



Violent behavior and aggression in schizophrenia: Prevalence and risk factors. A multicentric study from three Latin-America countries

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ABSTRACT

Objective: The aim of the present study was (i) to assess the prevalence of Violent Behavior in Schizophrenia (VBS) in a sample of community-dwelling outpatients in three middle-income countries of Latin America and (ii) to determine the clinical and socio-demographical risk factors associated with VBS and aggression level.

Methods: The study included 253 stabilized outpatients with schizophrenia and their principal caregivers from 3 public ambulatory psychiatric care centers in Bolivia (N = 83), Chile (N = 85), and Peru (N = 85). VBS was defined according to the Overt Aggression Scale (OAS) score and the aggression level was measured by the aggression subscore of the Agitated Behavior Scale of Corrigan. We collected socio-demographic information and clinical data. Multiple linear and logistic regressions were performed to determine which variables were associated with VBS and aggression level.

Results: The prevalence of VBS differed statistically between the three countries ($p < 0.001$) with 3.5% in Chile, 14.6% in Peru and 55.4% in Bolivia. After adjustment for confounding factors, VBS was associated with a younger age, a more severe psychotic symptomatology, a lower family income and unemployment. After adjustment for confounding factors, aggression level was associated with a more severe psychotic symptomatology, a lower family income, a younger age at illness onset and higher number of hospitalizations in the last 3 years.

Conclusion: These results may guide future health policies to specifically provide social support and rehabilitation care to VBS patients in middle-income countries, including psychoeducation and a more integrated work between the treating medical team and the social workers.

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1. Introduction

There is consensus in the literature concerning a modest but consistent association between violent behavior, aggression and schizophrenia (SZ) (Fazel et al., 2009; Large and Nielssen, 2011; Witt et al., 2013; Knezevic et al., 2015; Fleischman et al., 2014; Iozzino et al., 2015; Dack et al., 2013). Violent Behavior in Schizophrenia (VBS) evaluation is crucial for social and clinical prognosis of schizophrenia as well as for personalized care of VBS patients.

A recent meta-analysis assessed the VBS-associated socio-demographical variables (Witt et al., 2013). Overall, VBS was moderately

associated with homelessness, being male, and weakly associated with non-white ethnicity and a lower socio-economic status. VBS was also strongly associated with psychotic symptomatology (including delusions, hallucinations, hostility, lack of insight and mood symptomatology). However, most of the included studies were carried out in inpatient samples. Including only inpatients is associated with a potential recruitment bias and with VBS risk factors associated with hospitalization (e.g., involuntary hospitalization) (Hodgins and Müller-Isberner, 2014).

Outpatients' studies are therefore needed to correctly evaluate VBS prevalence and associated risk factors in the real world. However, only a small number of VBS studies have been carried out in community-dwelling SZ patients. In the USA, a subgroup analysis of the CATIE study in 1410 SZ outpatients concluded that minor violence (estimated in 19.1% of the sample) was associated with co-occurring substance abuse and interpersonal and social factors (Swanson et al., 2006). Serious violence (3.6%) was associated with psychotic and depressive symptoms, childhood conduct problems, and victimization in this

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study. In Spain, 5% of 895 SZ outpatients were found to have shown verbal violence in the last week, and 47% were defined as VBS according to the study's criterion (Bobes et al., 2009). In this study, VBS was associated with more past episodes of violence, higher psychotic relapses and lower satisfaction with treatment. In the UK, a study conducted in 251 SZ outpatients concluded that VBS (20.1% of the sample) was significantly and positively associated with childhood conduct disorder, current use of illicit drugs, positive, threat-control-override, and depression symptoms (Hodgins and Riaz, 2011). Similar findings come from a study of 421 SZ Japanese outpatients (Imai et al., 2014). More recently, another study carried out in 331 SZ outpatients in France found that self-reported higher aggression level was associated with younger age, lower education level, and higher psychotic symptomatology independent of type of treatment (Fond et al., 2015). In this last study, no VBS prevalence was determined because there was no cut-off on the self-reported scale used to assess aggression level. Moreover most of the VBS studies to date were carried out in North America and in Europe, with none in Latin America.

The aim of the present study was (i) to assess the prevalence of VBS in sample of community-dwelling SZ outpatients in three middle-income countries of Latin America (Bolivia, Chile, and Peru) and (ii) to determine the clinical and socio-demographical risk factors associated with VBS and aggression level.

2. Method

2.1. Study participants

Overall, 253 stabilized outpatients with schizophrenia and their primary caregivers were consecutively recruited between May 2012 and February 2013 in three public ambulatory psychiatric care centers of three areas: Arica, northern Chile (N = 85, 33.6%), Tacna, southern of Peru (N = 85, 33.6%), and La Paz, Central-Western of Bolivia (N = 83, 32.8%). The three centers shared similar characteristics in terms of size, type of treatment given to patients, professionals and free access of care.

2.1.1. Inclusion criteria

All stabilized community-dwelling patients diagnosed with schizophrenia according to the criteria of International Classification of Diseases (ICD), 10th version (WHO, 1992) were included in this study.

2.1.2. Non-inclusion criteria

Patients with a history of neurological disorders (including stroke, epilepsy and head injury) or other illnesses affecting the central nervous system (blindness, deafness) were not included in the present study.

2.2. Procedures

Two psychologists, who were part of the research team, trained for scale evaluation, and supervised by the principal researcher (AC-U), conducted the evaluations of the participants under the auspices of the mental health services of each country. The length of time of the evaluation was between 20 and 30 min.

2.3. Data collection

2.3.1. Demographic and illness characteristics variables

The variables assessed were sex, age, ethnicity (Aymara and non-Aymara), educational level (≥ 12 years or < 12), employment status (unemployed or employed), marital status (single or in couple), family income (measure of the total salary per month for all members of the family, expressed in US dollars), age at onset of the disorder, duration of untreated psychosis (DUP), the number of hospitalizations in the last 3 years. All patients were administered antipsychotics. The presence or absence of add-on integrated treatment (defined by psychotherapy,

family psychoeducation, and/or day care hospital in addition to pharmacological treatment) was also reported.

Concerning ethnicity, the Aymara is the largest ethnic group in the region, with a population of 2 million people, and has lived in the Andes Mountains for centuries. Recent generations of Aymara have undertaken a massive migration from rural towns to large cities and, thus, receive healthcare services from the same clinics as non-Aymara individuals (Köster, 1992; Van Kessel, 1996; Gundermann et al., 2007; Núñez & Cornejo, 2012).

2.3.2. Psychotic symptomatology

Psychotic symptomatology was evaluated with the Positive and Negative Syndrome scale for Schizophrenia (PANSS) (Kay et al., 1987). This 30-item, 7-point (1–7) rating scale is specifically developed to assess psychotic symptoms in individuals with schizophrenia and comprises 5 different subscales: positive, negative, cognitive, depressive and excitement scales (Fresán et al., 2005a). The PANSS has been translated into Spanish and validated in Spain by Peralta and Cuesta (1994) and in Mexico by Fresán et al. (2005a). Insight into illness was specifically assessed by the G12 item of the PANSS. G12 is a global clinical assessment of lack of judgment and insight. It measures one's level of insight by assessing one's ability to recognize psychiatric illness, need for treatment, decision-making, and planning.

2.3.3. VBS and aggression assessment

The patient's overall level of violence and aggression was assessed by the caregivers using two widely used and validated scales: the *Overt Aggression Scale* (OAS) (Yudofski et al., 1986) and the *Agitated Behavior Scale* (ABS) (Corrigan, 1989). VBS was defined according to the OAS score (Yudofski et al., 1986). The OAS is a standardized behavioral checklist that rates episodes of aggression in four main categories, representing escalating violent behavior: 1) verbal aggression, 2) physical aggression against self, 3) physical aggression against objects, and 4) physical aggression against others. Scores range from 0 to 4 where 0 indicates nonaggression and 4 indicates extreme aggression. The individual total OAS scores are calculated by adding the scores of the four subcategories of OAS, ranging from 0 to 16. This instrument is widely used due to its documented reliability and validity. The Spanish version of this scale was utilized (Páez et al., 2002; Fresán et al., 2004). As recommended in the validation study, the VBS group (VBS+) was defined by a score ≥ 7 (sensitivity: 0.80; specificity: 0.97) (Fresán et al., 2004). Patients with a score < 7 were not considered as violent (VBS-).

The aggression level was measured by the aggression subscore of the ABS (Corrigan, 1989). The ABS is a 14-item instrument to objectively assess the agitation of patients in three domains: disinhibition, aggression and lability. In this study work, we utilize the aggression subscale as an indicator of VBS. This measure uses a rating of severity from 1 (absent) to 4 (present to an extreme degree). No cut-off score was defined in the validation study (Corrigan, 1989).

The OAS and ABS has been developed to evaluate aggressive behavior during a specific period of time (Yudofski et al., 1986; Corrigan, 1989). In this study, the period was the 4 weeks before evaluation.

2.3.4. Attitude towards treatment

The *Drug Attitude Inventory* (DAI-10) (Hogan et al., 1983) is a 10-item self-report scale that assesses the current attitude, experience and beliefs about antipsychotic drugs. The DAI-10 is considered to be a good predictor of adherence to treatment in schizophrenia (Hogan et al., 1983; Nielsen et al., 2012). Scores ranged from -10 (very poor attitude) to +10 (best possible attitude). It is a simple and easy-to-use self-report instrument with satisfactory psychometric properties that assesses a clinical dimension relevant to nonadherence (Nielsen et al., 2012). DAI-10 scores that are analyzed here were obtained from patients. The DAI-10 is a time point report of the patient's attitude towards treatments and has no specific period of time.

2.4. Ethical considerations

Before the start of the study, written informed consent was requested and received from the patient and her/his primary caregiver. The objectives of the study were explained as well as the voluntary nature of participation. No compensation was offered for participating in the study. The study was approved by the Ethics Committee of the University of Tarapacá and the National Health Service of Chile.

2.5. Statistical analysis

Descriptive analyses for the socio-demographic and clinical variables are presented as frequencies and percentages for categorical variables and as means and standard deviations for continuous variables. Chi-squared or t-tests were conducted to compare the variation on sociodemographic and clinical characteristics of the study sample based on the OAS cut-off for the absence or presence of violent behavior. Pearson's correlation coefficients or t-tests were used to assess the association between the characteristics of the study sample and the aggression ABS score. Multiple regression analyses were then performed to identify variables potentially associated with violence behavior, after adjusting for confounding factors. Due to the multicollinearity induced by the strong association between country and economic and health factors, we did not include the country in our univariate and multivariate analyses. Each country has not been analyzed separately due to the relatively small sample size for each country. Variables relevant to the model were selected based on their sociodemographic interest and/or a threshold p-value (≤ 0.02) in univariate analysis. Logistic regression analysis was used to estimate the adjusted Odds ratio (OR) for risk factors associated with the dichotomous OAS measure, and a linear regression was used to estimate the standardized β coefficients for risk factors associated with the continuous aggression ABS score.

Statistical significance was defined as $p < 0.05$ in two-sided tests. The statistical analyses were performed using the SPSS version 18.0 software package (SPSS Inc., Chicago, IL, USA).

3. Results

3.1. Sample characteristics (Table 1)

Two hundred and fifty-three stable community-dwelling SZ outpatients were enrolled in the present study. The mean age of patients was 35.6 years (SD = 12.5), 164 (66.4%) were men, 213 (84.2%) had low educational level (<12 years), 176 (69.6%) were unemployed and 117 (46.2%) were Aymara. The median monthly family income was 331.6 US dollars (interquartile range = 144.9–517.9). The mean duration of illness was 14.6 (± 11.8) years. The patients had moderately severe symptoms with a total PANSS score of 71.3 (SD = 28.2).

Overall, 61 (24.4%) participants were considered as VBS+ according to their OAS score. The prevalence of VBS differed statistically between the three countries ($p < 0.001$) with 3.5% in Chile, 14.6% in Peru and 55.4% in Bolivia. The socio-demographic data, clinical characteristics, violent behavior and aggression severity level in Bolivia, Chile and Peru are presented in Online supplement.

3.2. VBS associated factors (Table 1)

In univariate analyses, VBS+ participants were found to be younger ($p = 0.001$), indigenous (Aymara) ($p = 0.008$), with low educational level ($p = 0.007$), unemployed ($p = 0.025$), poorer ($p < 0.001$), with more severe psychotic symptomatology and poorer insight of into illness (PANSS total, $p < 0.001$) including positive ($p < 0.001$), negative ($p < 0.001$), cognitive ($p < 0.001$), depressive ($p = 0.004$), excitement ($p = 0.002$) symptomatology and insight into illness ($p < 0.001$), with higher number of hospitalizations in the last 3 years ($p < 0.001$), and with lower adherence to pharmacological treatment (DAI-10) ($p = 0.009$) in comparison with VBS – patients.

In the multivariate analysis, younger age, unemployment, family income and global severe psychotic symptomatology remained significantly associated with VBS.

Table 1
Socio-demographic and clinical associated risk factors of Violent Behavior in Schizophrenia (VBS).

	Whole sample N = 253	Univariate analysis			Multivariate logistic regression analysis	
		VBS+ N = 61	VBS– N = 189	p-Value	Adjusted OR [IC95] ^b	p-Value
Sex (Male)	164 (66.4)	44 (72.1)	119 (63.0)	0.216	1.20 [0.23;6.36]	0.828
Age (years) ^a	35.6 (12.5)	31.2 (10.2)	37.8 (12.9)	0.001	0.91 [0.83;0.99]	0.020
Ethnicity (Aymara)	117 (46.2%)	37 (60.7)	78 (41.3)	0.008	2.83 [0.66;12.2]	0.163
Low educational level (≤ 12 years)	213 (84.2%)	58 (95.0)	152 (80.4)	0.007	1.25 [0.14;11.10]	0.842
Marital status (single)	233 (93.6)	57 (93.4)	174 (92.0)	0.683	–	–
Unemployed	176 (69.6%)	49 (80.3)	121 (64.0)	0.025	4.18 [1.1;15.71]	0.034
Mean monthly family income (USD) ^a	417.6 (429)	231.2 (163.5)	473.7 (470.4)	<0.001	0.99 [0.98;0.99]	0.003
Age at onset of the disorder (years) ^a	20.9 (6.5)	19.4 (5.9)	21.2 (6.5)	0.066	0.95 [0.82;1.12]	0.559
Duration of untreated psychosis (years) ^a	2.7 (4.9)	3.2 (4.5)	2.6 (5.0)	0.365	–	–
PANSS total score ^a	71.3 (28.2)	90.3 (31.2)	65.4 (24.7)	<0.001	1.04 [1.01;1.07]	0.002
Positive factor	8.3 (4.6)	11.5 (7.3)	7.3 (4.2)	<0.001		
Negative factor	18.6 (8.4)	22.8 (8.6)	17.3 (7.9)	<0.001		
Cognitive factor	7.3 (4.0)	9.2 (4.5)	6.7 (3.6)	<0.001		
Depressive factor	6.4 (3.7)	7.9 (4.8)	5.9 (3.1)	0.004		
Excitement factor	11.5 (5.9)	14.0 (7.3)	10.6 (5.1)	0.002		
Insight (G12)	2.9 (2.0)	3.9 (2.0)	2.6 (5.0)	<0.001		
Mean number of hospitalizations in the last 3 years ^a	1.3 (1.5)	2.3 (1.7)	0.9 (1.3)	<0.001	1.40 [0.90;1.17]	0.132
Attitudes towards medications – DAI-10 score ^a	3.0 (4.8)	1.7 (5.5)	3.5 (4.5)	0.009	0.95 [0.82;1.12]	0.420
Pharmacological treatment only ^c	222 (87.7)	56 (91.8)	163 (86.2)	0.252	–	–

Significant associations are in bold ($p < 0.05$).

VBS was defined by an Overt Aggression Scale (OAS) score ≥ 7 , evaluated by the primary caregiver of each patient.

PANSS: Positive and Negative Syndrome Scale for Schizophrenia. DAI: Drug Attitude Inventory.

^a (SD): Standard Deviation.

^b Adjusted Odds ration [95% interval confidence].

^c Without add-on psychotherapeutic or social interventions.

3.3. Aggression level associated factors (Table 2).

In the univariate analyses, higher aggression level (according to the aggression subscore of the ABS) was associated with lower family income ($p = 0.002$), more severe psychotic symptomatology and poorer insight of into illness (PANSS total, $p < 0.001$) including positive ($p < 0.001$), negative ($p < 0.001$), cognitive ($p < 0.001$), depressive ($p < 0.001$), excitement ($p < 0.001$) symptomatology and insight into illness ($p < 0.001$), with higher number of hospitalizations in the last 3 years ($p < 0.001$), with lower adherence to pharmacological treatment ($p = 0.03$) and with the absence of psychotherapy/social intervention ($p = 0.021$).

In the multivariate analysis, higher aggression level remained associated with lower family income ($p = 0.048$), younger age at illness onset ($p = 0.007$), more severe psychotic symptomatology ($p < 0.001$) and with higher number of hospitalizations in the last 3 years ($p = 0.024$).

Table 2
Socio-demographic and clinical characteristics associated with aggression severity level.

	Univariate analysis		Multivariate analysis	
	Aggression ABS score M (S.D.) ^a or R ^b	p-Value	β^c	p-Value
Sex				
Men	25.3 (12.0)	0.400	0.15	0.105
Women	26.7 (13.0)			
Age (years) ^a	−0.10	0.112	0.09	0.333
Ethnicity				
Aymara	27.9 (12.7)	0.601	0.03	0.680
Non-Aymara	29.2 (12.1)			
Educational level				
Low (≤ 12 years)	26.5 (12.8)	0.136	0.03	0.680
High	23.7 (10.1)			
Marital status				
Without a partner	26.1 (12.4)	0.674	–	–
With a partner	24.7 (13.3)			
Occupation				
Unemployed	25.4 (12.0)	0.641	−0.10	0.199
Employed	26.1 (12.7)			
Monthly family income (USD dollars)	−0.21	0.002	−0.17	0.049
Age at onset of the disorder (years) ^a	−0.12	0.062	−0.28	0.007
Duration of untreated psychosis (years) ^a	0.03	0.645	–	–
Severity – PANSS total score ^a	0.51	<0.001	0.44	<0.001
Positive factor	0.43	<0.001		
Negative factor	0.31	<0.001		
Cognitive factor	0.40	<0.001		
Depressive factor	0.29	<0.001		
Excitement factor	0.51	<0.001		
Insight (G12)	0.36	<0.001		
Number of hospitalizations in the last 3 years	0.32	<0.001	0.19	0.024
Attitudes towards medications – DAI-10 ^a	−0.14	0.030	−0.07	0.507
Type of mental health treatment				
Pharmacological treatment only	7.6 (3.6)	0.021	−0.01	0.896
Pharmacological + psychotherapy/social treatment	6.3 (2.8)			

Bold values: $p < 0.05$. Aggression level was measured according to the Agitation Behavior Scale (ABS) aggression subscore.

^a M (S.D.): mean (standard deviation).

^b R: Pearson's correlation coefficient.

^c β , standardized beta coefficient (β represents a change in the standard deviation in the satisfaction score resulting from a one standard deviation change in the independent variable).

4. Discussion

Our main results may be summarized as follows: (i) the prevalence of VBS in our sample of 253 Latin America community-dwelling SZ patients varied strongly between countries, from 3.5% in Chile to 14.6% in Peru and 55.4% in Bolivia. (ii) After adjustment for confounding factors, VBS was associated with a younger age, a more severe psychotic symptomatology, a lower family income and unemployment. After adjustment for confounding factors, aggression level was associated with a more severe psychotic symptomatology, a lower family income, a younger age at illness onset and higher number of hospitalizations in the last 3 years.

This VBS study was the first to be carried out in Latin America. Higher rates of VBS were found in Bolivia and Peru, in comparison with Chile and studies performed in western countries, e.g. the United States (3.6% serious violent behavior) (Swanson et al., 2006) and Spain (2.4%) (Bobes et al., 2009). This finding may be explained by lower economic resources for patients and their caregivers, and lower-quantity or quality mental health system in Bolivia and Peru than in Chile and some western countries. For example, in terms of income, in Bolivia, 13.6% of the population lives on less than US\$1 per day compared to 5.9% in Peru and <2.0% in Chile (OMS, 2013). There are also striking differences in access to mental health services (OPS, 2013; Caqueo-Urizar et al., 2015). In terms of psychiatric care facilities (per 100,000 inhabitants), Bolivia has 0.1 psychiatric hospitals, while Peru has 0.01 and Chile 0.003. With regard to mental health staff, the number of psychiatrists (per 100,000 inhabitants) in Bolivia is 0.1; Peru: 0.1 and Chile: 0.6; Day hospitals (per 100,000 inhabitants) are Bolivia: 0.1; Peru <0.1 and Chile: 0.5. The economic growth between 1999 and 2008 differed substantially between the 3 countries (3.2% in Bolivia, 4% in Peru and 4.6% in Chile) and the total public health spending varied from 369 million (USD) in Bolivia, 1384 million in Peru and 2670 million in Chile (Urcullo et al., 2008). Future studies should specifically explore the reasons for such differences of VBS prevalence between these three countries.

We found that VBS and aggression level were both associated with more severe psychotic symptomatology, which is consistent with inpatient studies and with the previous European and American outpatients studies (Witt et al., 2013; Bobes et al., 2009; Hodgins and Riaz, 2011; Fond et al., 2015). Psychotic symptomatology was assessed by the PANSS scale, which includes items that are directly related to VBS, like hostility and inner tension. It also includes items that were strongly demonstrated to be associated with VBS (namely delusions, hallucinations, lack of insight and mood symptomatology) (Witt et al., 2013). Our results, combined with those of previous outpatients studies, suggest that psychotic symptomatology is associated with VBS, not only during acute episodes and hospitalizations, but also during the ambulatory follow-up.

VBS was associated with younger age in our study, which is consistent with previous studies (Fond et al., 2015; Swanson et al., 2006). Adolescence and young adulthood are critical periods at risk for violent behavior. Multiple factors including brain development, substance abuse and social adversity (including unemployment and separation, which were also found in our results as VBS risk factors) were suggested as etiological factors for violent behavior onset in this population (Fond et al., 2015; Swanson et al., 2006).

Aggression level was associated with younger age at illness onset in our study, independently of sociodemographic factors, treatment adherence and symptomatology. This finding is similar to the recently found by Huber et al. (2016). These authors attribute the results to trait variable, e.g. antisocial personality disorder that is more prominent in early-onset psychosis and may be related to more aggressive incidents and suicidality. Early onset schizophrenia has been suggested to differ from classical forms of schizophrenia, with potential specific genetic and cognitive patterns as well as potentially more childhood abuse, more complications during mother's pregnancy and more comorbid substance use disorders (Fraguas et al., 2016; Bora et al., 2014;

Wang et al., 2013; Ni et al., 2013; Myles et al., 2012). All these factors may increase aggression level and further studies should unravel the role of each factor in aggression level. Moreover, three distinct phenotypes of offenders with schizophrenia have been recently identified: individuals with a childhood onset of conduct disorder who display antisocial and aggressive behavior both before and after schizophrenia onset, individuals with no history of conduct problems who begin engaging in aggressive behavior at the onset of illness, and individuals who engage in a severe physical assault after many years of illness (Hodgins and Müller-Isberner, 2014). It was not possible to identify these three types of offenders in the present study and further studies are needed to understand the psychopathological pathways of VBS onset in schizophrenia.

Treatment adherence was associated with both VBS and aggression level, but only in univariate analyses and not in multivariate analyses, suggesting that the association between treatment adherence and respectively VBS and aggression level may be explained by other confounding factors including younger age, unemployment or younger age at illness onset. Future studies should further explore the relationship between treatments, adherence and violence.

Aggression level was associated with a higher risk of having been hospitalized in the last 3 years, independently of all sociodemographic and clinical variables. This suggests that the risk of hospitalization is associated with a higher aggression level, which means that more aggressive VBS patients tend to be hospitalized more often. This is consistent with the results of Swanson et al. (2006), who distinguished minor and major violence. However, these hospitalizations were also described as a risk factor for higher aggression level (Zhou et al., 2015; Iozzino et al., 2015; Dack et al., 2013). This bidirectional association appears as a potential vicious cycle. Prevention and ambulatory care with specific intervention (including pharmacological and non-pharmacological treatments and social support) appears as the first-line recommended therapeutic options, if possible.

No association between male gender and VBS or aggression level was found in our study. The association between gender and VBS varies across studies and is probably influenced by the community structure (Swanson et al., 2006; Bobes et al., 2009; Hodgins and Riaz, 2011; Imai et al., 2014; Fond et al., 2015). For example, in Swanson et al. study, the sex effect in the final model was influenced by a subgroup of younger women with substance abuse problems and history of arrest (Swanson et al., 2006). Further studies are needed to determine under what conditions VBS varies by gender.

Considering socio-demographic data, monthly family income (but not low educational level and ethnicity) remained significantly associated with VBS and aggression level in multivariate analyses. This suggests that lower income in Latin America may be associated with a higher risk of VBS onset, independently of education level, age, ethnicity, marital status, employment or psychotic symptomatology. The significant association between unemployment (and therefore monthly income) and VBS in our results is further support for this hypothesis. Our results underscore how social inequalities could influence VBS onset. VBS patients in this study receive half of household income compared to the non-VBS patients. This association was not explored in previous outpatient VBS studies, however our results are consistent with those of inpatients studies (Fresán et al., 2005b, 2005c; Knezevic et al., 2015; Volavka et al., 1997).

Limitation and strengths. There were some limitations that should be considered in this study. First, the study is cross-sectional and thus cannot establish temporal ordering or causality among the variables. Second, the sample may not be representative of the entire Latin American population of patients with schizophrenia. Larger studies of more diverse and larger groups of patients are needed to confirm our findings. Third, we did not include several variables that may have helped to explain VBS and aggression level, including substance abuse, the general class of antipsychotic treatment and benzodiazepine administration, premorbid functioning, childhood abuse, conduct disorder during

childhood and history of patient's aggressive behavior, which is a major limit of this study.

The limitations should be considered in the light of its strengths. First, this was the first study carried out with VBS patients in Latin America, in a multicentric international study. Second, only subjects with ICD-10 schizophrenia diagnosis were included. Third, multiple confounding factors were taken into account in multivariate analyses.

5. Conclusion

Altogether, these results may guide future health policies to specifically provide social support and rehabilitation care to VBS patients. Psychoeducation has also been shown to improve family attitude towards VBS, which may be recommended to diminish the risk of VBS onset (Rahmani et al., 2015; Asmal et al., 2014) as well as the caregiver burden in schizophrenia. A more integrated work is necessary between the treating medical team and the social workers. Addressing both sides would be probably associated with the best VBS prevention in these patients. Further studies should assess the effectiveness of such interventions.

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Conflict of interest

The authors have declared that there are no conflicts of interest in relation to the subject of this study.

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