



Mediating Factors of a Brazilian School-Based Drug Prevention Program

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Abstract

This study aimed to evaluate the mediating mechanisms of a Brazilian school-based program to prevent drug use among adolescents. In this study, we enrolled 4,030 students in two cluster randomized controlled trials to evaluate two PROERD curricula (fifth and seventh grades) in 30 public schools. Mediation analysis was used to evaluate the program's indirect effects on drug use through communication skills, decision-making skills, attitudes toward drugs, and refusal skills. Evidence regarding differences in mediator variables and drug use between the intervention and control groups is lacking. A clear association was noted between drug use and mediators, independent of group allocation; therefore, program activities should be revised and improved to influence these mediators.

Keywords Prevention · Drugs · Alcohol · Adolescents · Mediation analysis · Randomized controlled trials

Adolescent drug use is considered a public health issue, significantly impacting the population's mental health and morbimortality (Hall et al., 2016; Whiteford et al., 2013). School-based programs are the most frequently implemented preventive interventions that aim to delay and reduce adolescent drug use; among them, the life-skills intervention has demonstrated the most positive preventive effects (Strøm et al., 2014; UNODC, 2018).

In Brazil, the Drug and Violence Resistance Educational Program (Programa Educacional de Resistência às Drogas e à Violência [PROERD]) is implemented in schools by trained police officers and is the most widely implemented prevention program in the country (Pereira & Sanchez, 2020). PROERD current two curriculums (fifth and seventh grades) are the Portuguese translated versions of the North American DARE-Keepin'it REAL (DARE-kiR) program, without cultural adaptation, renamed in Brazil as "PROERD-Caindo na Real". DARE-kiR is disseminated in the US by Drug Abuse Resistance Education (D.A.R.E.) and is an adapted version of the kiR curriculum implemented by police officers in the United States. KiR is an evidence-based universal drug use prevention

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program that teaches communication skills, social skills, and drug resistance strategies to enhance anti-drug norms through culturally oriented prevention messages (Gosin et al., 2003; Hecht et al., 2003). PROERD and DARE-kiR are translate version of the same program, share the same theoretical model of their original version (kiR program). The main difference between the programs is that kiR is implemented by teachers, and DARE-kiR and PROERD are implemented by police officers.

Even though DARE-kiR curriculum has been widely implemented in United State (US) schools, we didn't find any published evaluation of their results on drug use prevention, only on secondary outcomes (Day et al., 2017). On the other hand, many studies reported efficacy results from the original version of kiR before it was adapted by DARE and became DARE-KIR. We found consistently favorable kiR results on the prevention of drug use for the seventh curriculum in the US (Hecht et al., 2003), Guatemala (Kulis et al., 2019), Mexico (Kulis et al., 2021), and Spain (Cutrín et al., 2021). However, there is a lack of evaluations for the kiR 5th grade curriculum, and the only published study showed a significantly increased prevalence of substance use (Elek et al., 2010).

Considering that none of the previously published studies refer to the Portuguese translated version of the DARE-kiR, implemented in Brazil by PROERD, and adding up that no cultural adaptation of the DARE-kiR was performed before implementation in Brazilian schools, it was mandatory that we evaluate PROERD effectiveness. The main results of this evaluation showed no evidence of the direct effect of PROERD on the prevention of drug use (Sanchez et al., 2021).

When an iatrogenic or neutral result is found in the evaluation of a program, the crucial *next step is the understand of the reasons underlying the program's failure*. Even in the absence of direct intervention effects (path c), mediation analysis is a valuable tool for program evaluation by providing a conceptual overview of how programs work and evaluating if there is an indirect effect (path a*b) of the program via mediators (O'Rourke & MacKinnon, 2018). Considering that mediators are part of the behavior change theories of the programs, there is always a theoretical reason for analyzing them. It can contribute to determining which program components need to be strengthened or require improved measures. The effect of the program on drug use is not direct, that is, it depends on the effect of the program on a mediator, which will then produce the effect on drug use. However, the fact that a program does not change the outcome does not imply that it is not affecting the mediator. The failure of the intervention could be a failure in the conceptual theory, i.e., program may affect mediator, but the mediator may not affect the outcome the mediator may not be related to the outcome (path b); or yet, the program also did not affect the mediator and, consequently, did not affect drug use (MacKinnon et al., 2007).

The theoretical model of the intervention (kiR) proposes that PROERD would reduce or delay drug consumption by changing the targeted mediating variables. According to kiR developers, training in decision-making, communication skills, and refusal skills was one of the mediators of the causal process of the program (Hecht et al., 2008b). Norms and attitudes toward drugs are also expected to be affected by the intervention (Hecht et al., 2003). The program is designed to reduce the effects of peer pressure in the drug use initiation process by increasing youth's repertoire of drug resistance skills, promoting nonpermissive substance attitudes, and engaging adolescents to make more informed decisions (Gosin et al., 2003).

Despite the importance of understanding the mechanisms through which preventive programs work, that is, if they effectively increase the mediators defined in the logical model and if these are reducing drug use, published studies evaluating the indirect effect of the DARE-kiR or even other versions of the kiR program through mediators are unavailable.

However, some studies have analyzed the direct effect of the kiR program on the mediator's variables as a short-term secondary outcome. The only DARE-kiR study, reporting findings from fifth grade curriculum, showed promising effects on resisting peer pressure, confidence in explaining refusal to cigarette use, and responsible decision-making knowledge and skills (Day et al., 2017). In contrast, other studies showed that fifth-grade kiR curriculum did not change students' resistance or decision-making skills (Hecht et al., 2008a). Results from kiR's seventh-grade curriculum showed positive effects with respect to intentions to refuse substances (Kulis et al., 2005); norms, attitudes, and resistance strategies (Hecht et al., 2003); acquisition of drug resistance skills; and less drug use expectancies (Kulis et al., 2019, 2021). Although the impact of school-based interventions in preventing drug use has been well studied, evidence regarding the potential mediating mechanisms underlying the effect of the interventions is lacking (Liu & Flay, 2009).

This study aimed to evaluate the mechanisms of PROERD—the Brazilian translated version of the North American school-based prevention program DARE-kiR—through mediation analysis that could influence the initiation of adolescent drug use (alcohol, cigarette, marijuana, and binge drinking), implemented through two curricula: fifth and seventh grades. We hypothesize that the program would change the mediators which in turn will change the drug outcomes.

Methods

Given that PROERD integrates two different curricula (fifth and seventh grades), their effectiveness was evaluated by two cluster randomized controlled trials conducted on 4,030 students (1,727 fifth and 2,303 seventh graders) in 30 public schools in the city of São Paulo (Brazil) in 2019. Both intervention groups (fifth and seventh grades) received PROERD delivered by trained police officers, whereas the control group received no intervention. The 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 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). All procedures in the present study followed 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. Written consent to participate in the study was obtained from the school directors before randomization and from the students after randomization.

Sampling

Two different sample sizes were calculated, one per curriculum. The necessary sample size calculated for fifth grade was 1,820 participants (70 students per group) for a power of 80%, a significance level of 5%, an effect size of 0.3, and an interclass correlation of 0.02 (Ahn et al., 2014). Concerning the seventh grade, the minimum sample size necessary (Donner & Klar, 2010) was calculated to be 1,608 participants (67 per group) for a power of 80%, a significance level of 5%, a difference of proportions of 7%, and an interclass

correlation of 0.02. The parameters used were based on the results of a study by KiR USA (Marsiglia et al., 2011).

Randomization

An external collaborator performed the randomization procedure that was first drawn from the list of all eligible schools from the city of São Paulo according to the following inclusion criteria: (a) state public schools in the city of São Paulo, (b) schools offering both grades of interest (fifth and seventh grades), and (c) schools did not receive the PROERD program within 3 years before the study. Then, eligible schools were randomly assigned to the intervention or control groups using Efron's biased coin, which maintained a 1:1 allocation ratio, using the PASS version 22. For more information, please see Sanchez et al. (2021).

Intervention

The PROERD "Caindo na Real" is a Brazilian-Portuguese translated version of the American school-based DARE-kiR program for substance use prevention. PROERD consists of 10 weekly classes that use interactive methods with an average duration of 50 min. Trained police officers implemented the program through the 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 delivered the program were trained in an 80-h training session offered by the Military Police, under the guidance of American developers (DARE America).

Fifth and seventh grades curriculum are based in well known core elements of preventive interventions such as communication competence, narrative-based knowledge, social norms as motivators in substance use, social and emotional learning of life skills and drug resistance strategies. Both curricula intend to enhance social, psychological, and emotional competencies that protect youth from substance use through interactive techniques (Elek et al., 2010; Hecht et al., 2003). Although all elements received consideration during the creation of the fifth and seventh grades curriculum, each curriculum emphasizes more one element or another. So they didn't share the same mediators nor the same activities. The main focus of the fifth-grade curriculum lessons is on the social and emotional learning element, teaching students how to perform responsible and healthy decisions through decision-making skills. The program's activities are based on the program's decision-making skills model taught through a four-step model: Define, Analyze, Act, and Evaluate (Elek et al. 2010). On the other hand, the seventh-grade curriculum gives special emphasis on drug use resistance strategies, teaching through a four strategies model how to resist offers of substance use: Refuse, Explain, Avoid, and Leave (REAL) (Hecht et al., 2003).

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 shows that PROERD has only been translated into a different language without considering cultural adaptation.

Instruments and measures

The instrument used for data collection was a self-reported audio-guided questionnaire administered by the researchers through smartphones, as described in detail in Sanchez et al. (2021).

The fifth- and seventh-grade outcomes analyzed were the initiation of alcohol, cigarette, marijuana, and binge drinking evaluated as “yes/no.” First drug use was defined as students who self-reported no lifetime use of drugs at baseline but then changed to lifetime use at the follow-up time point (no to yes). For this assessment, questions such as “Have you ever tried marijuana?” were used. The pattern of binge drinking was defined as the consumption of five or more alcoholic drinks on one occasion.

The mediator variables analyzed for the fifth grade were communication and decision-making skills. For the seventh grade, the mediator variables analyzed were communication skills, decision-making skills, attitude toward drugs (positive and negative), and refusal skills. More details about the measurement model underlying the mediator variables can be found in Valente and Sanchez (2021), where an item-level analysis was conducted using confirmatory factor analysis.

Communication skills were analyzed using a five-point Likert scale ranging from “very hard” to “very easy” (Giannotta et al., 2014) based on five items. The common stem was “How easy or difficult would you find to....” The stem was completed with “Say something nice to a friend,” “Ask for a favor,” “Saying ‘no’ when someone asks me to do something I do not want to,” “Call for help when I have problems,” and “Help someone who needs help.” Students’ replies were summed to create a score for communication skills (ranging from 0 to 15). Higher scores represented higher levels of communication skills. The scale was used in its translated version for the seventh grade; however, the fifth grade required an adapted version where available answers were only “easy” or “hard.” Fit indices demonstrated a good unidimensional model, with $X^2 = 4.915$ and $p = 0.2961$, RMSEA estimate = 0.013, RMSEA probability = 0.975, CFI = 0.996, and TLI = 0.989 (Valente & Sanchez, 2021).

Decision-making skills were analyzed using a nine-item (agree or disagree) scale developed by the European Drug Addiction Prevention Trial (EU-DAP) (Giannotta et al., 2014), with questions such as the following: “I often make up my mind without thinking about the consequences,” “I weigh up all the choices before I decide on something,” and “Sometimes I change my mind about something several times a day.” Students’ replies were summed, creating a score ranging from 0 to 9; the higher the score, the higher the level of decision-making skills. Fit indices demonstrated a good unidimensional model, with $X^2 = 119.125$ and $p < 0.001$, RMSEA estimate = 0.053, RMSEA probability = 0.269, CFI = 0.882, and TLI = 0.830 (Valente & Sanchez, 2021).

Attitudes toward drugs were analyzed using an 11-item scale (agree or disagree) developed by the EU-DAP (Giannotta et al., 2014), which contained six items where the response option “agree” indicated a “drug-negative” response and five items where the response option “disagree” indicated a “drug-positive” response. Positive attitudes (agree or disagree) toward drug use included questions such as the following: “Using drugs can be a pleasant activity,” “Using drugs is fun,” and “The police should not annoy young people who try drugs.” The negative attitudes (agree or disagree) related to drug use included questions such as the following: “The laws about drugs should be made stronger” and “A young person should never try drugs.” Students’ replies were assessed based on two scores: one related to the five positive items (ranging from 0 to

5) and the other to the six negative items (ranging from 0 to 6). Fit indices demonstrated a good two-dimensional model (positive drug use attitudes and negative drug use attitudes), with $X^2 = 121.025$ and $p < 0.001$, RMSEA estimate = 0.039, RMSEA probability = 0.994, CFI = 0.966, and TLI = 0.955 (Valente & Sanchez, 2021).

Refusal skills for cigarettes, marijuana, and alcohol were analyzed using three dichotomous questions (I would say yes or don't know versus I would say no) developed by the kiR program (Hecht, Elek, et al., 2008a): The common stem was "What would you do if?" The stem was completed with "a member of your family offered you alcohol," "a close family friend offered you marijuana," and "a schoolmate offered you a cigarette?"

The covariates were age, sex, socioeconomic status (SES), and baseline assessment outcomes. SES was assessed using the scale of the Brazilian Association of Research Companies (ABEP), which considers the education level of the head of the household and goods and services used. The ABEP was scored from 1 to 100 points, with categories ranging from A (highest) to D/E (lowest) according to the cutoff points established in the literature: A (45–100), B (29–44), C (17–28), and D/E (0–16) (ABEP 2016).

To match individual questionnaires from different evaluation periods with anonymity and confidentiality (Galanti et al., 2007), students provided a code formed by letters and numbers of their personal information, as previously used in other studies (Valente et al., 2018). The code was matched using the Levenshtein algorithm, which identifies similarities between a set of characteristics (Levenshtein, 1965).

Statistical analysis

Data were initially submitted for descriptive analysis; categorical variables are summarized using numbers and percentages and continuous variables using means and standard deviations. All descriptive analyses were performed using the STATA 16 software.

For each outcome (initiation of alcohol, cigarette, marijuana, and binge drinking), a mediation model, which included all mediators simultaneously, was analyzed for each grade. Consequently, four in-parallel mediation models were analyzed to determine if random assignment to the intervention (PROERD) influenced the outcome variable indirectly through the program's theoretical mediators.

Figure 2 shows the mediation model: path A (effects of the exposure on the mediator), path B (effects of the mediator on the outcome), path C (effects of the exposure on the outcome), and indirect effect (product between path A and path B). It should be noted that the covariates were regressed at the same time for two mediators and the outcomes.

To deal with the multilevel structure of data (children nested in schools), we applied a post-estimation adjustment to the standard errors to account for nesting, using maximum likelihood estimation with robust standard errors to account for the nonindependence of the observation, as proposed by Asparouhov (2006). The standard error was then computed using a sandwich estimator with the complex option in the analysis command in conjunction with the cluster options of the variable command (Muthén & Muthén, 2017). Full information maximum likelihood (FIML) was used to deal with 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, fulfilling the intention-to-treat paradigm following the Consolidated Standards of Reporting Trials (CONSORT) statements (Schulz et al., 2010). Based on FIML, it is assumed that the data loss mechanism is random (missing at random), 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 (Enders, 2001). The following were used as variables in the nonrestricted model: sex, age, SES score, and baseline outcomes. The level of significance was set at 5%. All mediation analyses were performed using Mplus version 7.4.

Results

Of the 2,152 fifth graders from the 72 classrooms of the 28 schools randomized in the study, 1,727 answered the baseline questionnaire and 1,334 answered the follow-up questionnaire 9 months post-baseline (77.24%). Of the 2,890 seventh graders from the 90 classrooms of the 30 schools randomized in the study, 2,303 answered the baseline questionnaire and 1,739 answered the follow-up questionnaire (75.51%), as presented in Fig. 1.

Figure 2 shows the conceptual mediation models for the fifth and seventh PROERD curricula. Four models were performed separately for each outcome drug (alcohol, binge drinking, cigarette, and marijuana) for each grade.

Table 1 presents the characteristics of the fifth- and seventh-grade students who participated in the baseline assessment of the PROERD RCT. The intervention and control groups were homogenous at baseline concerning all variables, except sex, in the fifth grade, which was included as an adjustment variable in all analyses. Alcohol was the most commonly used drug in both grades at baseline.

Table 2 shows the impact of all mediators on outcomes through direct effects (path B). The results show that the mediators are associated with drug use initiation. Among the fifth

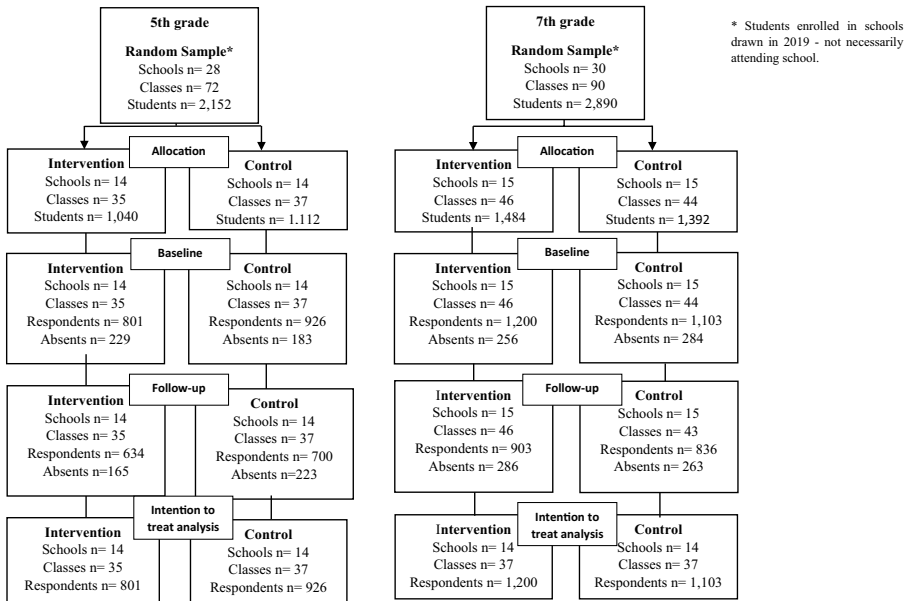


Fig. 1 Flowchart of the randomized controlled trial to assess the effect of the drug use prevention program PROERD, among 5th and 7th grade students

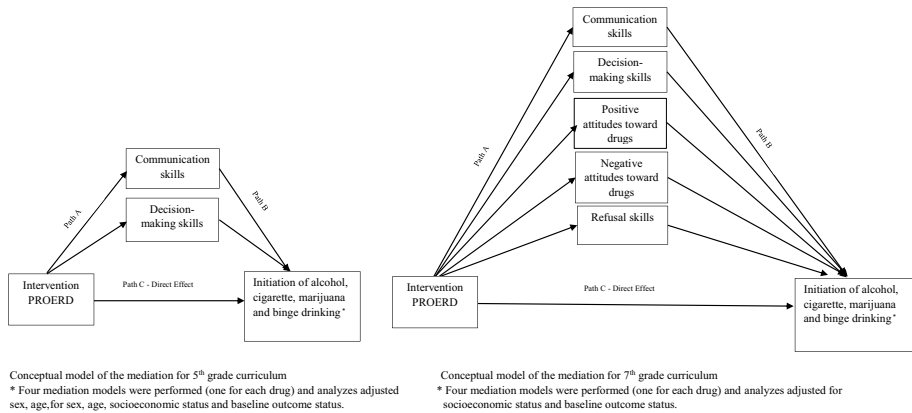


Fig. 2 Conceptual model of the mediation analysis**

graders, decision-making skills demonstrated to be the mediators associated with more types of drug consumption (alcohol, binge drinking, and cigarette). For example, higher decision-making skills are protective factors against alcohol consumption (OR = 0.787; 95% CI = -0.706–0.877). Among the seventh graders, decision-making skills also play an important role in adolescent drug use, since we found a negative association between this mediator and alcohol, cigarette, and marijuana use (e.g., cigarette OR = 0.777; 95% CI = 0.686–0.880). Positive attitudes and refusal skills were positively associated with all drugs' consumption among seventh graders. Students who had higher scores for positive attitudes toward drug consumption (e.g., alcohol OR = 1.418; 95% CI = 1.205–1.668) and refusal skills (e.g., binge drinking OR = 7.464; 95% CI = 4.950–11.256) had a higher chance of reporting drug use initiation. We also found an effect of negative attitudes on drug consumption except for cigarettes and marijuana among seventh graders (e.g., alcohol OR = 0.899; 95% CI = 0.827–0.978), which means that students with higher negative attitudes were less likely to report alcohol consumption and binge drinking.

Table 3 shows the direct and indirect effects of the randomization on drug use through mediators; direct and indirect effects are reported on a logit scale. There was a lack of significance regarding the indirect effects from the random assignment of all types of drug use (alcohol, binge drinking, cigarettes, and marijuana) via mediators for both grades. Thus, the results suggest that PROERD did not reduce drug use through mediators, as expected by the program's logic model.

Discussion

The present study aimed to investigate the mediating mechanisms of the Brazilian school-based prevention program PROERD for preventing youth drug use initiation. Evidence for the program's indirect effect on reducing drug use via mediators, as proposed by its theoretical model, was missing. We found a strong association between mediators and drug use, independent of the intervention effect. Higher decision-making skills, refusal skills, and negative attitudes toward drugs were associated with lower levels of drug use. In contrast, higher positive attitudes toward drugs were related to higher drug consumption, independent of group allocation.

Table 1 Distribution of 5th and 7th grade students according to sociodemographic, drug use and allocation group in the cluster randomized controlled trial of the PROERD program, at baseline

	Total		Intervention		Control		p-value
	N	%	N	%	N	%	
5 th grade students	(N = 1,727)		(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	
Lifetime Drug Use							
Alcohol	303	17.54	148	18.48	155	16.74	0.344
<i>Binge drinking^a</i>	33	1.92	15	1.88	18	1.95	0.924
Tobacco	31	1.80	16	2.01	15	1.62	0.553
Marijuana	10	0.58	3	0.38	7	0.76	0.298
7 th grade students (N = 2,303)			(N = 1,200)		(N = 1,103)		
Gender							0.835
Male	1,187	51.54	621	51.75	566	51.31	
Female	1,116	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	1,222	53.64	629	53.13	593	54.20	
D-E	153	6.72	65	5.49	88	8.04	
Lifetime Drug Use							
Alcohol	866	37.68	439	36.64	427	38.82	0.283
<i>Binge drinking^a</i>	229	9.97	127	10.61	102	9.28	0.289
Tobacco	112	4.88	51	4.26	61	5.55	0.155
Marijuana	78	3.40	41	3.43	37	3.37	0.935

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

* Socioeconomic classification according to ABEP

This study suggests that PROERD was not successful in changing decision-making skills, attitudes toward drugs, refusal skills, and communication skills, as proposed by the theoretical model. To the best of our knowledge, there is no published study presenting a mediation analysis of the DARE-kiR program (the American version of PROERD) or even other versions of the kiR program. However, we found some previous studies (kiR and DARE-kiR) that evaluated the program's short-term effect on the mediator's variables and found positive preventive results in the US (Day et al., 2017; Hecht et al., 2003; Kulis et al., 2005, 2019, 2021). PROERD's inability to reproduce the findings of previous DARE-kiR and kiR studies suggests that lessons

Table 2 The direct effect and covariate effects on the initiation of the drugs (Alcohol, Binge Drinking, Cigarette and Marijuana) examined in the cluster randomized controlled trial of the PROERD program

	Alcohol				Binge Drinking ^a				Cigarette				Marijuana			
	OR	95%CI	p-value	OR	95%CI	p-value	OR	95%CI	p-value	OR	95%CI	p-value	OR	95%CI	p-value	
5 th grade (n = 1727)																
Communication Skills	1.142	0.966;1.350	0.119	0.797	0.527;1.204	0.281	0.942	0.627;1.415	0.773	0.613	0.390;0.965	0.035	0.613	0.390;0.965	0.035	
Decision Making	0.787	0.706;0.877	< 0.001	0.695	0.555;0.872	0.002	0.695	0.560;0.864	0.001	0.833	0.612;1.133	0.245	0.833	0.612;1.133	0.245	
7 th grade (n = 2303)																
Communication Skills	1.059	0.993;1.129	0.080	1.068	0.997;1.143	0.060	1.013	0.952;1.077	0.690	1.077	0.978;1.185	0.132	1.077	0.978;1.185	0.132	
Decision Making	0.914	0.870;0.960	< 0.001	0.910	0.812;1.021	0.107	0.777	0.686;0.880	< 0.001	0.775	0.644;0.932	0.007	0.775	0.644;0.932	0.007	
Positive Attitudes	1.418	1.205; 1.668	< 0.001	1.611	1.400;1.853	< 0.001	1.528	1.292;1.807	< 0.001	2.288	1.874;2.792	< 0.001	2.288	1.874;2.792	< 0.001	
Negative Attitudes	0.899	0.827; 0.978	0.013	0.860	0.762;0.972	0.016	1.082	0.916;1.278	0.356	0.883	0.765;1.018	0.087	0.883	0.765;1.018	0.087	
Refusal Skills	6.844	5.418; 8.645	< 0.001	7.464	4.950;11.256	< 0.001	4.207	2.523;7.015	< 0.001	2.904	1.497;5.634	0.002	2.904	1.497;5.634	0.002	

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

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

Intention to Treat via Full Information Maximum Likelihood*

Bold indicates statistical significance

Table 3 Direct and Indirect effects from PROERD 5th and 7th grade curriculum on drug use initiation (alcohol, binge drinking, Cigarette and Marijuana) via program mediators

	Alcohol			Binge Drinking ^a			Cigarette			Marijuana		
	Coef	95%CI	p-value	Coef	95%CI	p-value	Coef	95%CI	p-value	Coef	95%CI	p-value
5 th grade (N=1727)												
Direct effect:	-0.017	-0.358; 0.324	0.922	-0.003	-0.667; 0.661	0.992	-0.224	-0.843; 0.396	0.480	-0.301	-1.363; 0.762	0.579
Group on Outcome via Mediator												
Com- muni- cation Skills	-0.003	-0.014 ; 0.008	0.592	0.005	-0.015; 0.025	0.631	0.001	-0.009; 0.012	0.811	0.011	-0.029; 0.050	0.591
Decision Making	0.019	-0.009 ; 0.046	0.179	0.029	-0.019; 0.078	0.238	0.029	-0.020; 0.078	0.240	0.015	-0.023; 0.053	0.430
7 th grade (n=2303)												
Direct effect:	0.061	-0.164; 0.286	0.596	0.056	-0.226; 0.339	0.697	0.151	-0.229; 0.530	0.437	-0.115	-0.659; 0.430	0.679
Group on Outcome via Mediator												
Com- muni- cation Skills	0.004	-0.009; 0.016	0.560	0.004	-0.012; 0.020	0.606	0.001	-0.003; 0.005	0.712	0.005	-0.013; 0.022	0.591

Table 3 (continued)

	Alcohol			Binge Drinking ^a			Cigarette			Marijuana		
	Coef	95%CI	p-value	Coef	95%CI	p-value	Coef	95%CI	p-value	Coef	95%CI	p-value
Decision Making	0.007	-0.007; 0.021	0.311	0.008	-0.009; 0.025	0.381	0.020	-0.025; 0.065	0.388	0.020	-0.027; 0.067	0.404
Positive Attitudes	0.002	-0.023; 0.026	0.901	0.003	-0.030; 0.036	0.853	0.002	-0.027; 0.032	0.874	0.002	-0.056; 0.059	0.959
Negative Attitudes	0.014	-0.007; 0.036	0.199	0.021	-0.010; 0.052	0.193	-0.010	-0.039; 0.018	0.472	0.017	-0.012; 0.045	0.252
Refusal Skills	-0.007	-0.090; 0.076	0.873	-0.007	-0.092; 0.078	0.874	0.040	-0.007; 0.088	0.098	0.030	-0.014; 0.074	0.179

^aBinge drinking was considered the consumption of five or more drinks of alcohol on one occasion

* Analyzes adjusted for sex, age, socioeconomic status and baseline outcome status

Intention to Treat via Full Information Maximum Likelihood*

should be revised. All these versions of the kiR curriculum are based on cultural grounding theory, suggesting that cultural values must be addressed in all preventive communications. The developers state that students' narratives, knowledge, and experiences should be capitalized to create a program that reflects the culture and learning styles of the target audience (Hecht & Krieger, 2006). In this context, the simple translation of the DARE-kiR curriculum can be a hypothesis that explains the lack of ability of the program to impact the mediators, which is in line with previous studies of PROERD (Sanchez et al., 2021; Valente & Sanchez, 2021). When youth cannot recognize themselves as represented in the proposed activities, they are less likely to engage in the program's activities (Gosin et al., 2003).

The findings highlight the well-supported necessity of cultural adaptation of programs when implemented in a new context, even more in the case of culturally grounded programs (Hecht & Krieger, 2006). Cultural adaptation should go deep into the program's activities, taking into account the norms and values of the target population (Castro et al., 2004). Culturally adapted interventions have the potential to increase engagement, adoption, fidelity, and, consequently, intervention effectiveness (Barrera et al. 2017).

Despite the lack of effect on the mediation analysis, we found a clear association between almost all mediators and students' drug use, corroborating international guidelines (UNODC, 2018). These results show that investing in decision-making skills, attitudes toward drugs, and refusal skills as mediators seem to be valuable for reducing drug use, as already evidenced in other studies (Bate et al., 2009; Komro et al., 2001; Orlando et al., 2005; Vigna-Taglianti et al., 2021).

Decision-making skills can act as a protective factor for drug use in both fifth and seventh-grade curricula, increasing students' ability to make responsible decisions about using drugs (Sussman et al., 2004). Decision-making skills are one of the personal competencies proposed for the social-emotional learning theory, which suggests that drug use can be prevented by integrated efforts to develop students' social and emotional skills (Durlak et al., 2011). Decision-making skills are especially important in prevention programs that target students in elementary schools that benefit most from enhancing personal competencies but are also related to positive results among early adolescents (Onrust et al., 2016).

Attitudes toward drugs seem to be associated with drug use among seventh-grade students. Attitudes toward drugs are well documented as strong predictors of drug use (Cooke et al., 2016; Cutrín et al., 2020; Garcia-Cerde et al., 2021). This association is explained by the theory of planned behavior, which proposes that attitudes are one of the most important determinants of the intention to perform some behavior, such as drug use. Attitudes are an individual's positive or negative evaluation of performing a behavior (Ajzen, 2020). Preventive programs that target social norms are related to positive results among early adolescents once it teaches to correct misperceptions of peers' substance use and acceptance levels (Onrust et al., 2016).

Moreover, refusal skills are negatively associated with adolescent drug use among seventh-grade students, in line with previous literature (Hopfer et al., 2013; Kulis et al., 2008). Refusal skill is the ability to respond to an offer or opportunity to use drugs and is an important part of the skill set necessary to resist peer pressure (Hecht et al., 2008b). Despite the evidence pointing out the association between refusal skills and less drug use, training this ability in preventive interventions is controversial. Some studies suggest that training on refusal skills is not always a successful strategy in preventive interventions and must always be associated with social norms and drug attitude components (Onrust et al., 2016). Modeling resistance strategies can lead to an increase in the perception of peer drug use, which can contribute to an increase in drug use initiation (Hecht et al., 2008b). In addition, in a developmental stage where students become increasingly concerned with peer relationships, instructing them not to follow their peers may be less advisable (Onrust et al., 2016).

This study had some limitations. First, loss of data due to follow-up may have introduced bias in the mediation analysis. However, this is expected in longitudinal studies (Saiepour et al., 2019) and statistical missing data techniques were applied to address this limitation. Second, our sample may not be representative of all schools in São Paulo, since the sample was chosen from public state schools that did not receive the evaluated program 3 years before our study. Owing to the inclusion criteria, the selected schools were incidentally located in more areas of the city with lower income. The impact of this limitation must be considered in the external validation of these findings.

The results of this study suggest a lack of an indirect effect of PROERD on preventing adolescent drug use. In particular, when the program presents null or negative impacts, mediation analyses should be a priority to understand how the prevention program is working and provide information to improve the program. Decision-making skills, negative attitudes toward drugs, and refusal skills seem to be potential protective factors against drug use, whereas positive attitudes toward drugs were identified as possible risk factors for drug use. However, the program itself was not associated with these variables, suggesting that they did not act as program mediators. The program's activities aimed at influencing these mediators should be revised and improved to produce the intended effects, as expected by the theoretical model created by the developers.

Author Contributions The submitted manuscript has been read and approved by all authors. All authors acknowledge that they have exercised due care in ensuring the integrity of the work. JYV wrote the first version of the paper and also was responsible for the statistical analysis. ZS designed the original study and review the final version of the manuscript, helped interpreting the results and was responsible for the final approval of the version to be published. None of the original material contained in the manuscript has been submitted for consideration nor will any of it be published elsewhere.

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Declarations

Competing Interest The authors have no relevant financial or non-financial interests to disclose.

Ethics Approval 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 Consent to participate in the study was written and obtained from the schools' directors before randomization and from students after randomization.

Conflict of Interest Authors declare that they have no conflict of interest.

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