First admissions for psychoses in Eastern Piedmont-Italy

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ABSTRACT – *Background and Objectives*: 1) To identify the sociodemographic, anamnestic characteristics and presentation symptoms of patients, at the time of first hospitalization, associated with a discharge diagnosis of schizophrenic *versus* non-schizophrenic psychoses; 2) to define risk factors, at the time of the first admission, for a rehospitalization, regardless of reasons for readmission; 3) to assess the diagnostic stability between first and second hospitalization.

Methods: This study includes 245 patients first admitted to the University Psychiatric Clinic of Novara in a period of seven years, discharged with a diagnosis of psychosis as reported in the Discharge Register (ICD-9-CM codes 290-299). Data were collected by consulting medical records and registers of community-based services of the South Novara Mental Health Department. A logistic regression model was used to determine the characteristics associated with a discharge diagnosis of schizophrenia. The relationship between the risk of rehospitalization and patients characteristics was studied using Cox's regression analysis.

Results: Risk factors for a discharge diagnosis of schizophrenia were age, compulsory admission, positive symptoms, and previous non-psychotic psychiatric episodes. Risk factors for rehospitalization were a diagnosis of schizophrenia, an age of less than 40 years, the absence of a stable affective relationship, and living with the family of origin. The 92% of the patients diagnosed as schizophrenic on the first hospitalization had the same diagnosis on readmission.

Conclusions: Schizophrenia differs from other psychoses in terms of the greater prevalence of both some symptomatological characteristics and an history of previous non psy-

chotic episodes. Some sociodemographic and clinical characteristics at the time of the first hospitalization can provide indications useful in preventing rehospitalization.

Background and objectives

A psychotic episode may be due to many conditions, including schizophrenia, mood disorders, substance use or a medical general condition. Particularly, substance use or the presence of a general medical condition may influence the presentation symptoms of any psychiatric disorder and eventually determine a psychotic breakdown in schizophrenic and manic patients. It may be difficult to make a differential diagnosis at the time of presentation although this is important for defining prognosis and therapy.

Most psychotic episodes can be attributed to schizophrenia, a ubiquitously widespread pathology throughout the world[1-3] that has a cumulative lifetime incidence between 0.5% and 1.6%[4], whereas the totality of psychotic syndromes was found to have an estimated cumulative incidence of 3-3.4%[5]. The first hospitalization due to schizophrenia often marks the end of a prodromic period that lasts an average of five years; depressive and negative symptoms appear first, followed by the first signs of cognitive decline and social dysfunctioning[6-11].

Some recent studies indicate that early intervention improves the prognosis of both schizophrenia and schizoaffective disorder and that starting treatment later leads to a more severe symptoms and to a worse drug therapy response[12-14]. Otherwise a recent report indicates that the intensive early-intervention program improved clinical outcome after 2 years, but the effects were not sustainable up to 5 years later[15].

As the prodromic period of schizophrenia often passes unobserved, the first hospitalization represents the first contact with psychiatric services in many cases, and can therefore be considered a good indicator of the incidence of the illness[16]. In accordance with Italian law, such admissions may be voluntary or compulsory (for a renewable period of 7 days, that can also be revoked earlier)[17].

The first aim of the study was to identify which of the characteristics present at the time of the first hospital admission were associated with a discharge diagnosis of schizophrenic or non-schizophrenic psychoses. The second aim was to define which of the factors assessed at the time of the first admission indicates a risk of rehospitalization. The third aim was to assess, in patients readmitted to hospital, the concordance of the discharge diagnosis between first and second hospitalization.

The University Psychiatric Clinic, in which the study was conducted, belongs to the South Novara Mental Health Department (Piedmont, Italy). The catchment area of the Department has a population of about 182,000 people, 56% of whom are resident in the town of Novara. In addition to the University Psychiatric Clinic (14 beds, with 1.7 members of hospital staff per bed), the Department has three Day Hospitals (one

inside the hospital), two Day Centres, seven Residential Facilities (two Therapeutic Communities and five apartment blocks with a total of about 60 beds), and outpatients clinical activity[18]. There is also a liaison with Pediatric Neuropsychiatry across staff meetings and possibility of consultation of clinical charts.

Methods

The study includes 245 patients first admitted to the University Psychiatric Clinic of Novara in a period of seven years, resident in the same area, and discharged with a diagnosis of psychosis as reported in the Discharge Register (ICD-9-CM codes 290-299).

We have considered the following diagnoses: pre-senile and senile states (code 290), alcohol induced syndromes (code 291), drug induced psychosis (code 292), transient organic psychotic states (code 293), schizophrenic psychosis (code 295), paranoid states (code 297), other non organic psychoses (code 298). Affective psychoses (code 296) include single maniacal episode (code 296.0), single/recurrent depressive episode with psychotic symptoms (codes 296.24 and 296.34), bipolar disorder (codes 296.4, 296.5, 296.6, 296.7). We have finally divided the study patients in two diagnostic groups: schizophrenic psychosis (ICD-9-CM code 295) and non schizophrenic psychoses.

Medical records were reviewed in order to collect the following data: gender, age, education, occupational history, marital status, living circumstances (alone, with their family of origin, with their own family, or in a community), family history of psychiatric illness (i.e. the presence of a first-degree rel-

ative with a current or previous history of a disorder requiring the intervention of the psychiatric services), the type of admission (compulsory or not), the number of days spent in hospital, and any previous psychiatric history (defined as any known contacts with public or private psychiatrists, public or private hospital admissions, continuous contacts with a pediatric neuropsychiatrist because of non-psychotic symptoms).

Family and personal history of psychiatric illness were assessed by consulting clinical charts and the registers of the diversified community-based services belonging to the South Novara Mental Health Department.

The symptoms present at the time of the first hospitalization were evaluated by reading the admission reports, in which positive and negative symptoms of PANSS (Positive and Negative Syndrome Scale) two sub-scales are systematically considered, by means of a specific checklist, in terms of present or not present[19]. We have considered the presence of at least one symptom for each subscale in order to classify the two categories: "presence of positive symptoms" and "presence of negative symptoms". We have also considered confusion and agitation in terms of present or not present.

In order to identify which of the characteristics present at the time of the first hospital admission were associated with a discharge diagnosis of schizophrenic or non-schizophrenic psychosis (first aim), a logistic regression model, using the forward selection method, was applied. The odds ratios and 95% confidence interval (95% CI) were calculated. The significance of each individual variable was assessed using the likelihood ratio test (LRT), with a p value < 0.05 being considered statistically significant.

With regards to the risk factors for readmission (second aim), rehospitalization curves

were constructed on the basis of a survival analysis. We have considered as follow-up the period of time from the date of first hospitalization to the date of second admission or the last known information by reading medical records. All of the patients had a follow-up of at least one year.

The risk of rehospitalization was considered regardless of reasons for readmission; diagnosis at the time of rehospitalization was evaluated in terms of diagnostic stability or not.

The cumulative risk was calculated using the Kaplan-Meier method[20], and the 95% CI using Greenwood's formula[21].

The rehospitalization curves were constructed on the basis of gender, age (< 40 *versus* ≥ 40 years), education (high school diploma or degree *versus* middle school diploma or less), occupational history, marital status (single or widowed or separated *versus* married), living circumstances (family of origin, own family, community *versus* living alone), family history of psychiatric illness (yes *versus* no), personal history of previous psychiatric episodes (yes *versus* no), type of admission (compulsory *versus* voluntary), days of hospitalization (> 10 *versus* ≤ 10 days), psychomotor agitation at the time of the first hospitalization (absent *versus* present), confusional symptoms (absent *versus* present), positive symptoms (present *versus* absent), negative symptoms (present *versus* absent), and a discharge diagnosis of schizophenia *versus* other diagnoses. The significance of the differences between the curves was assessed using the log-rank test for homogeneity, with p values < 0.05 being considered statistically significant.

The relationship between the risk of rehospitalization and patients characteristics was studied using Cox's regression analysis (or proportional risks model), and the hazard ratio

(HR) was calculated: a value of HR > 1 indicates a higher risk in the group with a given characteristic than in the reference group.

The concordance between first and second hospitalization (third aim) with regards to diagnosis was also studied.

STATA v8 (Stata Corporation, College Station, TX, USA) and SAS software (release 8.2, SAS Institute Inc., Cary, NC, USA) were used to perform all statistical analyses.

Results

Table I and Table II show the sociodemographic, anamnestic characteristics and presentation symptoms of the study patients by discharge diagnosis of schizophrenic psychosis (142 patients, 58%) or non-schizophrenic psychoses (103 patients, 42%).

Figure 1 shows the diagnostic breakdown of the 103 patients discharged with a diagnosis of non-schizophrenic psychosis.

With regards to the first aim of the study, the multivariate logistic regression analysis showed that the main characteristics at the time of first admission associated with a discharge diagnosis of schizophrenic psychosis were age (OR = 0.90 per year; 95%CI 0.88-0.93), type of admission (compulsory *versus* voluntary: OR = 4.18; 95%CI 1.34-13.0), positive symptoms upon admission (present *versus* absent: OR = 2.22; 95%CI 1.06-4.66), and a history of previous non psychotic episodes (present *versus* absent: OR = 2.19; 95% CI 1.0-4.8). The likelihood ratio test value of the model including all these variables (df = 4) was 114.6 (p < 0.0001). The other considered variables were not statistically significant.

Table I
Percentage distribution of the sociodemographic and anamnestic characteristics of the study patients by discharge diagnosis of schizophrenic psychosis or non-schizophrenic psychoses

	Schizophrenic psychosis	Non-schizophrenic psychoses	Total
Gender			
Males	72 (50.7%)	41 (39.8%)	113 (46.1%)
Females	70 (49.3%)	62 (60.2%)	132 (53.9%)
Mean age, years (SD)	34.7 (11.9)	58.0 (18.9)	44.5 (19.1)
Education			
Middle school diploma or less	81 (57.0%)	72 (70.0%)	153 (62.4%)
High school diploma or degree	54 (38.0%)	22 (21.3%)	76 (31.0%)
Unknown	7 (5.0%)	9 (8.7%)	16 (6.6%)
Working history			
Currently working	59 (41.5%)	29 (28.2%)	88 (35.9%)
Used to work	61 (43.0%)	65 (63.1%)	126 (51.4%)
Never worked	18 (12.7%)	3 (2.9%)	21 (8.6%)
Unknown	4 (2.8%)	6 (5.8%)	10 (4.1%)
Marital status			
Married	43 (30.3%)	43 (41.7%)	86 (35.1%)
Single, widowed, separated	97 (68.3%)	56 (54.4%)	153 (62.4%)
Unknown	2 (1.4%)	4 (3.9%)	6 (2.4%)
Living circumstances			
Alone	20 (14.1%)	27 (26.2%)	47 (19.2%)
With family of origin	59 (41.5%)	15 (14.6%)	74 (30.2%)
With own family	46 (32.4%)	44 (42.7%)	90 (36.7%)
Community setting	12 (11.6%)	12 (11.6%)	24 (9.8%)
Unknown	5 (4.9%)	5 (4.9%)	10 (4.1%)
Family medical			
History			
Positive	39 (27.5%)	21 (20.4%)	60 (24.5%)
Negative	39 (27.5%)	34 (33.0%)	73 (29.8%)
Unknown	64 (45.0%)	48 (46.6%)	112 (45.7%)
Personal psychiatric history			
No	41 (28.9%)	36 (35.0%)	77 (31.4%)
Yes	95 (66.9%)	51 (49.5%)	146 (59.6%)
Unknown	6 (4.2%)	16 (15.5%)	22 (9.0%)
Type of first admission			
Involuntary	29 (20.4%)	12 (11.7%)	41 (16.7%)
Voluntary	113 (79.6%)	91 (88.3%)	204 (83.3%)
Mean duration of hospitalisation, days (SD)	12.6 (7.5)	12.2 (7.0)	12.4 (7.3)

Figure 2 shows rehospitalization curves in the two study groups and Table III shows the results of the Cox univariate and multivariate analyses with the hazard ratio (HR) and 95% confidence intervals of the variables significantly associated with the risk of rehospitalization (second aim of the study).

One hundred patients (41%) were rehospitalized: three years after the first admission, the cumulative risk of a second hospitalization was 36.7%; 21% of the subjects were followed up for a period of less than three years. The mean time of follow-up between the first hospitalization and the second one or the end of follow-up (whichever occurred first) was 3.1±2.5 years. Among subjects with a diagnosis of schizophrenic psychosis the mean time of follow-up was

Table II
Presentation symptoms of the patients in the two diagnostic groups at the time of the first admission:
agitation, confusion, 'positive' and 'negative' symptoms are reported in terms of present or absent

	Schizophrenic psychosis	Non-schizophrenic psychoses	Total
Agitation			
Present	79 (55.6%)	54 (52.4%)	133 (54.3%)
Absent	63 (44.4%)	49 (47.6%)	112 (45.7%)
Confusion			
Present	26 (18.3%)	35 (34%)	61 (24.9%)
Absent	116 (81.7%)	68 (66%)	184 (75.1%)
Positive symptoms			
Present	84 (59.2%)	42 (40.8%)	126 (51.4%)
Absent	58 (40.8%)	61 (59.2%)	119 (48.6%)
Negative symptoms			
Present	60 (42.3%)	50 (48.5%)	110 (44.9%)
Absent	82 (57.7%)	53 (51.5%)	135 (55.1%)
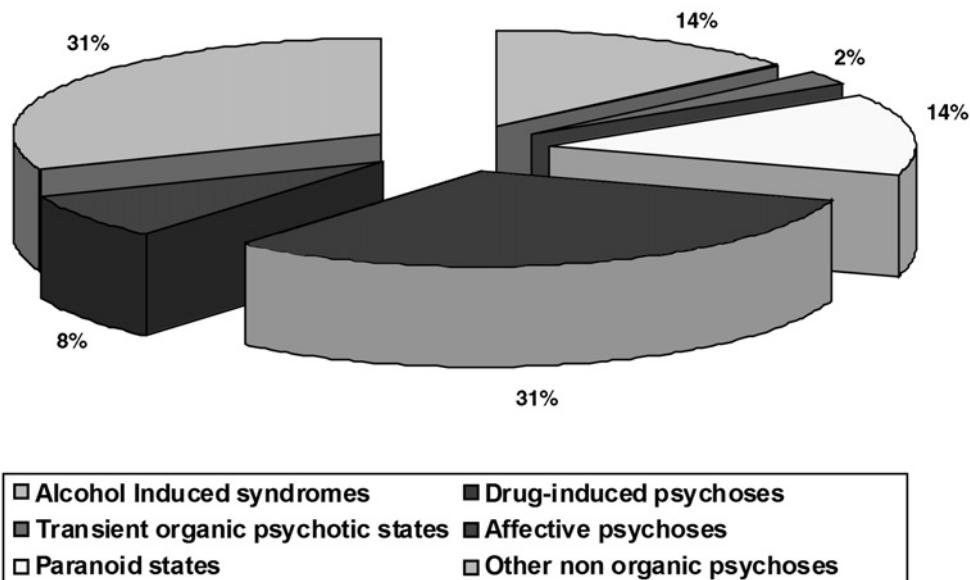
Figure 1. Diagnostic breakdown of the 103 patients discharged with a diagnosis of non-schizophrenic psychosis.
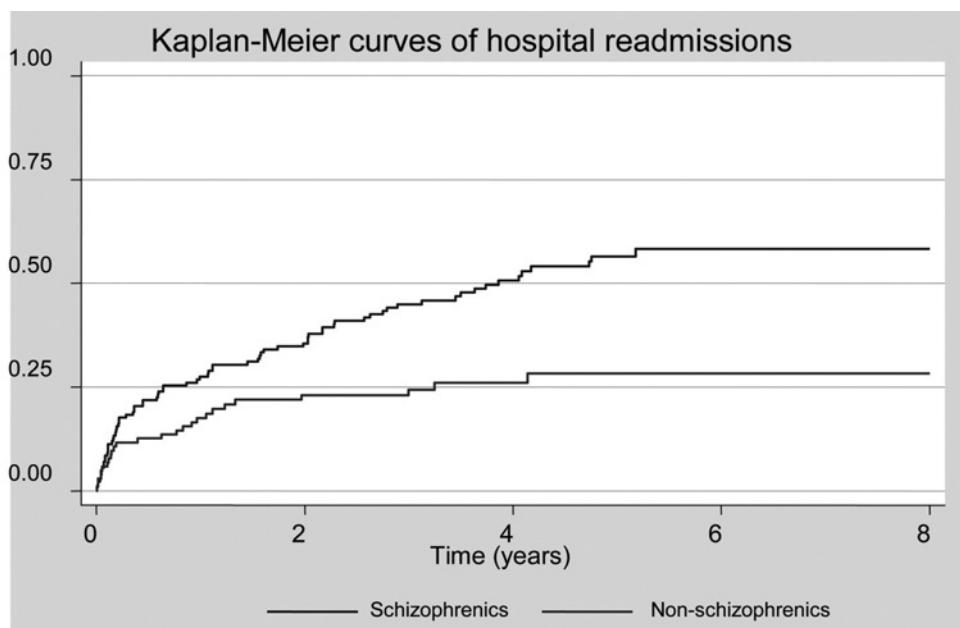
Figure 2. Rehospitalization curves in the two study groups.

Table III
Cox univariate and multivariate analyses: variables significantly associated with the risk of rehospitalization. In the multivariate analysis younger age, single status, and the absence of confusional symptoms are significantly associated with the risk of rehospitalization; the diagnosis of schizophrenia is only significant in the univariate model

	HR (CI 95%) (Multivariate model)	HR (CI 95%) (Univariate model)
Age		
< 40 years	1.96 (1.17-3.28)	2.51 (1.64-3.84)
> 40 years	1*	1*
		LR = 19.7; p-value < 0.0001
Marital status		
Single/widowed/separated	1.84 (1.16-2.93)	1.98 (1.26-3.12)
Married	1*	1*
		LR = 9.7; p-value = 0.0018
Confusion		
Absent	1.70 (1.01-2.87)	1.76 (1.06-2.94)
Present	1*	1*
		LR = 5.3; p-value = 0.0208
Schizophrenia		
Yes	1.21 (0.71-2.09)	2.21 (1.41-3.45)
No	1*	1*
	LR = 31.3; p < 0.0001	LR = 13.4; p-value = 0.0003

*Reference category

3.0 ± 2.4 years, and 3.4 ± 2.5 years among subjects with non-schizophrenic psychosis (Figure 2).

The multivariate analysis showed that the variables significantly associated with the risk of rehospitalization were age (< 40 *versus* ≥ 40 years: HR = 1.96; 95% CI 1.17-3.28), marital status (single *versus* married: HR = 1.84; 95% CI 1.16-2.93), and the absence of confusional symptoms at the time of first admission (absent *versus* present: HR = 1.70; 95% CI 1.01-2.87) (Table III).

The diagnosis of schizophrenia was not statistically significant in the multivariate model (HR = 1.21; 95% CI 0.71-2.09), but it was significant in the univariate model (HR = 2.21; 95% CI 1.41-3.45). The likelihood ratio test of the multivariate model (df = 4) was 31.3 (p < 0.0001). Particularly age is one of the most important predictor of readmission; HR of schizophrenia adjusted by age was 1.45 (95% CI 0.86-2.50) (Table III). The mean age of patients readmitted was 37.4±15.4 years, and 49.4±19.8 for the patients not readmitted.

The univariate analysis, but not the multivariate one, also showed that patients living with their family of origin were at significantly greater risk of readmission than those living alone (HR = 1.73; 95% CI 1.01-2.97). Patients living with their own family (HR = 0.59; 95% CI 0.32-1.07) or in a community (HR = 1.3; 95% CI 0.61-2.68) were not at greater risk of readmission than those living alone. The likelihood ratio test of the univariate model (df = 3) was 19.1 (p = 0.0003).

With regards to the third aim of the study**,** 92% of the patients diagnosed as schizophrenic on the first hospitalization had the same diagnosis on readmission. The 84% of the 100 patients readmitted to hospital had the same discharge diagnosis on both hospitalizations.

Conclusions

The published literature generally considers three diagnostic groups when referring to psychotic episodes: schizophrenic spectrum psychoses, bipolar disorder, and major depressive disorders with psychotic symptoms[22]. In our sample the most frequent discharge diagnosis was schizophrenia according to ICD-9-CM. Affective psychoses were less represented.

With regards to the first aim, we found some risk factors, at the time of the first hospitalization, for a discharge diagnosis of schizophrenic versus non-schizophrenic psychosis.

With regards to age, in our sample it has been shown that the risk of a diagnosis of schizophrenic psychosis decreases with age at a rate of about 10% per year. In literature, at the general population level, the age-specific incidence of schizophrenia is highest in the early 20s and decreases with age[23-26]. However, a recent study conducted in Finland suggests that increasing age does not decrease the risk of schizophrenia up to age of 40[27].

In terms of symptoms, we found that the presence of at least one of the PANSS positive symptoms was a risk factor for a diagnosis of schizophrenia. On the other hand the PANSS negative symptoms were equally prominent in the two study groups. Some published data, regarding first episode psychotic patients, indicate that symptoms classified as "negative" upon admission are more frequent in subjects finally recognized as schizophrenic than in those with affective disorder, but at the time of the first hospitalization it can be difficult to differentiate between "negative" symptoms and depressive symptoms[28]. The literature also suggests that "negative" symptoms can be already present at the time of the first psychotic episode in schizophrenic patients[29].

We found that the presence of any previous non psychotic episode is related to a greater risk for a discharge diagnosis of schizophrenia. Published data report that first episode psychotic patients later diagnosed as schizophrenic frequently have a history of psychiatric illness corresponding to prodromic symptoms, such as previous psychotic or neurotic symptoms, or emotional or behavioural disorders[30]. Other studies have demonstrated that changes in mood precede the first admission by some years[31]. In literature various approaches have been used to assess the duration of untreated illness (DUI) in schizophrenia. Very few studies have separately examined DUI from prodromal versus psychosis onset in the same patients[32-34]. This suggests that an accurate collection of anamnestic data especially about the presence of previous psychiatric episodes in first admitted patients can be helpful in making a correct differential diagnosis. In comparison with patients with other psychoses, schizophrenic patients have a longer period of disease before the diagnosis is made[35], and only 12% has been in contact with psychiatric services before their first hospitalization[36].

Regarding the type of admission, we found that compulsory first admission is a risk factor for a discharge diagnosis of schizophrenia. In other samples including first episode psychotic patients, the literature indicates a diagnosis of schizophrenia as a risk factor for compulsory hospitalization[36]. In a recent national survey conducted in Italy about patterns of admission to acute psychiatric in-patient facilities, non affective psychoses accounted for a large extent of compulsory admissions[37]. Sociodemographic characteristics, a positive family history of any psychiatric illness, and any non-positive symptoms, were all not significantly associated with a discharge diagnosis

of schizophrenia. Our failure to find any statistically significant differences in terms of sociodemographic characteristics confirms previously published data concerning affective and schizophrenic psychoses[38]. In our sample there is no substantial gender difference in the prevalence rate of schizophrenia versus other psychoses. In literature it has been found that the incidence of schizophrenia is higher in males[39,40].

About the second aim of the study, our multivariate analysis showed that the risk of rehospitalization was almost twice in subjects aged less than 40 years at the time of the first admission. Younger age was also associated with a greater risk for a diagnosis of schizophrenia, which resulted in higher rehospitalization in the univariate but not in the multivariate analysis: in our sample younger age resulted more important than diagnosis for the risk of rehospitalization. A possible explanation is that elder patients are often hospitalized in other services different from psychiatric emergency units. Consistent with this consideration, the absence of confusional symptoms, prominent in senile psychoses, was a risk factor for readmission.

Some published data show that schizophrenic spectrum psychoses are not associated with rehospitalization rates higher than those of affective disorders with psychotic symptoms[38] also because the prognosis and course of schizophrenia is variable[41]. In literature some data indicate that 60% of the patients diagnosed as having schizophrenia become chronically affected, but only 25% are rehospitalized within 5-6 years of diagnosis[42]. In another recent study only 20% of patients require rehospitalization within the first year of diagnosis[43]. It is important to underline that prognosis of schizophrenia depends on a correct diagnosis but also on the definition of specific outcomes such as remission or full recovery[44].

In our study the characteristics of the familial and social context at the time of first admission proved to be statistically significant in determining the risk of rehospitalization: not having a stable affective relationship (i.e. being single, widowed or separated) was significant in both the univariate and the multivariate models, whereas living with the family of origin rather than alone was only significant in the univariate model. The absence of one's own family, which may reflect a difficulty in psychosocial adaptation, therefore worsens functional outcome regardless of the underlying illness. The greater probability of rehospitalization of patients living with their family of origin compared to those who live alone may reflect a greater attention to clinical conditions requiring hospitalization or less tolerance to even milder symptoms, thus leading the patients to be brought to the attention of psychiatric services.

There are published data indicating that the existence of stable interpersonal relationships with friends and relatives improves the quality of life and the prognosis of schizophrenia[45,46]. On the other hand, patients with a better course of the disorder and less associated complications (i.e. substance abuse, law violations) are also able to maintain a valid network of friends and relatives, resulting in a better social support than those who have a worse course and outcome of schizophrenia.

The other clinical and sociodemographic characteristics considered at the time of first hospitalization, the type of admission and the duration of hospitalization were not significantly associated with the risk of rehospitalization.

With regards to the third objective of the study, we found a high percentage of diagnostic stability in schizophrenic patients. Some published data indicate that diagnostic stability is greater in adult patients than in adolescents at the time of first admission; the mean age of our sample was 34 years[47]. A four-year follow-up study has found that the diagnosis of schizophrenia is more stable over time than the other psychoses[48]. The positive predictive value of a diagnosis of schizophrenia is reported to be more than 90%[49].

Some limitations, however, must be considered when drawing inferences from the present data.

In our study we referred to routine clinical diagnoses as reported in the Discharge Register according to ICD-9-CM codes without using a structured diagnostic interview, and the clinical diagnosis is the primary diagnosis regardless of comorbidity. Moreover, evaluation of symptoms like anxiety or depression at the time of admission and of attempted suicides should be considered and based on specific instruments and scales. We considered an heterogeneous group of non schizophrenic psychoses including very different diagnoses such as dementia and organic psychoses, substance abuse and bipolar disorder, even if age and sex differences may have affected the distribution of some of the characteristics examined.

About patients' previous contacts with private psychiatrists or clinics we could only refer to our anamnesis records, which however include specific items regarding this kind of previous information.

In conclusion, in our sample, only some symptomatological characteristics (particularly the presence of at least one PANSS positive symptom at the time of first admission) and a positive history of previous psychiatric non psychotic episodes seem to be the most significant risk factors for a diagnosis of schizophrenia. This suggests that other more specific factors (such as biological factors) should be considered at the time of first ad-

mission to hospital. Schizophrenic patients are certainly at greater risk of rehospitalization, although the diagnosis itself seems to be less important than other variables.

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