

Prediction of Relapse After Cognitive-Behavioral Treatment of Gambling Disorder in Individuals With Chronic Schizophrenia: A Survival Analysis

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Gambling disorder (GD) in individuals with chronic schizophrenia is relevant because there are higher rates of GD in schizophrenic populations (10%) than in the nonschizophrenic population (1%–5%). In addition, these patients have more severe alcohol use disorder (i.e., meeting at least 6 of the DSM-5 11 criteria for diagnosis of this disorder), higher depression scores, a poor adherence to treatment, and more frequent use of outpatient mental health care. One of the main problems in GD is therapeutic failure (defined as three or more lapse episodes during treatment) or relapse (three or more lapse episodes in the follow-up period). Predicting a relapse of GD in individuals with chronic schizophrenia can be useful in targeting the patients for aftercare services. The main aim of this study was to estimate the time to a GD relapse (survival rate) and to evaluate some of the qualitative and quantitative variables related to a GD relapse by a survival analysis. The sample consisted of 35 patients with chronic schizophrenia and GD who were treated with pharmacological and cognitive-behavioral therapy. The therapeutic failure rate in the treatment period was 43%, and it was associated with the

number of episodes of schizophrenia, the age of gambling onset, and the age of the patients. The relapse rate in the follow-up period was 32%, and it was associated with the patients' age, educational level, and weekly allowance. The implications of this study for future research are discussed.

Keywords: gambling disorder; chronic schizophrenia; therapeutic failure; relapse; predictive variables

ACCORDING TO THE DATA of the only cross-sectional study in an outpatient setting of individuals with schizophrenia/schizoaffective disorder and problem/disordered gambling, there are higher rates of gambling disorder (GD) in schizophrenic populations (10%) than in the nonschizophrenic population (1%–5%) (Desai & Potenza, 2009). Actually, in an Australian national survey of people with psychotic disorders, 6.4% of the people were moderate risk gamblers, and 5.8% of them were problem gamblers (Haydock, Cowlshaw, Harvey, & Castle, 2015). These patients have more severe alcohol use disorder (i.e., meeting at least 6 of 11 of the DSM-5 criteria for diagnosis of this disorder), higher depression scores, a poor adherence to GD treatment, and more frequent use of outpatient mental health care. Co-occurring GD contributes substantially to the financial costs and emotional burden of schizophrenia for patients, their families, and the mental health system (Chen, Barnett, Sempel & Timko, 2006; Green, Drake, Brunette, & Noordsy, 2007).

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There may be a bidirectional relationship between schizophrenia and GD. Individuals with schizophrenia who have positive symptoms (e.g., delusions, hallucinations, or disorganized thinking) may present an optimistic bias in the perception of risk (Ligneul, Sescousse, Barbatat, Domenech & Dreher, 2012; Yakovenko, Clark, Hodgins & Goghary, 2016). The intensity of symptomatology can affect the risk of a gambling relapse. In turn, the negative consequences of GD in these people, such as falling into debt or feeling pressure from creditors, may trigger acute psychotic episodes (Borras & Huguelet, 2007). In other cases, gambling to fill a need for activity and gambling to connect with society/world are the reasons for engaging in disordered gambling (Yakovenko et al., 2016).

The presence of GD and psychotic symptoms poses special diagnostic and treatment challenges. Mental health services, hospitals, and primary care settings are concerned with these challenges. With dual disorders, the personal, family, and social problems of these patients increase and contribute to relapses in GD (Kassani, Niazi, Hassanzadeh, & Menati, 2015; Yakovenko et al., 2016). This increases the number of hospitalizations and the cost of treatment, so there is a need for a comprehensive assessment and an integrated intervention that addresses the multiple problems associated with these co-occurring disorders (Abbou-Saleh, 2004; Potenza & Chambers, 2001; Ziedonis, Steinberg, Smelson, & Wyatt, 2009).

Among the different therapeutic approaches aiming to deal with this dual disorder, cognitive-behavioral therapy (CBT) seems to be particularly promising for the treatment of GD in individuals with schizophrenia. The utility of this approach has been tested both in case reports (Borras & Huguelet, 2007; Potenza & Chambers, 2001) and in the only controlled clinical trial until now (Echeburúa, Gómez & Freixa, 2011).

Research that evaluates program efficacy tends to emphasize the factors that predict successful treatment outcomes. Typically, clinical research in the area of GD does not include the factors associated with poor treatment outcomes. Perhaps this is because dropouts and noncompliant subjects are eliminated from the pool of treatment participants. Actually, there are no studies dealing with the prediction of therapeutic failures or relapses in individuals with schizophrenia/schizoaffective disorder and GD. There are only three specific studies that have examined the predictors of relapses in patients with GD only; however, even in these studies, the results (i.e., alcohol abuse in Echeburúa, Fernández-Montalvo & Báez, 2001; impulsivity, maladjustment in everyday life, and early age of gambling onset in González-Ortega,

Echeburúa, Corral, Polo-López & Alberich, 2013; and impulsivity in Ramos-Grille, Gomà-i-Freixanet, Aragay, Valero, & Vallés, 2015) have not been conclusive because of their small sample size and because they do not take into account comorbid disorders. Therefore, the relative importance of the different predictive variables has not been definitively determined. According to this prior research, the variables tested to determine the significant variables that were included in the final model were both qualitative (gender, marital status, education, professional status, and adherence to treatment) and quantitative (age, monthly income, financial family support, alcohol/substance use, gambling episodes per week, time spent per gambling episode, amount of money spent per week, age of gambling onset, gambling severity, age of onset of the first episode of schizophrenia, number of admissions to a hospital and number of acute psychotic episodes). Based on the literature review, our hypotheses were that an early age of onset of both the first episode of schizophrenia and the gambling behavior, a large number of admissions to a hospital, a great amount of money spent per week, a low educational level, and a poor adherence to treatment would predict a higher rate of therapeutic failure and relapse.

The survival function is the probability of survival as a function of time. A therapeutic failure during treatment is defined as patients having three or more episodes of gambling and investing more money than the weekly sum of money assigned for personal expenses in the observation period. A relapse is considered when patients have three or more lapse episodes in the follow-up period (Echeburúa et al., 2001; Echeburúa, Gómez & Freixa, 2011; Echeburúa, González-Ortega, Corral & Polo-Lopez, 2011).

Therefore, the main aim of this paper is to predict the risk of therapeutic failure or a relapse of GD in these patients with a survival analysis. To do this, we will determine the time intervals with an increased risk of therapeutic failure or a relapse and evaluate with a Cox regression model the association of all the significant variables with the failure or relapse in GD. The study is designed to identify factors associated with the treatment failures and relapses within 1 year following CBT.

Method

PARTICIPANTS

The sample for this study consisted of patients who were diagnosed with chronic schizophrenia and were receiving pharmacological treatment for this disorder at several mental health centers in Barcelona (Spain). The inclusion criteria for the study were as follows: (a) being in treatment for chronic schizophrenia; (b) meeting an additional diagnosis of GD according

to the DSM-5 and having a score equal to or above 4 on the South Oaks Gambling Screen (SOGS; Lesieur & Blume, 1987); (c) being aged 18–65 years; and (d) taking part in the study voluntarily, after having been properly informed of its characteristics.

After screening, out of the 71 patients who came to the therapeutic program for individuals with dual diagnoses (i.e., chronic schizophrenia and GD), the sample was reduced to 44 subjects, according to the inclusion criteria. The excluded subjects (27) did not meet the criteria for admission because they had poor medication adherence at the beginning of the study (17), or they did not properly meet the diagnosis of GD (10).

The average age of the participants was 38.45 years old ($SD = 7.053$). Most of them were men (93.2%), and single (81.8%), and had affective and financial family support (72.8%). Even though 22.7% of the participants were inpatients in mental institutions, most of them lived with their relatives. Their educational level was rather low (72.8% with only primary school). In regards to employment status, most of the participants were pensioners (86.4%), and their socioeconomic level was low (93.2%).

Following the assessment phase, the participants were consecutively assigned to either the experimental group or the control group. Thus, the resulting modalities were as follows: (a) experimental group ($n = 23$ [21 men and 2 women]): CBT for GD and standard drug therapy for schizophrenia; and (b) waiting list control group ($n = 21$ [20 men and 1 woman]): only standard drug therapy for schizophrenia. The CBT for GD was based on the manualized therapist's guide included in Fernández-Montalvo and Echeburúa (1997). This program consisted of 26 weekly sessions (20 in an individual format and 6 in a group format) lasting 60 minutes each, and was led by a clinical psychologist. The main components of the program were psychoeducation, stimulus control, gradual "in vivo" exposure with response prevention, and relapse prevention. There were repeated measures of assessment (pretreatment, posttreatment and 1-, 3-, 6- and 12-month follow-up assessments). Nine participants refused to engage in the treatment, so 35 patients (33 men and 2 women) were included in this study, and 28 (26 men and 2 women) completed the treatment. After the end of the observation period, all of the patients in the control group were treated for ethical reasons. In this paper, all of the patients, after being treated with CBT, are together in only one group to increase the sample size, so there are no group comparisons.

EXPERIMENTAL DESIGN

A survival analysis was used to deal with the analysis of time duration until three or more lapse episodes

(relapses) happened, according to prior research (Echeburúa et al., 2011; González-Ortega et al., 2013). A survival analysis attempts to answer certain questions (e.g., What is the proportion of a population that will survive past a certain time? How do particular circumstances or characteristics increase or decrease the probability of survival?). The survival function captures the probability that the system will survive beyond a specified time. In our study lifetime is defined as the period between the beginning of treatment and the third lapse episode.

PROCEDURE

For subjects entering the study, informed consent was obtained after they had been given a verbal description of the study. The participants were assessed individually using the SOGS and a semistructured interview (Fernández-Montalvo & Echeburúa, 1997), which had a high interrater reliability in the original version ($\kappa = 0.94$), and focused on different aspects of gambling behavior. In this study, the interrater reliability for a GD diagnosis was $\kappa = 0.92$. This interview was carried out in the different assessments (i.e., pretreatment, posttreatment, and 1-, 3-, 6- and 12-month follow-up assessments). The treatment program was conducted on an outpatient basis at no charge by a clinical psychologist (the second author of this paper) with 10 years of experience in the cognitive-behavioral treatment of GD.

DATA ANALYSIS

The gathered data from the 35 subjects who began the treatment and from the 28 subjects who completed treatment were analyzed using SPSS-21 software through the life table, a Kaplan-Meier analysis and a Cox regression model, which are applicable statistics methods for analyzing studies conducted as time follow-up designs. The level of significance was considered 0.05.

To define the survival function, two periods were assessed: the treatment period (182 days; $n = 35$) and the follow-up period (367 days; $n = 28$).

Results

In Table 1, the rate and the time to therapeutic failures (survival time) are described. A total of 43 percent of patients had therapeutic failures during the survival time in the treatment period. The failures usually happened within the first 2 months of treatment (60%).

A Cox regression model with a conditional forward method was used to evaluate the association of all of the significant variables with failures in treatment for GD. The final model is indicated in

Table 1
The Therapeutic Failure Status of Subjects Using the Life Table Method during the Treatment Period (n=35)

Follow-up Interval, days	With Drawl, No.	Exposed to Risk, No.	Patients with a relapse	Relapse Rate	Survival Rate	Cumulative Survival	Hazard Rate
0	35	35,000	2	,06	,94	,94	,04
20	33	33,000	2	,06	,94	,89	,05
40	31	31,000	3	,10	,90	,80	,07
60	28	28,000	2	,07	,93	,74	,07
80	26	26,000	1	,04	,96	,71	,08
100	25	25,000	1	,04	,96	,69	,08
120	24	24,000	1	,04	,96	,66	,08
140	23	23,000	1	,04	,96	,63	,08
160	22	22,000	2	,09	,91	,57	,08
180	20	10,000	0	,00	1,00	,57	,08

Table 2
Variables Associated With Therapeutic Failure in Gambling Disorder in a Cox Regression Model during the Treatment Period (n=35)

	B	SE	Wald	df	Sig.	Exp(B)	95,0% CI for Exp (B)	
							Lower	Upper
Number of episodes of schizophrenia	,523	,245	4,544	1	,033	1,687	1,043	2,727
Age of gambling onset	,907	,442	4,209	1	,040	2,477	1,041	5,894
Age	-1,962	,859	5,220	1	,022	,141	,026	,757

^a Abbreviations: B, Unstandardized (B) coefficient; SE, Standard Error; df, Degrees of Freedom; Sig., Significance; CI, Confidence Interval.

Table 2. The best predictors of treatment failures were the young age of patients, the higher number of episodes of schizophrenia, and the older age of gambling onset (Table 2).

In Table 3 and Figure 1, the rate and the time to a relapse episode (survival time) are described. A total of 32% of patients had relapsed during the follow-up period. Although lapse episodes could happen at any time of the follow-up period, most of them happened within the first 6 months in the follow-up period (67%). The probability of a nonrelapse before 6 months after treatment is 0.65.

A Cox regression model with a conditional forward method was used to evaluate the association of all of the significant variables with a relapse to GD.

The final model is indicated in Table 4. The best predictors of a gambling relapse were the young age of the patients and a small weekly allowance.

Discussion

People with psychosis are four times more likely to have a gambling problem than the general population (Desai & Potenza, 2009). The strategies for the identification of disordered gambling in psychosis could initially involve the use of brief tools administered to people during treatment intake and regularly during ongoing clinical contact (Haydock et al., 2015).

In the current study, the rate and the time to a therapeutic failure or a relapse (survival time) and

Table 3
The Relapse Status of Subjects Using the Life Table Method during the Follow-up Period (n=28)

Follow-up Interval, days	With Drawl, No.	Exposed to Risk, No.	Patients with a relapse	Relapse Rate	Survival Rate	Cumulative Survival	Hazard Rate
0	28	28,000	1	,04	,96	,96	,04
60	27	27,000	2	,07	,93	,89	,06
120	25	25,000	1	,04	,96	,86	,07
180	24	24,000	2	,08	,92	,79	,08
240	22	22,000	0	,00	1,00	,79	,08
300	22	22,000	2	,09	,91	,71	,09
360	20	10,500	1	,10	,90	,65	,10

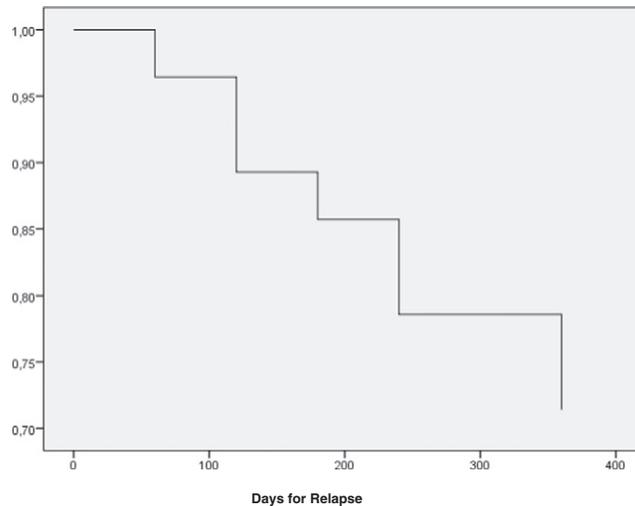


FIGURE 1 Survival function of time in days since the start of monitoring to first relapse during the Follow-up Period.

their determinants during and following treatment for GD are described. The therapeutic failure rate during treatment was 43%. Based on the life table model, most of the failures took place within the first 2 months of treatment (60%). These results were similar to the relapse rates summarized by other studies (Echeburúa & Fernández-Montalvo, 2005; Echeburúa et al., 2001).

The only predictive variables of treatment failure that were significant were the number of episodes of schizophrenia, the age of gambling onset, and the age of the subjects. That is, patients failed more frequently to complete a successful treatment when they were younger, they began gambling at an older age and they had a higher number of episodes of schizophrenia. There are not any other studies in the literature evaluating these variables. In a study with a different perspective (Jiménez-Murcia et al., 2010), a younger age of gambling onset was related to greater GD severity in pathological gamblers, but in this study patients were not diagnosed with a dual disorder and the authors failed to adequately

control for participant age when examining the relation between age of onset and relapse.

Regarding the relapse status of the patients, a total of 32% of patients had relapsed during the follow-up period. Lapse episodes took place at any time of the follow-up period, but they usually occurred within the first 6 months of the follow-up period (67%). Weekly allowance and age of the patients had an inverse relationship with a relapse. Data related to relapse rate are consistent with other studies in the field of disordered gambling (Hardoon, Gupta & Derevensky, 2004) or other addictions (Kassani et al., 2015). These results suggest that an early age may be a risk factor for a relapse in GD and may highlight the need to focus on prevention and treatment interventions.

This is a preliminary study regarding clinical consequences derived from the results. If there is a direct relationship between therapeutic failure and an earlier age of gambling onset and a higher number of episodes of schizophrenia, an intensive treatment should be focused on the patients with these features,

Table 4
Variables Associated with a Relapse to Gambling Disorder in a Cox Regression Model during the Follow-Up Period^a (n=28)

	B	SE	Wald	Df	Sig.	Exp(B)	95,0% CI for Exp (B)	
							Lower	Upper
Age	-,156	,068	5,215	1	,022	,856	,748	,978
Weekly allowance	-,826	,393	4,414	1	,036	,438	,203	,946
Educational level	,939	,545	2,971	1	,085	2,558	,879	7,441

^a Abbreviations: B, Unstandardized (B) coefficient; SE, Standard Error; df, Degrees of Freedom; Sig., Significance; CI, Confidence Interval.

and the parents should make efforts in gambling prevention for teenagers. Further studies with larger samples should investigate the role of weekly allowance in relapse. Existential therapy components could help these individuals find meaning in life and develop a self-identity beyond the diagnosis and the label of schizophrenia (Yakovenko et al., 2016). In addition, if lapse episodes take place mostly within the first 6 months of the follow-up period (67%), there should be more frequent and intensive contact between the clinicians and the patients during this critical period.

The limitations of these data should be considered when interpreting the study findings. First, the relatively small sample size, nearly exclusively restricted to men, precludes a definitive conclusion about the predictors of a GD relapse. This should be expanded to give the study more weight (Echeburúa, González-Ortega, et al., 2011). Further studies should include larger samples of the patients with this dual pathology and a longer follow-up period. Second, regarding the methodology, it is important to remember that the treatment seekers might not be representative of the gamblers in the general population. Third, a more comprehensive assessment of the mental symptoms and comorbid disorders needs to be carried out in future research (Haydock et al., 2015). Finally, the self-reported nature of the data can lead to recall bias.

In summary, the interest of this study is to contribute to identifying the factors that may be associated with a GD relapse. It is important to examine the impact of these factors on the severity of GD and thus be able to tailor treatment to specific patients' needs according to individual characteristics (Echeburúa, Fernández-Montalvo & Báez, 2000). Clinicians should screen for comorbid gambling problems in people with psychosis. In particular, future research should examine gambling behaviors alongside psychological functioning and suggest treatment approaches to address specific goals according to these differences (González-Ortega et al., 2013). There is a strong need to provide empirically supported service guidelines and treatment recommendations for people with comorbid psychosis and disordered gambling (Yakovenko et al., 2016).

Conflict of Interest Statement

The authors declare that there are no conflicts of interest.

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