

Predictors of Suicide in First-Episode Affective and Nonaffective Psychotic Inpatients: Five-Year Follow-Up of Patients From a Catchment Area in Vitoria, Spain

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Objective: To determine the baseline demographic and clinical characteristics associated with suicide attempts over 5 years following a first admission for psychosis and to assess the relationship between suicidal behavior during 5-year follow-up and clinical factors.

Method: All inpatients consecutively admitted between February 1997 and January 1999 with a first psychotic episode from a specific catchment area in Spain were included at baseline; they were followed up yearly over a 5-year period with an extensive protocol that included the Structured Clinical Interview for DSM-IV, the Positive and Negative Syndrome Scale, and the 21-item Hamilton Rating Scale for Depression. The primary outcome measure was suicide attempts. Comorbidity with alcohol and drug abuse was recorded, as were all suicidal acts made by patients over the follow-up period. Relationships between suicidal outcome and baseline clinical features were examined. Logistic regression modeling was used to test the significance and independence of associations of relevant factors to suicidal status.

Results: Of 83 first-episode psychotic patients, 14.5% displayed suicidal behavior within the 5 years following the first admission, and 2.4% died by suicide. Suicide rate was 0.48%/year and attempt rate was 2.89%/year, with a 1.5-fold (95% CI = 1.07 to 2.22) greater risk for each depressive symptom at index episode and with an 8-fold (95% CI = 1.45 to 44.40) higher risk among patients with baseline stimulant abuse (cocaine and amphetamine).

Conclusions: Patients with a first-episode psychotic disorder seemed to be a high-risk population for suicidal behavior. Depressive symptoms during the index psychotic episode and comorbidity with stimulant abuse at baseline were relevant predictive factors for suicidal behavior during the first years of first affective and nonaffective psychotic episodes.

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Since suicide is the most severe consequence of psychotic disorders. Since it is a relatively frequent cause of premature death in psychotic patients, looking for predictive factors for suicidal behavior is crucial in this group. Prospective studies have identified history of suicide attempt before first hospitalization,^{1,2} recent discharge from hospital,^{3,4} and early course of illness^{5,6} as the strongest predictive factors of suicide attempts. Among clinical predictors, depressive symptoms as well as substance abuse and dependence are the most strongly correlated psychiatric symptoms associated with suicide in schizophrenia^{7,8} and other psychosis,^{6,9–12} but little is known about whether these depressive symptoms were already present during the first episode, as the majority of studies were done retrospectively in chronic patients.

On the other hand, the risk of suicidal behavior may change as the illness evolves, so prospective studies done in patients with a first psychotic episode are required. Indeed, young people with early psychosis are at particularly high risk of suicide,^{2,3,13,14} and suicidal risk seems to

be higher during the first year of the psychotic disorder.¹ In addition, the cumulative incidence of suicidal behavior has been found to increase from 11% at 2 years from the index episode,¹ to 23% at 4 years,¹⁵ and 25% at 10 years.¹⁶

Nevertheless, little is known about suicide in first-psychotic episode samples followed up over several years, and data until now have been contradictory. An association has been found between suicide and history of suicide attempts before first hospitalization, longer duration of first admission, substance misuse, and more readmissions.¹ However, the role of positive psychotic symptoms in predicting suicide is not clear at all in 1- and 2-year follow-up studies.^{1,2} With regard to predictive value of depressive symptoms, depressive feelings in the index episode were found to predict suicide during the first year² and even over a 10-year follow-up.¹⁶ These results were not confirmed in another recent 1-year follow-up study with a larger sample, however.¹⁷ Prospective studies combining larger first-psychotic episode samples and longer follow-up periods are required. The absence of convincing results is probably due to the size of the samples, the length of the studies, and especially the rates of patients lost to follow-up in longitudinal research. Recruiting patients in well-coordinated catchment areas can minimize this latter effect.

Consequently, specific early predictive variables of future suicidal risk have yet to be found in patients with a first psychotic episode. This article examines whether it is possible to identify high-risk suicidal patients from the onset of the psychotic disorder, whether the presence of substance abuse is predictive, and finally, what the role of affective symptomatology is in predicting suicidal behavior at the onset of the illness.

Baseline demographic and clinical characteristics associated with suicide attempts over 5 years following a first admission for psychoses were therefore determined, and the relationship between suicidal behavior during follow-up and baseline factors was assessed. The study was performed in a geographically circumscribed and well-coordinated catchment area where coordination after patient discharge is excellent, thereby reducing the rate of patients lost to follow-up. Hospital Santiago Apóstol in Vitoria (Spain) is the reference center for all acute psychiatric hospitalizations in the province. When patients are discharged, they are treated by their corresponding psychiatric ambulatory services.

METHOD

Subjects

Data were gathered on first-psychotic episode patients consecutively admitted from February 1997 through January 1999 to a general hospital psychiatric ward. The hospital provides psychiatric care to all inhabitants of the catchment area (300,000) independently of their socio-

economic status. There is only 1 emergency room for psychiatric patients, and if necessary, patients are hospitalized in the psychiatric department of the general hospital, as there are no other hospitalization units (public or private) in the area. Therefore, the sample represents the whole psychotic population with a first psychotic episode needing inpatient psychiatric treatment. Patients were included in the study after informed consent to participate was obtained.

Assessments

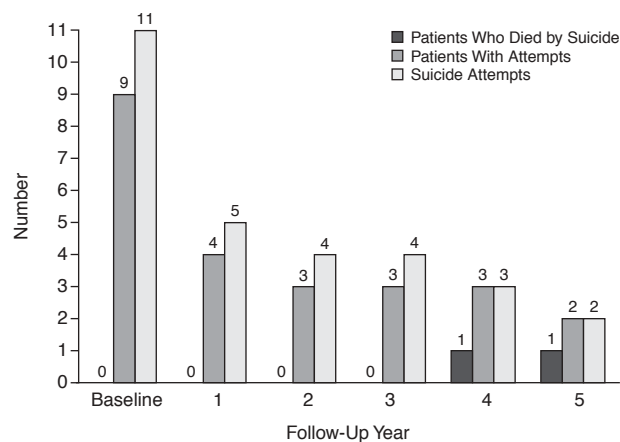
First psychotic episode was defined as the first time a patient displayed positive psychotic symptoms of delusions or hallucinations. *Suicidal behavior* was defined as a self-destructive act sufficient to require medical evaluation and carried out with suicidal intent, as well as completed suicide. In addition, we used the Spanish National Statistical Register to document all deaths in the sample, and we consulted medical and forensic records to determine causes of death and to establish any diagnoses of probable suicide. All subjects were aged 15 to 65 years and met DSM-IV¹⁸ criteria for schizophreniform disorder, schizoaffective disorder, schizophrenia, delusional disorder, brief psychotic disorder, atypical psychosis, bipolar I or II disorder, or major depressive disorder with psychotic symptoms. Patients diagnosed with bipolar I or II disorder, schizoaffective disorder, or major depressive disorder with psychotic symptoms were considered "affective psychotic patients"; meanwhile, patients with the other diagnoses were considered "nonaffective psychotic patients." Subjects with mental retardation, organic brain disorders, or drug abuse as a primary diagnosis were excluded. The DSM-IV¹⁸ Axis I diagnosis was made using the Structured Clinical Interview for DSM-IV (SCID-I).¹⁹

The day after admission, patients with first-onset psychotic symptoms were assessed with a protocol that included SCID-I¹⁹ and the following clinical scales: Positive and Negative Syndrome Scale (PANSS)²⁰ and Hamilton Rating Scale for Depression (HAM-D-21).²¹ Other relevant clinical and demographic variables were also collected, i.e., history of parasuicide, gender, age, and comorbidity with alcohol and drug abuse. The evaluations were performed during a clinical interview lasting about 90 minutes and pertaining to the previous week. The interview was carried out by 2 psychiatrists (A.G-P., F.M.) who had reached good interrater reliability for SCID-I diagnoses ($\kappa = 0.88$).

Patients were evaluated by direct interview with the same methodology once a year over a period of 5 years, which finalized in January 2004. Those patients who could not be contacted during the study period were considered lost to follow-up. All suicidal attempts committed by patients were recorded over the 5-year follow-up.

Additional information from clinical records, family informants, and staff observations were incorporated into

Figure 1. Frequency of Suicidal Acts at Baseline (N = 112) and During 5-Year Follow-Up (N = 83)



the rating process. The patients were treated with medications as clinically appropriate.

Statistical Analysis

Suicidal/nonsuicidal outcome subgroups were initially contrasted with univariate models (Mann-Whitney U tests, 2-sample t tests based on analysis of variance) for continuous variables and contingency tables (χ^2 or Fisher exact p test when cell $N \leq 10$), all with significance defined as 2-tailed $p < .05$ at stated degrees of freedom. In addition, we employed multivariate logistic regression modeling to test the independence and significance of associations of sociodemographic and clinical factors with a suicidal outcome that were at least suggestively associated in the initial univariate contrasts ($p \leq .10$).

RESULTS

Patients diagnosed with a first affective or nonaffective psychotic episode ($N = 112$) were included in the study; 37 (33%) were affective and 75 (67%) were nonaffective psychotic patients. The mean $\pm$ SD age of the patients was 28.86 ± 10.27 years (range, 16–61 years), and 37 (33%) were women.

Only 7 patients were lost in the first year of follow-up. The rate of missing patients increased slightly during the follow-up. Most of the initial sample, i.e., 83 patients (74%), was followed up for 5 years.

Nine inpatients (8% of the initial sample) had a history of suicidal behavior at admission. Over the follow-up period, 12 patients (14.5% of the followed sample) displayed suicidal behavior, but only 2 had previous suicide attempts. Nine of the suicidal patients were men. There were new patients with suicide attempts each year of follow-up. Seven patients made a single suicide at-

Table 1. Variables Studied in 5-Year Follow-Up of First-Episode Psychotic Inpatients

Variable	Nonsuicidal (N = 71), Mean $\pm$ SD	Suicidal (N = 12), Mean $\pm$ SD	Statistic	p
Age at illness onset, y	29.7 $\pm$ 10.9	23.8 $\pm$ 5.3	$t = 2.92$	< .01
No. of depressive symptoms	1.6 $\pm$ 1.8	2.8 $\pm$ 2.6	$t = -1.82$	.07
PANSS score				
Positive	24.65 $\pm$ 6.35	23.42 $\pm$ 7.56	$t = 0.61$	.55
Negative	19.07 $\pm$ 9.96	18.58 $\pm$ 9.66	$t = 0.16$	.88
General	41.72 $\pm$ 11.02	42.67 $\pm$ 9.86	$t = -0.28$	.78
Total	85.44 $\pm$ 20.53	84.67 $\pm$ 21.89	$t = 0.12$	.91
HAM-D-21 score	17.93 $\pm$ 7.98	18.42 $\pm$ 8.68	$t = -0.19$	.85
	% (N)	% (N)		
Nonaffective diagnosis	63.4 (45)	75.0 (9)	Exact	.53
Male	66.2 (47)	75.0 (9)	Exact	.74
History of suicide attempts	9.9 (7)	16.7 (2)	Exact	.61
Tobacco abuse	80.3 (57)	75.0 (9)	Exact	.70
Alcohol abuse	56.3 (40)	58.3 (7)	Exact	1.00
Cannabis abuse	46.5 (33)	50.0 (6)	Exact	1.00
Stimulant abuse (cocaine and amphetamine)	25.4 (18)	58.3 (7)	Exact	.037

Abbreviations: HAM-D = Hamilton Rating Scale for Depression, PANSS = Positive and Negative Syndrome Scale.

tempt during the 5-year period, 4 made 2 suicide attempts, and 1 made 3 attempts. Two patients, a man and a woman, committed suicide; 1 during the fourth and the other during the fifth follow-up year (Figure 1). The observed rate of suicide attempts during 5 years of follow-up was 2.89%/year (12/83/5) and of completed suicides was 0.48%/year (2/83/5).

Patients were treated after the first episode with atypical antipsychotics (62%–71%), with typical antipsychotics (7%–11%), or with mood stabilizers either as monotherapy or in combination with atypical antipsychotics (24%–28%) or received no treatment (0%–2%). Ranges in each treatment group indicate changes in the drugs administered during the follow-up.

Salient characteristics of suicidal and nonsuicidal subjects were compared in univariate analysis. There were associations of suicidal behavior with abuse of stimulating drugs (cocaine and amphetamine) and with a younger age at onset. Also, more baseline depressive symptoms measured by DSM-IV seemed to be strongly related to suicide. No associations were found with history of parasuicide, depressive symptomatology assessed by HAM-D-21, or positive, negative, or general psychotic symptomatology measured with the PANSS (Table 1).

We then used logistic regression modeling to test the significance and independence of associations of these factors to suicidal status. Among factors initially found to be significantly associated with suicidal behavior in the logistic regression model, we found that the strongest baseline predictors of suicidal behavior were abuse of

Table 2. Multivariate Analysis of Risk Factors for Suicidal Patients^a

Patients With Suicide Attempts ^b	Wald χ^2	p	OR	95% CI
Male	0.18	.68	0.68	0.11 to 4.18
Older age	3.14	.08	0.89	0.79 to 1.01
No. of depressive symptoms	5.39	.020	1.54	1.07 to 2.22
Stimulant abuse (cocaine and amphetamine)	5.74	.017	8.03	1.45 to 44.40

^aLogistic regression.^bDependent variable.

stimulating drugs (cocaine and amphetamine) and greater number of depressive symptoms measured by DSM-IV. Although earlier age at onset lost the association to suicide, there was a trend for older patients to be less suicidal (Table 2).

DISCUSSION

To our knowledge, the present research is the largest and longest prospective study of suicide risk factors in first-episode psychotic patients. The relationship was investigated between suicidal behavior during 5 years of follow-up and clinical and demographic baseline factors. Another strong point is that the study used an incidence cohort from a geographically circumscribed and well-coordinated area, so the study sample not only included all first-episode psychotic inpatients but also considerably reduced the risk of loss to follow-up.

High rates of suicidal behavior were found during the first years following a first psychotic episode. Around 14.5% of the patients in this study displayed suicidal behavior within the 5 years following the first admission, and the rate of suicide attempts remained stable over the time (4 suicidal patients during the first year; 3 during the second, third, and fourth years; and 2 during the fifth year). Nevertheless, severity of suicide attempts increased during the latter years of the study. One man and 1 woman (2.4% of the followed sample) committed suicide, 1 during the fourth year and the other during the fifth (Figure 1), with a rate of 0.48% per year. Other studies^{2,17} reported rates of 0.3% and 0.4% for completed suicide over 1 year. Although it is assumed that risk of suicide after the onset of psychosis decreases with time, our results do not support this hypothesis. Moreover, premature mortality due to suicide was not found in our sample at the beginning of the follow-up but was present 4 years after the first admission. In a recent study of mortality by suicide in schizophrenia in Taiwan, the authors found a higher rate of suicide in the first 4 years after first admission.²² Other epidemiologic studies in Europe found that the first years were the period of higher risk of suicide in both affective and nonaffective psychoses.^{23,24} Although our findings should be interpreted cautiously given the number of deaths, there may be cultural differences across countries

with regard to time to suicide in patients with severe mental disorders, but special care should be taken for at least 5 years after first admission in patients with a first psychotic episode.

On the other hand, the observed rates of suicide attempts (2.89%/year) or completed suicides (0.48%/year) during this study were higher than in the Spanish or international general populations. Spanish suicide rates have been rising over the past half-century and have recently (1995–2000) averaged 8.25 per 100,000/year (ca. 0.008%/year),²⁵ or about half the recent international average of approximately 0.015%/year.^{25,26} Estimated rates of attempts in international samples are typically 20 to 30 times higher,^{26,27} or about 0.172%/year for Spain.

Compared to other published first-episode studies, our rate for previous history of suicide attempts is relatively low, and it is not independently associated with risk of suicide, at least during this period of follow-up. Lifetime rate of suicide attempts at first admission in the present population was 8%, a figure lower than the 26.6% and 23% reported respectively in the studies of Cohen et al.²⁸ and Verdoux et al.,¹ but closer to the 15% in that by Addington et al.¹⁷ Once again, there are probably cultural differences in suicide rates. Spain has the lowest rate of suicide attempts of all European countries,²⁹ and cultural characteristics may change rates of suicide attempts.^{10,30} An alternative explanation is that this was an extremely carefully assessed sample of first-episode psychotic patients from a specific catchment area. Overly high figures of previous suicide attempts might be related to failure to detect previous psychotic episodes.

Abuse of stimulating drugs (cocaine and amphetamine) at baseline episode was a relevant factor for predicting suicidal risk. Although the impact of substance use disorders on clinical outcome has been studied in first-episode psychosis,^{31,32} to our knowledge this factor has previously been reported in only 1 other longitudinal study of suicide.¹ In our study, substance abuse was one of the factors independently linked with future suicide attempts. The risk of suicide in patients with stimulant abuse at the index psychotic episode was 8-fold higher within the 5 years following the first admission. Therefore, comorbidity of drug abuse, and specifically stimulant abuse (cocaine and amphetamine), is a relevant condition for predicting suicidal behavior during the early years of a first affective and nonaffective psychotic episode. This finding may have important clinical implications both in clinical samples and in the general population. Preventive programs are needed for all young people, who are increasingly abusing stimulant substances.³³ In this sense, special care must also be taken in children diagnosed with attention-deficit/hyperactivity disorder and treated with stimulant medication.³⁴

A previous study with a smaller sample reported that psychotic patients with drug and alcohol misuse at base-

line were nearly 3 times more likely to engage in suicide over a 2-year follow-up period.¹ Although no distinction was made for the different types of drugs, a relationship has also been found among drug abuse, higher impulsivity, and suicidality in samples of patients with schizophrenia and schizoaffective disorder^{12,35} and both in bipolar I^{10,36} and bipolar II³⁷ patients. There might therefore be a relationship among substance misuse, impulsivity, and suicidality, especially in younger patients.³⁸

Current thinking is that depressive symptoms are predictors of actual suicidality. A cross-sectional study with a first-episode schizophrenia spectrum disorder sample⁸ reported that more severe depressive symptoms heightened patients' risk of suicidality. Interestingly, depressive symptomatology was present in future suicidal patients from the onset of affective and nonaffective psychotic disorders.^{36,39} The existence of depressive symptoms during the index psychotic episode was associated with higher future suicide attempt risk over the course of the illness, and each DSM-IV depressive symptom at baseline increased the future risk of suicide attempt by 1.5 fold.

A few prospective studies have examined the role of these symptoms in predicting later suicidal behavior in samples of first psychotic episodes. Nordentoft et al.² reported that hopelessness expressed at baseline and depression were associated with suicidal attempts in the year following the index psychotic episode. More recently, another study¹⁶ suggested a relationship between suicide and more depressive symptomatology at baseline in a sample of adolescents with a first psychotic episode followed up for 10 years. The role of depressive symptoms in predicting suicidal behavior in the mid and long term was established in our study for a broad spectrum of first psychotic disorders. Independently of diagnosis, assessing and treating affective symptoms through intervention programs in first psychotic episodes can be useful in preventing future suicide attempts. Such programs at least seem able to diminish hopelessness ideation^{13,39} and indirectly reduce suicidal risk.

Younger age was associated with higher suicide risk, but the association disappeared in logistic regression analyses. Young people are probably more prone to stimulant abuse, and this fact might help to explain the association between lower age at onset and suicide risk that has also been reported in several studies with schizophrenic^{14,40} and bipolar¹⁰ patients. In fact, in a previous study on bipolar disorder, young age was related to suicide, but this relationship also disappeared after drug abuse was included in the statistical regression model.¹⁰

No associations were found in our study between suicidality over the follow-up and baseline psychotic symptomatology. The role of psychotic symptoms in predicting suicidal behavior has been widely studied, but the findings are contradictory, regarding not only future risk but also actual suicide attempts. Some authors have identified

presence and severity of psychotic symptoms as strong predictors of current suicidal risk,^{1,41} while others report no association.^{8,42} Moreover, the relationships between the severity of some psychotic symptoms at the onset of psychosis and the risk of suicide over the course of the illness are far from clear. One study² found that hallucinations and delusions were associated with greater suicide after 1 year of follow-up. In contrast, no relationship regarding risk of suicide was found between patients with and without psychotic symptoms during the index episode in a 6-year longitudinal study with depressive samples.⁴³ Furthermore, in first-psychotic episode samples, lower psychotic positive and negative symptoms were identified as baseline predictors of further suicide risk.^{1,16} In general, baseline psychotic symptoms have a limited predictive value on clinical and functional outcome of first-episode psychoses.⁴⁴⁻⁴⁸

A history of previous suicide attempt was not associated with further suicidal behavior during follow-up.¹⁷ Previous suicide attempts are considered as one of the most reliable and consistent risk factors for ultimate suicide.^{1,2,49} Most clinicians are particularly careful with patients who have already attempted suicide, as they run a high risk of further attempts. Clinical treatments for preventing suicide in such patients are currently available,⁵⁰ which might account for the lack of association between previous history of attempted suicide and risk of further attempts in our sample and in others.¹⁷ An alternative explanation is that 5 years is still too short to detect further self-harm in patients with a history of suicide attempts.

Finally, male sex was not associated with higher risk of suicide. Male sex overrepresented suicide patients as in other studies,^{3,7} but also overrepresented psychotic patients in this sample and was more frequent in subgroups of factors associated with suicide risk, such as drug abuse or younger age at onset.

This study has some limitations. The sample consisted of inpatients and not outpatients, and although the majority of patients with a diagnosis of a first psychotic episode need to be hospitalized, it would be interesting to include outpatients from the community sample.

In conclusion, depressive symptoms during the index psychotic episode were clearly associated with higher future suicide risk over the course of the illness. Comorbidity with stimulant abuse (cocaine and amphetamine) at baseline was a relevant predictive factor for suicidal behavior during the first years of affective and nonaffective psychosis in this sample. Considering depressive symptoms and stimulant abuse as important risk factors for further suicide attempts and completed suicide is a major clinical challenge in caring for patients with psychosis.

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