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## The role of drug use sequencing pattern in further problematic use of alcohol, tobacco, cannabis, and other drugs

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### Abstract

**Background**—There has been considerable debate regarding what typically occurs after experimentation with drugs throughout the life of young people who used various drugs.

**Aims**—To evaluate the clinical importance of the most common sequence for the first use of a drug by two models (the ‘gateway model’ and the ‘alternative model’, which is the most popular sequence for Brazilian university students according to a previous study) regarding the problematic use of alcohol, tobacco, cannabis and other illegal drugs, assessed by ASSIST.

**Method**—People who had already experimented with three or more drugs across different stages of the two models were selected from a representative sample of university students from 27 Brazilian capitals (n=12, 711).

**Findings**—There were no differences regarding the problematic use of the most consumed drugs in Brazil (alcohol, tobacco and cannabis) between the models. Multiple drug seekers and violators had more problematic use of illegal drugs other than cannabis than individuals in the model sequence. However, in the case of violators, this was only evident in the alternative model.

**Conclusions**—Multiple drug seekers and violators deserve special attention due to their increased risk of problematic use of other illegal drugs.

**Declaration of interest**—None.

### Keywords

sequence of drug experimentation; abuse; dependence; problematic use; university students

## 1. Introduction

The 'Gateway model' (Kandel, 1975) predicts that the use of alcohol and/or tobacco occurs during the first step, followed by cannabis in the second step and other illegal drug use in the third step\*. Alcohol and tobacco are usually the first drugs that adolescents experiment with, according to several international studies (Van Etten et al., 1997, Wagner & Anthony, 2002, Herrera-Vazquez et al., 2004, Wells & McGee, 2008, Caris et al., 2009, Mayet et al., 2010), which may be why these two drugs have the highest prevalence of use over the lifespan in most countries. The second step generates more controversial data. In countries with a high prevalence of cannabis use, such as Germany, Ukraine and New Zealand, the classic sequence seems to be most common (Degenhardt et al., 2010). Violators are those individuals who try alcohol, tobacco or cannabis after first experimenting with other drugs or who experiment with alcohol or tobacco after cannabis. In the U.S., one study showed that one of these violations was more common in a specific ethnic group (Vaughn et al., 2008).

There is another category, namely that of people who in theory, actively experiment with new drugs. Curiosity may be an important factor in the drug experimentation of these individuals (Yang et al., 2009). These people experiment with drugs from different steps (e.g., cocaine and alcohol) within a short time interval (<1 year). For this group, the sequence of drug use experimentation loses importance, and they are best characterised as a separate group. Wagner & Anthony (2002) defined this group as 'drug seekers'.

Recently, our group investigated the most common sequences of drug use in the Brazilian university student population (Author 1 et al., 2013). This previous study found the most common sequence of drug use in this population to be the following: alcohol and/or tobacco use in the first step, cannabis and/or inhalants in the second step, and other drugs in the third step. In the present study this proposal is referred to as the 'Alternative model'†.

As adolescence usually involves the first use of several drugs, the subsequent period, during which many individuals attend a university, is an interesting one within which to assess the age of first drug use in general, given that most drug use initiations have occurred recently, which minimises memory bias. Bearing this in mind, the present study seeks to investigate whether the most common sequence correlates with the problematic use of any specific drug(s) among Brazilian university students.

## 2. Methods

The project was previously evaluated and approved by the local Institutional Review Board (IRB). Data collection was completed between May–December of 2009.

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\*In the last decade, there has been considerable debate about what typically occurs regarding experimentation with drugs sequencing pattern throughout the life of young people who used various drugs (Morril et al., 2002, Fergusson et al., 2006). This debate has been rekindled because of recent data from a study with laboratory animals that found the previous use of a legal substance (e.g., nicotine) increased the likelihood of becoming addicted to an illegal substance (e.g., cocaine) after its first use (Levine et al., 2006), but the reverse pattern was not found. Moreover, recent cross-national epidemiological data suggest that instead of finding a single universal sequence, the incorporation of the characteristics of each population will determine the most common sequence (Degenhardt et al., 2010) for that population.

†This model is consistent with the moderately high lifetime prevalence of inhalant use (24.6%), which is similar to that of cannabis use (35.4%) within this population (Wagner et al., 2007). The moderately high prevalence of inhalant lifetime use is a feature of the general population in Brazil (Fonseca et al., 2010).

## 2.1. Sample

The target population of this study was university students who were enrolled in undergraduate courses at Higher Education Institutions (HEIs), both public and private, in the 27 Brazilian state capitals. Undergraduate degrees take approximately 4 to 6 years to complete in Brazil. After agreeing to participate, students completed and signed an informed consent statement. There was no incentive to participate and they were not part of their course. A random sample was stratified and recruited with clusters of unequal sizes<sup>‡</sup>.

## 2.2. Measures

A structured, self-administered, anonymous questionnaire consisting of 98 closed questions was developed with an emphasis on drug use and related disorders, risky behaviours and screening for psychiatric morbidity (e.g., depressive symptoms and psychotic and nonspecific psychological complaints). The content of this questionnaire was based on the World Health Organization's research questionnaire (Andrade et al., 1997, Stempliuk et al., 2005).

## 2.3. Drug Use

The data on drug use were collected through a series of questions with multiple response options. First, students reported whether they had ever used the following drugs: alcohol, tobacco, cannabis, inhalants and solvents, cocaine, hallucinogens, ketamine, ayahuasca, ecstasy, steroids, tranquilisers, prescription opioids, anticholinergics, heroin, amphetamines, and synthetic drugs. In the second part of the questionnaire, students reported the age that they first used each of the previous drugs. In addition, the ASSIST (Alcohol, Smoking and Substance Involvement Screening Test) was applied for each drug.

**2.3.1. Division of the polydrug user groups**—Figure 1 presents the division of individuals by the type of sequence of their first drug use. Analyses were performed with two different forms of group separation for the polydrug users depending on their sequences of first use of the drugs. The individual could then be allocated into one of the following three groups: (i) model sequencers (MS), meaning s/he passed through the stages in the order of the sequence; (ii) violators (VT), meaning s/he passed through the stages in a different order than the sequence; or (iii) multiple drug seeker (MDS), meaning s/he used two drugs from different stages at the same age. The two methods of dividing the sample were as follows:

- 'Gateway model': Stage 1-Alcohol and/or Tobacco; Stage 2-Cannabis; Stage 3-Other Drugs.
- 'Alternative model': Stage 1-Alcohol and/or Tobacco; Stage 2-Cannabis and/or Inhalants; Stage 3-Other Drugs

<sup>‡</sup>The sampling was conducted in two stages, such that a sample of HEIs was selected, and a sample of student classes was chosen from this selection. Given that the sizes of the HEIs and the classes (in terms of the number of universities) were not always the same, the conglomerates were of unequal sizes. The final response rate for this study was approximately 72.1% when the estimated size of the college student sample was taken into consideration (12, 721/17, 651). The analysis of the survey data complied with the following characteristics of the sampling plan: (i) a complex sample, (ii) the use of stratification, (iii) clustering and (iv) dissimilar selection probabilities. The dissimilar selection (DM) probability was one aspect of the sampling plan that was considered when analysing the data. Two weighting factors were obtained to deal with DM.

With regard to the age of first use of drugs, there were a significant number of people who did not declare all of the ages necessary, which excluded them from the analyses<sup>§</sup>.

**2.3.2. The ASSIST scores**—The ASSIST instrument is translated and validated for the Portuguese language, which is spoken in Brazil (Henrique et al., 2004). First, we calculated the ASSIST scores for all drugs for all of the individuals. Then, these values were stratified into the following two tracks: (i) normal use – 0 to 3 points; or (ii) problematic use – 4 points or more (which merge risk of abuse and dependence). We combined the ASSIST scores for illegal drugs other than cannabis into a single class called ‘other drugs’ as follows: if an individual obtained a problematic score on a drug, he would be allocated into the range of ASSIST problematic. An individual should have a normal ASSIST score for all of the drugs included in this class to be considered as a ‘normal user’.

## 2.4. Statistical analysis

We used the statistical package STATA version 11 to run the analyses. All of the analyses were performed within the survey option with weights, strata and primary sampling units. Differences were considered valid at the  $p < 0.05$  level. Initially, we ran a descriptive analysis with chi-square tests. We selected all of the people who had used alcohol to analyse for possible differences in ASSIST scores that were stratified by alcohol among the three groups and then comparing each group against each other in pairs. The same procedure was followed for tobacco, cannabis and other drugs. Data were analysed using logistic regression models for categorical outcomes with the inclusion of 14 socio-demographic variables: gender, age, religion, practice of the religion, years of education of the head of the family, ethnic group, marital status, children, employment status, driver license, area of the undergraduate course, year of the under graduation, happy with the under graduation course, and all-day course.

## 3. Results

The majority of MS were male in both models (67.8% in the ‘Gateway model’ and 60.2% in the ‘Alternative model’) while the opposite was true for VT (male were 42.2% and 31.1%, respectively). MDS were more balanced between the two genders. Regarding age, the majority of MS, VT and MDS in both models were older than 21 year-old. Figure 1 presents the division of the groups following the criteria for the ‘Gateway model’ and the ‘Alternative model’.

### 3.1. Gateway model

Table 1 presents the results of the descriptive analyses with chi-squared test according to the classical model. Regarding the problematic use of alcohol and tobacco, there was no difference between groups. However, in relation to the problematic use of cannabis, there were differences among the three groups. When the groups were analysed in pairs, there was

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<sup>§</sup>Figure 1 presents the number of people in each group. A logistic regression with an adjustment for socio-demographic variables was run to determine whether there were significant differences between the individuals who declared all of the ages (and were included in the study) compared with those who did not. Additionally, people who declared all of their ages of first use did not complete all of the questions on the ASSIST and were therefore excluded from the analysis (Figure 1). Only minor differences were found between individuals included in the study and those excluded because of missing data for both models (‘Gateway’ and ‘Alternative’).

more problematic use of cannabis among the MS(35.8%) compared to the VT(18.2%) with  $p < 0.05$ . A difference was also evident in the MS(35.8%) compared with the MDS(18.0%) with  $p < 0.05$ . There was a reverse situation regarding the problematic use of other drugs. MDS had more problematic use(27.9%) than the MS(16.3%) with  $p < 0.05$ .

After the inclusion of several socio-demographic variables in the logistic regression models(table 2), it is evident that all of the differences in the problematic use of cannabis were not supported given that the 95% confidence intervals passed through 1.00. The only difference that remained significant was regarding the problematic use of other drugs in MDS compared to the MS(aOR=8.52, 95% CI=1.20–60.27,  $p < 0.05$ ) with greater problematic use in the MDS.

### 3.2.Alternative model

Table 1 presents the many statistically significant differences that were found in the descriptive analyses using chi-squared test according to the 'Alternative model. There were no significant differences between MDS and VT regarding problematic use of alcohol(63.9% and 69.9%, respectively). However, problematic use of alcohol occurred in 83.5% of MS, which was significantly different from the VT( $p < 0.01$ ) and the MDS( $p < 0.01$ ), and the difference among all the groups was also significant( $p < 0.01$ ). With regard to problematic use of tobacco, there was no significant difference between the MS and the MDS(49.3% versus 45.4%,  $p > 0.05$ ). However, 26.6% of the VT had problematic use of tobacco, which was significantly different from the MS( $p < 0.01$ ) and the MDS( $p < 0.01$ ), and a significant difference was found among all of the groups( $p < 0.01$ ). Regarding problematic use of cannabis, all the analyses generated significant differences( $p < 0.05$ ), with 35.8% of the MS, 9.3% of the VT and 17.6% of the MDS reporting problematic use of that drug. The problematic use of other drugs was higher in the MDS(41.7%) than the VT(29.4%) and the MS(20.3%), leading to significant differences between all of the groups( $p < 0.001$ ). This difference was only confirmed between MDS and MS( $p < 0.001$ ).

None of the significant findings in the exploratory analyses were significant in the logistic regression models(table 2). Regarding the use of alcohol, tobacco and cannabis, all of analyses generated 95% confidence intervals that encompassed 1. However, there were significant differences in the problematic use of other drugs between the MDS and the MS(aOR=5.10, 95% CI=1.65–15.78,  $p < 0.01$ ), with higher problematic use in the MDS, and between the VT and the MS(aOR=0.31, 95% CI=0.11–0.91,  $p < 0.05$ ), with more problematic use in the VT.

## 4.Discussion

The aim of this study was to compare the prevalence of an unfavourable clinical outcome(i.e., the problematic use of alcohol, tobacco, cannabis and other drugs) among three groups of polydrug users with different trajectories in a representative sample of university students from the 27 Brazilian capitals. These polydrug users were divided by the most common paths for drug use in the U.S.(i.e., the 'Gateway model')(Kandel, 1975) and for Brazilian university students(i.e., the 'Alternative model')(Author 1 et al., 2013), according to previous studies. There were no differences in the problematic use of the three

most consumed psychoactive substances in Brazil(Fonseca et al., 2010), which are alcohol, tobacco and cannabis, according to either model. However, MDS had more problematic use of other drugs, which are drugs other than alcohol, tobacco and cannabis, than those individuals in the classical sequence in both models. In addition, when using the ‘Alternative model’, there was more problematic use of other drugs in VT than in the MS, which argues for including the characteristics of each population when studying the sequences of drug use.

Although several studies have evaluated the transitions of first drug use in several countries(Van Etten et al, 1997, Herrera-Vazquez et al., 2004, Wells & McGee, 2008, Caris et al., 2009, Chen et al., 2009, Posada-Villa et al., 2009, Makanjuola et al., 2010, Degenhardt et al, 2010, Mayet et al., 2010, Author 1 et al., 2013) and have presented how the use of one drug increases or decreases the chances of using a second drug, little to no literature compares the clinical outcomes of the different groups of polydrug users. Recently, Tarter et al.(2012) presented the results of a prospective study that followed people from 10–22 years of age, which were similar to ours regarding cannabis. The most common sequence for experimenting with drugs(i.e., illegal drug use before the use of cannabis) had no effect on the problematic use of cannabis later. Their study did not consider the last step of the classical sequence(i.e., cannabis use before the use other illegal drugs), which was examined in this study. In a cross-sectional study of individuals from the U.S.(Degenhardt et al, 2009) ‘Gateway model’ violations were largely unrelated to later dependence risk, with the exception of small increases in risk of alcohol and other illegal drug dependence for those who initiated use of other illegal drugs before cannabis. In this study, the clinically unfavourable outcome of dependence was assessed with the Composite International Diagnostic Interview(CIDI), and only the ‘Gateway model’ was considered. Our study was different in that we used the ASSIST and combined the suggestive use of abuse and dependence into one single class(problematic use). We also created one group consisting of different polydrug users, which were the MDS, and we analysed two models(i.e., the ‘Gateway’ and ‘Alternative’ ones). With regard to the comparable data between the two studies, which involves the differences between the VT and MS, we did not find a clinically unfavourable outcome(problematic use) of alcohol, but did find of illegal drug.

We must remember that although it is a representative sample of university students from the 27 capitals of a country with diverse cultural, economic and social differences(Victora et al., 2010), we are still dealing with a specific population. University students in this country are not representative of the general population given that only 13.9% of young adults have access to higher education. Almost 50% of university students study in private institutions, which sets them apart from the general population. Furthermore, cross-sectional data like this are especially prone to a memory bias, which in this case may affect the memory of the exact date of the first use of drugs. However, as previously noted, given that most of experimentation with drugs occur in adolescence and early adulthood, examining students attending a university is the best time period as it may attenuate this bias. Still, as one would expect, there were a lot of people who did not remember all of the ages of their first use, yet a statistical comparison showed that there were no differences regarding the use of the most popular drugs.

Studies in other populations should be conducted to test this hypothesis. In addition, the role of psychiatric comorbidity could be investigated regarding drug use sequencing pattern. Moreover, VT of the classical sequence, when considering the most common sequence for each country, may have an increased risk of pathological use of illegal drugs other than cannabis. These data also need further study to analyse different countries' cultures. Interventions, such as secondary prevention, could be particularly interesting for MDS and VT.

In practical terms, careful attention must be paid to two aspects of the present study. Firstly, this study suggests that three types of individuals have an elevated risk of 'other drugs' abuse/dependence: (i) those who experiment with cannabis/inhalants before alcohol/tobacco; (ii) those who experiment with 'other drugs' before alcohol/tobacco/cannabis/inhalants; and those who experiment with drugs from a different step for a short period (<1 year). Secondly, our results show that a large number of the university students went through the three steps of the two models of experimentation with drugs. These findings deserve special attention by health policy makers and practitioners. Strang et al. (2012) suggested brief interventions targeted at select groups who have a higher risk of drug problems. This approach seems to suit individuals who experiment with many drugs within a short period of time, as well as those who violate the most classical drug experimentation sequence for Brazilians who attend university. Adolescence and university/college years seem highly appropriate for this end.

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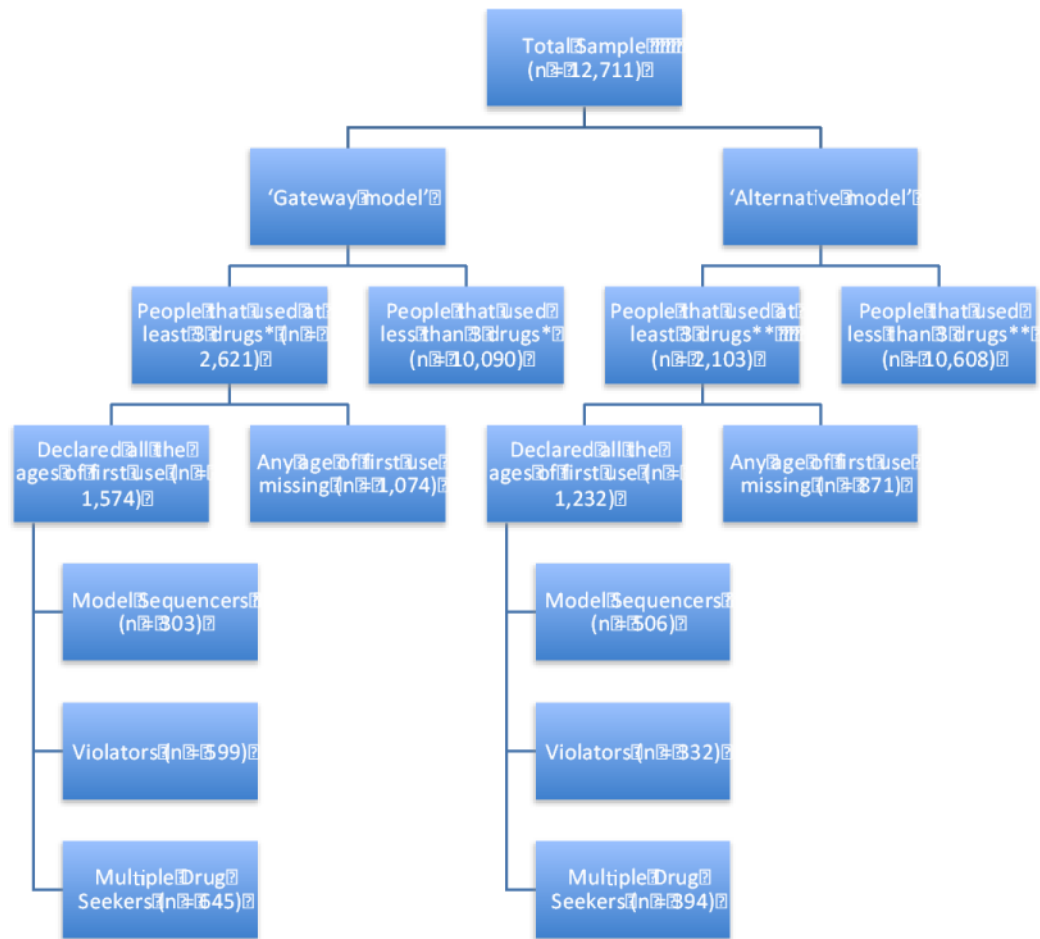
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**Figure 1.** Distribution of samples per type of model and sequence of drug use among Brazilian university students, 2009.

\*In this criteria, alcohol or tobacco use meant just an unique drug use

\*\*In this criteria, alcohol or tobacco use meant just an unique drug use, and cannabis or inhalants use meant just another unique drug use

Descriptive analysis of drug experimentation sequences among a representative sample of Brazilian university students, 2009.

Table 1

Gateway model	Groups						Chi-square tests(p)		
	ASSIST	Total	MS*	V*	MDS*	All Groups	MS vs V	V vs MDS	MDS vs MS
<b>Alcohol</b>	1451(100%)	286(100%)	566(100%)	599(100%)	599(100%)	0.289	0.456	0.406	0.081
<i>Occasional Use</i>	360(26.7%)	51(20.0%)	164(24.9%)	145(30.6%)	145(30.6%)				
<i>Problematic Use</i>	1091(73.3%)	235(80.0%)	402(75.1%)	454(69.4%)	454(69.4%)				
<b>Tobacco</b>	1423(100%)	279(100%)	562(100%)	496(100%)	496(100%)	0.462	0.322	0.109	0.725
<i>Occasional Use</i>	637(50.9%)	163(53.5%)	405(66.0%)	355(58.8%)	355(58.8%)				
<i>Problematic Use</i>	500(49.1%)	116(46.5%)	157(34.0%)	227(41.8%)	227(41.8%)				
<b>Cannabis</b>	1401(100%)	268(100%)	562(100%)	571(100%)	571(100%)	<b>0.049</b>	<b>0.043</b>	0.962	<b>0.048</b>
<i>Occasional Use</i>	1116(78.6%)	189(64.2%)	498(81.8%)	429(82.0%)	429(82.0%)				
<i>Problematic Use</i>	285(21.4%)	79(35.8%)	64(18.2%)	142(18.0%)	142(18.0%)				
<b>Other Drugs</b>	1180(100%)	246(100%)	454(100%)	480(100%)	480(100%)	0.312	0.526	0.524	<b>0.014</b>
<i>Occasional Use</i>	961(76.0%)	205(83.7%)	368(77.7%)	388(72.1%)	388(72.1%)				
<i>Problematic Use</i>	219(24.0%)	41(16.3%)	86(22.7%)	92(27.9%)	92(27.9%)				
Alternative model	Groups						Chi-square tests(p)		
ASSIST	Total	MS*	V*	MDS*	All Groups	MS vs V	V vs MDS	MDS vs MS	
<b>Alcohol</b>	1153(100%)	482(100%)	302(100%)	365(100%)	<b>0.002</b>	<b>&lt;0.001</b>	0.403	<b>&lt;0.001</b>	
<i>Occasional Use</i>	292(25.7%)	89(16.5%)	112(36.1%)	91(30.1%)					
<i>Problematic Use</i>	861(74.3%)	393(83.5%)	194(63.9%)	274(69.9%)					
<b>Tobacco</b>	1137(100%)	468(100%)	313(100%)	356(100%)	<b>0.005</b>	<b>0.003</b>	<b>0.007</b>	0.526	
<i>Occasional Use</i>	714(56.9%)	263(50.7%)	231(73.4%)	220(54.6%)					
<i>Problematic Use</i>	423(43.1%)	205(49.3%)	82(26.6%)	136(45.4%)					
<b>Cannabis</b>	1128(100%)	458(100%)	317(100%)	353(100%)	<b>&lt;0.001</b>	<b>&lt;0.001</b>	<b>0.037</b>	<b>0.007</b>	
<i>Occasional Use</i>	878(76.8%)	321(64.2%)	288(90.7%)	269(82.4%)					
<i>Problematic Use</i>	250(23.2%)	137(35.8%)	29(9.3%)	84(17.6%)					

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Alternative model	Groups						Chi-square tests( <i>p</i> )		
	Total	MS*	V*	MDS*	All Groups	MS vs V	V vs MDS	MDS vs MS	
<b>ASSIST</b>	918(100%)	398(100%)	244(100%)	276(100%)	<0.001	0.148	0.094	<0.001	
<b>Other Drugs</b>	701(70.3%)	322(79.7%)	179(70.6%)	200(58.3%)					
<i>Occasional Use</i>	217(29.7%)	76(20.3%)	65(29.4%)	76(41.7%)					
<i>Problematic Use</i>									

\* MS = Model sequencers; V = Violators; MDS = Multiple drug seekers.

**Table 2**

Results of logistic regression on two drug experimentation models among a representative sample of Brazilian university students, 2009.

Gateway model		Logistic Regression **		
ASSIST	All groups	MS* versus VT*	VT* versus MDS*	MDS* versus MS*
<b>Alcohol</b>				
aOR	0.68	0.50	0.66	0.79
95%CI	0.46–1.01	0.18–1.41	0.43–1.02	0.45–1.38
<i>p</i>	0.061	0.192	0.062	0.418
<b>Tobacco</b>				
aOR	0.91	1.20	0.99	0.45
95%CI	0.61–1.35	0.48–2.99	0.75–1.30	0.08–2.48
<i>p</i>	0.647	0.686	0.981	0.356
<b>Cannabis</b>				
aOR	0.82	0.80	0.86	0.56
95%CI	0.58–1.15	0.34–1.86	0.63–1.16	0.17–1.87
<i>p</i>	0.250	0.609	0.331	0.349
<b>Other drugs</b>				
aOR	1.01	0.45	0.96	<b>8.52</b>
95%CI	0.67–1.51	0.19–1.05	0.69–1.33	<b>1.20–60.27</b>
<i>p</i>	0.954	0.066	0.807	<b>0.032</b>

Alternative model		Logistic Regression **		
ASSIST	All groups	MS* versus VT*	VT* versus MDS*	MDS* versus MS*
<b>Alcohol</b>				
aOR	1.01	0.92	0.98	0.91
95%CI	0.73–1.40	0.44–1.90	0.68–1.41	0.50–1.66
<i>p</i>	0.915	0.823	0.935	0.774
<b>Tobacco</b>				
aOR	0.92	1.26	1.00	0.43
95%CI	0.56–1.52	0.54–2.94	0.65–1.54	0.14–1.27
<i>p</i>	0.761	0.575	0.991	0.128
<b>Cannabis</b>				
aOR	0.87	1.83	1.02	0.50
95%CI	0.64–1.18	0.65–5.14	0.69–1.51	0.22–1.15

Alternative model	Logistic Regression **			
	ASSIST	All groups	MS* versus VT*	VT* versus MDS*
<i>p</i>	0.380	0.248	0.889	0.103
<b>Other drugs</b>				
aOR	1.34	<b>0.31</b>	1.15	<b>5.10</b>
95%CI	0.73–2.47	<b>0.11–0.91</b>	0.71–1.85	<b>1.65–15.78</b>
<i>p</i>	0.335	<b>0.033</b>	0.546	<b>0.005</b>

\* MS = Model sequencers; VT = Violators; MDS = Multiple drug seekers

\*\* 14 socio-demographic variables were included in the regression models.

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