Suicidal behaviour in first-episode non-affective psychosis: Specific risk periods and stage-related factors

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Abstract
Suicide is a major cause of premature death in psychosis. Earlier stages have been associated with higher risk. However, such risk periods have not been specifically determined and risk factors for suicidal behaviour may change over those periods, which may have crucial implications for suicide prevention. The aim of this study was to determine and characterize the highest risk period for suicide in a representative sample of first-episode psychosis (FEP) patients. Suicidal behaviour prior to first presentation of psychosis and during a 3-year follow-up was examined in a sample of 397 individuals. Risk factors for suicidal behaviour during specific time periods were investigated and compared. The greatest suicide risk was found during the month before and 2 months after first contact with psychiatric services (i.e., 'early' attempts). Severity of depressive symptoms and cannabis use emerged as predominant risk factors across time. 'Early' attempters were characterized as being male, living in urban areas, having poor premorbid adjustment, requiring hospitalization, scoring higher on anxiety measures and unusual thought content than non-attempters. Greater suspiciousness and more severe depressive symptoms distinguished the 'late' attempters. In conclusion, there is a specific high risk period for suicide in FEP around the time of the first presentation. Early intervention programmes targeting phase-specific risk factors, particularly psychotic symptoms

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management and secondary depression prevention strategies may be useful for suicide prevention in psychosis.

1. Introduction

The lifetime risk of suicide following first-episode psychosis (FEP) is approximately 5% (Dutta et al., 2010; Hor and Taylor, 2010; Palmer et al., 2005). Between 15% and 26% of FEP patients have made at least one suicide attempt by their first treatment contact, and 2–11% attempt to end their lives over the first year after treatment onset (Melle et al., 2006).

A history of previous suicide attempts and severity of depressive symptoms have been repeatedly associated with a higher suicide risk (Bakst et al., 2010a; Large et al., 2011; Pompili et al., 2011). Other potential contributors include being young and male (Hor and Taylor, 2010); possessing a high IQ and better neurocognitive functioning, in particular higher executive function (Lara et al., 2015; Nangle et al., 2006); a high level of education and high socio-economic status, poor premorbid adjustment, living alone, the severity of psychotic symptoms, a longer duration of untreated psychosis, types of insight, a family history of suicide and a higher rate of substance abuse (Drake et al., 2004; Harvey et al., 2008; Hor and Taylor, 2010; Lopez-Morinigo et al., 2012; Serafini et al., 2012). Compliance with treatment has been demonstrated to reduce suicide risk (Qin et al., 2006).

Some studies show that the periods of the greatest risk of suicide in FEP patients are shortly before and after hospitalization (Harvey et al., 2008; Melle et al., 2006). Flanagan and Compton, 2012 found nearly one-quarter of patients endorsed a history of suicidal ideation in the two weeks prior to first admission and should be carefully monitored among initiating treatment and during the early course of illness. It should be pointed out that such a history may influence clinicians in the decision to admit and hence this is observation is somewhat circular. To our knowledge, little is known about this period of extreme risk because studies that specifically investigated suicidality surrounding admission are limited (Fedyszyn et al., 2010; Melle et al., 2006). The highest suicide risk period in FEP patients remains unclear, as do possible changes to the contributors to suicide risk over the early stages of the psychotic illness. To address this further, there is a need for studies on large FEP samples and longitudinal designs.

1.1. Aims of the study

The aim of this study was to determine and characterize the highest risk period for suicide in a representative sample of FEP patients. We focused on examining premorbid, demographic, clinical, insight and neurocognitive characteristics that are potentially related to suicide risk before the first presentation to psychiatric services and over the follow-up period. We hypothesized that 1) suicide attempts will be more likely to occur in the period around the first contact with psychiatric services and related to psychotic symptoms and neurocognitive function and 2) suicide attempts later in the follow-up period will be linked to insight, depressive symptoms and certain specific premorbid and demographic characteristics.

2. Experimental procedures

2.1. Study design and setting

Data for the present study came from a large epidemiological and 3-year longitudinal study of first-episode psychosis (PAFIP) conducted at the outpatient clinic and the inpatient unit at the University Hospital Marques de Valdecilla, Santander, Spain. This study was approved by the local institutional review board and informed consent from participants was obtained. A more detailed description of our programme has been previously reported (Pelayo-Teran et al., 2008).

All referrals to PAFIP over 2001–2010 were screened with the following inclusion criteria: age 15–60 years; living in the catchment area; experiencing their first episode of psychosis; no prior treatment with antipsychotic medication or, if previously treated, a total life time of adequate antipsychotic treatment of less than 6 weeks; meeting DSM-IV criteria for brief psychotic disorder, schizophreniform disorder, schizophrenia, or schizoaffective disorder. DSM-IV criteria for drug dependence and mental retardation and having a history of neurological disease or head injury were exclusion criteria.

Three hundred and ninety seven patients who met inclusion criteria were included in the PAFIP program during this time interval. Diagnoses were made using the Structured Clinical Interview for DSM-IV (SCID-I) (First et al., 1996), which was carried out by an experienced psychiatrist (BC-F) 6 months after the baseline visit. In particular, the baseline diagnoses of our FEP patients (i.e. six months after first contact) were as follows: schizophrenia ($N=224$), schizophreniform disorder ($N=96$), schizoaffective disorder ($N=5$), brief psychotic disorder ($N=41$), psychosis NOS ($N=29$) and delusional disorder ($N=2$). At three years, diagnoses were: schizophrenia ($N=274$), schizophreniform disorder ($N=60$), schizoaffective disorder ($N=17$), brief psychotic disorder ($N=22$), psychosis NOS ($N=22$), and delusional disorder ($N=1$).

2.2. Measures

2.2.1. Premorbid and sociodemographic variables

Information was obtained from patients, relatives and medical records. This included sex, age at admission, age at onset and duration of untreated psychosis (DUP). Other sociodemographic variables collected were: years of education, relationship status ("married/cohabiting" vs. "single/divorced/separate or widowed"), living status ("alone" vs. "other"), socio-economic status derived from the parents' occupation ("low" vs. "other"), employment status ("employed" vs. "unemployed"), living area ("urban" vs. "rural", which included those living in areas with less than 10,000 inhabitants), cannabis and alcohol use (self-reported as yes/no) and first degree family history of psychosis (yes/no). Premorbid social adjustment (PAS) (Cannon-Spoor et al., 1982) was split around the

median to create a binary variable. Additionally, hospitalization (yes/no) and days in hospital were collected.

2.2.2. Baseline clinical, insight and neuropsychological measures

Clinical symptoms of psychosis at study entry were assessed with the Scale for the Assessment of Negative Symptoms (SANS) (Andreasen, 1983) and the Scale for the Assessment of Positive Symptoms (SAPS) (Andreasen, 1984). Global scores were used to generate three symptomatic dimensions: positive, disorganized and negative (Grube et al., 1998). General psychopathology was assessed with the Brief Psychiatric Rating Scale (BPRS) (Flemenbaum and Zimmermann, 1973). The above variables were dichotomized by splitting the sample through the median (resulting in, for example, mild vs. severe symptomatology). Depressive symptoms were evaluated using the Calgary Depression Scale for Schizophrenia (CDSS) (Addington et al., 1992), and a cut-off point of 6 was used, which supported 82% specificity and 85% sensitivity for predicting a major depressive episode (Addington et al., 1993). Patients were also classified into two diagnostic groups: "schizophrenia" and "other psychoses".

The shortened version of the Scale to Assess Unawareness of Mental Disorder (SUMD) (Amador et al., 1994) was used to measure three insight dimensions: insight into mental illness, insight into need for treatment, and insight into social consequences of illness. 'Poor' insight was defined as SUMD scores greater than 1, and a score of 1 designated 'good insight'. Patients were classified in two groups (good and poor insight).

The neuropsychological assessment was carried out when patient clinical status permitted good cooperation, and occurred at a mean of 10.5 weeks after intake. A detailed description of the assessment has been reported elsewhere (Gonzalez-Blanch et al., 2007). A subset of measures was selected to asses eight major ability areas: (1) verbal memory was assessed with the Rey Auditory Verbal Learning Test (RAVLT; (Rey, 1964), delayed recall; (2) visual memory was assessed with the Rey Complex Figure (RCF; (Osterrieth, 1944), delayed reproduction; (3) executive functioning was assessed with the Trail Making Test (TMT; (Reitan and Wolfson, 1985), time to complete TMT-B minus TMT-A; (4) working memory was assessed with the WAIS-III Backward Digits scale (Weschsler, 1997, total subscore); (5) processing speed was measured with the WAIS-III Digit Symbol subtest, standard total score; (6) motor dexterity was assessed with the Grooved Pegboard Handedness (GP; Lezak, 1994), time to complete with dominant hand; (7) attention was assessed with the Continuous Performance Test (CPT; Cegalis and Bowlin, 1991), total number of correct responses; and (8) premorbid IQ was determined using the WAIS-III Vocabulary subtest (Lezak, 1995), standard total score.

2.2.3. Suicide attempts information

Suicide-related behaviours, i.e. potentially self-injurious behaviour for which the person intended to kill himself/herself (O'Carroll et al., 1996), were taken from medical records by psychiatrist trainees (BVH and EGA). In particular, any self-harm act before first contact with psychiatric services and any further suicidal behaviours were registered, which included suicide attempts and suicide completions. Information on suicidal behaviour was available for the whole sample, $N=397$ patients. The method of suicide was dichotomized according to Asberg et al.'s (1976) criteria into 'violent' (hanging, jumping from a height, jumping in front of a vehicle, cutting him/herself, setting fire) and 'non-violent' (self-poisoning).

2.3. Statistical analysis

The Statistical Package for Social Science, version 19.0 (SPSS Inc., Chicago, IL, USA), was used for statistical analyses. Univariate analyses were conducted to explore specific characteristics of suicide attempters. Appropriate statistics, such as t-tests or the chi-square, were used. Multivariate analyses explored suicide attempt risk factors by entering the significant variables from the above analyses into binary logistic regression models. In particular, Nagelkerke's R^2, which is a measure of the proportion of explained variation in the logistic regression models, was investigated. In addition, the logistic regression analyses yielded odds ratios (ORs), which provided an additional measure of the strength of association. All of the above analyses were two-tailed and significance level was set at 95%.

3. Results

The sample comprised 397 individuals. Sixty patients (15.11%) made a suicide attempt. Before first presentation, 25 (6.3%) individuals had attempted suicide; of these 8 (2.11%) were persistently suicidal after the treatment began. Forty-three patients (10.83%) attempted suicide at least once over the follow-up period, and, of these, 12 (3.02%) made two attempts and 5 (1.26%) made three attempts. Six subjects (1.51%) completed suicide over the 3-year follow-up period.

In 22 (88%) of the 25 attempters before first contact with psychiatric services, the attempt occurred during the 31 days (mean 5.36) before entering our FEP program. The remaining 3 cases had made attempts 2, 3 and 8 years before first contact. In 6 (22.2%) of the 27 patients who attempted suicide for the first time after first presentation, these attempts occurred within the first 46 days (mean 5). All these patients were therefore considered 'early' attempters, while the remaining subjects were classified as 'late' attempters. See Figures 1 and 2. Of note, four fatal attempts occurred within 60 days (mean 36) after first presentation.

3.1. Differences between all attempters and non-attempters

The 60 suicide attempters were more likely to be male (70%, $p=0.026$), cannabis users (55%, $p=0.043$), more severely depressed (25.4%, $p=0.002$), have poorer premorbid adjustment (49%, $p=0.031$) and require hospitalization more frequently (76.7%, $p=0.032$) than non-attempters. This group also showed a trend toward not living alone (97.3%, $p=0.064$) and living in urban areas (82.3%, $p=0.073$). The risk of attempting suicide before cohort inception was 46.3%. See Table 1. Neuropsychological results presented in Table 2 show that only information processing speed was significantly ($p=0.046$) more impaired in attempters.

To further assess possible relationships between suicidality and selected variables, the data were analyzed by splitting the cohort into 'early' and 'late' attempters. We found that the 32 early attempters were more frequently male (75%, $p=0.026$), living in an urban area (90.6%, $p=0.024$), more severely depressed (25.8%, $p=0.014$), with poorer premorbid adjustment (58.3%, $p=0.012$) and a higher rate of hospitalization (84.4%, $p=0.013$) than non-attempters. The most frequent suicide method in 'early' attempters was self-injury (71.4%). The 25 'late' attempters, in comparison with non-attempters showed a shorter DUP ($p=0.014$), more severe depression (26.7%, $p=0.011$)
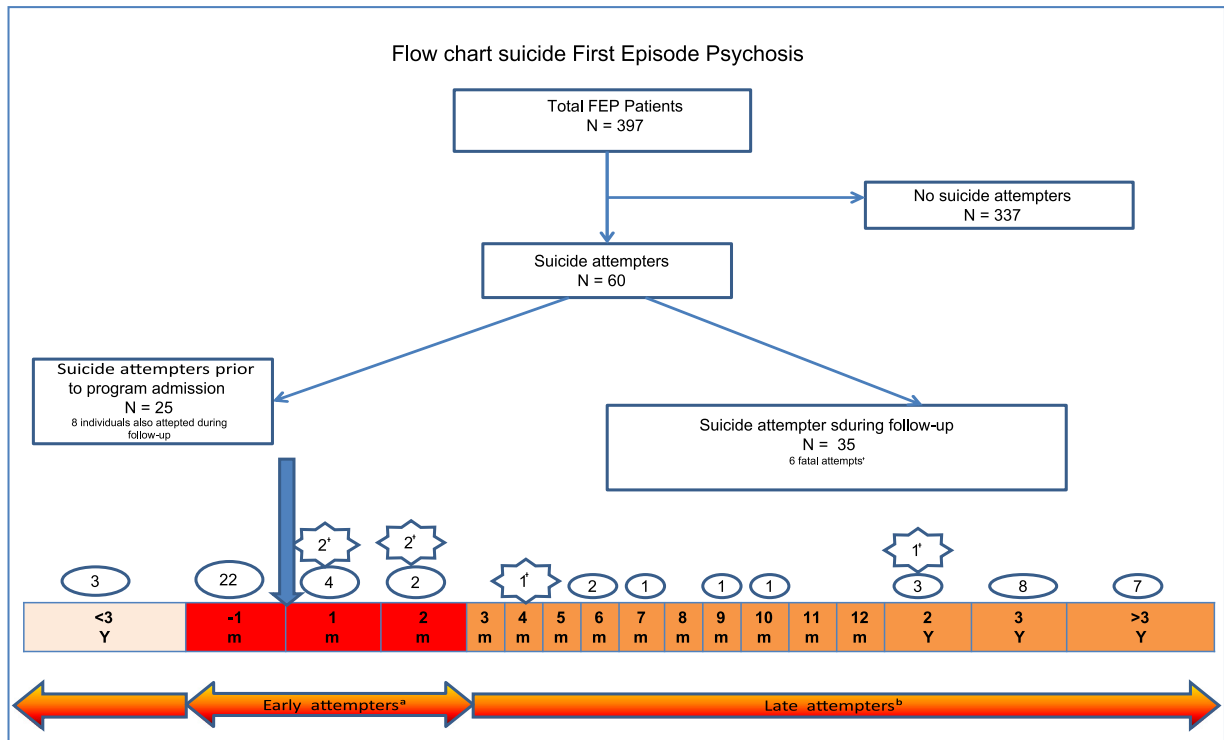
Flow chart suicide First Episode Psychosis

^aSuicide attempters between < 1 month before and < 2 months after admission; N=32 (22 attempters <1 month before; 10 attempters < 2months after; 4 fatal attempts) ; ^bSuicide attempters > 2 months after admission ; N=25 (23 first attempters; 2 fatal attempts)

Figure 1 (a) Suicide attempters between <1 month before and <2 months after admission; N=32 (22 attempters <1 month before; 10 attempters <2 months after; 4 fatal attempts); (b) Suicide attempters >2 months after admission; N=25 (23 first attempters; 2 fatal attempts).
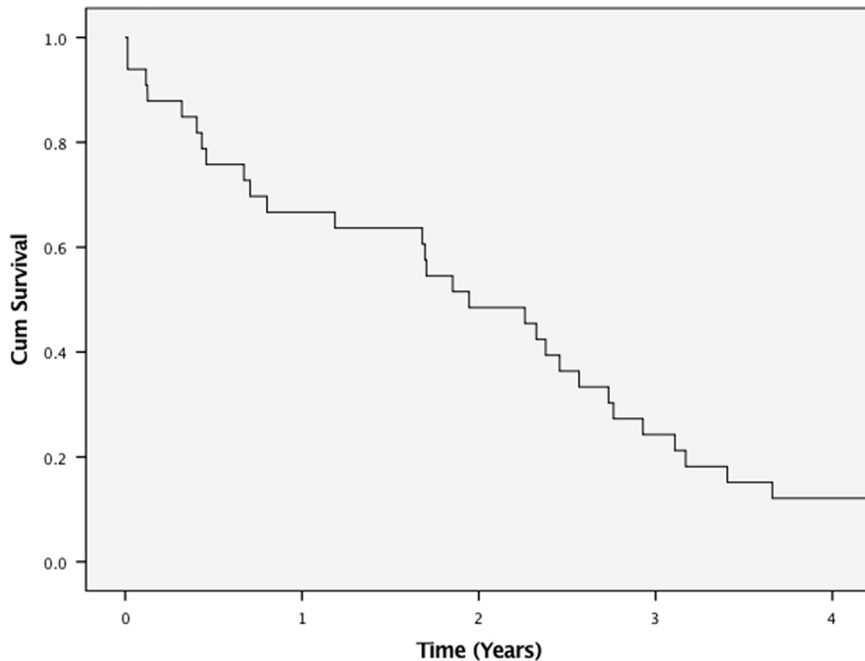

Figure 2 Survival function.

and a trend regarding cannabis use (58.6%, p=0.065). A suicide attempt before first presentation was made by 20.7% of the sample, and the most frequent method used by 'late' attempters was self-poisoning (55.2%). Neuropsychological measures did not significantly differ across groups, including comparisons of early and late attempters with non-

Table 1   Differences between suicide attempters and non-attempters FEP.

	Total sample (N=397)	Attempters (N=60)	Non-attempters (N=337)	Test statistic	P
Demographic variables					
Age, years: mean (s.d.)	28.94 (9.46)	28.35 (8.56)	30.11 (9.61)	$t=1.32$	0.185
Age at illness onset, years: mean (s.d.)	28.65 (9.01)	26.97 (7.62)	28.94 (9.21)	$t=1.55$	0.12
DUP, days: mean (s.d.)	417.00 (925.26)	407.95 (993.64)	418.58 (914.32)	$t=0.08$	0.935
Education, years: mean (s.d.)	10.24 (3.35)	9.8 (3.17)	10.32 (3.39)	$t=1.11$	0.27
Male sex (%)	226 (56.9)	42 (70)	184 (54.6)	$\chi^2=4.96$	0.026
Unmarried (%)	83 (21.0)	49 (81.7)	264 (78.6)	$\chi^2=0.29$	0.587
Living alone (%)	339 (85.6)	4 (6.7)	53 (15.8)	$\chi^2=3.43$	0.064
Unemployed (%)	220 (55.6)	31 (51.7)	145 (43.2)	$\chi^2=1.49$	0.222
Urban area (%)	293 (74.0)	50 (83.3)	243 (72.3)	$\chi^2=3.31$	0.073
Cannabis (%)	171 (43.1)	33 (55)	138 (40.9)	$\chi^2=4.1$	0.043
Alcohol (%)	215 (54.3)	33 (55)	182 (54.2)	$\chi^2=0.01$	0.905
Family history of psychosis (%)	88 (22.2)	14 (23.79)	74 (22)	$\chi^2=0.09$	0.763
Low socio-economic status (%)	207 (52.8)	33 (55)	174 (52.4)	$\chi^2=0.14$	0.711
Poor premorbid adjustment (%)	117 (35.3)	24 (49)	93 (33)	$\chi^2=4.68$	0.031
Clinical variables					
BPRS total: mean (s.d.)	62.42 (12.58)	64.18 (11.6)	62.11 (12.74)	$t=-1.18$	0.24
SAPS total: mean (s.d.)	13.50 (4.31)	13.18 (3.81)	13.56 (4.4)	$t=0.62$	0.536
SANS total: mean (s.d.)	7.07 (6.25)	7.7 (7.1)	6.95 (6.1)	$t=-0.85$	0.394
CDSS total: mean (s.d.)	2.34 (3.28)	3.81 (3.97)	2.08 (3.07)	$t=-3.186$	0.002
Severe positive symptoms (%)	192 (48.4)	25 (41.7)	167 (49.6)	$\chi^2=1.27$	0.260
Severe negative symptoms (%)	172 (43.3)	28 (46.7)	144 (42.7)	$\chi^2=0.32$	0.571
Severe disorganazed symptoms (%)	177 (44.6)	24 (40)	153 (45.4)	$\chi^2=0.68$	0.438
Severe depression (%)	51 (13.0)	15 (25.4)	36 (10.8)	$\chi^2=9.46$	0.002
SUMD: insight mental illness (%)	125 (35.5)	20 (40)	105 (34.8)	$\chi^2=0.51$	0.474
SUMD: insight need treatment (%)	188 (53.4)	24 (48)	164 (54.3)	$\chi^2=0.68$	0.408
SUMD: insight social consequences (%)	218 (61.9)	31 (62)	187 (61.9)	$\chi^2=0$	0.991
Hospitalization (%)	256 (64.5)	46 (76.7)	210 (62.3)	$\chi^2=4.58$	0.032
Schizophrenia diagnosis (%)	224 (56.4)	39 (65)	185 (54.9)	$\chi^2=2.11$	0.146
Previous admission self-harm (%)	25 (6.29%)				

Abbreviations: DUP=Duration of untreated psychosis; BPRS=Brief Psychiatric Rating Scale; SAPS=Scale for the Assessment of Positive Symptoms; SANS=Scale for the Assessment of Negative Symptoms; CDSS=Depression Scale for Schizophrenia; SUMD=Scale to Assess Unawareness of Mental Disorder.

attempters and, early with late attempters. (Data available upon request.)

3.2.   Factors predicting any attempt

The regression model included sex, cannabis consumption, depression, premorbid adjustment, hospitalization at admission, living status, living area and previous suicide attempts for 325 patients. These variables predicted 'any attempt' with 91.4% accuracy and correctly classified 98.9% of "non-attempters" and 46.8% of "attempters". Due to multicollinearity, previous suicide attempts and living status were not considered. Information on processing speed did not survive multivariate analyses and it was not included in the model presented since it would reduce the sample size from 325 to 272 individuals. Depression was found to be the exclusive significant predictor (OR=4.52; 95% CI 1.72-11.85;

$p=0.002$), while cannabis use showed a trend (OR=2.33; 95% CI 0.93-5.83; $p=0.069$). See Table 3.

3.3.   Factors predicting early and latter attempts

With regard to early attempts, the regression model included sex, depression, premorbid adjustment, living area and hospitalization. These variables had an accuracy of 91.4% in predicting early attempts and correctly classified 98.9% of the "non-attempters" and 4.2% of the "early-attempters". Severe depression (OR=4.41; 95% CI 1.6-12.18; $p=0.004$) and hospitalization (OR=5.02; 95% CI 1.37-18.41; $p=0.015$) were the most significant predictors, followed by being male (OR=4.52; 95% CI 1.72-11.85; $p=0.002$), living in an urban area (OR=0.18; 95% CI 0.04-0.85; $p=0.031$) and having worse premorbid adjustment (OR=0.4; 95% CI 0.16-0.99; $p=0.047$). See Table 4.

Table 2 Comparison of neurocognitive performance between attempters and non-attempters.

	Attempters		Non-attempters			
	N	Mean (SD)	N	Mean (SD)	t-test	p
Cognitive domain						
Premorbid IQ						
WAIS-III vocabulary	41	8.46 (3.26)	251	9.18 (2.73)	1514	0.131
Information processing speed						
WAIS-III digit symbol	44	5.91 (2.96)	258	6.87 (2.94)	2005	0.046
TMT A (sec)	43	49.37 (17.94)	259	46.02 (19.12)	−1.075	0.283
Motor dexterity						
Grooved Pegboard dominant hand (sec)	42	77.62 (20.36)	248	72.3 (24.97)	−1.309	0.192
Working memory						
WAIS-III digits backward	44	5.45 (1.81)	259	5.52 (2.06)	0.19	0.85
Verbal memory						
RAVLT list delayed recall	43	6.7 (3.38)	259	7.49 (3.28)	1467	0.144
Visual memory						
Rey figure delayed recall	43	16.46 (7.75)	256	18.19 (2.34)	1501	0.134
Attention						
CPT total correct	42	65.52 (18.16)	236	69 (14.34)	1381	0.168
Executive fuction						
TMT B-A (sec)	42	62.6 (47.6)	252	61.88 (50.94)	−0.084	0.933

Abbreviations: IQ=Intelligence quotient; WAIS-III=Wechsler Adult Intelligence Scale III; TMT A=Trail Making Test A, TMT B=Trail Making Test B; RAVLT=Rey Auditory Verbal Learning Test; CPT=Continuous Performace Test.

Table 3 Predictors of any suicide attempt in FEP.

	B	SE	Wald	Significance	OR	95% CI
Predictors (N=325)						
Male	0.017	0.474	0.001	0.971	1018	0.402-2.578
No living alone	18.46	4536.17	<0.001	0.997	–	–
Rural area	−0.93	0.59	2.47	0.116	0.396	0.125-1.257
Cannabis consume	0.85	0.467	3298	0.069	2335	0.935-5.832
Premorbid social adjustment	−0.73	0.448	2686	0.101	0.48	0.199-1.155
Depression	1.51	0.49	9.38	0.002	4.52	1.72-11.85
Hospitalization at admisssion	−0.123	0.447	0.076	0.783	0.884	0.368-2.122
Previous attempt	−38.45	8235.33	<0.001	0.996	–	–

Model $\chi^2(8)$=117.92, $p<0.001$, R^2 Nagelkerke=0.54

The regression model for 'late' attempters included DUP, depression, cannabis consumption and previous admission attempts. These variables had 93.6% accuracy and correctly classified 100% of the "non-attempters" and 17.9% of the "late-attempters". The exclusive significant predictor was depression (OR=2.98; 95% CI 1.09-8.18; $p=0.033$). See Table 5.

3.4. Differences in psychotic symptoms between attempters and non-attempters

To further explore psychopathological differences between attempters and non-attempters, analyses with SAPS, SANS and BPRS items were performed. When considering attempters as a whole, this group presented with more severe delusions ($p=0.007$), unusual thought content ($p=0.014$), suspiciousness ($p=0.009$) and guilt ($p=0.04$), but had lower scores on elated mood ($p=0.01$), motor hyperactivity ($p=0.03$), excitement ($p=0.02$), distractibility ($p=0.02$) and disorientation ($p=0.007$) than non-attempters. Late attempters showed more suspiciousness ($p=0.001$) and more severe depression ($p=0.04$) than non-attempters. Early attempters presented with more severe delusions ($p=0.001$), unusual thought content ($p=0.001$), anxiety ($p=0.005$) and lower mood ($p=0.001$). Finally, early attempters had higher scores on anxiety ($p=0.04$), unusual thought content ($p=0.02$) and suicidality ($p=0.003$), and lower scores on motor retardation ($p=0.04$) and tension ($p=0.049$) than late attempters. See Table 6.

4. Discussion

Two major findings emerged from our study, which were relatively in line with our hypotheses. First, it seems that

Table 4 Predictors of early attempt in FEP.

	B	SE	Wald	Significance	OR	95% CI	
Predictors (N=302)							
Male	1.095	0.544	4.048	0.044	2.988	1.029	8.678
Rural area	−1.692	0.783	4.671	0.031	0.184	0.040	0.854
Premorbid social adjustment	−0.917	0.462	3.940	0.047	0.400	0.162	0.989
Depression	1.484	0.518	8.204	0.004	4.412	1.598	12.183
Hospitalization at admisssion	1.613	0.663	5.909	0.015	5.017	1.367	18.414

Model $\chi^2(5)=30.95$, $p<0.001$, R^2 Nagelkerke$=0.23$

Table 5 Predictors of later attempt in FEP.

	B	SE	Wald	Significance	OR	95% CI	
Predictors (N=361)							
Duration of untreated psychosis	0.000	0.000	0.366	0.545	1.000	0.999	1.001
Depression	1.091	0.511	4.555	0.033	2.977	1.093	8.106
Cannabis consume	0.593	0.441	1.814	0.178	1.810	0.763	4.292

Model $\chi^2(4)=32.87$, $p<0.001$, R^2 Nagelkerke$=0.207$

there is a critical temporal pattern of self-harm behaviour in FEP patients. In particular, the month preceding first contact with psychiatric services and the 2 months after the first contact are the times of greater risk, which also tends to be characterized by the use of methods of high lethality and includes most cases of suicide completion in our sample. Second, 'early' and 'late' suicidal behaviours in FEP seem to differ in terms of risk factors; 'early' attempts appear to be more related to acute psychosis, while 'late' attempts appear to be the result of having developed secondary depression.

Although the period between the onset of psychotic symptoms and first contact with services has been reported to be a time of major concern, few studies have examined this period in detail. Recent studies have focused on suicidality over the period of untreated psychosis (DUP) and shortly prior to study entry (Barrett et al., 2010; Flanagan and Compton, 2012). Barrett et al., 2010 found that such suicide attempts were associated with more depressive episodes, younger age at illness onset, drug use and longer DUP. In Flanagan et al.'s study (Flanagan and Compton, 2012), depression, insight and suicidality were found to be predictors of suicidal ideation prior to the initial hospitalization. Fedyszyn et al. (2010) found that the suicide risk was higher in the first month of treatment and decreased rapidly over the next 6 months. Tarrier et al. (2006) showed that the first six weeks after admission were significantly associated with suicidal behaviour severity, more severe positive psychotic symptoms, greater insight, lower self-esteem, and greater depression. In agreement with Pompili et al. (2011) findings, we confirmed that the highest self-harm rates occurred before psychiatric hospitalization and shortly after discharge. Therefore, the first hospital admission does not necessarily represent illness onset and similarly, discharge from hospital may not necessarily suggests illness remission.

We found that 46% of our FEP attempters had made suicide attempts prior to the study inception, which was

also the strongest predictor of future suicide attempts in line with previous research (Bakst et al., 2010a; Challis et al., 2013; Tarrier et al., 2006) including a recent meta-analysis (Large et al., 2011). Nevertheless, we also found novel differences with regard to 'early' and 'late' suicide attempts in FEP, which are discussed below.

With regard to baseline predictors for 'early' suicide attempts in our FEP sample, being male, living in urban areas, requiring hospitalization, having poor premorbid adjustment and more severe depression appeared to increase the risk, which is consistent with the previous literature. Thus, although the association between being male and increased suicide risk has been consistently reported in schizophrenia (Hor and Taylor, 2010), some FEP studies failed to replicate this finding (Dutta et al., 2011). Moreover, some of these studies revealed similar suicidal risk across genders (Large et al., 2011) or even a greater risk for females (Thorup et al., 2007).

In terms of residence area, early suicide attempts were more frequent in individuals living in urban areas. In contrast to our results, however, Searles et al., 2013 found that suicide rates were higher in rural areas, which was linked to limited access to mental healthcare and availability of firearms in rural areas. In keeping with this, (Burrows et al., 2013), lower levels of urbanicity were associated with higher risk of suicide by firearms and lower risk of use of jumping to take one's life. Hence, urbanicity, as opposed to living in rural areas, may have different associations with suicide risk across countries. Specifically, we speculate that living in rural areas in Cantabria behaved as a protective factor for suicide due to increased social cohesion.

In our study, self-harm behaviour led to hospital admission in 7 (31.8%) of the 22 early attempters, which is consistent with previous studies (Harkavy-Friedman et al., 1999) reporting on the severe lethality of suicide methods used by patients with psychosis, who are therefore more likely to require medical attention after a suicidal event.

Table 6 Differences in psychotic symptoms between attempters and non-attempters.

	Attempters (n=60) Mean (SD)	Non-attempters (n=337) Mean (SD)	t-test	P
SAPS				
Hallucinations	2.2 (2.34)	2.63 (2.3)	t=1.321	0.187
Delusions	4.95 (0.22)	4.83 (0.6)	t=−2.711	0.007
Bizarre behaviour	4.15 (1.33)	3.84 (1.63)	t=−1.379	0.169
Positive Formal Thought Disorder	1 (1.64)	1.13 (1.8)	t=0.545	0.586
Inappropitate Affect	0.88 (1.55)	1.12 (1.72)	t=1.004	0.316
SANS				
Affective flattening	1.62 (1.78)	1.31 (1.55)	t=−1.248	0.216
logia	1.07 (1.66)	0.93 (1.52)	t=−0.653	0.514
Apathy	1.40 (1.97)	1.27 (1.8)	t=−0.522	0.602
Anhedonia	1.97 (1.91)	1.61 (1.84)	t=−1.371	0.171
Attention	1.65 (1.89)	1.84 (1.9)	t=0.704	0.482
BPRS				
Somatic concern	2.13 (1.96)	2.25 (2.08)	t=0.411	0.681
Anxiety	2.17 (1.59)	2.57 (1.73)	t=1.692	0.091
Depression	2.70 (2)	2.20 (1.65)	t=−1.821	0.073
Suicidality	2.72 (2.29)	1.35 (1.05)	t=−4.547	<0.001
Guilty	2.23 (2.04)	1.67 (1.45)	t=−2.06	0.043
Hostility	3.48 (2.38)	3.18 (2.24)	t=−0.946	0.345
Elated Mood	1.1 (0.4)	1.29 (0.95)	t=2.568	0.011
Grandiosity	1.33 (1.1)	1.44 (1.43)	t=0.562	0.575
Suspiciousness	6.67 (1.17)	6.19 (1.79)	t=−2.661	0.009
Hallucinations	3.57 (2.88)	3.94 (2.81)	t=0.955	0.34
Unusual thought content	6.82 (0.5)	6.59 (1.17)	t=−2.484	0.014
Bizarre behaviour	5.5 (2)	5.3 (1.97)	t=−0.714	0.467
Self-neglect	1.87 (1.57)	1.63 (1.32)	t=−1.261	0.208
Disorientation	1	1.08 (0.56)	t=1.146	0.007
Conceptual disorganization	2.33 (2.11)	2.3 (2.1)	t=−0.125	0.901
Blunted affect	2.73 (2.08)	2.41 (1.77)	t=-1.256	0.265
Emotional withdrawal	3 (2.1)	2.77 (2.04)	t=−0.787	0.432
Motor retardation	2.17 (1.71)	1.91 (1.47)	t=−1.209	0.227
Tension	2.58 (1.85)	2.49 (1.79)	t=−0.383	0.702
Uncooperativeness	2.43 (2.01)	2.67 (2.06)	t=0.835	0.404
Excitement	1.73 (1.34)	2.2 (1.85)	t=2.327	0.022
Distractibility	1.27 (0.82)	1.56 (1.26)	t=2.328	0.022
Motor hyperactivity	1.22 (0.69)	1.45 (1.18)	t=2.157	0.033
Mannerisms and posturing	1.43 (1.25)	1.65 (1.55)	t=1.025	0.306

Abbreviations: SAPS=Scale for the Assessment of Positive Symptoms; SANS=Scale for the Assessment of Negative Symptoms; BPRS=Brief Psychiatric Rating Scale.

However, the extent to which an admission reduces long-term suicide risk remains controversial. Thus, although the main determinant for an admission tends to be acute psychosis (Hunt et al., 2012), perceived humiliation by the individual over the admission process, particularly when an involuntary admission is required, should be taken into account in order to lessen the negative impact on self-esteem, which may increase later suicide risk (Svindseth et al., 2007).

In spite of the held notions about the relationship between cognition and suicide recently summarized by Lara et al. (2015), and specifically between the preserved cognitive function and suicidal attempts in psychotic disorders (Nangle et al., 2006), in our FEP sample suicide risk did not correlate with overall cognition. Similar negative results have been shown previously by Potkin et al. (2003).

Although attempters showed significantly poorer information processing speed, this association did not survive the multivariate analyses. However, as mentioned above, cognitive decline may prevent patients with schizophrenia and related disorders from dying by suicide (De Hert et al., 2001; Fenton, 2000). Thus, further research is warranted to clarify whether or not cognitive impairment prevents schizophrenia patients from suicide. As stated by Martinez-Aran and Vieta (2015), exploring relevant topics such as the role of cognitive reserve and cognitive enhance in clinical outcomes, are the close future of investigation and intervention.

In keeping with prior studies, we replicated the association of premorbid functioning with suicide attempts (Bakst et al., 2010b; Muller et al., 2005). Hence, a specific assessment of this domain might help to identify high-risk

FEP patients. Also, depression was found to play a crucial role in suicidality in our FEP patients, consistent with previous studies (Barrett et al., 2010; Bertelsen et al., 2007; Flanagan and Compton, 2012; Harvey et al., 2008; Kontaxakis et al., 2004). Furthermore, early attempters showed more severe acute psychotic symptoms, such as delusions, unusual thought content, excitement and anxiety, tension and motor retardation, which is in line with previous work, particularly the association between thought disorder (Bakst et al., 2010a) or distress, related to acute psychosis and suicide risk at first presentation (Harvey et al., 2008). Interestingly, shorter DUP, cannabis use and depression were found to be associated with 'late' risk of suicide, although only depression survived the multivariable regression models. Hence, depression seems to be a high risk factor for suicide in both early and later stages of FEP.

In the light of our findings, we might postulate that 'early' and 'late' depression may have different phenomenological correlates. Thus, a recent 12-month follow-up first-episode psychosis study found that while malevolent voices, use of safety behaviour and subordination to persecutors were associated with depression in the acute FEP, post-psychotic depression was linked to loss, shame, low level continuing positive symptoms, and longer duration of untreated psychosis (Upthegrove et al., 2014). For instance, depressive symptoms observed in attempters around hospital admission might be related to anxiety and distress related to psychotic symptoms (Harvey et al., 2008) and the negative impact of hospitalization (Svindseth et al., 2007); while hopelessness, social isolation and impaired quality of life as a consequence of psychosis might underlie depressive symptoms in late attempters (Barrett et al., 2010). In line with our results, a previous first episode study from our group found an association between suicidal behaviour preceding first contact with services and depression at that point (Lopez-Morinigo et al., 2014). Also, depression in the prodromal stage was reported to predict suicidality at first presentation and further depressive episodes both in the acute and recovery stages of FEP (Upthegrove et al., 2010), which appears to challenge the so-called demoralization syndrome (Drake and Cotton, 1986). Moreover, despite the kraepelinian classification of psychoses, depression should be understood as a pathological dimension in its own right both in first episode psychosis (Peralta et al., 2013) and schizophrenia (Siris, 2004). Hence, depression appears to play a crucial role in risk of suicidal behaviour both in schizophrenia (Hawton et al., 2005) and FEP (Pompili et al., 2011). However, there is little guideline in the management of depression in schizophrenia and related disorders (Siris, 2000) and further research in this area is therefore needed.

Regarding cannabis use, previous FEP studies (Melle et al., 2010) reported on the role of substance misuse in suicide risk, particularly conjointly with depression. Therefore, the impact of substance abuse on suicide risk in FEP should not be overlooked in early intervention services which may focus on other aspects of the management of psychosis.

Interestingly, shorter DUP was associated with a higher risk of late attempts. Previous studies found an association between longer DUP and suicide risk, particularly in association with depression and severity of psychiatric symptoms (Barrett et al., 2010; Clarke et al., 2006; Mitter et al., 2013). A possible explanation for our results is that a shorter DUP might be associated with greater levels of awareness of psychotic symptoms, which was also linked to suicidal history preceding first presentation with psychosis, and subsequent feelings of hopelessness, thus increasing long-term suicide risk (Lopez-Morinigo et al., 2014).

4.1. Strengths and weaknesses

To our knowledge, this is the first FEP study aimed at investigating suicide risk over specific periods of the course of the illness, including a 3-year follow-up period. Of note, we recruited a relatively large sample ($N=397$) of FEP patients, which allowed us to conduct further exploratory analyses. Moreover, our sample included both in- and out-patients from urban and rural areas, which is therefore highly representative of our catchment area population. In addition, a wide range of potential contributing variables was analysed.

However, several study limitations should be borne in mind when interpreting our results. First, follow-up information on suicidal behaviour was taken retrospectively from the medical records, which might have resulted in under-estimating suicide attempts. In addition, some FEP patients may have completed suicide before first contact with psychiatric services, thus also increasing the risk of under-estimation. Second, the sample size of suicide attempters subgroups may have reduced the statistical power of some statistical analyses. Third, other non-tested variables may contribute to suicide risk in FEP. Fourth, several variables were dichotomized due to little variability of scores across patients, which may have increased the risk of false positives. Finally, 'baseline' predictors may have changed over the follow-up period and therefore their associations with suicide risk should be taken cautiously, particularly regarding late attempters.

5. Conclusion

In summary, our results suggest the existence of a critical period for suicide attempts around first presentation with psychosis, which differs meaningfully from 'later' suicidal acts. More specifically, early high-risk individuals tend to be males who live in urban areas, with poorer premorbid adjustment and are more likely to require hospital admission. However, depression and substance use were the strongest predictors of suicide risk in our whole FEP sample, in addition to severity of symptoms in the early risk period. Hence, better management of psychosis, depression and substances misuse emerges as the main focus for early intervention programmes which aim to reduce suicide in patients with psychosis.

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Contributors

All the authors have participated and have made substantial contributions to this paper.

RAA: design, statistical analysis, interpretations of data and drafting the article.

EGA and BVH: revision of medical records, design and revising the article.

RPI, JDLM and RD: statistical analysis, interpretations of data and revising the article.

ASD, RTS and BCF: conception, design and revising the article.

Conflict of interest

The authors have no conflicts of interest concerning the subject of the study.

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