia, F. F. (2007). Promoting reduced and discontinued substance use among adolescent substance users: Effectiveness of a universal prevention program. *Prevention Science, 8*(1), 35–49. 10.1007/s11121-006-0052-3.

Levenshtein, V. (1965). Binary codes capable of correcting deletions, insertions and reversals. *Doklady Akademii Nauk SSSR, 163*(4), 845–848.

Li, M., Chen, N., Cui, Y., & Liu, H. (2017). Comparison of different LGM-based methods with MAR and MNAR dropout data. *Frontiers in Psychology, 8*. 10.3389/fpsyg.2017.00722.

Lynam, D. R., Milich, R., Zimmerman, R., Novak, S. P., Logan, T. K., Martin, C., Leukefeld, C., & Clayton, R. (1999). Project DARE: No effects at 10-year follow-up. *Journal of Consulting and Clinical Psychology, 67*(4), 590–593. 10.1037/0022-006X.67.4.590.

Marsiglia, F. F., & Hecht, M. L. (2005). *Keepin'it REAL: An evidence-based program*. ETR Associates.

Marsiglia, F. F., Kulis, S., Martinez Rodriguez, G., Becerra, D., & Castillo, J. (2009). Culturally specific youth substance abuse resistance skills: Applicability across the U.S.—Mexico border. *Research on Social Work Practice, 19*(2), 152–164. 10.1177/1049731507303886.

Marsiglia, F. F., Kulis, S. S., Booth, J. M., Nuño-Gutierrez, B. L., & Robbins, D. E. (2015). Long-term effects of the Keepin' it REAL model program in Mexico: Substance use trajectories of guadalajara middle school students. *Journal of Primary Prevention, 36*(2), 93–104. 10.1007/s10935-014-0380-1.

Marsiglia, F. F., Kulis, S., Yabiku, S. T., Nieri, T. A., & Coleman, E. (2011). When to intervene: Elementary school, middle school or both? Effects of Keepin' it REAL on substance use trajectories of Mexican heritage youth. *Prevention Science, 12*(1), 48–62. 10.1007/s11121-010-0189-y.

Marsiglia, F. F., Medina-Mora, M. E., Gonzalvez, A., Alderson, G., Harthun, M., Ayers, S., Gutiérrez, B. N., Corona, M. D., Melendez, M. A. M., & Kulis, S. (2019). Binational cultural adaptation of the Keepin' it REAL substance use prevention program for adolescents in Mexico. *Prevention Science, 20*(7), 1125–1135. 10.1007/s11121-019-01034-0.

Mcpherson, S., Barbosa-leiker, C., Mamey, M. R., Mcdonell, M., Enders, C. K., & Roll, J. (2014). A ' missing not at random ' (MNAR) and ' missing at random ' (MAR)

growth model comparison with a buprenorphine /naloxone clinical trial. *Addiction*, 51–58. 10.1111/add.12714.

Moos, R. H. (2005). Iatrogenic effects of psychosocial interventions for substance use disorders: Prevalence, predictors, prevention. *Addiction, 100*(5), 595–604. 10.1111/j.1360-0443.2005.01073.x.

Muthén, L. K., & Muthén, B. O. (2017). *Mplus Version 8. Base Program and Combination Add-On (64-Bit)* (No. 8).

Newton, N. C., Teesson, M., Vogl, L. E., & Andrews, G. (2010). Internet-based prevention for alcohol and cannabis use: Final results of the climate schools course. *Addiction, 105*(4), 749–759. 10.1111/j.1360-0443.2009.02853.x.

OECD. (2020). *Development co-operation report 2020*. OECD. 10.1787/f6d42aa5-en.

Penna, G. (2010). Pesquisa Nacional de Saúde do Escolar (PeNSE). *Ciência & Saúde Coletiva, 15*(suppl 2) 3006–3006. 10.1590/S1413-81232010000800001.

Pereira, A. P. D., & Sanchez, Z. M. (2020). Characteristics of school-based drug prevention programs in Brazil. *Ciência & Saúde Coletiva, 25*(8), 3131–3142. 10.1590/1413-81232020258.28632018.

Pereira, A. D., Paes, Â. T., & Sanchez, Z. M. (2016). Factors associated with the implementation of programs for drug abuse prevention in schools. *Revista de Saúde Pública, 50*, 1–10. 10.1590/S1518-8787.2016050005819.

Pettigrew, J., Graham, J. W., Miller-Day, M., Hecht, M. L., Krieger, J. L., & Shin, Y. J. (2014). Adherence and delivery: Implementation quality and program outcomes for the seventh-grade Keepin' it REAL program. *Prevention Science, 16*(1), 90–99. 10.1007/s11121-014-0459-1.

PISA. (2016). Brasil no PISA 2015: Análises e reflexões sobre o desempenho dos estudantes Brasileiros. Fundação Santillana.

Sanchez, Z. M., Valente, J. Y., Galvão, P. P., Gubert, F. A., Melo, M. H. S., Caetano, S. C., Mari, J. J., & Cogo-Moreira, H. (2021). A cluster randomized controlled trial evaluating the effectiveness of the school-based drug prevention program #Tamojunto2.0. *Addiction, 116*, 1580–1592. 10.1111/add.15358.

Sanchez, Z. M., Valente, J. Y., Sanudo, A., Pereira, A. P. D., Cruz, J. I., Schneider, D., & Andreoni, S. (2017). The #Tamojunto drug prevention program in Brazilian schools: A randomized controlled trial. *Prevention Science, 18*(7), 772–782. 10.1007/s11121-017-0770-8.

Sanchez, Z. M., Valente, J. Y., Sanudo, A., Pereira, A. P. D., Schneider, D. R., & Andreoni, S. (2018). Effectiveness evaluation of the school-based drug prevention program #Tamojunto in Brazil: 21-Month follow-up of a randomized controlled trial. *International Journal of Drug Policy, 60*(2017), 10–17. 10.1016/j.drugpo.2018.07.006.

Sloboda, Z., Stephens, R. C., Stephens, P. C., Grey, S. F., Teasdale, B., Hawthorne, R. D., Williams, J., & Marquette, J. F. (2009). The adolescent substance abuse prevention study: A randomized field trial of a universal substance abuse prevention program. *Drug and Alcohol Dependence, 102*(1–3), 1–10. 10.1016/j.drugalcdep.2009.01.015.

Strøm, H. K., Adolfsen, F., Fossum, S., Kaiser, S., & Martinussen, M. (2014). Effectiveness of school-based preventive interventions on adolescent alcohol use: A meta-analysis of randomized controlled trials. *Substance Abuse Treatment, Prevention, and Policy, 9*(1), 48. 10.1186/1747-597X-9-48.

Tobler, N. S., Roona, M. R., Ochshorn, P., Marshall, D. G., Streke, A. V., & Stackpole, K. M. (2000). School-based adolescent drug prevention programs: 1998 M eta-analysis. *Journal of Primary Prevention, 20*(4), 275–336. 10.1023/A:1021314704811.

Trudeau, L., Spoth, R., Lillehoj, C., Redmond, C., & Wickrama, K. A. S. (2003). Effects of a preventive intervention on adolescent substance use initiation, expectancies, and refusal intentions. *Prevention Science, 4*(2), 109–122. 10.1023/A:1022926332514.

International standards on drug use prevention—Second updated edition (p. 58. (2018).

Valente, J. Y., Cogo-Moreira, H., Swardfager, W., & Sanchez, Z. M. (2018). A latent transition analysis of a cluster randomized controlled trial for drug use prevention. *Journal of Consulting and Clinical Psychology, 86*(8), 657–665. 10.1037/ccp0000329.

Warren, J. R., Hecht, M. L., Wagstaff, D. A., Elek, E., Ndiaye, K., Dustman, P., & Marsiglia, F. F. (2006). Communicating prevention: The effects of the Keepin' it REAL classroom videotapes and televised PSAs on middle-school students' substance use. *Journal of Applied Communication Research, 34*(2), 209–227. 10.1080/00909880600574153.

Werch, C. E., & Owen, D. M. (2002). Iatrogenic effects of alcohol and drug prevention programs. *Journal of Studies on Alcohol, 63*, 581–590.

Whiteford, H. A., Degenhardt, L., Rehm, J., Baxter, A. J., Ferrari, A. J., Erskine, H. E., . . . Vos, T. (2013). Global burden of disease attributable to mental and substance use disorders: Findings from the global burden of disease study 2010. *Lancet, 382*(9904), 1575–1586. 10.1016/S0140-6736(13)61611-6.