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# Confirmatory factor analysis (CFA) of the Crack Use Relapse Scale (CURS)

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## Abstract

**Background:** When it comes to crack/drug use, relapse is a relatively common event in the first weeks after the end of treatment. However little is known about what happens to patients who relapse after discharge. **Objective:** To report the confirmatory factor analysis (CFA) of the Crack Use Relapse Scale (CURS) in an inpatient population. **Methods:** A five-point Likert scale with 25 items and, initially, 9 theoretical factors was generated and utilized in a cross-sectional study with a sample of 333 hospitalized male crack users. **Results:** CFA indicated a well-fitting model for the CURS. **Discussion:** The CFA shows that the CURS model is appropriate and well-fitting for assessment of latent variables common to psychiatric and psychological constructs – in this case, relapse of crack cocaine use after inpatient treatment.

Pedroso R et al. / Arch Clin Psychiatry. 2016;43(3):37-40

**Keywords:** Crack cocaine, drug, substance abuse, relapse, inpatient, scale.

## Introduction

When it comes to crack/drug use, relapse is a relatively common event in the first weeks after the end of treatment, in both inpatient and outpatient care<sup>1</sup>. Recent data shows that crack users have increasingly sought care from rehabilitation facilities, but, still, little is known about what happens to patients who relapse after discharge as there are very few studies that focus on this subject<sup>1-4</sup>.

A qualitative study<sup>5</sup> in which 14 crack users were interviewed showed that family, emotions, feelings, coping, sex, treatment, crime, positive expectations and craving are factors associated with relapse. Those reports served as basis for the instrument presented in another paper<sup>6</sup>.

This study aims to describe the confirmatory factor analysis of CURS/Crack Use Relapse Scale, it is a unique and specific tool for assessing crack users relapse. The CURS assesses risk factors that may cause the user to slip back soon after discharge from treatment that may serve to help creating new strategies to increase their self-efficacy and coping skills over relapse to the specific use of crack.

## Methods

### Development of the scale

The development of the scale, presenting the pilot study and initial psychometric validation emphasizing the exploratory factor analysis can be accessed, respectively, in two previous publications<sup>5,6</sup>.

### Sample

Using a cross-sectional design, a convenience sample of male crack users hospitalized in a public psychiatric hospital in Porto Alegre, Brazil, was recruited. The total sample comprised 333 participants, most of whom were white (74.47%). Only a minority of subjects claimed to live in a marital relationship (16.52%). Mean age (25.9 years, SD 7.96) and educational attainment, were also noteworthy characteristics: n = 239 (71.8%) – incomplete elementary school, n = 65 (19.5%) – high school, n = 24 (7.2%) – Higher Education and n = 5 (1.5%) – illiterate.

All research participants had a DSM-5<sup>7</sup> diagnosis of Cocaine Dependence – specifically, crack cocaine dependence – established by psychologists and psychiatrists specializing in drug dependence.

All subjects reported crack as their drug of choice. No subjects were excluded from analysis.

### Instruments

- Semi-structured interview: conducted to evaluate the socio-demographic profile of the sample and describe the pattern of psychoactive substance use, that is, to determine and record any other psychoactive substances subjects may have used before turning to crack cocaine.
- Crack Use Relapse Scale/CURS<sup>6</sup>: a 25-item scale, each item consisting of a statement on factors that may influence crack use relapse. Respondents are asked to score near agreement with each statement on a five-point Likert-type<sup>8</sup> scale, where 1 corresponds to “completely disagree” and 5, to “completely agree” (Table 1).

### Data analysis

The exploratory factor analysis (EFA) was performed to classify the common items in clusters. The Kaiser-Meyer-Olkin test (KMO), was used to evaluate sampling adequacy, and Bartlett's test, to test for sphericity of CURS, to assess the suitability of the data for exploratory factor analysis and as a criteria of good adjustment of the scale<sup>6</sup>.

Cronbach's alpha was used to test the reliability of internal consistency<sup>9</sup>. Analysis was performed for each factor individually and for the 25-item scale as a whole. The kappa coefficient was used to assess inter-rater reliability<sup>6</sup>. Confirmatory factor analysis (CFA) in this study, with the factors defined in the EFA<sup>6</sup> the confirmatory factor analysis was performed in the AMOS v.18 software environment<sup>10</sup>. Factor confirmation was based on the following fit indices, all of which range from 0 to 1, with values nearer 1 suggesting good model fit<sup>11,12</sup>: overall fit (OF), root mean square error of approximation (RMSEA). It is measured by the chi-square statistic (RMSEA) which estimates how well the model parameters reproduce the population covariance where values less than 0.05 indicate good fit, and values up to 0.08 represent reasonable error; goodness-of-fit index (GFI) and adjusted goodness-of-fit index (AGFI) that measure the relative amount of variance and covariance explained, where the latter suffers a penalty by the inclusion of an additional parameter will be included as indices of adjustments. Values near to 1 indicate a good fit of the model of the scale; comparative fit index (CFI), and Tucker Lewis index (TLI).

**Table 1.** Crack Use Relapse Scale (CURS)

The following list presents several risk factors that may influence the relapse of crack users. Read each item and circle the number that best reflects your opinion on how much you disagree or agree, in relation to your use of crack during the past six months:

1	Family conflicts	I disagree completely	1	2	3	4	5	I agree completely
2	Intimate relationship conflicts ( <i>e.g.</i> , with partner)	I disagree completely	1	2	3	4	5	I agree completely
3	Feelings of sadness	I disagree completely	1	2	3	4	5	I agree completely
4	Feelings of loneliness	I disagree completely	1	2	3	4	5	I agree completely
5	Feelings of anxiety	I disagree completely	1	2	3	4	5	I agree completely
6	No hope	I disagree completely	1	2	3	4	5	I agree completely
7	Dissatisfaction	I disagree completely	1	2	3	4	5	I agree completely
8	Feelings of pleasure	I disagree completely	1	2	3	4	5	I agree completely
9	Feelings of euphoria	I disagree completely	1	2	3	4	5	I agree completely
10	Excessive self-confidence	I disagree completely	1	2	3	4	5	I agree completely
11	Craving for crack	I disagree completely	1	2	3	4	5	I agree completely
12	Craving for crack after the use of another drug	I disagree completely	1	2	3	4	5	I agree completely
13	Exchange of sex for crack when craving strikes	I disagree completely	1	2	3	4	5	I agree completely
14	HIV infection	I disagree completely	1	2	3	4	5	I agree completely
15	Infection with sexually transmitted diseases other than HIV	I disagree completely	1	2	3	4	5	I agree completely
16	Difficulty accessing treatment in the public health service	I disagree completely	1	2	3	4	5	I agree completely
17	Imprisonment due to crack use	I disagree completely	1	2	3	4	5	I agree completely
18	Theft and robbery due to crack use	I disagree completely	1	2	3	4	5	I agree completely
19	Involvement with the drug trade	I disagree completely	1	2	3	4	5	I agree completely
20	Unemployment	I disagree completely	1	2	3	4	5	I agree completely
21	Favorable social environment for the consumption of crack	I disagree completely	1	2	3	4	5	I agree completely
22	Inability to cope with situations posing a high risk of crack use	I disagree completely	1	2	3	4	5	I agree completely
23	Lack of perspectives for a new lifestyle	I disagree completely	1	2	3	4	5	I agree completely
24	Lack of healthy habits, <i>e.g.</i> involvement in sports	I disagree completely	1	2	3	4	5	I agree completely
25	Lack of spirituality	I disagree completely	1	2	3	4	5	I agree completely

## Methodology of final scores

In a previous publication<sup>6</sup>, the factor loadings of each item in each domain were discriminated. These loadings are important for the development of the final scores. We realize that the largest factor loading links the item to its corresponding factor. For example, the first 7 items that have larger loadings 0.579 that are related with higher intensity to the factor 1 contributing more of the other items.

## Ethical aspects

The study was approved by the Institutional Review Board of Hospital de Clínicas de Porto Alegre.

## Results

### Dimensionality of the CURS

After EFA, the CURS had a six-factor model. The six factors represent the scale in its entirety<sup>6</sup>. The KMO found was 0.774 and the Bartlett's test was significant ( $p < 0.001$ ). The composite model with 6 factors explained 62.2% of the variability of 25 items.

### Six-factor model

Factor 1 – Emotions, family and affect – assesses feelings of loneliness, anxiety, hopelessness, sadness, and dissatisfaction; Factor 2 – Coping – assesses strategies used to cope with crack use, as well as lifestyle, habits, and spirituality; Factor 3 – Health, sex and treatment – assesses aspects pertaining to physical health, sexuality, and treatment access; Factor 4 – Legal and social aspects – assesses involvement in crime (theft, robbery, drug trafficking), imprisonment, and unemployment; Factor 5 – Positive expectations – assesses beliefs regarding crack consumption, euphoria, pleasure, and self-confidence; and Factor 6 – Craving – assesses users' cravings for crack cocaine.

## Confirmatory factor analysis

OF was 775.9 with 258 degrees of freedom ( $p < 0.001$ ). GFI and AGFI were 0.851 and 0.812 respectively, indicating good fit. CFI was 0.848 and TLI, 0.824. The RMSEA was 0.078 ( $< 0.080$ )<sup>13</sup>. All indices had satisfactory values, suggesting a well fitting model (Figure 1).

The Figure 1 shows the six factors of the CURS (represented by the large circles). Each rectangle represents one item of the questionnaire, linked to its parent factor by a single-headed arrow. The double-headed arrows connected to items 1, 2, 6, and 7 represent covariance between two latent variables. Only for items 6 and 7 was simplification of statements believed to facilitate understanding.

### Reliability

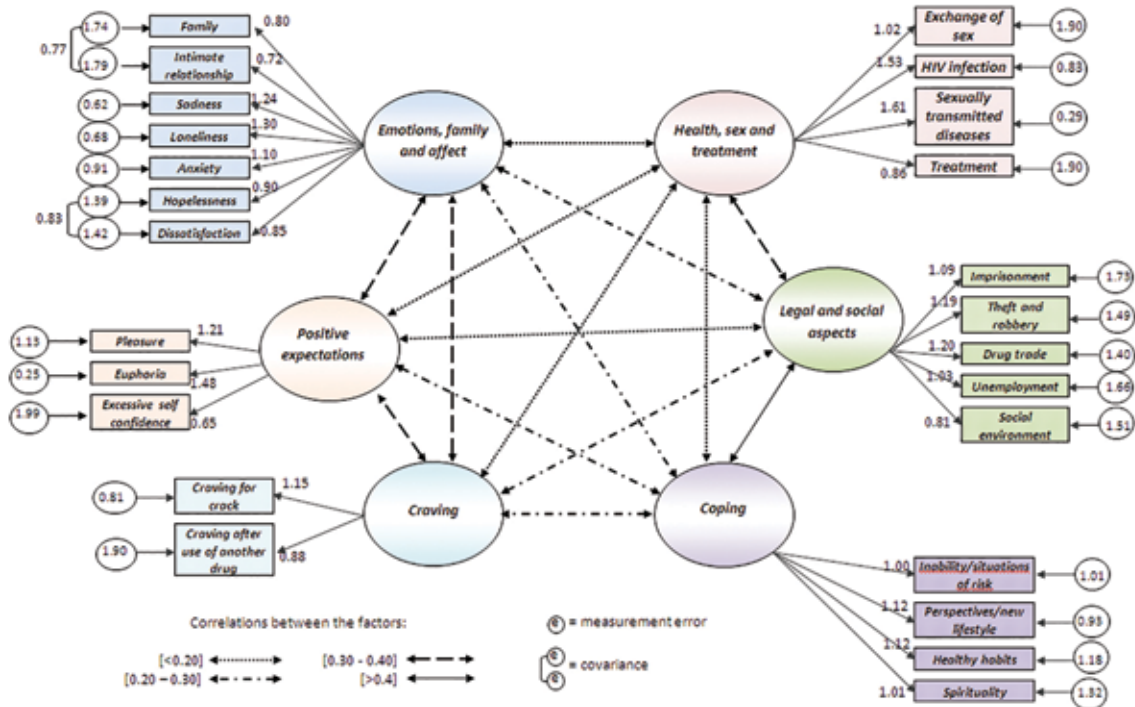
The Cronbach's alpha values obtained for the total scale (0.86) and each of the six factors were high, suggesting high internal consistency, as the literature states that values  $> 0.60$  are considered acceptable<sup>9</sup>.

## Discussion

Our findings show that the CFA then demonstrated satisfactory values for all fit indices, confirming the good fit of the underlying model of the scale and, consequently, the adequacy of the scale to measure its proposed construct. CFA is fully able to evaluate this adequacy, aiding the development of psychological, psychiatric and social models, particularly those designed to measure abstract constructs (latent variables), as in the present study<sup>11,12</sup>.

Significant aspect of the study was demonstrated by CFA, which ratified all *prior* psychometric analyses and enabled assessment of the structural model underlying the CURS in a reliable, scientific manner, bearing in mind that the evaluation of latent variables (factors) can be particularly challenging, and these variables cannot be observed directly when the construct of interest is both biological and psychosocial in nature<sup>12</sup>. Therefore, we chose to simplify items





**Figure 1.** Path diagram of confirmatory factor analysis of the CURS items and their respective factors.

6 and 7 to “No hope” and “Dissatisfaction” respectively. On the basis of our theoretical knowledge in the results of prior studies conducted by our team<sup>5</sup>, we had developed a priori postulates on the relationships between the measured variables and the factors defined initially. If on one hand the adjustment indices CFI, AGFI and TLI were moderate and the RSEMA index was fully satisfactory, indicating the appropriate model CURS, which was confirmed at the time that the scale was applied crack users by the adequacy of goodness-of-fit indices<sup>11-13</sup>.

We are aware of some limitations of this study. A heterogeneous, diverse sample is usually advised for validation studies, but our sample was entirely male, as male crack users are still more likely to receive treatment in Brazil<sup>5</sup>. The facility where the study was conducted has a dedicated unit for treatment of male users, but no such unit for women, even though we believe studies of female samples would be important. It bears stressing that this study presents satisfactory results for the first-ever scale developed for assessment of crack use relapse, which can now act as an alternative to – at least partially – bridge the gap in preventive strategies for coping with high-risk situations in this population. According to the media, over 70% of crack cocaine users treated at inpatient drug dependence care facilities will relapse after discharge. However, scientifically sound data on what really happens to this population after discharge are still lacking<sup>5</sup>. The CURS proved adequate for assessment of risk factors associated with relapse after discharge and can also be used for follow-up interviews within a psychosocial treatment model<sup>3</sup>, which we believe to be an essential intervention for following the trajectory of crack users after discharge from rehabilitation and, perhaps, even modifying the now almost-certain outcome that is relapse.

**Conclusions**

The six-factor model produced by exploratory factor analysis of the CURS reflects the several dimensions of the construct “crack use relapse”, designating satisfactory values and good psychometric properties, including validity and reliability<sup>14</sup>.

Finally, we believe the greatest efficacy in preventing relapse among crack users can be achieved through the fact that users know their own vulnerabilities, as enshrined in the health belief model, according to which individuals are able to carry out preventive behaviors with respect to a certain condition merely by believing they are susceptible to the condition and subsequently taking preventive action to modify their behavior. Possibly, the CURS is an instrument capable of providing these data to researchers and clinicians working with crack cocaine users<sup>15</sup>.

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**Authors’ contributions**

RSP managed the data collection, conducted preliminary data analysis, drafted the manuscript, conducted the final data analysis and revised the manuscript. LBZ, MP, JNS and VMG conducted preliminary data analysis and revised the manuscript, LSPG undertook interpretation of data, the statistical analysis and revised the manuscript, FHPK undertook interpretation of data, conducted preliminary data analysis and revised the manuscript, FP designed the research questions and was responsible for general coordination and revision of the manuscript. All authors read and approved the final manuscript.

**Conflict of interest statement**

The authors have no competing interests.



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# Early emotional trauma in alcohol-dependent men: prevalence, associations and predictive value

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## Abstract

**Background:** Several studies have indicated that early emotional traumas (EET) are highly prevalent in alcohol-dependent individuals, and that these traumas work as risk factors for the development of this disorder. **Objective:** The aim of the current study is to evaluate the EET associations and predictive value regarding active alcohol dependence among male individuals from a developing country. **Methods:** The sample consisted of two groups. The first was composed by adult male individuals diagnosed as alcohol dependents (AG, N = 110), and the second with no alcohol abuse and/or dependence diagnosis (CG, N = 110). Both groups were evaluated using Structured Clinical Interview based on the Diagnostic and Statistical Manual of Mental Disorders; Early Emotional Trauma Inventory; and a sociodemographic questionnaire. **Results:** All trauma subtypes (general, physical, emotional and sexual) were more prevalent among AG than CG. However, only traumas categorized as general and emotional worked as risk factor for alcoholism development and they increased the chances to develop this disorder by 1.45 and 1.23 times, respectively. **Discussion:** EETs are important factors that should be taken into account in interventions that aim to prevent, minimize and/or treat this clinical condition and its impact and/or severity, especially in countries such as Brazil.

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**Keywords:** Dependence, alcoholism, emotional early trauma, risk factors.

## Introduction

It is known that alcohol consumption is quite significant worldwide: approximately two billion people consume this substance and 76.3 million of them show some disorder associated with alcohol abuse<sup>1</sup>. Considering these statistics, it is possible to assume that the impacts associated with this consumption habit are extremely negative and lead to a series of damages to both the alcohol-dependent individual and the society.

By investigating the factors that predispose individuals to alcoholism, it is possible to emphasize the following: genetic aspects<sup>2</sup>, age<sup>3-5</sup>, social influences<sup>6</sup>, personality factors<sup>7</sup>, the experience of early emotional trauma (EET)<sup>8</sup>, among others.

The EETs refer to one or more traumatic events experienced from childhood up to 18 years of age. They may involve general and unexpected situations, such as witnessing natural disasters or living with parents that abuse on alcohol or drugs, as well as more specific situations, such as the experience of being physically, sexually or emotionally neglected and/or abused<sup>9-11</sup>. The literature has shown data regarding the association between alcoholism and EET.

Mirsal *et al.*<sup>8</sup> showed that the frequency of EET experienced by a sample comprising alcohol-dependent individuals (37.2% emotional abuse, 31.1% physical abuse; 11.1% sexual abuse) was significantly higher than that found in the group without such disorder (22.24% emotional abuse; 18.1% physical abuse; 3.1% sexual abuse). According to a different perspective, Fitzpatrick *et al.*<sup>12</sup> and Trent *et al.*<sup>13</sup> found that individuals who were victims of severe mistreatment during childhood showed very high alcoholism rates in adulthood, reaching up to 84%, depending on the type of EET they experienced.

Alcoholism risk factors associated with EET seem to differ between genders. Potthast *et al.*<sup>14</sup> conducted a study comprising individuals undergoing alcohol-dependence treatment. They pointed out that although the different types of traumas assessed in their study were alcoholism predictors, the emotional abuse experience was the main risk factor to predict alcohol dependence severity (ODDS = 4.33) among men. In addition, the studies by Elliott *et al.*<sup>15</sup> and by Fenton *et al.*<sup>16</sup>, who also used clinical sample, emphasized that

sexual abuse was the strongest alcoholism predictor (ODDS = 2.99;  $p < 0.01$ ) among men.

Regarding the female gender, Magnusson *et al.*<sup>17</sup> highlighted the existence of a synergistic relationship between parental alcoholism and EET. Sexual abuse and emotional neglect worked as risk factors for alcoholism in women, but only when they had parental history of alcoholism. It indicates both genetic vulnerability and gender influence on the possible associations between EET and alcoholism. Thus, gender should be considered an independent variable within this context.

The previous literature indicates that the link between EET and alcoholism in adulthood may be explained by the fact that EETs favor a series of emotional regulation deficits. These deficits are related to difficulties in accepting and overcoming traumatic experiences, in realizing and/or expressing feelings, and in socially relating with partners, among others. Thus, alcohol may be used as a way to compensate or alleviate such damages. Accordingly, it is worth emphasizing the study by Cardinal *et al.*<sup>18</sup> who showed the association between experiencing EET and brain volume reduction in the *dorsomedial prefrontal cortex*. It is known that this region plays an important role in regulating emotional experiences<sup>8,12,13</sup>. In addition, Hong *et al.*<sup>19</sup> also indicated that the link between EET experience and emotional dysregulation may be explained by the fact that children who experience EET have difficulties in establishing and/or forming healthy relationships with their peers, as well as in acquiring social skills related to emotional regulation and social interaction. Hence, these children show compromised social relations in adulthood.

Thus, there seems to be no doubt about the solid relationship between alcoholism and EET. However, it is worth conducting studies on this issue, by evaluating a) the impact and associations of different traumatic situations; b) the samples from developing countries such as Brazil, where the socioeconomic conditions increase the vulnerability to experience EETs<sup>20</sup>; c) the specificities of the gender variable within this context.

Therefore, the aim of the current study is to evaluate the EET associations and predictive value regarding active alcohol dependence among male individuals from a developing country.

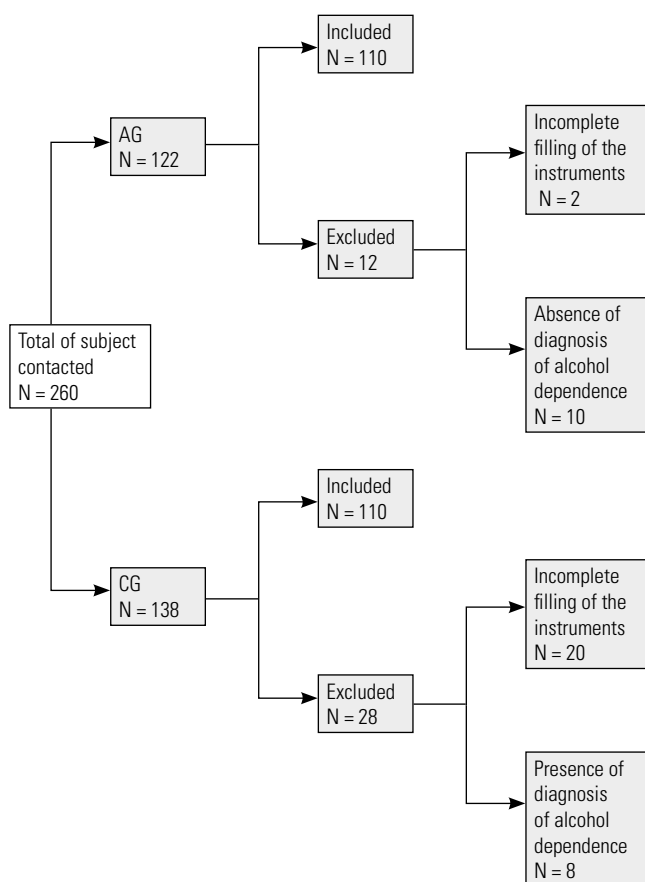
## Materials and methods

### Sample

The sample in the current study comprised two distinct groups, namely:

a) The AG (alcohol-dependent group) comprised male individuals over 18 years old, who were recruited in the alcoholic liver disease treatment clinic of a university teaching hospital and diagnosed as alcohol dependent according to the criteria listed in the fourth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV).

b) The CG (control group) comprised male individuals over 18 years old, who were recruited among the general population, especially in primary health care services and in a non-governmental organization. These individuals had no alcohol abuse and/or dependence diagnosis, according to the DSM-IV criteria. The study aimed to pair the sociodemographic variables from both the CG and AG groups, namely: gender, age and education. The exclusion criterion adopted for both groups was the incorrect filling of the instruments. Figure 1 below shows the flowchart of the sample composition trajectory.



**Figure 1.** Flowchart of inclusion and exclusion of participants.

### Instruments

The following instruments were used to assess the individuals:

A. Structured Clinical Interview based on the DSM-IV (SCID-IV): suggested by First *et al.*<sup>21</sup> and translated and adapted into Portuguese by Del-Ben *et al.*<sup>22</sup>. This instrument is used to make psychiatric clinical diagnosis based on the DSM-IV. The current study used the E module to perform alcohol abuse and/or dependence diagnostic investigation.

B. Early Trauma Inventory Self Report – Short Form (ETISR-SF): self-applied instrument composed of 27 items scored in “Yes” or “No” answers that evaluate trauma occurrence during childhood and adolescence. The current study used the Brazilian Portuguese version translated and validated by Osório *et al.*<sup>23</sup> The version presented 0.83 internal consistency (Cronbach’s alpha) and test-retest reliability > 0.78.

C. Clinical and sociodemographic questionnaire: instrument developed for the current study. It aims to collect additional data on the sociodemographic and clinical features of the sampling group.

### Data collection and analysis

The current study met the human research ethical parameters and was approved by the local Ethics Committee (HCRP Process n. 2316/2011).

Data were individually collected and inserted in a database. Subsequently, they were analyzed using a) descriptive statistics (analyses of the sampling group sociodemographic and clinical features); b) parametric statistics: Student’s t test (comparison between the groups); c) Pearson’s correlation test (correlation of variables) and d) multivariate logistic regression – backward technique (predictive variable analysis – the variables showing  $p < 0.20$  in the comparison between the groups were included in the initial model). The significance level was set at  $p < 0.05$ .

### Results

The clinical sample had mean age of 53 years (SD = 8.24). Fifty-eight point two percent (58.2%) of the individuals were married and 83.6% of them had children. As for education, individuals with up to 8 years of education (56.4%) were prevalent. Regarding the control group, the mean age was 53 years and there was also the prevalence of married individuals (71.8%) with children (78.2%), and education level of up to 8 years (54.6%). Both groups did not statistically differ in these variables. However, it is noteworthy that the AG group presented higher inactivity rates regarding employment (56.4%) than the CG group (19%). This result was statistically significant ( $p < 0.001$ ).

The mean number of doses the alcohol-dependent group consumed daily was 7.64 and the mean alcohol use time was 29.36 years. It is noteworthy that 77.3% of the individuals showed clinical alcoholic liver cirrhosis symptoms and 22.7% of them showed clinical liver disease symptoms.

The main data regarding the experienced EETs are presented in Table 1.

Table 1 shows that there were statistically significant differences between AG and CG in all trauma categories, and traumas were more often found in AG.

It is important to emphasize that 94% of AG individuals experienced some traumatic event during childhood. There was high co-occurrence rate of different EET types, since the average number of traumatic events was 8.39 (SD = 5.93) per individual.

Significant correlations were not observed ( $p > 0.41$ ) when EET categories were correlated with alcoholism time and with the number of consumed doses. Accordingly, no significant correlation was observed by correlating the different trauma categories: General ( $p > 0.11$ ), physical ( $p > 0.09$ ), emotional ( $p > 0.37$ ) and sexual traumas ( $p > 0.09$ ).

Table 2 details the most frequent EET subtypes experienced by both groups.

It is observed that the traumatic situations in the “general” category were the most commonly found in the AG sample, especially in the case of situations involving witnessing the death and/or serious injury of a friend and/or caregiver. The sexual trauma category was less frequently experienced in both groups, but it still showed rates between 11 and 22% in AG. The groups did not show any differences only in three traumatic situations: severe accident, being slapped in the face, and being pushed.

**Table 1.** The frequency and percentage of different categories of early emotional traumas experienced by the sample, according to the alcoholic and control groups

Trauma categories		AG (N = 110)	CG (N = 110)	Statistics
General traumas	Mean (SD)	4.30 (3.20)	1.69 (1.85)	$t = -7.390; p < 0.001^*$
	Minimum n.	0	0	
	Maximum n.	11	9	
	%	85.5%	63.6%	
Physical punishment	Mean (SD)	1.77 (1.89)	1.12 (1.32)	$t = -2.931; p = 0.004^*$
	Minimum n.	0	0	
	Maximum n.	5	5	
	%	60.9%	52.7%	
Emotional traumas	Mean (SD)	1.31 (1.94)	0.60 (1.22)	$t = -3.235; p \leq 0.001^*$
	Minimum n.	0	0	
	Maximum n.	5	5	
	%	30.9%	27.3%	
Sexual traumas	Mean (SD)	0.89 (1.76)	0.26 (0.73)	$t = -3.434; p = 0.001^*$
	Minimum n.	0	0	
	Maximum n.	6	5	
	%	30.9%	17.3%	
Total	Mean (SD)	8.39 (5.93)	3.90 (4.01)	$t = -6.56; p \leq 0.001^*$
	Minimum n.	0	0	
	Maximum n.	28	22	
	%	94%	71%	

SD: standard deviation; AG: alcoholic group; CG: control group; Minimum and Maximum n.: minimum and maximum number of traumatic events/situations experienced in the category; *t*: Student's *t* test; *p*: significance level; \*: statistically significant difference; %: percentage of individuals who experienced at least one traumatic event/situation in the category.

**Table 2.** The frequency and percentage of different early emotional trauma subtypes/situations experienced by the sample, according to the alcoholic and control groups

EET Category	EET <sup>(A)</sup> Subtype	AG		CG		Statistics
		N	%	N	%	
General traumas	1.1. Natural disasters	18	16.4	7	6.4	$\chi^2 = 5.46; p = 0.01^*$
	1.2. Severe accident	29	26.4	23	20.9	$\chi^2 = 0.90; p = 0.34$
	1.3. Injury/Illness	44	40.0	18	16.4	$\chi^2 = 15.18; p < 0.01^*$
	1.4. Death/Illness of parents	54	49.1	21	19.1	$\chi^2 = 22.03; p < 0.01^*$
	1.5. Divorce	49	44.5	14	12.7	$\chi^2 = 27.24; p < 0.01^*$
	1.6. Death/Injury of siblings	53	48.2	10	9.1	$\chi^2 = 41.12; p < 0.01^*$
	1.7. Death/Injury of friends	58	52.7	20	18.2	$\chi^2 = 28.68; p < 0.01^*$
	1.8. Violent situations	49	44.9	18	16.4	$\chi^2 = 20.62; p < 0.01^*$
	1.9. Mental disorder in the family	41	37.3	19	17.3	$\chi^2 = 11.09; p < 0.01^*$
	1.10. Alcohol/Drug use by parents	39	35.5	13	11.8	$\chi^2 = 17.02; p < 0.01^*$
	1.11. Murder	39	35.5	23	20.9	$\chi^2 = 5.74; p < 0.01^*$
Physical traumas	2.1. Slap in the face	47	42.7	34	30.9	$\chi^2 = 3.30; p = 0.07$
	2.2. Burnt with water/cigarette	35	31.8	16	14.5	$\chi^2 = 9.21; p < 0.001^*$
	2.3. Punched/Kicked	39	35.5	21	19.1	$\chi^2 = 7.42; p < 0.01^*$
	2.4. Thrown objects	35	31.8	20	18.2	$\chi^2 = 6.28; p < 0.01^*$
	2.5. Pushed	39	35.5	33	30.0	$\chi^2 = 0.743; p = 0.39$
Emotional traumas	3.1. Ridiculed	28	25.5	16	14.5	$\chi^2 = 4.09; p = 0.04^*$
	3.2. Ignored	30	27.3	15	13.6	$\chi^2 = 6.28; p < 0.01^*$
	3.3. Told that he/she was not good	28	25.5	10	9.1	$\chi^2 = 10.30; p < 0.01^*$
	3.4. Lack of affection/Love	29	26.4	11	10.0	$\chi^2 = 9.90; p = 0.02^*$
	3.5. Parents did not understand the his/her needs	29	26.4	14	12.7	$\chi^2 = 6.50; p < 0.01^*$
Sexual traumas	4.1. Touching body parts	22	20	9	8.2	$\chi^2 = 6.34; p = 0.01^*$
	4.2. Rubbing genitals	20	18.2	10	9.1	$\chi^2 = 3.86; p = 0.05^*$
	4.3. Touching intimate parts of another	17	15.5	2	1.8	$\chi^2 = 12.96; p < 0.01^*$
	4.4. Sex against his/her will	16	14.5	3	2.7	$\chi^2 = 9.73; p = 0.02^*$
	4.5. Oral sex	12	10.9	2	1.8	$\chi^2 = 7.62; p = 0.01^*$
	4.6. Sexualized kiss	11	10	3	2.7	$\chi^2 = 4.88; p = 0.03^*$

A: non-exclusive categories; AG: alcoholics group composed of individuals with alcohol dependence diagnosis; CG: control group composed of individuals with no diagnosis of alcohol abuse and/or addiction; N: frequency; %: percentage; *p*: significance level;  $\chi^2$ : chi-square test; \*: statistically significant difference; EET: early emotional traumas.

Regarding the joint analysis of the variables, no significant correlations were observed when the categories were compared. Two multivariate logistic regression models were tested to evaluate the alcohol dependence EET predictive value.

Firstly, an analysis was performed by taking under consideration the four EET categories all together. Results showed that general (odds ratio (ODDS) = 1.45; Confidence Interval ([CI] = 1.27-1.65;  $p < 0.001$ ) and emotional traumas (ODDS = 1.23, CI = 1.01 – 1.50,  $p = 0.003$ ) worked as risk factor for alcoholism development. Thus, each general and emotional trauma situation experienced by these individuals increased by 45 and 23%, respectively, their chance of developing alcoholism in comparison to individuals who had not faced such traumatic experiences.

Next, a second initial logistic regression model tested all different EET subtypes/specific situations that were statistically significant according to the analysis described in Table 2 (those with significance value lower than 0.05 set the final model shown in Table 3).

As it can be seen in Table 3, four EET-specific situations worked as risk factor for alcoholism. They increased the chance of developing the disorder when the event was experienced from 2.77 to 8.66 times.

## Discussion

The current study aimed to determine possible links between EETs and alcohol dependence. In addition, it sought to associate specific EET situations and alcoholism as well as to check the EET role as risk factor for alcohol dependence development in a sample, which exclusively comprised male individuals from a developing country. These specificities stand out as the study differential when it is compared to previous studies found in the literature.

The findings in the current study corroborate those of previous studies<sup>24-26</sup> regarding the close relationship between EET and alcoholism pointed out in the literature. Alcohol-dependent individuals showed EET percentages higher than the non-dependent ones. They also showed bigger EET co-occurrence number (about twice as much). This finding is not unusual, since international statistics show that the combined occurrence of different EET types is quite high in this group of individuals and that it reaches rates up to 84%<sup>12,27,28</sup>.

In addition, the high EET rates draw attention not only to the alcohol-dependent individuals sampling group, but also to the controls (17.3% to 63.6%); mainly when they are compared to the trauma prevalence in the general Brazilian population, which was estimated approximately 7 years ago (5.7 to 12%)<sup>29</sup>. These data are a warning sign about the increase and severity of these indicators, and they require special attention from governmental institutions and from programs targeted to protect the health and integrity of local children and adolescents<sup>30</sup>.

The increased EET rates found in the current study, in comparison to other international indicators, may be partly explained by the Brazilian social context and by that of several other developing countries. This social context enhances the exposure to other risky situations. In this particular context, part or much of the population belong to disadvantaged social strata and live in families with big number of children coming from multiple marriages. Such fact may favor the emergence of conflicts and aggressions resulting from the correction strategy applied, in most cases, to children by stepfathers or stepmothers due to their bad behavior<sup>31-33</sup>. In addition, high

unemployment and underemployment rates, and even the need for parents and/or caregivers to work in multiple jobs to supplement the family income, favor stress, personal dissatisfaction, parental distancing from the children, family conflicts, substance abuse, among other potentially harmful aspects<sup>34</sup>. All these factors together may broaden the experience of early stressors and increase children's vulnerability to different EETs.

By analyzing the EET categories, it was possible to see that categories such as "general" and "physical" traumas were the most frequent in the AG sample. Elliott *et al.*<sup>15</sup> and Fenton *et al.*<sup>16</sup> had previously reported this finding regarding physical trauma; however, its occurrence (25% to 31%) was lower than that found in the current study (60.9%). The high prevalence of physical trauma in the AG in the current study, in comparison to that reported in the literature, may be justified by the fact that corporal punishment is still widely used as educational practice in the current family context, despite the child protection efforts that include judicial proceedings (ordinary law 13.010 from June 26<sup>th</sup>, 2014)<sup>35</sup>.

The herein categorized "general" traumas were not investigated in the aforementioned studies, probably because the authors used measurement instruments such as the "Childhood Trauma Questionnaire" (CTQ), which does not assess these types of occurrences and/or experiences (natural disasters, collapses, among others). Thus, this finding appears to be innovative and it mainly draws the attention of clinicians and researchers in the field towards the impact caused by experiences such as injury or illness in people close to the children, violence, divorce, psychiatric disorder of the parents, natural disasters and death-associated experiences. It is worth emphasizing the risk factor for alcoholism associated with this type of trauma, because its occurrence increases by 45% the chance of developing the disorder.

Similarly, "emotional" and "sexual" traumas were most often found in AG than in CG, with statistically significant differences. These data meet those found in the previous literature, which suggests that approximately 34% of the alcohol-dependent individuals<sup>8,35</sup> experienced emotional traumas and 3-21% of them experienced sexual traumas<sup>36-38</sup>.

It is also important to highlight that EET subtypes/specific situations also individually worked as risk factor for the disorder. It is worth emphasizing the role played by children interaction with parents and/or caregivers who had history of alcohol and other substances use or abuse, as it was previously documented<sup>39,40</sup>. Therefore, alcohol use by caregivers may model the child learning by signaling that addictive behaviors are acceptable or even expected within certain contexts. On the other hand, Souza and Carvalho<sup>41</sup> found that children of alcohol-dependent parents show increased risk of experiencing other EET types, such as living in unstable home environments, suffering physical and verbal aggression, parental divorce and parental affectivity reduction, which may be secondarily associated with alcohol abuse.

Some specific EET subtypes also worked as risk factor for alcoholism, namely: "witnessing the death or injury of siblings", "hearing that they are not important" and "touching intimate body parts of another person". The literature suggests the significant impacts felt by the individual when he/she experiences the aforementioned EET subtypes. These impacts cause damages to the physical and psychosocial development. Such damages may show up in the short, medium and long term<sup>42</sup>. In the short term, it is possible

**Table 3.** Final logistic regression model for predicting alcoholism using different traumatic subtypes/situations as independent variables

Variables	B	S.E.	p	O.R.	CI = 95%	
					Lower	Higher
Death/Injury of siblings	2.15	0.40	$p < 0.001^*$	8.66	3.93	19.05
Alcohol/Drug use by parents	1.01	0.40	$p = 0.01^*$	2.77	1.24	6.17
Told that he/she was not good	1.17	0.45	$p = 0.01^*$	3.24	0.90	1.33
Touching intimate parts of another	2.02	0.81	$p = 0.01^*$	7.58	1.52	37.64

B: beta value; S.E.: standard deviation of the estimate; p: significance level; O.R.: odds Ratio; CI: confidence interval.

to see the development of low self-esteem, learning problems, and difficulty in engaging in interpersonal relationships. In the medium and long terms, it is possible to see neurological damages and increased susceptibility to develop depression, anxiety and abusive behaviors related to alcohol and drug use<sup>43-45</sup>.

In short, it is concluded that EETs are in fact significantly associated with addictive behaviors in adulthood, such as alcohol dependence. Thus, EETs are important factors that should be taken into account in interventions that aim to prevent, minimize and/or treat this clinical condition and its impact and/or severity, especially in countries such as Brazil. The prevalence rates are higher in these countries and the public health policies as well as the policies to protect the underage teenager welfare are ineffective when they are compared to the same policies in developed countries such as the United States and England<sup>46-49</sup>.

It stands out as limitations of the current study: a) the use of clinical sample, in particular with significant liver comorbidities, which limits the generalizability of the findings to other clinical groups and to the general population; b) the use of cross-sectional methodology to document a temporal relationship considering the presence of EET grounded only in memory-based reports. Although previous studies<sup>26,50</sup> indicate similar EET rates both in retrospective and in prospective studies, this proviso should be taken into consideration.

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# Posttraumatic growth measures: translation and adaptation of three self-report instruments to Brazilian Portuguese

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## Abstract

**Background:** Posttraumatic growth is one of the most commonly used concepts to evaluate positive changes after trauma. The principal scales used internationally to evaluate this phenomenon have not yet a Brazilian Portuguese version. **Objectives:** This study aimed to translate and adapt to the Brazilian context the Posttraumatic Growth Inventory (PTGI), the Core Beliefs Inventory (CBI), and the Event Related Rumination Inventory (ERRI). **Methods:** The procedures included translation, back translation, expert committee's evaluation, and pilot testing in the target population. **Results:** All items of all three instruments had a good content validity index after evaluation by four experts and three reformulations. The back translation of the final version also demonstrated that all Brazilian Portuguese versions convey the same meaning as the original English version. The final version was pilot tested with 30 undergraduate students, and all the items were above the cut-off point. **Discussion:** This study was able to produce Brazilian versions of the PTGI, CBI, and ERRI. Further studies are underway to determine the reliability, factorial validity, and convergent validity of the subscales of the instruments.

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**Keywords:** Transcultural adaptation, posttraumatic growth, trauma, PTSD, psychometrics.

## Introduction

Although it is estimated that 40 to 90% of people will be exposed to at least one traumatic event in the course of life, only 10% of those will develop psychiatric disorders, such as posttraumatic stress disorder (PTSD)<sup>1,2</sup>. These figures suggest that negative outcomes are not the only type of experience in the aftermath of trauma. Several studies have shown that an individual's struggle with a traumatic event can produce negative, positive, and, perhaps even more typically, a mixture of negative and positive experiences<sup>3,4</sup>.

Posttraumatic growth (PTG) is one of the most commonly used concepts to evaluate the positive outcomes of trauma. PTG is defined as a positive change experienced as a result of the struggle with a major life crisis or traumatic event, a change beyond mere adjustment and recovery<sup>5,6</sup>. The underlying idea is that it is not the event itself that defines the outcome, but how this experience challenges people's beliefs about the world and self<sup>3,4</sup>. PTG can be achieved as a consequence of the process of attempting to understand the event (*e.g.*, deliberate rumination) and the cognitive effort to redefine those beliefs and the assumptive world<sup>7,8</sup>.

Previous studies have shown an association of PTG with greater life satisfaction, well-being and quality of life in the long term after not only traumatic events but also extremely adverse situations, such as cancer<sup>9</sup> and coronary heart disease<sup>10</sup>. Even though PTG has received empirical support, the theoretical model should be further developed many hypotheses have yet to be tested<sup>3</sup>.

A widely used inventory for investigating PTG is the Posttraumatic Growth Inventory (PTGI)<sup>5</sup>, which consists of 21 self-report items scored on a six-point Likert scale. A total score can be used, but the scale also has a five-factor model that reflects different domains of growth: Relating to others (RO); Personal strength (PS); New possibilities (NP); Appreciation of life (AL); and Spiritual change (SP)<sup>5,11</sup>. The internal consistency for the total score and subscales of the PTGI has been reported as satisfactory ( $\alpha$  coefficient for the total score = .90, RO = .85, NP = .84, PS = .72, SP = .85, and AL = .67), just as the test-retest reliability ( $r = .71$ )<sup>5</sup>. The PTGI has already been translated and adapted to different languages, such as Chinese<sup>12</sup>, Spanish<sup>13</sup>, Dutch<sup>14</sup>, Japanese<sup>15</sup>, and European Portuguese<sup>16</sup>.

For a broader understanding of PTG, it is necessary to consider not only the subjectively perceived gains but also the cognitive,

emotional and social factors that facilitate the growth process<sup>17</sup>. One critical factor that has been theorized to facilitate the PTG process is the confrontation with core beliefs. In this sense, a traumatic event is considered a psychologically shattering experience or an experience that challenges a person's core beliefs, forcing individuals to reexamine them<sup>7</sup>. Core beliefs are defined as a general set of beliefs that a person has about the world and their individual place within it. These beliefs also include assumptions about how one believes people will behave, how events should unfold, and one's personal ability to influence events<sup>18</sup>. After trauma, the psychological struggle triggered by the disruption of core beliefs could facilitate identification of positive changes in their worldview and a connection with others that would not have existed otherwise, resulting in the experience of PTG<sup>4</sup>. Empirical studies have supported that the reexamination of core beliefs is more closely related to growth than the perceived stressfulness of the event<sup>19,20</sup>.

To measure the degree of disruption of core beliefs after a traumatic event, the Core Beliefs Inventory (CBI) was developed. The CBI consists of nine self-report items, and responses are made on a six-point scale. Psychometric studies of the scale indicate a single-factor model and the internal reliability was good in a two-stage study ( $\alpha$  time 1 = .82;  $\alpha$  time 2 = .87) and the test-retest reliability was acceptable ( $r = .69$ )<sup>20</sup>.

Another cognitive process that facilitates PTG is the effort to review and understand the traumatic event in order to reintegrate the shattered beliefs. Empirical and theoretical studies suggest that intrusive rumination is associated with negative reactions to trauma, whereas deliberate rumination is associated with meaning and growth<sup>21</sup>. Aiming to investigate the role of both styles of rumination in the growth process, the Event Related Rumination Inventory (ERRI) was designed<sup>7</sup>. The ERRI consists of 20 self-report items that are scored on a four-point scale. The original psychometric ERRI study confirmed the two-factor model, with a good internal reliability in both subscales (intrusive,  $\alpha = .94$ ; deliberate,  $\alpha = .88$ ).

Despite the increasing interest in PTG worldwide, to the best of our knowledge, there are no studies addressing this issue in the Brazilian population. The purpose of this study was to describe the steps of the process of translation and cultural adaptation to Brazilian Portuguese of the three main scales used internationally to evaluate

the PTG phenomenon: PTGI, CBI, and ERRI. In the process of adaptation of a psychological measure to a different language and culture, content validity must be considered. The content validity is the degree to which the items of an instrument are representative of the construct being measured<sup>22</sup>. In this sense, careful translation and adaptation methods are important to ensure that the construct remains the same as that of the original instrument<sup>23</sup>. We hope that with this adaptation the scales can be psychometrically validated and used as clinical and research tools in the Brazilian context.

## Methods

The translation and adaptation of the three instruments were based on the guidelines of the International Test Commission and previous studies<sup>24,25</sup> and followed six steps: (1) translation, (2) expert committee's evaluation, (3) review by linguistic experts, (4) pretest in the target population, (5) back translation, and (6) original authors' evaluation. The study was approved by the Research Ethics Committee of the institution where it was conducted (protocol no. 247.127).

## Results

### Translation

Two native Portuguese-speaking authors, fluent in English, independently translated the original versions of the ERRI and CBI into Brazilian Portuguese. These versions were then merged into one initial translated version of each scale. The Brazilian version of the PTGI was based on the existing European Portuguese version<sup>16</sup>, and only minor semantic changes were made.

### Expert committee's evaluation

The translated versions of the ERRI, CBI and PTGI were evaluated by an expert committee composed of four judges: two psychologists (MSc) with expertise in PTSD and two psychologists (PhD) with expertise in psychological assessment. The content validity index (CVI)<sup>26</sup> was used to objectively measure the experts' evaluation. This index is based on a five-point Likert-type scale on which experts rate the items according to (1) clarity of language, which measures how understandable the items are to the target population; (2) practical relevance, which measures how adequate each item is to evaluate the target population; and (3) theoretical relevance, which measures how much the items are in agreement with the construct theory<sup>27</sup>. For each item, values  $> 0.7$  were considered satisfactory<sup>28</sup>. Items with lower scores were rephrased and resubmitted to the four judges for evaluation until the CVI reached a value of  $> 0.70$ . Table 1 summarizes the items that were modified at this stage.

### Review by linguistic experts

This phase consisted of a meeting between two linguistic experts and the authors of the study. The translated versions were compared with the original English versions not only to verify whether all items expressed the same ideas but also to ensure semantic, idiomatic and conceptual equivalence between the source-language and adapted versions. As a result of this evaluation, some expressions in the adapted versions were modified.

In the instructions for use of the CBI, the term "event" was considered problematic. In Portuguese, the most similar word to "event" is "evento", a term that generally means "party"; thus, this word was changed to a semantically similar word: "situação", which means "situation". Also, in some items of the CBI, the expression "examined" used in "I seriously examined the degree to which I believe things..." was modified considering that, in Portuguese, the most similar word to "examined" is "examinei", a verb that means to test or evaluate something. Aiming to preserve the original meaning, the word was changed to "repensei", which means thinking again.

In the ERRI, some items needed to be completely modified. Item 7 "Reminders of the event brought back thoughts about my experience" was rewritten considering that there is no similar word or expression in Portuguese to "reminders" in the context of "reminding by association". In this case, it was decided to explain the entire sentence in more detail: "*Coisas do meu cotidiano relacionadas à situação me fizeram ter pensamentos sobre o que vivi*", which may be literally translated as "Things that happen in my daily life related to the situation made me think about what I have experienced". In the original ERRI, item 13 aims to investigate a deliberate effort to cope with the event: "I forced myself to think about my feelings about my experience". The experts considered that the literal translation of "I forced myself" (i.e., "*eu me forcei*") may have a negative connotation. The item was then changed to "*Eu me esforcei para refletir sobre os meus sentimentos acerca da situação*", which may be literally translated as "I made an effort to think about my feelings about the situation".

### Pretest in the target population

The adapted versions of all three instruments were administered to a sample of the target population in a pilot study. The understanding of each item in the three questionnaires was evaluated using a five-point verbal numeric rating scale, ranging from "1- Incomprehensible" to "5- I completely understood". The sample consisted of 30 university students (10 men and 20 women), with a mean (SD) age of 24 (5.4) years. Most students were psychology undergraduates (86%).

Satisfactory understanding was defined as a mean score  $\geq 3$ , a cut-off point based on previous studies<sup>29,30</sup>. None of the items of any of the three scales needed to be modified at this stage because participants rated all the items as completely understandable. All items had a mean score of four or higher.

### Back translation

After all items were considered appropriate by the evaluators and understandable by the students, the adapted version of each scale was back translated by two independent, bilingual native English speakers, who were blinded to the original instrument. These two back-translated versions were merged by the authors of this study into a single back-translated version of each scale.

### Original authors' evaluation

The Brazilian Portuguese adapted versions, the back-translated versions and the results of all stages were submitted to the authors of the original versions for evaluation and subsequent approval.

## Discussion

This study aimed to adapt three self-report measures used to investigate PTG. In the adaptation process, the scales were evaluated and expressions were modified to preserve the content validity of the instrument in the Brazilian Portuguese version.

In the psychometric literature, the content validity of translated scales should be investigated with methodological rigor and include cross-cultural adaptation addressing both linguistic and cultural issues. Although several methods have been proposed for adaptation of existing instruments, how to conduct this process in a reliable and objective manner is still debatable. Moreover, these methodological guidelines do not cover linguistic specificities, requiring a case-by-case examination. This precaution was taken in the present study by using the CVI. This index provided quantitative data to evaluate the adequacy of the scales regarding clarity of language, practical and theoretical relevance.

A major limitation of this study was the pilot phase, since all participants were university students, mostly psychology students. As most studies investigating PTG have obtained their initial data from university students, our pilot study provides sufficient reliability

**Table 1.** Results of expert committee's evaluations

Measure	Primeira versão	CL	PR	TR	Versão reformulada	CL	PR	TR
PTGI								
11	Sou capaz de fazer coisas melhores com a minha vida	0,64	0,89	0,89	Agora sou capaz de fazer coisas melhores com a minha vida	0,84	0,99	0,99
14	Apareceram oportunidades que não teriam aparecido de outra forma	0,69	0,74	0,79	Surgiram oportunidades que não teriam surgido de outra forma	0,84	0,99	0,99
17	É mais provável eu mudar as coisas que precisam ser mudadas	0,69	0,99	0,99	Agora é mais provável que eu mude coisas que precisam ser mudadas	0,94	0,99	0,99
ERRI								
Intro	Após uma experiência como a que você reportou, as pessoas – às vezes, mas não sempre – se dão conta de estar pensando sobre a experiência mesmo quando não estão voluntariamente tentando pensar sobre isso. Indique, para os itens abaixo, se você teve essas experiências descritas, e com qual frequência, durante as últimas semanas	0,69	0,99	0,99	Após uma experiência como a que você reportou, as pessoas às vezes se dão conta de estar pensando sobre a experiência mesmo quando não estão voluntariamente tentando pensar sobre isso. Indique para os itens a seguir se você teve essas experiências descritas e com qual frequência, durante as últimas semanas	0,94	0,99	0,99
7	Coisas que me lembravam do evento me fizeram pensar sobre a minha experiência.	0,64	0,94	0,99	Coisas do meu cotidiano relacionadas à situação me fizeram ter pensamentos sobre o que vivi	0,94	0,99	0,99
9	Outras coisas me mantêm pensando sobre a minha experiência	0,69	0,94	0,99	Outras coisas me levaram a ficar pensando sobre a minha experiência	0,89	0,99	0,99
12	Eu pensei se as mudanças na minha vida vieram de eu ter que lidar com a minha experiência	0,44	0,79	0,99	Eu pensei se as mudanças na minha vida vieram como consequência de eu ter lidado com esta experiência	0,84	0,99	0,99
13	Eu me forcei para pensar sobre os meus sentimentos acerca da minha experiência	0,64	0,94	0,99	Eu me esforcei para refletir sobre os meus sentimentos acerca da situação	0,94	0,99	0,99
20	Eu me forcei para enfrentar os meus sentimentos em relação ao que aconteceu	0,39	0,99	0,99	Eu me esforcei para enfrentar os sentimentos que tive em relação à situação	0,94	0,99	0,99
CBI								
Intro	Alguns eventos que as pessoas vivenciam são tão impactantes que “abalam seu mundo” e as levam a examinar seriamente suas principais convicções sobre si mesmas, o mundo, as outras pessoas e sobre o futuro. Por favor, reflita sobre a situação sobre a qual você está reportando e indique qual o grau que esta leva você a repensar cada uma das convicções abaixo:	0,69	0,99	0,99	Algumas situações que as pessoas vivenciam são tão impactantes que “abalam seu mundo” e as levam a reexaminar seriamente suas principais convicções sobre si mesmas, o mundo, as outras pessoas e o seu futuro. Por favor, reflita sobre a situação sobre a qual você está relatando e indique o quanto esta situação leva você a repensar cada uma das convicções abaixo:	0,84	0,99	0,99

CL: clarity of language; PR: practical relevance; TR: theoretical relevance.

for use in research and to replicate these studies in Brazil. However, one must proceed with caution when conducting further studies with individuals with lower education.

Previous studies have shown that the PTGI domains may vary across cultures<sup>15</sup>. One of the main reasons is that growth is a response that depends closely on cultural meanings of negative life events, personal strength, and thriving<sup>31</sup>. In this sense, the transcultural adaptation of the three PTG-related measures is particularly important. The content validity of these measures can provide a basis for future studies indicating, in the case of psychometric data, different factors of the original instrument in the factor analysis. In this case, for instance, different findings could be attributed to the Brazilian culture rather than to differences in the item's content. Further studies are underway to determine the reliability and psychometric validity of these scales.

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### Conflict of interest

There are no conflicts of interest concerning the publication of this article.

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# Level of paranormal beliefs and its relationship with explanatory models, treatment adherence and satisfaction

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## Abstract

**Background:** Paranormal beliefs are common among patients with mental illness. Such beliefs may mediate conceptualization of illness, treatment satisfaction and medication adherence. **Objective:** To study the level of paranormal beliefs and its relationship with explanatory models, treatment adherence and satisfaction using standardized assessment tool. **Methods:** Eighty nine patients with mental illness in remission were assessed with Sociodemographic proforma, Revised Paranormal Belief Scale (RPBS), Mental Distress Explanatory Model Questionnaire (MMAS), Morisky Medication Adherence Scale (MMAS) and Short Assessment of Patient Satisfaction (SAPS). **Results:** Results revealed a high level of paranormal beliefs on RPBS (Mean 83.96, SD ± 23.91). Variables that had a statistically significant group difference on the score of RPBS were domicile status ( $p < .05$ ), diagnosis ( $p < .001$ ), method of treatment sought before ( $p < .001$ ). In a linear regression analysis four variables explained 35.4% of the variance ( $R^2 = .38$ ,  $R^2$ Adjusted = .35,  $F = 13.04$ ,  $p < .001$ ) in RPBS Score. These variables were total score of MDEM (Beta = .308,  $t = 3.435$ ,  $p < .001$ ), total score of MMAS (beta = .357,  $t = 3.716$ ,  $p < .001$ ) and magico-religious treatment received earlier (beta = .306,  $t = 3.52$ ,  $p < .001$ ) and SAPS. **Discussion:** Based on the finding of this study, it may be concluded that the level of paranormal beliefs may vary with some demographic variables. Levels of paranormal beliefs is positively associated with explanatory models and adherence in patients with mental illness in remission.

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**Keywords:** Paranormal belief, explanatory model, patient satisfaction, medication adherence, mental illness in remission.

## Introduction

Paranormal belief (PB) is the beliefs which violate currently accepted scientific theories. In India, it is common in general population and patients with mental illness; and related to evil spirits, witchcraft, astrological influences, bad deeds of previous birth and punishment for a sin<sup>1,2</sup>. Few attempts have been made to explore the paranormal belief in India. Kate *et al.* in his study found that more than 50% of patient with schizophrenia had paranormal beliefs; particularly among males, older age, married and with lower levels of education; and initially approached to a magico-religious healers<sup>3</sup>. Swain *et al.* assessed the level of paranormal beliefs using revised paranormal belief scale in a small sample of patients with schizophrenia, and compared it with their siblings and controls. He observed a significant correlation of paranormal beliefs with age, gender and education<sup>4</sup>. Chakraborty *et al.* studied the perceptions about the cause of psychiatric disorders and subsequent help seeking<sup>5</sup>. A questionnaire was designed and assessed some paranormal beliefs. A high prevalence of supernatural beliefs in relatives of patients with schizophrenia (96.8%), anxiety disorder (40%) and depressive disorder (27.3%) was observed. Educated patients sought more medical help (58.3%) than illiterate and supernatural beliefs had a positive correlation with seeking of religious remedies.

In patients with mental illness, PB may play a role in conceptualizing their illness known as an explanatory model (EM)<sup>6</sup>. It is a socio-anthropological approach to understand the subjective experiences of distress that can be applied in psychiatric practice<sup>7</sup>. EM and PB may influence treatment adherence and satisfaction that have a bearing on the outcome of any psychiatric disorder<sup>8,9</sup>. Skeptics believe that patients with paranormal beliefs are prone to be misguided by a traditional healer which may lead to non-compliance to medication<sup>10</sup>. However, there is dearth of study that examined this issue. This study was carried out to study the level of paranormal beliefs and its relationship with explanatory models, treatment adherence and satisfaction using standardized assessment tool. We hypothesises that: 1) The level of paranormal beliefs is positively associated with explanatory models, and negatively associated with medication adherence and patients' satisfaction.

## Methods

This hospital based cross sectional study was conducted at the outpatient department of psychiatry of a tertiary care general hospital in south India, after approval from the institution ethics committee. Eighty nine patients (40 males & 49 females) with mental illness who were living in the community after the improvement with treatment, and came for follow-up were consecutively recruited over a period of six months after obtaining an informed consent. The inclusion criteria were: both male and female patients with a psychiatric diagnosis of axis I psychiatric disorder currently in remission as per the International Statistical Classification of Diseases and Related Health Problems, Diagnostic criteria for research (ICD-10 DCR), aged 14-65 years and > 2 consultation visits.

Patients with a comorbid chronic physical illness, diagnosis of unexplained physical complaint and involvement (self or any family member) in delivering faith or other type of healing practices were excluded from this study as they may independently influence PB, EM, patient satisfaction and treatment adherence. Patients with an ICD 10 DCR diagnosis of mental retardation and dementia were also excluded due to reliability issues. All participants were evaluated by a qualified physician and a qualified psychiatrist. Patients who satisfied the selection criteria were administered the assessment tools (Kannada translation) in the following order:

1. Socio-demographic and clinical proforma designed for this study: this proforma assess Gender, Occupation, Religion, Education, Marital status, Family type, Domicile, Family history of mental illness, Knowledge of treatment option, Source of information, Knowledge of the course of illness, Preferred method of treatment, Referred by, and Treatment type sought before.

2. Revised Paranormal Belief Scale (RPBS)<sup>11</sup>: this scale was used to assess the paranormal beliefs. The scale has 26 items, seven point rating (1-7) for each item, 7 subscales (Traditional religious belief, Psi, Witchcraft, Superstition, Spiritualism, Precognition, Extraordinary Life Forms) with a possible score of maximum 182 and minimum 26. The sum of all items is indicative of a general tendency to adopt a paranormal belief, while subscales can be used to measure specific dimensions of paranormal belief.



3. Mental Distress Explanatory Model Questionnaire (MDEMQ)<sup>6</sup>: MDEMQ was used to assess the patients' conceptualization of mental illness. This questionnaire consists of 45 items with 5 points (1-5) item rating. The items can be clustered into four explanatory categories; Western Physiology, Non-Western Physiology, Supernatural and Stress. Possible minimum score is 45 and the maximum score is 225.

4. Morisky Medication Adherence Scale (MMAS)<sup>12</sup>: eight items MMAS was used to assess medication adherence. Each item can be rated at 2 points (0-1). Adherence is low when the score is > 2, medium when the score is 1-2, and high when score is 0.

5. Short Assessment of Patient Satisfaction (SAPS)<sup>13</sup>: SAPS was used to assess the level of satisfaction. This scale has 7 items, with a 5 point rating (0-4), and possible scores of maximum 28 and minimum of 0. Lower score indicates less satisfaction while higher score indicate greater satisfaction.

SPSS Version 16 was used for Statistical analysis. For categorical data, frequency and percentage were used while continuous data were expressed with mean and standard deviation. After analysis of distribution of data, relationships between variables were analysed using ANOVA and linear regression analysis. For all the test significance threshold was set to  $p < .05$ .

## Results

### Demographic characteristics

In this study majority of the patients were married Hindu, literate, unemployed, belonged to the urban area having nuclear family. The majority preferred the Allopathic method of treatment (mainstream medicine) and health professionals were the major source of information about their illness (Tables 1 and 2).

Table 1 reveals mean and standard deviation of scores on age, duration of illness, MDEMQ (Mean 95.44, SD  $\pm$  22.18), MMAS (Mean 7.3, SD  $\pm$  1.6) and SAPS (Mean 8.13, SD  $\pm$  3.58).

### Relationship of paranormal belief with demographic and clinical variables

Level of paranormal beliefs was analysed using descriptive statistics and ANOVA. The sample had a mean score of 83.96 (SD  $\pm$  23.91) on RPBS. Variables that had a statistically significant group difference on the score of RPBS were domicile status ( $p < .05$ ), psychiatric diagnosis ( $p < .001$ ), method of treatment sought before ( $p < .001$ ) (Tables 1 and 2).

### Relationship of paranormal belief with explanatory model, treatment satisfaction, medication adherence and demographic variables

A linear regression analysis was conducted (using the enter method) to see if any demographic variables, MDEMQ score, MMAS score and SAPS score can predict the value of RPBS (Table 3). Four variables explained 35.4% of the variance ( $R^2 = .383$ , Adjusted  $R^2 = .354$ ,  $F = 13.044$ ,  $df = 4$ ,  $p < .001$ ). These variables were total score of MDEMQ (Beta = .308,  $t = 3.435$ ,  $p < .001$ ), total score of MMAS (beta = .357,  $t = 3.716$ ,  $p < .001$ ) and magico-religious treatment received earlier (beta = .306,  $t = 3.352$ ,  $p < .001$ ) and SAPS. However the total score of SAPS did not significantly predict the value of total RPBS (beta = -.007,  $t = -.079$ ,  $P = .938$ ).

A linear regression analysis was also conducted to know if subscales of MDEMQ can predict the participants' scores on RPBS (Table 4). Two subscales that explained 43.5% of the variance ( $R^2 = .435$ , Adjusted  $R^2 = .408$ ,  $F = 16.185$ ,  $df = 4$ ,  $p < .001$ ) were non-western physiology (beta = .291,  $t = 2.269$ ,  $p < .05$ ) and supernatural subscale (beta = .416,  $t = 3.454$ ,  $p < .001$ ).

## Discussion

### Demographic and clinical characteristics

We observed that the majority of patients had a preference for the allopathic method (mainstream medicine) of treatment. This was a contradictory finding to the general belief that Indians have an inclination for magico-religious treatment. Probably this reflects an increased popularity and acceptance of mainstream medicine over the years<sup>14-16</sup> due to its higher efficacy (compared to other methods of treatment) and its role in controlling the disorders associated with high stigma in Indian culture. Medical practitioners trained in mainstream medicine are now the first caregivers than the faith healer, though in some part of India vice versa is true<sup>17-19</sup>.

### Level of paranormal belief

In this study, we observed a higher level of PB (83.96, SD  $\pm$  23.91) as compared to other study who reported lower levels of PB (58.46, SD  $\pm$  24.57) from India<sup>1</sup>. This could be due to difference in demographic characteristics and the presence or absence of mental illness in the study sample<sup>5</sup>. Dharma (as essence of eternal life, moral law and righteousness); Veda, Yoga and Sidhi (teaching of psychokinesis); and Vastushastra, Numerology, and Palmistry are supported by Indian culture that may maintain paranormal beliefs<sup>20-23</sup>.

**Table 1.** Clinical characteristics

Variables	Minimum	Maximum	Mean	Std. Deviation
Total duration of illness	1.00	28.00	6.2	5.9
Age	15.0	65.0	35.9	11.6
Total score on Morisky medication adherence scale	1.0	8.0	7.3	1.6
Total score on Short Assessment of Patient Satisfaction	2.0	19.0	8.3	3.3
Score on Mental distress explanatory model questionnaire	59.0	191.0	95.4	22.1
Score revise paranormal belief scale	27.0	121.0	83.96	23.91
Traditional religious belief	6.0	27.0	18.57	5.21
Psi	4.0	19.0	12.44	3.53
Witchcraft	4.0	21.0	10.85	5.03
Superstition	3.0	19.0	12.67	4.05
Spiritualism	4.0	21.0	11.74	5.37
Precognition	4.0	23.0	14.48	4.88
Extraordinary life forms	1.0	5.0	1.97	1.26

**Table 2.** Relationship of paranormal believe with sociodemographic & clinical variables

Variables	n	%	Mean	Std. Deviation	Sum of Squares	df	Mean Square	F	Sig.	Eta squared
Gender										
Male	40	44.9	83.80	22.96	2.00	1	2.00	.003	.953	.000
Female	49	55.1	84.10	24.88						
Occupation										
Employed	57	64.0	84.00	24.82	.180	1	.18	.000	.986	.000
Unemployed	32	36.0	83.90	22.58						
Education										
Illiterate	14	15.7	90.50	18.26	3326.1	6	554.3	.968	.452	.066
Primary	11	12.4	85.27	28.42						
Middle	6	6.7	96.83	22.48						
High school	22	24.7	78.90	21.42						
Higher secondary	22	24.7	86.18	25.42						
Graduate	12	13.5	75.66	28.28						
Post graduate	2	2.2	73.50	4.94						
Marital status										
Married	64	71.9	84.48	21.05						
Single/divorced/widow	25	28.1	80.34	30.72	1571.6	2	785.8	1.387	.255	.031
Family type										
Nuclear	74	83.1	81.95	25.06	1768.2	1	1768.2	3.169	.079	.035
Joint	15	16.9	93.86	13.84						
Domicile										
Rural	36	40.4	91.08	20.92	3062.0	1	3062.0	5.638	.020	.061
Urban	53	59.6	79.13	24.77						
Religion										
Hindu	75	84.3	83.14	24.41	779.2	2	389.6	.676	.511	.015
Muslim	14	15.7	86.76	21.27						
Preferred treatment										
Magico-religious	16	18.0	86.75	27.49	151.1	1	151.1	.262	.610	.003
Allopathic	73	82.0	83.35	23.21						
Psychiatric diagnosis										
F10&20	18	20.2	71.51	21.0	8320.8	3	2773.6	5.615	.001	.165
F30	58	65.2	82.82	21.87						
F40	13	14.6	69.23	26.64						
Knowledge of course										
Continuous	24	26.9	84.91	23.24	928.6	3	309.5	.533	.661	.018
Recurrent	56	62.9	84.67	23.84						
Other	9	10.2	75.44	27.86						
Family history										
Absent	69	77.5	83.78	22.61	10.3	1	10.3	.018	.894	.000
Present	20	22.5	84.60	28.59						
Source of information										
Media	2	2.2	83.50	17.67	412.8	3	137.6	.234	.872	.008
Family & society	27	30.3	83.74	22.16						
Health professionals	60	67.5	84.42	25.19						
Knowledge of treatment option										
Pharmacological only	64	71.9	85.85	22.58	1257.5	3	419.1	.726	.539	.025
Pharmacological & Psychological	21	23.6	78.04	27.56						
Magico-religious	3	3.4	89.66	29.28						
Ayurvedic	1	1.1	70.00							
Referred by										
Self	15	16.9	78.40	27.89	2344.2	3	781.4	1.385	.253	.047
Family members	60	67.4	87.36	21.15						
Health professionals	14	15.7	80.50	29.44						
Method of treatment sought before										
Magico-religious	38	42.7	96.39	18.58	10730.1	2	5365.0	11.658	.000	.213
Allopathic	49	55.1	74.08	23.62						
Ayurvedic	2	2.2	90.00	4.24						

**Table 3.** Relationship of paranormal belief with explanatory model, treatment satisfaction, medication adherence

Model	Variables	Unstandardized Coefficients		Standardized Coefficients		Sig.
		B	Std. Error	Beta	t	
1	(Constant)	3.470	14.674		.236	.814
	Magico-religious treatment received	14.725	4.392	.306	3.352	.001
	Total MDEMQ score	.332	.097	.308	3.435	.001
	Total MMAS score	1.971	.530	.357	3.716	.000
	Total SAPS score	-.049	.624	-.007	-.079	.938

$R^2 = .383$ , Adjusted  $R^2 = .354$ ,  $F = 13.044$ ,  $df = 4$ ,  $p < .001$ .

Dependent variable = RPBS Score.

**Table 4.** Relationship of paranormal belief with subscales of MDEMQ

Model	Variables	Unstandardized Coefficients		Standardized Coefficients		Sig.
		B	Std. Error	Beta	t	
1	(Constant)	69.170	8.991		7.694	.000
	Stress	-.473	.253	-.199	-1.874	.064
	Western Physiology	-.551	.522	-.121	-1.056	.294
	Non-Western Physiology	3.172	1.398	.291	2.269	.026
	Supernatural	.738	.214	.416	3.454	.001

$R^2 = .435$ , Adjusted  $R^2 = .408$ ,  $F = 16.185$ ,  $df = 4$ ,  $p < .001$ .

Dependent variable = RPBS Score.

The result revealed that domicile status had a group difference on the score of RPBS. In comparison with rural, urban status gives an ample opportunity for education and exchange of scientific information that help people to update their knowledge and modify their belief<sup>1,24</sup>. We observed that diagnosis had a significant group difference on the score of RPBS. This finding has some similarity with the observation made by others, who reported variation in belief with the diagnosis<sup>5,25</sup>. In the absence of evidence of cause (as seen with physical disease), people tend to attribute supernatural forces for symptoms of mental illness, and such beliefs are maintained by prevalent witch doctors in rural India<sup>24</sup>. Group difference on the score of RPBS was also observed with the type of treatment received in the past for the mental illness. The majority of the participants had received mainstream treatment (Allopathic), magico-religious and Ayurvedic method of treatment before participating in this study. This finding is congruent with common explanatory models prevailing in Indian about an illness (medical and supernatural model)<sup>3,26,27</sup>. It appears that depending upon the explanatory model of illness, patients sought a treatment method<sup>26</sup>. Those with a medical model continued with the next level of treatment (primary care to tertiary care) while those with non-medical model changed their strategy and shifted to the medical model after an inadequate response to the treatment<sup>19</sup>.

#### Relationship of paranormal belief with explanatory model, treatment satisfaction, medication adherence and demographic variables

Consistent with our hypothesis, the level of paranormal beliefs had a significant positive association with Non-Western Physiology & Supernatural subscales of MDEMQ in this study. This may be because both are rooted in the collective explanatory model (a model shared by most members of the Indian community). PB explains mostly personalistic cause (e.g. religious, supernatural) while MEMQ explains both personalistic and naturalistic causes (situations, psychobiological). Indians attribute more of a personalistic cause such as God's will, supernatural force and astrological cause for

suffering or problems<sup>28</sup>. Prevalent astrological beliefs such as Shani (Saturn), Rahu (the ascending node of the moon) and Ketu (descending node of the Moon) is often believed to determine good or bad happening in daily life. Ayurveda, an ancient method of treatment (that is prevalent in India since centuries) describes three types of life forces (tridoshas): pitta dosha (fire and water), kapha dosha (water and earth) and vata dosha (space and air). Excited Vayu (gas) of the vata dosha has been mentioned as causes of mental illness<sup>29,30</sup>. Some disorder such as Dev-unmada (psychological disturbances due to God), Bhoot-unmada (due to ghost) described in Ayurveda attributes supernatural force as the cause of mental illness<sup>30</sup>. Other indigenous method of treatment such as faith healing & Jadi-Buti also supports the supernatural cause of mental illness. Lagna and Raasi are common horoscopic supernatural factors often attributed to determine the health, fortune or misfortune depending upon the astrological status, such as the position of planets & the moon<sup>31</sup>. The significant association (positive) of the past magico-religious treatment and paranormal belief indicates the congruence of belief and treatment.

Consistent with our hypothesis, we found a statistically significant negative association of paranormal belief with medication adherence. This is consistent with other reports, that supernatural belief is associated with unfavorable compliance<sup>26,32</sup>. Those who subscribe to a supernatural cause of mental illness, their decision to continue medication may be influenced by belief, they may have a negative attitude toward medication, and more likely to go with the idea that magicoreligious rituals are helpful<sup>2,3</sup>. Since medical treatment is based on the medical model of illness, which may not go with a patient's model of illness the patient may be less adherent to medication.

We could not find any association of paranormal belief and satisfaction, and this is not consistent with our hypothesis. Possible reason could be that patient's belief alone may not determine the satisfaction, but other factors such as doctor patient relationship, quality of service provided and improvement in symptoms are important determinants of satisfaction<sup>33</sup>.

## Conclusion

Based on the finding of this study, it may be concluded that level of paranormal beliefs varies with some demographic variables. Levels of paranormal beliefs is positively associated with non-western physiology and supernatural dimension of explanatory models and negatively associated with adherence in patients with mental illness in remission availing services at tertiary care.

Though our hypothesis appears to be partly true, this study finding should be interpreted in the context of Indian culture. The limitations of this study were a heterogeneous patient group, no control population for comparison, small sample size; purposive sampling method and knowledge about the illness was not assessed (especially biomedical model). Further studies are needed to address the limitations of this study.

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## Conflict of interest

Nil.

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# Deconstructing the myth of Pasewalk: Why Adolf Hitler's psychiatric treatment at the end of World War I bears no relevance

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## Abstract

**Background:** Even more than 70 years after the end of WW II, questions regarding the personality of dictator Adolf Hitler (1889-1945) remain unresolved. Among them, there is a focus on the problem of his state of mental health, in particular on the possible relevance of the medical treatment he received for a war injury at the military hospital of the small German town of Pasewalk in the last days of WW I. Some authors have come to postulate a profound change of his personality due either to a psychic trauma suffered or a hypnotic therapy he supposedly underwent for curing a hysterical blindness. **Objectives:** The assumptions about Hitler's war injury which rely on only two significant sources shall be assessed for their validity. **Methods:** Existing historical sources and inferred hypotheses will be discussed in the light of alternative interpretations. **Results:** The mentioned suppositions reveal their highly arbitrary character: neither a hysterical blindness of Hitler's nor a hypnotic treatment at Pasewalk military hospital can be substantiated. **Discussion:** Given the fact that Hitler's medical sheet is most likely irrevocably lost, the authors plea for the acceptance of the limitations of historical research, even more so since the occurrences in Pasewalk lack any deeper importance for a historic assessment of Hitler's personality.

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**Keywords:** Adolf Hitler, Edmund Forster, Ernst Weiß, Pasewalk, hysterical blindness.

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## Introduction

Though more than 70 years have passed since the end of World War II, that outburst of extreme violence in Central Europe remains somewhat enigmatic: how could a country like Germany, which considered itself among the world's most civilized nations, become the perpetrator of such extreme destructiveness? One of the explanations easily at hand points to the person of Adolf Hitler (1889-1945) and his charismatic, even hypnotic aura. But then again, another problem arises: how could such a mediocre figure, a failed landscapist, turn into such a powerful and highly influential creature?

Here is where some authors make the assumption that psychiatry plays a role, stating that Hitler underwent a profound personality alteration at the end of World War I, when he fought with the rank of lance corporal in a Bavarian infantry division. They postulate that the presumed change was the result of either a severe psychic trauma suffered when his unit was attacked with mustard gas in the trenches close to the Belgian town of Ypern in October 1918, or from the psychiatric treatment he supposedly received afterwards in the Northern German town of Pasewalk, where he was a patient at the local military hospital from October 21 to November 19 of that year. The incident on the Western front, Hitler's temporary blindness, and his medical treatment in the Pomeranian town can be considered proven facts. However, the speculations that rise from them cannot claim any reliable evidence in their favour. Yet they spread rapidly, even finding their way into Brazilian and Portuguese scientific literature<sup>1-6</sup> and thus creating what the authors of this paper have come to call the "myth of Pasewalk". This study aims to acquaint the reader with the main arguments brought forth by the advocates of this delineated narrative, to scrutinize their reliability and, finally, to reveal their highly speculative and implausible nature. And, while it cannot prove the opposite, this study makes a strong plea for the intellectual honesty of accepting the limitations of historical research.

## State of the discussion in general

A vast number of studies dealing with questions of Hitler's overall health have been published in English and German. Some of them

come from his followers or ex-doctors and must be read with due caution<sup>7-9</sup>, but there are also more recent studies<sup>10-12</sup>.

When focusing on Hitler's mental health, we find some remarkable statements already made by renowned German psychiatrists of the time. University professor Oswald Bumke (1877-1950), teaching in cities such as Rostock, Leipzig, Munich and then German Wrocław, claimed to have hinted strongly at Hitler when lecturing on prestige-craving ("geltungsbedürftig") hysterical personalities and schizoid, autistic fanatics, as the terminology of the time called it<sup>13</sup>. The best-known statement from the time comes from Karl Willmanns (1873-1945). He is said to have explained Hitler's 1918 blindness as a hysterical reaction in a 1933 lecture<sup>14-16</sup>. Supposedly because of this, he lost his position as a full professor at Heidelberg University. A similar story has been told about Hans Gruhle (1880-1958). Even up to the present, psychiatrists maintain the hypothetical diagnosis of a hysteria<sup>17</sup>.

Literature provides an even wider spectrum of mental disorders Hitler may have suffered from, ranging from a paranoid personality accentuation with ideas of persecution and grandeur over a narcissistic and hysterical psychopathy including hysterical blindness or paresis respectively, or, alternatively, a schizoidia up to a paranoid schizophrenia with hallucinations of cadaveric poison, coenesthesias, bacillophobia and delusions of persecution and blessedness. The pathographic compilation "Genie, Irrsinn und Ruhm" ("Genius, insanity, and glory") provides a comprehensive survey of these psychiatric hypotheses, as well as of a number of physical diseases like Parkinson's, encephalitis and a syphilis with ocular symptoms<sup>18</sup>; see also the recent overview<sup>19</sup>. However, all of these vast allegations lack any objective basis in terms of reliable historical documents.

## Hitler in Pasewalk

In recent years, the debate has concentrated on a brief episode in late 1918, when the young Adolf Hitler, a low-ranking soldier in the German army at the time, received medical treatment at the military reserve hospital in the Pomeranian town of Pasewalk, about 150 km north of Berlin. In 1976, the American historian Rudolph Binion made

the assumption that the German psychiatrist Edmund Robert Forster (1878-1933), then chief surgeon in service of the German imperial navy, but in civil life first senior doctor at the Berlin University Hospital Charité, and from 1925 onwards professor at Greifswald University Hospital, had been in charge of Hitler's treatment and that this and the fear of reprisal was the reason for Forster's subsequent suicide<sup>20</sup>. By applying a so-called psycho-historical approach, developed by Lloyd deMause in the 1970s, Binion postulated that, in the last days of WW I, Hitler turned into a charismatic leader personality and a fervent anti-Semite, demonstrating characteristics he never had before. Binion holds Edmund Forster's supposed "miraculous cure" responsible for this alteration.

This study focuses on the validity of this hypothesis, which relies almost exclusively on two very special documentary sources, given that Hitler's medical charts are still missing. The first is a US Navy intelligence report from March 1943, reporting a testimony given in Reykjavik by the Jewish refugee Karl Kroner (1878-1954), who had worked as a neuropsychiatrist in Berlin and claimed to have been present at Hitler's medical examination. The report, entitled "ADOLF HITLER'S BLINDNESS (A psychological study)"<sup>21</sup> draws a connection between Hitler, Forster (though incorrectly referring to him as "Förster") and the diagnosis of hysteria. Additionally, Kroner accused Hitler not only of murdering Edmund Forster because of what he knew about his former patient, but also of killing his own niece, Geli Raubal, for refusing to submit to her uncle's sexual perversions. Furthermore, Kroner denounced Hitler as a coward in war, undeserving of his military decorations. Unfortunately, Kroner died too soon for historians to interview him about his allegations after the war, but the British neuropsychologist David Lewis had the opportunity to talk to his son, who provided some insight into his father's situation at the time he delivered this testimony. Having barely escaped a German concentration camp, Karl Kroner found it difficult to make a living in Iceland because his medical diploma wasn't recognized by the local authorities<sup>22</sup> (pp279-81; in Portuguese: 3 p282). Thus, he may have tried to accelerate his visa process to the US by making himself irreplaceable. Given the obvious exaggerations and distortions in his narrative and the tremendous pressure he was under, he may serve as a witness for a number of things – but certainly not for such a crucial aspect of history as the one in question here. After all, Kroner did nothing but repeat rumors that were circulating in the academic world at that time<sup>14</sup> (p75). This leads to the second, and even less "documentary" piece of evidence Binion and subsequently various other present: a novel, written by the desperate emigrant author Ernst Weiß (1882-1940). Given that all of Binion's successors<sup>1-6,22-26</sup> emphasize its significance, the novel shall be closely examined below.

### Fact or fiction – Fiction for fact

Weiß came from a unique cultural context that, like so many others in Europe, has ceased to exist: the ambience of German-speaking Jewish intellectuals and artists in an area that now belongs to the Czech Republic. A relatively well-known author in his time, writing predominantly in the sober style of New Realism (Neue Sachlichkeit), which became popular in German language literature after the loss of World War I, he was friends with Franz Kafka (1883-1924), with whom he shared this specific background<sup>27</sup>. Born in Brno, Moravia, Weiß began studying medicine in Prague and then moved to Vienna, where he may have attended Sigmund Freud's lectures<sup>28</sup> p15, <sup>29</sup> p136, <sup>30</sup> p143, <sup>31</sup> p186, <sup>32</sup> p10, <sup>33</sup> p18). He specialized in surgery, working with some of the era's leading authorities, such as Theodor Koch (1841-1917) in Bern, the first surgeon to win the Nobel Prize. Although his interest in literature eventually got the upper hand and led him to give up his medical work in 1920, his entire oeuvre shows his profound concern with the psychological and ethical intricacies of his original profession<sup>33,34</sup>, and mental health issues in particular<sup>35</sup>. He fled from the Nazis when Hitler seized power and settled under miserable circumstances in Paris, where he committed

suicide the day German troops invaded the city in 1940. His last novel *The Eyewitness* (German original: *Der Augenzeuge*, in Portuguese *A Testemunha Ocular*), written in 1938 under tremendous pressure, had fallen into oblivion until it was published posthumously, 25 years later<sup>36</sup>, and was subsequently translated into English, Spanish and French. Like many of his other novels, it consists of a fictitious (auto) biography of a physician, in this case a psychiatrist. Similar to Weiß's experience, the protagonist and narrator serves in the war as a physician<sup>37</sup> (pp11,107-8). By the end of the war, he is assigned the duty of providing special care for the mentally afflicted in the psychiatric department of Pasewalk military hospital, where, among his patients, he encounters a sleepless, rambling, unappealing anti-Semite called A. H., ill with mild conjunctivitis and a psychogenic blindness. Since the young doctor himself had suffered long-lasting humiliation both in his private and professional life, he sees his chance to excel, and attempts to cure his patient by applying a strong suggestion to him: possibly being as extraordinary a man as Jesus or Mohammed, A.H. might be able to overcome his ailment through pure willpower – in order to fulfil his destiny as a savior of defeated Germany<sup>36</sup> (p118). The cure turns out to be a success, and events take their well-known course.

The novel has been frequently misinterpreted with claims of it being of documentary value and representing real occurrences in that specific period of Hitler's life. Yet there is no historical evidence whatsoever that Weiß had privileged access to Hitler's lost medical files or any other source of in-depth information<sup>38</sup> (p224). Quite the contrary: a careful reading of *The Eyewitness* reveals the various efforts Weiß took with the aim of making it very clear that he was by no means to be confused with the fictitious narrator of the story<sup>37</sup> (p113). A good look at his other novels emphasizes the literary nature of the book, as many of them deal with questions of power and helplessness in medical affairs<sup>39</sup> (pp36-7). The assumption that Weiß's novel provides something like a docu-fiction for potentially crucial days in Hitler's life can neither be proven nor refuted<sup>33</sup> (p99,6). It simply needs to be taken as purely hypothetical.

### Critical voices

In the light of the insufficiency of the provided sources, we advocate being extremely careful about a possible mental disorder on Hitler's record<sup>39,40</sup>. No one has been able to come forth with reliable historical material for the allegations made, whether on the making of Ernst Weiß's novel or on Edmund Forster's biography. We also cannot be sure that Forster was present at Pasewalk at all during Hitler's treatment, nor do we know of any positive proof that his involvement with Hitler could be considered a motivation for his suicide. Quite the contrary: documentary sources at Greifswald University provide strong evidence that Forster fell victim to a personally motivated attack by a former member of staff and subsequently was dismissed by Nazi authorities – a chain of events that caused the ambitious scientist to fall into a deep depression and take his own life<sup>41</sup>. Another open question continues to be how Forster is supposed to have transferred information on Hitler and his medical sheet to Ernst Weiß in Paris<sup>39,40</sup>. The aforementioned arguments that construe a link between Hitler's hypothesized treatment in Pasewalk and Edmund Forster's death are based on vague evidence, the sources for which can most likely be traced back to Forster himself. These aspects have been prudently challenged before by Maranhão-Filho and da Rocha e Silva<sup>6</sup>.

After all, the evidence provided by Forster's relatives as insinuated by Lewis can hardly be considered convincing: the only thing the son Balduin, a thirteen-year-old boy at the time of his father's suicide, remembers for sure is his mother's statement saying that Forster had assessed Hitler and called him a hysteric<sup>42</sup>. Yet the context of this assessment and whether it involved some kind of therapy remain unknown.

Hitler's medical sheet, the only potentially conclusive document, no longer exists. The above-mentioned US intelligence dossier from 1943, discovered in the 1970s by Hitler's North American biographer



The image shows two pages of a handwritten medical record from 1918. The left page is a patient list with columns for name, denomination, marital status, diagnosis, and dates. The right page is a detailed medical record for a patient, including symptoms, diagnosis, and treatment notes.

**Figure 1.** Excerpt of the medical book (Hauptkrankenbuch) of Pasewalk (Source: Krankenbuchlager Berlin, Sammelurkunde Nr. 28103, HKB Res.-Laz. Pasewalk, p291); see row 2 for the only source available on Hitler's 1918 medical treatment: e.g. col 5 for his name, col 9 for his denomination (catholic), col 11 for his marital status (ledig = unmarried), col 14 for the diagnosis (Gasvergiftung = gas poisoning); compare informations for the blackened patient in the row above: Grippe = influenza which indicates that Hitler was not being treated in a specialized department), col 15 for date of entry, col 18 for date of dismissal.

John Toland<sup>43</sup> in the National Archives in Washington, at first seemed to shed light on Hitler's stay at Pasewalk. But as Katz remarked critically shortly afterwards, Kroner did not go beyond "reproducing" well-known opinions (of Forster's) – German psychiatrists were already discussing hysteria as a possible diagnosis of the self-proclaimed dictator at that time<sup>44</sup>. Based almost exclusively on this intelligence report as the only historical source, later authors such as Post (1998), Lewis (2003), Horstmann (2004), and Köpf (2005)<sup>22-24,26</sup> created a myth, the development and continuation of which have been investigated previously<sup>40</sup>.

Since the relevant sources are missing a factual consideration of Hitler's stay at Pasewalk military hospital, we are inevitably led to the conclusion that the issue of his alleged hysterical blindness simply cannot be resolved. Nor can the recent contributions made by historians Thomas Weber<sup>44</sup> and Henrik Eberle<sup>45</sup> change anything regarding the issue. Calling upon Lewis, Köpf and Horstmann, Weber presented a new narrative by introducing the German neurologist Otfried Foerster (1873-1941) as another colporteur of a mental disorder as yet unmentioned in academic discourse, but who was supposed to have had knowledge of Hitler's medical file<sup>44</sup> (p295). However, shortly afterward, Eberle proved him wrong by pointing out the administrative pathways of Pasewalk's files and presenting for the first time an excerpt of a so-called medical book used there in 1918 for a comprehensive documentation of all patients in the ward<sup>45</sup> (pp44-7). It is stored in the central archives of Berlin-Buch and indeed represents a quite specific document of the medical treatment performed in Pasewalk military hospital. For lance corporal Adolf Hitler, it definitively and exclusively shows the diagnosis of gas poisoning (Gasvergiftung) (Figure 1). This diagnosis is identical with what other documents from the Federal Archives Berlin reveal, which have been published by David Lewis in this journal<sup>3</sup> (Figure 1) some years ago.

This, of course, raises the question as to why anyone would register Hitler, a totally unknown, low-rank soldier at the time, under a false diagnosis. Supporters of the "hysteria hypothesis" still owe us an explanation for this. Eberle, on the other hand, emphasized that, contrary to their repeated claims, Pasewalk was by no means a specialized institution for psychiatric patients and that "gas poisoning" is one of the more frequent diagnoses to be found in the medical book, whereas some other patients were categorized as "nervenkrank" (literally "of ill nerves", a common expression at the time for the mentally disordered)<sup>45</sup> (p46).

## Conclusion

The reticence as shown by the majority of historians concerning Hitler's stay at Pasewalk military hospital continues to be more than appropriate. After all, with the medical sheet missing, there is no way of substantiating that he was ever treated by Edmund

Forster. Moreover, even if it were true, it wouldn't signify more than a marginal episode in Hitler's biography for a historical assessment of his person. Instead of adding to our knowledge by presenting new sources, recent contributions have publicized a myth that seems problematic in two ways: on one hand, it reduces Edmund Forster to having been Hitler's therapist, which doesn't do justice to his personality and achievements. On the other hand – and this weighs more heavily – it diminishes and relativizes Hitler's responsibility for his acts. In the opinion of the historian Ian Kershaw, it minimizes the complex developments that led to the mass murder of Jews during the Second World War to the alleged trauma of one single person in 1918<sup>46</sup> (p101). And, last but not least, this indirectly follows the logic of Hitler's "Mein Kampf", where he describes the shift his life allegedly took during his hospital stay, including his decision to become a politician<sup>47</sup> (pp221,225). This implicates the risk of continuing the Myth of Hitler (the so-called "Führer-Mythos"). In conclusion, it remains to be said that Hugh Redwald Trevor-Roper's\* 1947 statement remains valid: "Whatever Hitler's psychological condition may have been, [...] on such a subject, and in so unique a character, it would be imprudent to speculate"<sup>48</sup> (p53).

## Declaration of interest

There are no conflicts of interest.

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\* Hugh Redwald Trevor-Roper (1914-2003), an intelligence officer in World War II for British Secret Intelligence Service Military Intelligence Section 6 (SIS MI 6) and a professional historian, was assigned the task of investigating the final days of Hitler's life and the closer circumstances of his death. In 1947 he published his results in his book "The Last Days of Hitler".

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# Ten years after the FDA black box warning for antidepressant drugs: a critical narrative review

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## ABSTRACT

**Background:** The United States Food and Drug Administration (FDA) has warned about the increased suicidality risk associated with the use of selective serotonin reuptake inhibitors (SSRI) and venlafaxine in children and adolescents. **Objectives:** To critically appraise the available evidence supporting the FDA Black box warning concerning to the use of antidepressants in child and adolescents. **Methods:** A critical review of articles in Medline/PubMed and SciELO databases regarding the FDA Black box warning for antidepressants, and the impact of FDA warnings on antidepressant prescriptions and suicide rates. **Results:** The warning was based on surveys that did not report either cases of suicide nor a significant difference supporting an increased suicidality rate. The concept was defined in an ambiguous way and there is currently more available evidence to support such definition. The use of SSRI and venlafaxine has been associated to lower suicidality rates, but the prescription fall due to the warning increased suicide rates. **Discussion:** Suicidality is an inherent feature of depressive disorders so it would be desirable to consider how much of the phenomenon may be attributed to antidepressants *per se*. It would be appropriate to consider that suicide rates might increase also as a consequence of the warning.

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**Keywords:** Antidepressants, serotonin uptake inhibitors, suicide, United States Food and Drug Administration.

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## Introduction

Approximately 2 to 3% of children and 6 to 8% of teenagers suffer from major depressive disorder, considered the main determinant of suicide, and a leading cause of death among teenagers<sup>1</sup>. In fact, depression is present among 46 to 64% of suicidal adolescents<sup>2-4</sup>; an increase of over twenty times the risk of completed suicide<sup>5</sup>. Thus, suicidal conduct is included in the fifth edition of the Diagnostic and Statistical Manual of Mental Disorders as a diagnostic criterion to the affective disorders<sup>6</sup>.

While a positive correlation exists between the risk of suicide and the severity of affective disorders, subsequent treatment plays a role as a preventive measure. The introduction of new antidepressants (AD), particularly selective serotonin reuptake inhibitors (SSRI) have been a useful mechanism in the rehabilitation of depression, with some countries observing a decrease in suicide rates<sup>7</sup>.

Until the 1980s, depression was primarily treated with AD such as monoamine oxidase inhibitors and tricyclics. Since overdoses of these drugs are potentially lethal, in some cases they were even used as a way to carry out suicidal acts, a situation still worrisome among prescribers, and which opened a discussion surrounding suicidality<sup>8-10</sup>. Nevertheless, the notion that AD precipitate suicide in depressed people was noted by Kielholz and Battagay as early as 1958, relating it to “the rollback phenomenon”, which describes the risk associated with these medications in mobilizing severely depressed patients to attempt suicide as a consequence of psychomotor improvement during the first period of therapy, while still affectively impaired<sup>11</sup>.

The SSRI do not escape from inclusion in the discussion of suicide, on the grounds that Teicher *et al.* reported six cases of patients with suicidal ideas being treated with fluoxetine, highlighting that none had presented such phenomenon previously<sup>12</sup>. That report induced the United States Food and Drug Administration (FDA) to create a panel of experts that gave neither recommendations nor warnings regarding the drug. This despite blind randomized trials

which repudiated a link between previously mentioned AD and increased suicidality<sup>13</sup>. Subsequently, in 2004, the FDA created a new advisory committee that led to one of the most contentious debates linked to suicide: the association between SSRI consumption and the inducement of suicide in children and adolescents<sup>14</sup>. The current FDA warning alludes to an increase in suicidality, a vague concept ranging from mere ideation to the completion of suicide<sup>10-11</sup>, despite the lack of epidemiologic evidence showing a relationship between suicide rates and the prescription of new AD medications<sup>15</sup>.

This intent of this review is to provide a critical viewpoint concerning the FDA warning, its supporting evidence in terms of therapeutic (AD prescription) and epidemiological outcome (suicide rates), the studies that support it, and the research that reinforces the usage of AD.

## Methods

An exhaustive bibliographic search was done through the available articles on the database PubMed, Cochrane Central, SciELO, and on specialized consulting texts, using key words as “suicide”, “adolescence”, “antidepressants” and “FDA”. The date range of the search was from January 1988 through June 2014.

## Results

### Black box warning issued by the FDA

In 2003, the United Kingdom’s Department of Health and the FDA issued a public warning against the use of paroxetine in people younger than 18 years old. In August of the same year, Wyeth Laboratories, manufacturer of venlafaxine (dual AD), suggested that physicians should cease prescribing the aforementioned drug in children and adolescents, due to low efficacy and the risk of increasing hostile feelings and suicidal tendencies. Yet in October,

the FDA issued research results involving citalopram, fluoxetine, fluvoxamine, nefazodone, sertraline and venlafaxine, recommending physicians to be cautious in prescribing an AD, with insufficient data supporting the thesis of suicide increase<sup>16</sup>. In December, the British Medicines and Healthcare Products Regulatory Agency suggested that physicians cease prescribing AD for people younger than eighteen (excluding fluoxetine), based on three investigations that cited an apparent increase in suicidal tendencies among children and adolescents<sup>17</sup>. However, the only one of these investigations that were published examined paroxetine versus placebo in the treatment of major depressive disorder, and reported a 3% increase of suicidality for the AD (fourteen out of 378 patients) versus 2.5% for the placebo (seven out of 285 patients), indicating no statistically significant difference<sup>18</sup>. Additionally, the definition of suicidality or suicidal tendencies used was confusing, and included self-harm, suicidal planning and ideation, attempt or completed suicide. Neither of reports stated any death from suicide<sup>18,19</sup>.

The FDA alert, called the Black Box warning, was based on short-term investigations (between four and sixteen weeks) that showed a higher risk of suicidal tendencies (4% on average), the double researched for a placebo, without any accomplished suicides reported<sup>20</sup>. Such action provoked a marked decrease in AD prescription<sup>21</sup>. The American Medical Association and the American Psychiatric Association subsequently warned of the potentially negative consequences that a decline in AD access could have on patients, who might otherwise be significantly benefited by their prescription<sup>22</sup>.

Finally, in October 2004, after assessing a total of 24 studies, the FDA extended the Black Box warning to encompass all AD prescribed to people younger than eighteen. Many of these investigations have not been unveiled to the scientific community, so their methodological rigour could be arguable<sup>23</sup>. In February 2005, the warning was modified by the FDA, stating in a more precise way that the usage of AD would produce an increase in suicidal tendencies and ideations, but not in accomplished suicides<sup>24</sup>. In Table 1<sup>19</sup> suicidal risks for some AD are described, whereas Table 2 shows the results obtained by the FDA when re-analyzing the related events with suicidal acts in young people under AD treatment. For general pathologies the relative risk of suicidal events ascended up to 1.95, without witnessing a statistical superiority with placebo in any case<sup>23</sup>.

**Table 1.** Suicidality rate according to antidepressant versus placebo

Drug	N	Suicidality <sup>a</sup> Antidepressant (%)	Suicidality <sup>a</sup> Placebo (%)	P value
Fluoxetine	458	3.6	3.8	0.9
Sertraline	373	2.7	1.1	0.45
Citalopram	418	8.9	7.3	0.4
Paroxetine	663	3.7	2.5	0.5
Venlafaxine	334	2	0	0.25

<sup>a</sup>Ideation, suicide attempt or self-harm. Modified from Brent y Birhamer<sup>19</sup>.

**Table 2.** Relative risk for suicidal behaviors on clinical trials according to antidepressant

Antidepressant	Major depression studies	All pathologies studies
Citalopram	1.37	1.37
Fluvoxamine	No research	5.52
Paroxetine	2.15	2.65
Fluoxetine	1.53	1.52
Sertraline	2.16	1.48
Venlafaxine XR	8.84	4.97
Mirtazapine	1.58	1.58
Nefazodone	No events	No events
Bupropion	No research	No events
Total	1.66	1.95

Modified Cheung et al.<sup>23</sup>.

In a systematic FDA review, 24 studies were included, of nine SSRI and other AD families, with a total of 4,582 patients with anxiety and affective disorders. Their results showed a relative risk of suicidal behavior and ideation, and self-aggressive behaviors associated with the usage of SSRI in major depressive disorder above 1.66 (CI 95%, 1.02 – 2.68), whereas the relative risk in the total of AD examined for all evaluated pathologies was 0.002 (CI 95%, 0.01 – 0.03). At the same time, the Treatment for Adolescents with Depression Study, a multicenter randomized trial testing the efficacy of AD, reported a statistically significant higher relative risk for SSRI<sup>25</sup>. Also, a systematic review conducted by Hetrick *et al*, which looked at nineteen trials of a range of newer AD compared with placebo, with a total of 3,335 participants showed that those treated with AD had lower depression severity scores and higher rates of response/remission than those on placebo. However, there was evidence of an increased risk (58%) of suicide-related outcomes for those on AD. Nevertheless, the study's trials excluded young people at high risk of suicide and many co-morbid conditions, so participants were likely to be less unwell than those seen in clinical practice. Participants had limited information about the risk of bias, high dropout rates and issues regarding measurement instruments and the clinical usefulness of outcomes, which were often defined differently across trials. The authors concluded that: 1) Due to the methodological limitations of the included trials in terms of internal and external validity, the results must be interpreted with caution; 2) The size and clinical meaningfulness of statistically significant results are uncertain; 3) Fluoxetine might be the medication of choice if a decision to use medication is agreed given the guideline recommendations<sup>26</sup>. On the other hand, an independent meta-analysis, that included 39 studies of AD, did not reveal any significant difference in the ideation or risk of attempted suicide, where one in 147 patients would demonstrate an increased risk<sup>27</sup>. Dubicka *et al*. pointed out similar findings about pediatric depression, examining the suicidal and self-aggressive conduct rates. Total frequency for these events was 4.8% with an AD and 3% with a placebo. When using heterogeneity-sensitive random effects analysis, the relative risk did not encounter statistical significance (RR = 1.58; p = 0.083)<sup>28</sup>.

In May 2012, the American Academy of Child and Adolescent Psychiatry made a public announcement stating that SSRI and other AD would be useful in the treatment of depression<sup>29</sup>, suggesting that therapies with AD continue, but include informing and explaining to the patient's family the existing warning. Moreover, it was advised not to apply such warnings to all children prescribed AD for depression based on: 1) evidence that all AD are efficient in major depression (mainly supported for studies in people above eighteen years old); 2) The study reporting exacerbation of suicidal events does not have sufficient statistical power. Most psychiatrists think that if, in some cases that statement might be true, it is preferable to monitor them rather than to suppress therapy; 3) According to the FDA, only 2% to 3% of children and adolescents increased their suicidal ideations or self-aggressive behaviors after using AD, having no reports of actual suicide; 4) The cost of patients' depression is higher than an increase of 2% in suicidality; 5) At the onset of ideation or suicidal behavior in the beginning of AD treatment, or after a dose adjustment, close surveillance of the patient is recommended during the first month. This is to provide a list of alarm symptoms to be alert to, such as the appearance of or increase in symptoms such as anxiety, panic attacks, psychomotor agitation, akathisia, insomnia, irritability, hostility or aggressiveness, impulsivity, hypomania, and mania. Despite the aforementioned facts, there is no causal link between these symptoms and ideation or suicidal behavior; 6) If the symptoms were severe, had an abrupt start or were not initially present, a change in the therapeutic plan should be considered<sup>30,31</sup>.

Finally, in 2014 the results of a retrospective investigation were published that considered 36,842 children from ages six to eighteen who used fluoxetine, sertraline, paroxetine, citalopram, escitalopram, and venlafaxine, all of which were included in the FDA warning (fluoxetine is the only allowed AD to be prescribed in children and

adolescents by FDA). The research stated that the rates of attempted suicide did not differ significantly among people who received fluoxetine and the other AD not recommended by the FDA<sup>32</sup>.

### Evidence that supports the usage of antidepressants

The individual risk of suicide is multifactorial, but depression stands out as an important factor. Considering that the methodological quality of the research on AD therapy has improved since the warning issued by the FDA, the aspects that support the usage of AD will be described<sup>33</sup>.

### Usage of antidepressants and decrease in suicidal rates

Despite the FDA warnings, there is much AD treatment that results in reducing suicide risks. Thus, in the "Antidepressant Age" (1960-1992) suicide rates associated with affective disorders were reduced from 6.3 per thousand at the beginning of the Twentieth Century to 3.3 per thousand<sup>34,35</sup>. In a study, Kuba *et al.* found that suicidal ideation, self-mutilation and suicide attempts decreased from 47.1% to 22.9% after three months of AD therapy in patients with a mean age of 15.4 years<sup>36</sup>.

The Centers for Disease Control and Prevention indicate that the suicide rate of teenagers increased throughout the 1970's and 1980's<sup>14</sup>, followed by its decrease of 20% to 30%<sup>37</sup> associated with the introduction of SSRI in 1988<sup>38-41</sup>. In fact, between 1985 and 1999, the suicide rate in the US decreased from 12.4 to 10.7 per 100,000, while the prescription of AD (predominantly SSRI) was quadrupled<sup>42</sup>. In North American teenagers, for every 1% increase in AD prescription, there was a decrease of 0.23 suicides per 100,000 annually ( $p < 0.001$ )<sup>43,44</sup>. Additionally, the 13% increase in SSRI sales in 27 countries during 1999 reduced suicide rates by 2.5% in those countries. Particularly in Sweden, suicide fell by 25%, which was likely associated with the 400% increase in AD sales there<sup>45</sup>. Likewise, Bramness *et al.*, through observations made in Norway between 1980 and 2004, found a significant relationship between the rise of non-tricyclic AD sales and the decreased suicide rates<sup>46</sup>. On the other hand, SSRI were introduced in Japan in 1999, increasing its AD prescription by 54%. According to the Japanese Ministry of Health, suicide rates after that year decreased by 6%<sup>47</sup>.

### Elapsed time in antidepressant treatment

Simon *et al.* established a temporal correlation between the usage of AD and suicide rates, reporting that the instances of suicide were significantly lower than the month prior to the beginning of AD treatment. In a total of 65,103 users of AD, the suicide risk during the acute phase of the treatment was one per 3,000, while the suicide attempt was one per 1,000, without a significant association between an increase in these risks and SSRI therapy. Meanwhile, the suicide risk of children and teenagers during the six months following antidepressant indication was 314 per 100,000, this being higher than the month previous to the prescription, showing a decrease immediately after onset of medication and a decline during its usage. While the estimated risk remained relatively stable over the next six months, their confidence intervals were wide, validating the lack to the number of observed events. Researchers assert that a significant increase of suicide risks or serious suicidal attempts existed after initiating SSRI therapy<sup>48</sup>. These findings were confirmed by Simon & Savarino, thus proving the reduction in the suicide rate after AD treatment<sup>49</sup>. Similarly, Jick *et al.* found a strong relationship between suicidal behavior and the time elapsed since the beginning of the AD therapy. Compared to a group that had accomplished ninety or more days of treatment, those who had between one and nine days were four times more likely to commit a non-fatal suicidal act, while those that completed between ten and twenty-nine days were three times more likely, and those who completed reached between 30 and 89 days of treatment only 1.5 times more likely. Moreover, those

who had between one and nine days of treatment were 38 times more likely to commit suicide, those treated between ten and twenty-nine days, were 5.1 times more likely, and finally, those that completed between 30 and 89 days, twice as likely<sup>50</sup>.

### Usage of particular drugs in high risk cases

Mines *et al.* compared a series of clinical parameters and morbidity records in patients assigned to fluoxetine, citalopram and venlafaxine. The venlafaxine patients group was considered to be the most severe due to their psychopathological history with increased suicide risk. Confirming that statement, those treated with fluoxetine and citalopram showed 2.75 times and 2.43 times less suicidal behavior respectively, compared to those who received venlafaxine<sup>51</sup>.

Venlafaxine has been one of the most criticized AD by the FDA. Nevertheless, it has considerable prestige among clinicians for the treatment of severe depression, due in part to its being often prescribed to high-risk groups. Patients assigned to venlafaxine had 6.19 times more risk of being hospitalized for depression compared to patients assigned to fluoxetine, and 4.34 times more than those who received citalopram. Regarding drug history, 27.7% of the group of venlafaxine patients received two or more AD during the last year, while among fluoxetine and citalopram users, 5.5% and 11% respectively, reported such use. Table 3 illustrates the relative risks for general characteristics and behaviors related to suicide for venlafaxine, fluoxetine and citalopram<sup>51</sup>.

### Low plasma levels of antidepressants and discontinuation

Several toxicological studies have revealed that a low proportion of suicide victims had considerable plasmatic levels of AD, indicating that a large number of suicides occurred in people that were depressed and receiving no treatment, failed to adhere to indications, or who had discontinued the medication<sup>52-55</sup>. Relatedly, Isacson *et al.* conducted post-mortem studies of suicides, and did not find plasmatic levels of SSRI in children below fifteen years old, while in the group between fifteen and nineteen years of age, the presence of SSRI was minor compared to other types of AD. This suggests that the hypothesis of suicide being induced by SSRI was not supported by autopsy data<sup>56</sup>, while also concluding that the increase in AD usage in Sweden had been parallel to a significant decrease in suicide rates there.

Meanwhile, Leon *et al.* studied 66 suicides which occurred in New York City between 1993 and 1998, the first six years that paroxetine was available in the United States. Subjects were under eighteen years of age, and chromatographic methods did not find, plasma levels of paroxetine<sup>57</sup>. In other research conducted in New York City which looked at 44 suicides among subjects less than eighteen years old between 1999 and 2002, in only one case (2,8%) was sertraline and bupropion detected during the autopsy, while in all others no presence of any other AD was found<sup>58</sup>. From a sample of 1,635 suicide victims, Marzuk *et al.* showed that 16.4% had a psychotropic prescription, thus reinforcing the above evidence. From the toxicological analysis only 17.9% of deaths by poisoning were found, finding AD in less than half of these victims<sup>59</sup>. So it is supported that the presence of AD in suicidal teenagers is low, contradicting any direct relationship between SSRI usage and child and adolescent suicide<sup>14</sup>. Regarding the discontinuance of AD, Yerevanian *et al.* found that the risk of committing suicide increased five times after suspending AD therapy, claiming that its use would serve as an anti-suicidal protective factor<sup>60</sup>.

### Discussion

"Suicidal tendencies" are central to the FDA's stance against AD prescription, which raises the question: Is suicide an AD side effect or attributable to one of the affective disorders? In lieu of attributing suicidogenic characteristics to AD, we must bear in mind that the regulatory associations do not consider the essential factors

**Table 3.** Risk for behaviors and general characteristics related to suicide according to antidepressant

Characteristics	Venlafaxine N = 27,096	Fluoxetine N = 134,996	Citalopram N = 52,035	Relative risk	
	N (%)	N (%)	N (%)	Venlafaxine versus fluoxetine	Venlafaxine versus citalopram
<b>Previous diagnosis</b>					
Major depressive disorder	20,574 (75.9)	57,918 (42.9)	27,883 (53.6)	4.10	2.8
Bipolar disorder	423 (1.6)	452 (0.3)	328 (0.6)	4.83	2.51
Schizophrenia	705 (2.6)	1,343 (1)	714 (1.4)	2.70	1.91
Anxiety disorder	10,210 (37.7)	28,788 (21.3)	15,560 (29.9)	2.13	1.45
<b>1-year previous event</b>					
Suicidal behaviors	260 (1)	474 (0.4)	207 (0.4)	2.75	2.43
Suicidal behaviors that required hospitalization	99 (0.4)	177 (0.1)	67 (0.1)	2.79	2.84
Hospitalization due to depression	670 (2.5)	551 (0.4)	302 (0.6)	6.19	4.34
Another AD prescribed previously	19,651 (72.5)	37,318 (27.6)	20,563 (39.5)	6.91	4.04
<b>Number of prescribed AD in the last year</b>					
0	7,445 (27.5)	97,678 (72.4)	31,472 (60.5)	0.14	0.25
1	12,132 (44.8)	29,836 (22.1)	14,831 (28.5)	2.86	2.03
2 or more	7,519 (27.7)	7,482 (5.5)	5,732 (11)	6.55	3.1
<b>Current drug usage</b>					
Mood stabilizers	1,010 (3.7)	1,536 (1.1)	977 (1.9)	3.36	2.02
Anxiolytic	2,740 (10.1)	6,893 (5.1)	4,253 (8.2)	2.09	1.26
Antipsychotic	2,653 (9.8)	3,393 (2.5)	2,230 (4.3)	4.21	2.42

Modified from Mines et al.<sup>51</sup>.

that research has demonstrated, such as the severity of depressive symptoms, existence of initial suicide ideation, despair, impulsivity, previous suicide attempts, psychiatric disorder and suicide family records, comorbidities with other psychiatric disorders (e.g. alcohol or drug abuse), medical pathologies linked to pain, treatment adherence, pharmacokinetic parameters (e.g. increased metabolism with lower plasmatic concentrations than the therapeutic ones), and time elapsed since the onset of treatment<sup>61</sup>. Neither the psychosocial factors nor easy access to any suicidal methods are considered. It is questionable to not only attribute suicide to AD *per se* but to the presence and increase of suicidal behaviors, especially since these behaviors are inherent to mood disorders, estimating that between 60% to 70% of depressive people experience suicidal ideation and between 10% to 15% actually commit suicide<sup>62</sup>. At first glance, the fact that significant differences are observed in comparison with placebo may allow one to conclude that AD induce suicidality; nevertheless, those findings can be methodologically questioned, due to the fact that researchers would rarely administer any placebo or AD to groups of patients with similar depressive severity due to ethical constraints, rendering them hardly comparable. An inherent problem with the FDA's systematic review is the retroactive gathering of relevant information, and the lack of a clear definition pertaining to suicide-related events. In this sense, only the Treatment for Adolescents with Depression Study<sup>63</sup> comprehensively evaluated the phenomenon from initial quantities of suicidal ideation and associated behaviors. Suicide varies individually, thus only randomized trials with large sample sizes would have enough statistical significance to demonstrate any difference in the suicide rates linked to AD versus placebo. Nevertheless, with suicide being a low-frequency event, it is difficult to perform a clinical trial large enough to obtain a causal hypothesis. This is a problem that could be solved through meta-analyses of existing randomized clinical trials. However, the period of time clinical trials are usually conducted may be insufficient to establish long-term treatment benefits. Additionally, suicidal behaviors usually constitute exclusion criteria due to their ethical limitations and practical difficulties<sup>46</sup>.

Multiple factors exist which can be linked to the suicidality phenomenon. Firstly, not every AD is effective on any specific patient, nor is the prescribed dosage always sufficient to control the intensity of the symptoms. Another factor is the pharmacological

switch from depression to mania (particularly from dysphoric to irritable mania) in bipolar patients treated with AD in absence of mood stabilizers<sup>64</sup>, leading to self-aggressive behaviors. In terms of treatment temporality, there appears to be an inverted relationship between suicidal behaviors and AD exposure time, raising the question as to what methodology was used in the studies selected by the FDA looking at suicide risk during the first days of therapy compared to the risk in people who do not receive AD. Also, unlike adults with whom psychiatric assistance is often sporadic, in child and adolescent psychiatry the patient is commonly brought to treatment by their parents. As such, professional assistance may be sought once the responsible adult perceives that there may be a serious clinical disorder or if a suicide attempt has already occurred<sup>65,66</sup>.

The FDA clinical trials do not reflect sustained treatment, since in daily clinical practice the physician may prematurely interrupt the AD therapy due to unwanted adverse effects, to adjust the dosage or make changes to drug combinations<sup>67</sup>. It is precisely this type of practice-based AD treatment that has been successfully applied over the past thirty years in high-risk suicide depressive patients, mainly on an in-patient basis, whose follow up and control may have otherwise been adversely affected due to diverse constraints<sup>11</sup>. Considering that depression is the disorder most-linked to suicide<sup>68-70</sup>, it is reasonable to propose that a close surveillance of the patient could be a protector factor against the phenomenon, specially considering other variables, such as lack of response for SSRI (20% to 30%)<sup>71</sup>, patient non-compliance (15% to 20%)<sup>72</sup> and patients misreport about compliance (even higher in adolescents, particularly if there is no direct supervision). It is for this reason that fluoxetine, with a longer half life than the other SSRI, would not leave a "therapeutic gap" if the drug intake is irregular, which helps explain why fluoxetine has been the least challenged AD by the FDA.

Klein argue that the central concern of the FDA is that AD are potentially lethal, while it is unsupported by research on any case of suicide, instead using the concept of "suicidality" as a substitute for "suicide" and thus overstating the risk. Furthermore, the FDA's findings appear to be based on inferences, since the evidence was obtained in a manner that is not methodologically reliable, nor fulfilling the requirements of the definitions of "suicidal tendencies" utilized by the standardized scales<sup>22</sup>.

## What factors linked to antidepressants could increase suicidality?

Although Khan *et al.*<sup>73</sup> and Gunnell *et al.*<sup>74</sup> concluded that there was not an impact on suicide secondary to the use of AD, there was an increase of self-aggressive behaviors. Some proposed mechanisms to explain the relationship among AD, ideas, and suicidal behaviors<sup>75,76</sup>, are psychomotor stimulation, depression paradoxical deterioration, akathisia, panic attack or anxiety onset, pharmacological switch to mania, induction to obsessive concern with suicide, and aggressive “borderline reactions” or paroxysmal disorders to electroencephalogram that might alter impulse control<sup>61,73-76</sup>. For example, AD with short half-lives may induce, initially, serotonin level fluctuations, which may lead to akathisia, therefore increasing suicidal risk associated with desperation and unrest<sup>77</sup>.

In relation to genetic influence, Menke *et al.* did a genome-wide association study to identify genetic markers linked to emergent suicidal ideation resulting from the AD treatment, finding a very low proportion of genetic factors related to this phenomenon. The results suggest that combinations of some genetic markers could be used to identify patients with this risk<sup>78</sup>. Additionally, an investigation into clinical and genetic predictors of the increase of suicidal ideation by patients undergoing therapy with AD assessed the effects of paroxetine, venlafaxine, and clomipramine. The increase of suicidality was linked to the severity of the affective disorder and the AD treatment when some defined genetic sequences were present, with the exception of paroxetine, which did not show a significant relationship with the aforementioned risk. Some genome sequences were described as stronger guidelines than others in suicidal ideation increase across the therapy, whereas others exhibited a differential association according to the AD type. The FKBP5 gene that codifies proteins linked to glucocorticoid receptor would be associated with the misregulation of the hypothalamic-pituitary-adrenal axis during AD treatment, and the physiopathological mechanism was proposed as responsible for the increase in suicidal ideation. Nevertheless, the authors support the AD prescription in patients displaying suicidal ideation, taking into account the potential benefits of therapy<sup>79</sup>. Pan *et al.* described a crucial element of suicidality, independent of AD prescription, when reporting a new variant of guanosine triphosphate cyclohydrolase deficiency in young men with severe major affective disorder with multiple suicide attempts. This deficiency was linked to some biochemical mediators in the biosynthetic pathways of serotonin and dopamine in cerebral spinal fluid, demonstrating impairment in this metabolic pathway. Through the replacement of these mediators, suicidal ideation was lessened and there was significant improvement in the affective disorder<sup>80</sup>. Although these investigation trends are interesting, it would be overly-reductionist to only consider the biological-molecular aspects involved in the comprehension of suicide, regarding the inherent biopsychosocial nature of this topic.

## Epidemiological effects following FDA warning

Approximately one month after the FDA warning was published, the prescription of AD in the United States had decreased by 10%, and by June 2005 it had decreased an additional 10%<sup>81</sup>. Simultaneously, Hamilton *et al.* noted that after ten years of decrease in the annual suicide rates in North American children and teenagers, an increase of 18% was observed in people between one and nineteen years of age during 2003 and 2004, suggesting that this change may be the result of the FDA recommendation<sup>82</sup>. In a comparative analysis, Gibbons *et al.* found that the usage of SSRI in children and adolescents decreased by 20% in the Netherlands and the United States, proving a correlation with the increase of the 49% and 14% in suicide rates, respectively<sup>83</sup>. Nevertheless, Kurdyak *et al.* stated that the FDA warning was not associated with a significant change in AD prescription in Ontario (Canada) in patients under twenty years old. Meanwhile, the British warning about the prescription of paroxetine in this population

contributed to a significant decline in its prescription by 54% ( $p = 0.03$ ) immediately after the first warning by the *United Kingdom Committee on Safety of Medicines*. The authors argue that the drastic change in paroxetine usage in contrast with AD prescription was due to the British warning being more specific, since it only covered one AD. On the other hand, physicians in Ontario could have prescribed a substitute for paroxetine, while the FDA warning fell on an AD series, thereby leaving professionals without adequate replacement treatment options<sup>84</sup>.

These studies demonstrate a radically diametric effect from the warning issued by the FDA. It is clear that a posterior amplification of the black box warning had an additional impact on practice. In parallel, the FDA recommendation which suggests closer therapeutic contact does not consider the current problems of the mental health system, including low coverage by insurance plans for mental disorders, strict limits on visits to hospitalized and ambulatory patients, restricted access to mental health providers, *inter alia*. Additionally, the current deficit in professionals (child and youth psychiatrists in particular) is not expected to be reversed in the short term, which may be seen as a reason why this tight control becomes difficult<sup>85</sup>.

## Conclusions

Aside from being contradictory to present evidence, assigning a suicidogenic role to AD implies debugging every biological, social and psychological factor that impacts the act of suicide, which itself is a multifactorial phenomenon, and thus not attributable to a single cause. Indeed, many studies that underpin the FDA's stance on AD and suicide risk are still unknown to the scientific world, while others lack a rigorous methodology, or indicate results that do not reach statistical significance. Although the therapeutic effects of SSRI and venlafaxine in young patients may be limited, reasonable evidence does exist which supports its use in the treatment of depression. Based on this, the FDA warning itself might paradoxically be contributing to an increase in suicide rates.

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## Conflict of interest

The authors declare that there is no conflict of interests regarding the publication of this paper.

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