



Review

Suicide risk in first episode psychosis: A selective review of the current literature

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ABSTRACT

Many studies have confirmed that the risk of suicide in patients with first-episode psychosis (FEP) is high, and high rates of premature mortality, particularly from suicide, may occur in the early phases of schizophrenia. However, suicide rates are difficult to measure in FEP patients, even in carefully defined samples, and there is relatively little specific information about the risk of suicide at illness onset or retrospectively concerning the untreated psychotic period. This selected review of the literature investigates suicidal behaviour with particular regard to severe suicidality (plans and attempts) and risk factors associated with suicide in FEP patients. A search was performed to identify all papers and book chapters during the period 1965–2010, and approximately 100 studies met the inclusion criteria. Most of evidence suggests that risk of suicidal behaviour is relatively high in FEP patients. The research reports highlight the need for universal, comprehensive, public mental health interventions aimed, not only toward early detection, but also toward the rapid engagement in treatment of people with psychoses. These interventions should include an adequate assessment of suicidal behaviour in patients with FEP, and an examination of the efficacy of specific components of the interventions.

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1. Introduction

Excess mortality has been repeatedly reported in patients with schizophrenia (Bralet et al., 2000; Loas et al., 2008; Pompili et al., 2007, 2008, 2009; Roy and Pompili, 2009).

Suicide is one of the major contributors to the morbidity and mortality of schizophrenia, especially in first-episode psychosis (FEP) patients (Brown, 1997; Caldwell and Gottesman, 1992; Sartorius et al., 1987). Suicide accounts for approximately 2–5% of deaths in FEP patients as reported in long-term follow-up studies (Dutta et al., 2010, 2011; Palmer et al., 2005). Furthermore, several studies have demonstrated that, even prior to their first presentation, up to 10% (Bertelsen et al., 2007; Clarke et al., 2006; Harvey et al., 2008) or higher (Nordentoft et al., 2002) of FEP patients have made at least one suicide attempt (a non-fatal suicidal behaviour having suicidal intent), and a high percentage of undiagnosed

individuals complete suicide (Foley et al., 2008). The highest risk is among early onset patients (Krausz et al., 1995; Melle et al., 2006; Palmer, et al., 2005, Shrivastava et al., 2010).

A Danish study suggested that the standardized mortality ratio (SMR)¹ is increased in the first episode of schizophrenia and falls incrementally over the 5 years following a first episode of schizophrenia (Munk-Jorgensen and Mortensen, 1992). Brown (1997) reported that the excess mortality in schizophrenia was highest in FEP or early illness phase patients and suicide is the largest contributor to this excess. Specifically, suicide rates of FEP subjects are 2.7 times higher than in the chronic stages of the illness.

Haw et al. (2005) performed a systematic review of the international literature, including cohort and case-control studies of patients with schizophrenia or related diagnoses that reported deliberate self-harm (DSH) as an outcome and concluded that DSH was a strong predictor of suicide in schizophrenia.

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¹ The SMR is defined as the ratio of the observed deaths in the study population to the expected deaths controlling for the sex and age distribution of the study group.

Suicide happens in the early phases of schizophrenia and both genetic and environmental factors have been found to affect the suicidal risk, but the precise mechanism and the magnitude of these contributions are unclear.

Additionally, little is understood about the timing of suicidal risk in FEP patients. Suicide rates may be difficult to measure, even in carefully defined samples, because (1) there is diagnostic instability in early phases of psychotic disorders (Haahr et al., 2008); (2) studies of psychotic disorders have typically focused on suicidality in relation to the time of the first treatment rather than the time of the onset of the psychosis; and (3) few studies have investigated suicidality during the period of untreated psychosis, although this is considered to be a period of higher risk for violent suicide attempts compared to treated patients (Nielssen and Large, 2009).

Our aim is to conduct a selected overview of the current status of the international literature that would be of great value for researchers and clinicians. The objective of the present review was to assess suicide risk in patients with FEP and to search for the most relevant demographic and clinical predictors of suicidal behaviour.

2. Method

In order to provide a new and timely review of suicide in FEP, we performed careful MedLine, Excerpta Medica, PsycInfo and Index Medicus searches to identify all papers and book chapters in English during the period 1965–2010.

The patients included in the present study were those diagnosed with first episode schizophrenia and other types of schizophrenia-like psychoses (schizophreniform and schizoaffective disorders). We included only studies reporting rates of suicidal behaviour (completed suicide, deliberate self-harm, suicide attempts, suicidal ideation and plans) or suicidal risk (risk factors for completed suicide and prior suicidal behaviour). Where a title or abstract seemed to describe a study eligible for the inclusion, the full article was obtained and examined in order to assess its relevance based on the inclusion criteria.

The MedLine Search terms which were used were the following: “first episode psychosis” OR “first episode schizophrenia” AND “schizophrenia prodromal phase” OR “schizophrenia prodromal symptoms” AND “duration of untreated psychosis” AND “inpatients” OR “outpatients” AND “Suicide” OR “Suicidal risk” OR “Suicide rates” OR “Suicidal risk factors” AND “Prevention” AND “Pharmacological treatment” AND “Psychosocial treatment” AND “Rehabilitation”.

The combined search strategies yielded over 150 abstracts but, after an analysis of the abstracts, 111 full-text articles were reviewed. Approximately 54 studies met the inclusion criteria and were included. The relevance of papers was assessed by two independent researchers. Any discrepancies between the two reviewers who examined the studies for possible inclusion were resolved by consultation with a senior author (PG). The authors decided to focus on the most recent studies for the inclusion in the present review. Fig. 1 summarizes the search strategy followed for the inclusion of the studies in the current review.

3. Suicidal risk in FEP

Table 1 summarizes the most relevant studies reporting suicide rates in FEP patients. The highest suicide rate occurs after psychiatric hospitalization or soon after discharge. The first year of treatment is associated with a 60% increased risk of suicide compared to patients in other phases (Nordentoft et al., 2004). However, the suicide rates in FEP patients differ in the various studies.

Table 2 summarizes the most relevant studies on suicidal behaviour in FEP patients. The risk for suicidal behaviour is present over the course of schizophrenia, but the excess risk is higher in younger patients (Caldwell and Gottesman, 1990; Harkavy-Friedman et al., 1999; Malla and Payne, 2005; Tsuang, 1978).

3.1. Follow-up studies

3.1.1. Completed suicide

Krausz et al. (1995) found that the suicide rate in young patients who developed a schizophrenic psychosis between the ages of 14 and 18 was 13.1%, significantly higher than in studies of FEP patients who developed the psychosis at a later age. In the follow-up period of 11+ years, 21.5% of the men and 6% of the women completed suicide.

Nordentoft et al. (2004), in a nested case–control design, using data from four longitudinal Danish registers, reported a reduction in the suicide rate from 1981 to 1997 among patients with any schizophrenia spectrum disorder, similar to that observed in the general population (incidence rate ratio 1.00, 95% confidence interval 0.98 to 1.03). The authors reported that the suicide rate was highest in the first year after the first admission, particularly in the younger patients.

In a follow-up study of a randomized controlled trial of integrated vs. standard treatment in a cohort of 547 individuals with FEP spectrum psychosis (the OPUS trial), Bertelsen et al. (2007) reported that sixteen participants died during the 5-year follow-up, including 7 from suicide (1.3%) and an additional 6 whose cause of death could not be ascertained.

3.1.2. Deliberate self-harm

Verdoux et al. (2001), in a two-year follow-up study of 65 FEP patients assessed at 6-monthly intervals, reported that 11.3% of the patients displayed deliberate self-harm behaviour (non-fatal intentional, direct injuring of body tissue without suicidal intent – DSH). Baseline predictors of DSH were a lifetime history of parasuicide before the first admission (OR=5.9), lower positive scores on the Positive and Negative Symptom Scale (OR=0.8) and a longer duration of the first admission (OR=1.1). Patients with DSH had a longer duration of psychotic symptoms (OR=1.1) and a greater risk of being readmitted (OR=4.6). Patients with comorbid substance misuse were seven times more likely to engage in suicidal behaviour over the two-year period. The authors concluded that having a history of parasuicide, a deteriorating clinical course and substance misuse increased the risk of suicidal behaviour.

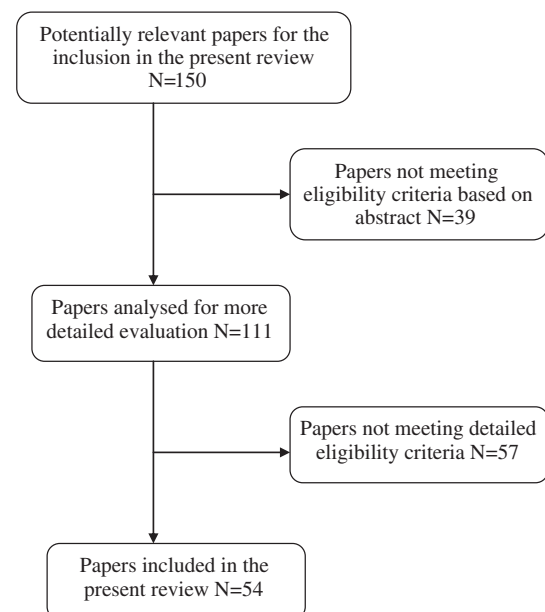


Fig. 1. The search strategy for the inclusion of studies in the current review.

3.1.3. Suicide attempts

In a one-year follow-up of a randomized controlled trial (the OPUS study), Nordentoft et al. (2002) studied a sample of 341 patients with a FEP spectrum disorder, randomly assigned to integrated treatment or treatment as usual. During the first year of treatment, 11.3% (31/275) of the patients attempted suicide. Attempting suicide was predicted by female gender, hopelessness and hallucinations.

In 444 participants in the Suffolk County Mental Health Project, Bakst et al. (2010) reported that worse premorbid functioning was associated with an increased likelihood of a suicide attempt prior to the first psychiatric hospital admission. Among the 126 participants with a previous suicide attempt, poor premorbid functioning was associated significantly with an increased likelihood of additional attempts during the 4 years after the first hospitalization. Levine et al. (2010) found that FEP patients admitted as a result of a suicide attempt (8.5% of the total FEP admissions) were more often college-educated, female and not married. Of the patients admitted after a suicide attempt, 31.6% (62/196) made another suicide attempt during the follow-up period of 4 to 7 years.

Addington et al. (2004) analysed a cohort of 238 patients assessed at initial presentation to a comprehensive early psychosis program and found that 15.1% had attempted suicide prior to program entry. After 1 year, 2.9% had made another attempt and 0.4% completed suicide, but no additional attempts were seen in those who had a history of attempted suicide prior to entry into the program.

In the follow-up study of a cohort of 547 individuals with FEP spectrum psychosis (the OPUS trial) mentioned above, Bertelsen et al. (2007) found that depressive and psychotic symptoms, especially hallucinations, at baseline predicted suicidal plans and attempts after 1 year, and persistent suicidal behaviour and ideation at baseline were associated with a greater risk of attempting suicide in the first year of follow-up. After entering all variables into a multivariate analysis, only having suicidal thoughts at baseline predicted suicidal plans during the 1-year follow-up, and suicidal plans at baseline predicted suicide attempts during the 1 year follow-up. Both in the univariate and the multivariate analyses, a strong association was reported between depression, suicidal thoughts, plans and previous attempts after 1 year of treatment with suicidal plans and attempts in the second year. Bertelsen et al. (2007) noted that a younger age predicted suicidal plans and attempts, and female gender predicted attempting suicide in the second year.

Melle et al. (2010) conducted a 2-year follow-up study of a comprehensive, integrated treatment regimen in two groups of FEP patients (118 from a region with an early detection program and 113 from a region without such a program). Low rates of completed suicide and suicide attempts in both groups were found after 2 years of treatment, with no between-group differences. Severe suicidality (plans and attempts) was predicted by drug abuse, dissatisfaction with life and severe suicidality at the start of treatment.

Robinson et al. (2010) followed up a cohort of 282 FEP patients for an average of 7.4 years who were treated at the Early Psychosis Prevention and Intervention Centre (EPPIC). Of these patients, 61 patients (21.6%) made a suicide attempt during the follow-up, including 12 who completed suicide. Patients with a history of self-harm at intake were more than four times as likely to attempt suicide during the follow-up. Suicidal tendencies, being depressed for >50% of the initial psychotic episode and hopelessness at intake each predicted a higher (more than twofold) risk of suicide attempts during follow-up. Alcohol abuse increased the risk of multiple suicide attempts. The authors concluded that the risk for suicide remains elevated for at least 7 years following treatment, and the key predictor of future suicidal behaviour was previous self-harm.

The rapid development of 'insight' is one of the most relevant risk factor for causing a state of hopelessness and depression in the immediate post-psychotic experience (Birchwood et al., 2000; Iqbal et al., 2000; Pompili et al., 2004, 2011).

Drake et al. (2004) found that the relationship between insight and depression diminishes with time in the 18 months after the diagnosis. Crumlish et al. (2005) found that insight increased with time over the 4 years after a FEP. Only 3% of patients have full insight at FEP onset vs. 37% after 4 years. Insight 6 months after intake predicted depression and attempting suicide by the time of the 4-year follow-up. However, prospective longitudinal studies investigating the association between insight in FEP patients and suicidality have been few, and those studies published on this topic have often produced mixed results.

In our opinion, the process of adjustment to schizophrenia is gradual, and 6 months after presentation is a pivotal point for insight, perhaps because it takes some time to grasp the full ramifications of a diagnosis of severe mental illness. Recognition of mental illness and a greater insight at this point may have an enduring negative effect on mood, as well as an impact on the likelihood of a suicide attempt. As suggested by Markova and Berrios (1992) insight is normally considered to be the ability to re-label unusual mental events as pathological, recognize the suffering due to the mental illness, and understand the necessity of treatment compliance. Its absence is usually considered to be a fundamental inability to realistically evaluate one's life circumstances (Hewitt, 2010), but its presence, as the illness progresses, may influence the subjective perception of impaired interpersonal interactions with the world and, thereby, impact on suicidal risk.

As a result of the results of studies such as those reviewed above, Nordentoft and Sogaard (2005) cautioned that all FEP patients who are treated after attempting suicide represent a high-risk group for suicide and need to be adequately supported and treated.

3.2. Cross-sectional studies

3.2.1. Suicide ideation and attempts in the early phases of FEP

Barrett et al. (2010) confirmed the association between suicidal ideation and attempts in FEP patients prior to treatment and in the early phases after treatment starts. They studied 170 patients with FEP from the ongoing Thematic Organized Psychosis Research (TOP) for diagnosis, suicidality, symptoms, substance use and premorbid functioning and found that, prior to entry into the study, 60 patients (35.3%) were nonsuicidal, 66 (38.8%) had suicidal ideation, and 44 (25.9%) had attempted suicide. Attempting suicide during the period of untreated psychosis was associated with more numerous depressive episodes and a younger age at illness onset, in addition to drug use in the last 6 months.

In a group of 578 young adults with an untreated FEP spectrum disorder (from the OPUS study), Thorup et al. (2007) found that men had more severe negative symptoms, worse premorbid functioning and social adjustment, smaller social networks, more substance abuse, and were more often unemployed and living alone while women had more severe hallucinations. Women were more likely to have attempted suicide in their lifetime (41% vs. 25%) and experienced lower self-esteem in spite of better social functioning.

Conus et al. (2010a,b) studied 658 FEP outpatients and found that 83% of the patients had been exposed to at least one stressful event during their lifetime, and 34% to sexual and/or physical abuse (SPA). SPA patients were more likely to have had post-traumatic stress disorder and substance use disorder before the onset of the psychosis, to have made a suicide attempt in the past, and to have worse premorbid functioning. SPA patients were more likely to attempt suicide during treatment.

Joia et al. (2009) compared 43 patients with onset of FEP before the age of 18 with 189 patients with FEP onset between 18 and 65 years of age and found that adolescent-onset patients had poorer premorbid functioning, a longer duration of untreated psychosis, higher suicidality (26% had lifetime suicidal plans or attempts vs. 12% in the older onset patients), and more depressive symptoms. They also

Table 1

The most relevant studies about suicide rates in FEP.

Study	Design	Sample size	Conclusions	Eventual follow-up	Suicide plans, ideation and attempts	Completed suicide
Cohen et al. (1994)	Cross-sectional study	184 psychotic inpatients	Those with a current attempt had significantly higher rates of lifetime history of major depression and less physical violence	No	42 (23%) had a suicide attempt history, and 52 (28% of the sample, 65% of attempters) were hospitalized for a suicide attempt	None
Krausz et al. (1995)	Long-term follow-up study including two follow-up periods after 5 and 11 years	Patients aged 14–18 years	The suicide rate was significantly higher than in studies of psychotic patients in a later period of life.	Yes	The suicide rate was 13.1%	21.5% of the men vs. 6% of the women
Verdoux et al. (2001)	Two-year follow-up study of first-admitted patients assessed at ½ year intervals over a 2-year follow-up	65 FEP patients	Baseline predictors of suicidal behaviour were a lifetime history of parasuicide before the first admission (OR = 5.9), lower positive scores on the PANSS (OR = 0.8) and a longer duration for the first admission (OR = 1.1). Having a history of parasuicide, a deteriorating clinical course and substance misuse increased suicidal risk.	At 2 years substance abusers were seven times more likely to engage in suicidal behaviour.	2 (1.3%) parasuicide during the first ½ year, 5 (3.25%) between ½ and 1 year, 1 (0.65%) between 1 and 1½ years and 1 (0.65%) between 1½ and 2 years	1 (0.65%) at 1 year of follow-up
Kontaxakis et al. (2004)	Cross sectional study comparing patients with and without suicidal thoughts	93 schizophrenia patients	Severity of depressive symptoms, motor retardation, guilt feelings, pathological guilt, and self-depreciation predicted the patients' suicidal ideation	No	20.4% patients reported suicidal thoughts during the last 15 days	None
Addington et al. (1998)	Longitudinal cohort study comparing level of depression in FEP and in a relapsing group	113 people during an acute relapse and 13 FEP patients	The median score on the Calgary Depression Scale for Schizophrenia was significantly higher in the FEP group during the acute phase	At ¼ and 1 year FEP group were significantly more depressed	No	None
Nordentoft et al. (2004)	Nested case–control design from 4 longitudinal Danish registers	18,744 who committed suicide between 1981 and 1997 individually matched with 20 controls (374 880 population controls)	The reduction in the suicide rate among schizophrenic patients was similar to the general population (incidence rate ratio 1.00)	The risk of suicide was highest in the first year after first admission, especially in the younger age groups	No	1665 among those admitted to psychiatric hospitals
Palmer et al. (2005)	Review study of 632 articles including 48,176 subjects	Follow-up studies divided in: 32 studies of 25 578 patients schizophrenics recruited at various illness points and 29 studies of 22 598 schizophrenics at illness onset or first admission	The lifetime suicide prevalence in those from the first admission or illness onset group was 5.6%. Mixed samples showed a rate of 1.8% (95% confidence interval, 1.4%–2.3%). Most of subjects will commit suicide during their lifetimes, usually near illness onset.	No	No	2361 (4.9%) will commit suicide
Melle et al. (2006)	Randomized controlled trial	Consecutive psychotic patients who sought initial psychiatric treatment in four catchment areas (two of these including 141 subjects were early detection communities)	Early detection programs that bring patients into treatment at lower symptom levels may reduce suicidal risk at first treatment contact.	No	48 (35%) from communities with no early detection program vs. 40 (29%) from early detection communities having suicidal thoughts; 8 (6%) vs. 7 (5%) having suicidal plans; 22 (16%) vs. 7 (5%) with suicidal attempts. Month preceding first treatment contact, 49 (35%) vs. 37 (26%) having suicidal thoughts; 10 (7%) vs. 4 (3%) having suicidal plans; 14 (10%) vs. 2 (1%) with suicidal attempts	None

Conus et al. (2010a,b)	Epidemiological FEP patient cohort	A cohort of 786 FEP patients of which 658 were analyzed, admitted between 1998 and 2000 at the Early Psychosis Prevention and Intervention Centre	652 (83%) had been exposed to stressful events and 267 (34%) to sexual and/or physical abuse (SPA). SPA patients were more likely to have made suicide attempts in the past, and to have had poorer premorbid functional levels.	No	180 (79.6%) among sexual and/or physical abusers had a past history of suicide attempts; 32 (14.3%) made suicide attempts in treatment	None
Robinson et al. (2010)	Naturalistic, prospective follow-up (7.4 years) study	A cohort of 413 FEP patients treated at an early psychosis centre. Follow-up data available for 282	History of self-harm, suicidal tendencies, being depressed for >50% of the initial psychotic episode and hopelessness and alcohol abuse increased the risk of suicide attempts. The key predictor was previous self-harm.	The risk of future suicide attempts was elevated for 7 years	61 subjects (21.6%) made a suicide attempt over the follow-up period. 46.7% of those with one or more suicide attempts reported past self-harm and 69.0% reported suicidal tendencies (defined as suicidal ideation or suicide attempt).	12 (4.25%)
Fedyszyn et al. (2010)	Longitudinal, uncontrolled cohort design, with a follow-up period of up to 1 year	696 patients treated between 2002 and 2005 from an Early Psychosis Prevention and Intervention Centre. 94 individuals met the study inclusion criteria	Suicide risk was highest in the first month of treatment, decreasing rapidly over the next 6 months. Intensive suicide screening across the course of treatment may facilitate identification and early management of FEP at suicide risk.	Yes	44 (53%) made suicide attempts during treatment	None
Bakst et al. (2010)	A 2 year follow-up study of first-admission inpatients	Data derived from 444 participants of the Suffolk County Mental Health Project	Worse premorbid functioning was significantly associated with an increased likelihood of a suicide attempt prior to first psychiatric hospital admission.	After 4 years, the poor premorbid functioning was associated with a higher likelihood of future attempts	Suicide attempts prior to first admission among 126 (27.7%) subjects with a prior attempt, 75 (59.5%) had poor functioning; at ½ year among 24 (19.2%) attempters before admission 18 (75%); at 1 year among 32 (25.4%) attempters 24 (75%) and at 2 years among 37 (29.4%) attempters 28 (75.7%)	None
Levine et al. (2010)	Retrospective data extracted from the National Psychiatric Hospitalization Case Registry of Israel	2293 FEP admitted between 1989 and 1992 and followed up until 1996	8.5% had attempted suicide at the time of first hospitalization and 6.6% over the following 4–7 years. The risk profiles together correctly classified 90.7% (137/151) of subsequent suicide attempts and had a long-term prognostic utility	No	196 (8.5%) attempted suicide at the first hospitalization and 151 (6.6%) over 4–7 years. 62/196 (31.6%) made a future suicide attempt during the follow-up (OR = 10.44)	None

Table 2

The most relevant studies about risk factors for suicidality.

Study	Design	Sample size	Conclusions	Eventual follow-up	Suicide plans, ideation and attempts	Completed suicide
Cohen et al. (1994)	Cross sectional study	184 hospitalized psychotic patients	Unipolar major depressive disorder; a lifetime major depressive episode; a less acute onset, worse pre-admission psychosocial functioning, and episodes of physical violence were significantly associated with having ever attempted suicide. Recently attempters more frequently had a lifetime history of major depression and less often had engaged in physical violence.	No	43 (23%) had a history of a suicide attempt, and 28 (15% of the sample; 65% of the attempters) made an attempt during hospitalization	None
van Os et al. (1996)	Cross-sectional study	A cohort of 166 consecutively admitted patients with functional psychosis of recent onset	An early and insidious onset of a negative syndrome associated with poor pre-morbid social functioning, in males and unmarried patients, predicted a worse course of illness. Lack of insight predicted more time in hospital and additional admission	No	No	None
Aguilar et al. (1997)	Longitudinal study over a period of 12 months	96 neuroleptic-naïve psychotic patients (49 schizophrenic and 47 with non-affective psychosis)	High hopelessness scores at baseline predicted poor short-term outcome in schizophrenic patients. Young severe schizophrenic patients with hopelessness are at higher risk of poor outcome.	Worse global functioning at 1 year follow-up	No	None
Addington et al. (1998)	Longitudinal cohort study	113 people during an acute relapse and 13 FEP patients	The median score on the Calgary Depression Scale for Schizophrenia was significantly higher in the FEP group during the acute phase	At ¼ and 1 year FEP subjects significantly more depressed	No	None
Verdoux et al. (2001)	Two-year follow-up study of first-admitted patients assessed at ½ year intervals over a 2-year follow-up	65 FEP patients	Baseline predictors of suicidal behaviour were a lifetime history of parasuicide before the first admission (OR = 5.9), lower positive scores on the PANSS (OR = 0.8) and a longer duration for the first admission (OR = 1.1). Having a history of parasuicide, a deteriorating clinical course and substance misuse increased suicidal risk.	At 2 years substance abusers were seven times more likely to engage in suicidal behaviour.	2 (1.3%) parasuicide during the first ½ year, 5 (3.25%) between ½ and 1 year, 1 (0.65%) between 1 and 1½ years and 1 (0.65%) between 1½ and 2 years	1 (0.65%) at 1 year of follow-up
De Hert et al. (2001)	Case-control study to identify specific risk factors for suicide	A cohort of 63 young schizophrenic patients who committed suicide and 63 controls matched by age in years at admission, sex, subtype of schizophrenia and year of index admission.	Risk factors were male gender, frequent relapses (OR 6.0), short hospitalizations, a negative attitude towards treatment (OR 7.0), impulsive behaviour (OR acting out 6.4, OR involuntary commitment 17), parasuicide, high pre-morbid IQ (OR 4.3), psychosis (OR 7.0) and depression (OR 36). Early defect onset (OR 6.3) and a daily activity (OR 4.2) were protective factors	No	Mean number of attempts in cases 2.19 (1.4%) and 0.37 (0.2%) in controls	6 (9.1%) men at a mean age of 28.4 years and 3 (4.2%) female at a mean age of 29.1 years
Nordentoft et al. (2002)	One-year follow-up of a randomized controlled trial	341 FEP patients randomized to integrated treatment or treated as usual	Baseline suicide attempts were associated with female gender, hopelessness, hallucinations and were the most significant predictors of a future suicide attempt. Integrated treatment reduced hopelessness	Yes	At 1 year of follow-up 38 (11%) attempted suicide.	None
Kontaxakis et al. (2004)	Cross sectional study comparing patients with/without suicidal thoughts	93 schizophrenia patients	Severity of depressive symptoms, motor retardation, guilt feelings, pathological guilt, and self-depreciation predicted the patients' suicidal ideation	No	20.4% patients reported suicidal thoughts during the last 15 days	None
Hawton et al. (2005)	Systematic review study of case-control and cohort studies of FEP patients	29 eligible studies identified	Previous depressive disorders (OR = 3.03), previous suicide attempts (OR = 4.09), drug misuse (OR = 3.21), agitation/motor restlessness (OR = 2.61), fear of mental disintegration (OR = 12.1), poor adherence to treatment (OR = 3.75), recent loss (OR = 4.03) increased suicidal risk, hallucinations reduced it (OR = 0.50)	No	No	None
Berger et al. (2006)	Review	–	Family history of a psychotic illness and a decline in functioning, or a history of a brief self-limiting psychotic episode were risk factors for suicide.	No	No	None
Melle et al. (2006)	Randomized controlled trial	Consecutive psychotic patients who sought initial psychiatric treatment in four catchment areas (two of these including 141 subjects were from early detection communities)	Early detection programs that bring patients into treatment at lower symptom levels may reduce suicidal risk at first treatment contact.	No	48 (35%) from communities with no early detection program vs. 40 (29%) with early detection having suicidal thoughts; 8 (6%) vs. 7 (5%) having suicidal plans; 22 (16%) vs. 7 (5%) with suicidal attempts. In the month preceding first treatment contact, 49 (35%) vs. 37 (26%) having suicidal thoughts; 10 (7%) vs. 4 (3%) having suicidal plans; 14 (10%) vs. 2 (1%) with suicidal attempts	None
Thorup et al. (2007)	Cross-sectional study	A group of 578 young adults with a FEP spectrum disorder	Men had more severe negative symptoms, worse premorbid functioning/social adjustment, smaller social networks, more substance abuse, and more often were unemployed/lived alone. Women had more severe hallucinations and lower self-esteem.	No	144.5 (25%) of men and 237 (41%) of women had attempted suicide at least once in lifetime	None

Bertelsen et al. (2007)	Longitudinal, prospective, 5-year follow-up with patients randomised to integrated vs. standard treatment	A cohort of 547 individuals with FEP spectrum psychosis.	Depressive and psychotic symptoms, especially hallucinations, predicted suicidal plans and attempts; and persistent suicidal behaviour and ideation were associated with a high risk of attempting suicide. At baseline suicidal thoughts at least once last week 123 (22.5), suicidal plans at least once in past week 54 (9.9), suicide attempts last year 100 (18.3), suicide attempts ever 154 (28.2)	At 1 and 2 years suicidal thoughts/plans/attempts, depressive/psychotic symptoms, young age were associated with suicidal plans/attempts	A stepwise regression analysis indicated that at 2-year follow-up, those who had suicidal plans in past year (compared to those who did not) had an OR of 5.11 (95% CI: 2.76-9.45) to have had suicidal plans at least once in the past week and an OR of 2.45 (95% CI: 1.04-5.74) to have attempted suicide in the past year. Those who had suicidal attempts in past year at 2-year follow-up (compared to those who did not) had an OR of 5.12 (95% CI: 1.68-15.58) to have had suicidal plans at least once in the past week, and an OR of 4.36 (95% CI: 1.63-11.6) to have attempted suicide in the past year.	16 died during the follow-up period, 7 from suicide. At 5 years follow-up, those subjects who died by suicide and those who died for any cause (compared to those who did not) had, respectively, an OR of 1.52 (95% CI: 0.17-13.0) and 2.08 (95% CI: 0.58-7.4) to have had suicidal plans, an OR of 0.55 (95% CI: 0.06-4.7), 0.74 (95% CI: 0.2-2.68), to have had suicidal thoughts, an OR of 1.12 (95% CI: 0.2-6.12) and 1.68 (95% CI: 0.58-4.85), to have attempted suicide
Boden et al. (2010)	Naturalistic cohort study comparing a 3-year before/after an assertive community treatment programme (mACT)	144 FEP patients in Uppsala County, Sweden	Patients in the mACT group, compared to those in the non-mACT group, had a borderline significant increased risk of having a poor 5-year outcome regarding positive psychotic symptoms [adjusted odds ratio (OR) 3.21].	At 5 years outcome, the implementation of mACT was not followed by an improvements	No	None
Cotton et al. (2009)	Retrospective study	661 (435 male, 226 female) FEP patients at the Early Psychosis Prevention and Intervention Centre	FEP females were more likely to have a history of suicide attempts and depression. Males had marked substance abuse before admission and more severe psychopathology/lower levels of functioning. At discharge, males had significantly lower functioning than females	No	Suicide attempts in treatment 32 male (7.4%) and 25 female (11.2%); 17 non-affective male (6.1%) and 14 female (11%)	None
Joa et al. (2009)	Cross-sectional study	43 non-affective FEP patients with onset <age 18 vs. >18 years	Early onset patients had poorer premorbid functioning, longer DUP, higher suicidality, more depressive symptoms, better cognition, fewer psychotic symptoms, and were more likely to be treated	No	11 early-onset psychosis (26%) and 22 (12%) having lifetime plans/attempts	None
Robinson et al. (2010)	Naturalistic, prospective follow-up (7.4 years) study	A cohort of 413 FEP patients treated at an early psychosis centre. Follow-up data available for 282 subjects	History of self-harm, suicidal tendencies, being depressed for >50% of the initial psychotic episode and hopelessness and alcohol abuse increased the risk of suicide attempts. The key predictor was previous self-harm.	The risk of future suicide attempts was elevated for 7 years	61 (21.6%) attempted suicide one or more times. Previous self-harm was 47 (28%) and suicidal tendencies 69.0 (40%) in attempters	12 (4.25%)
Levine et al. (2010)	Retrospective data from the National Psychiatric Hospitalization Case Registry of Israel	2293 FEP admitted between 1989 and 1992 and followed up until 1996	8.5% had attempted suicide at the time of first hospitalization and 6.6% over the following 4-7 years. The risk profiles together correctly classified 90.7% (137/151) of subsequent suicide attempts and have a long-term prognostic utility	No	196 (8.5%) attempted suicide at the first hospitalization and 151 (6.6%) over 4-7 years. 62/196 (31.6%) made a future suicide attempt during the follow-up (OR = 10.44)	None
Melle et al. (2010)	2 year follow-up study of an integrated treatment in two groups of FEP patients (early/non early detection programs)	231 patients completing the 2-year follow-up (113 not from an early detection area and 118 from an early detection area)	There were low rates of suicide attempts in both groups after 2 years of treatment, with no between-groups differences.	Severe suicidal plans/attempts were predicted by drug abuse, dissatisfaction, severe baseline suicidality	Until last month before treatment start, thoughts 35 (31%) from non-early detection area vs. 37 (32%) from early detection area; plans 6 (5%) vs. 7(3%); attempts 19 (17%) vs. 6. Last month before treatment start, thoughts 37 (33%) vs. 32 (27%); plans 8 (7%) vs. 4 (3%); attempts 12 (17%) vs. 2 (2%). At 1-year thoughts 43 (39%) vs. 20 (21%); plans 4 (4%) vs. 2 (2%); attempts 4 (4%) vs. 3 (3%). At 2-years thoughts 44 (39%) vs. 20 (18%); plans 0 (0%) vs. 3 (3%); attempts 7 (6%) vs. 6 (5%)	None
Bakst et al. (2010)	A 2 year follow-up study of first-admission inpatients	Data derived from 444 participants of the Suffolk County Mental Health Project	Worse premorbid functioning was significantly associated with an increased likelihood of a suicide attempt prior to first psychiatric hospital admission.	After 4 years, the poor premorbid functioning was associated with a higher likelihood of future attempts	Suicide attempts prior to first admission among 126 (27.7%) subjects with a prior attempt, 75 (59.5%) had poor functioning; at ½ year among 24 (19.2%) attempters before admission 18 (75%); at 1 year among 32 (25.4%) attempters 24 (75%) and at 2 years among 37 (29.4%) attempters 28 (75.7%)	None
Barrett et al. (2010)	Cross-sectional with suicidal behaviour measured retrospectively	170 FEP-patients	Suicide attempts during DUP were significantly associated with more depressive episodes and a younger age at illness onset, in addition to drug use the last 6 months.	No	44 (26%) attempted suicide and 66 (38.8%) had suicidal ideation prior to study entry. 119 (70%) were suicidal during the untreated period.	None
Barrett et al. (2010)	Cross-sectional	194 FEP-patients	More depressive symptoms, higher insight, negative beliefs about psychosis increase the suicidal risk in FEP. Suicidality was associated with depressive, schizophrenia symptoms, insight, beliefs about negative psychotic outcomes.	No	89 (46%) were currently suicidal	None
Ceskova et al. (2011)	Retrospective analysis whose participants were followed up for 10 years	162 patients consecutively hospitalized	All patients were young, single males and most of them suffered from paranoid schizophrenia. They had a higher number of psychiatric admissions. Suicides were associated with a severe relapsing form of the illness.	10 years	3 (1.8%) had previous suicidal ideas, behaviour or attempts	6 (3.7%)

had better cognition, fewer psychotic symptoms, and were more likely to be treated on an outpatient basis. The authors concluded that adolescents are at higher risk for longer treatment delays than adults, and a more targeted approach towards this group appears to be necessary.

3.2.2. Suicidal ideation and suicide attempts after the start of treatment

Barrett et al. (2010) assessed 194 FEP-patients for diagnosis, symptoms, functioning, substance use, suicidality, insight, and beliefs about psychosis. Nearly 46% of the patients had current suicidal ideation as measured by item 8 on the Calgary Depression Scale for Schizophrenia. More depressive symptoms, greater insight, and negative beliefs about psychosis were associated with current suicidal ideation. The authors suggested that monitoring insight is crucial in assessing suicide risk in FEP patients. Treating depression and counteracting negative beliefs about psychosis may possibly reduce the risk for future suicidality.

3.2.3. Suicidal ideation plans and attempts after hospitalization

Suicidal ideation is frequent among patients with acute schizophrenia, and suicidal plans and suicidal attempts may also be frequent among these patients, even if they are hospitalized and being treated. Melle et al. (2006) analysed consecutive patients treated in psychiatric units serving four catchment areas (two with an early detection program and two without such a program) and found that suicide plans and attempts were significantly more frequent in patients from communities without the early detection program.

Kontaxakis et al. (2004) found that 20.4% of psychiatric inpatients with acute schizophrenia reported suicidal ideation in the past 15 days. Suicidal ideation was predicted by the severity of depressive symptoms and the presence of motor retardation, pathological guilt and self-depreciation.

3.3. Retrospective studies

3.3.1. Risk factors for completed suicide

De Hert et al. (2001) studied the risk factors for suicide in a cohort of 63 young schizophrenic patients who committed suicide and 63 living schizophrenic inpatients. They found that risk factors for suicide were male sex, depression, involuntary commitment, acting out, a previous suicide attempt, a family history of suicide, a major loss in the prior 6 months, non-compliance with treatment, being psychotic at follow-up, frequent relapses (OR 6.0), more than five admissions, and a high pre-morbid IQ. There were protective factors, including receiving community-based care, engaging in useful daily activity, early onset of a “defect state” (not defined in the report), and being symptom-free.

Contrary to common views, psychotic symptoms, particularly command hallucinations, may only partially contribute to about 10% of suicides in schizophrenia (Hawton et al., 2005; Heila et al., 1997). In those with active psychotic symptoms, the risk of suicide is greater the higher the premorbid IQ, the higher the socioeconomic background, and the greater the degree of deterioration. Loss, stigma, poor social support and social exclusion/rejection may all increase the risk of suicide (Siris, 2001).

Suicidal risk may be increased in the acute psychotic period due to a reaction to dramatic psychotic phenomena, impaired functioning, and the accompanying acute distress. Suicidal tendencies may be drastically reduced when psychiatric services have engaged the patients and if the psychotic breakdown has been attenuated (Power et al., 1998).

Based on their review of the research, Berger et al. (2006) concluded that risk factors for completed suicide include a combination of a family history of a psychotic illness coupled with a decline in functioning, or a history of a brief self-limiting psychotic episode (even if triggered by drugs such as cannabis or amphetamines). They

suggested that the suicide rate in FEP patients is particularly high in the early phase of illness.

3.3.2. Risk factors for prior suicidal behaviour and attempts

In an epidemiological sample of 661 consecutive FEP treated at the Early Psychosis Prevention and Intervention Centre, Cotton et al. (2009) reported that, at intake, FEP females were more likely to have a history of suicide attempts and depression. Males were more likely to have substance use problems before the admission, and these problems persisted throughout treatment. Males also experienced more severe psychopathology and lower levels of functioning on the Global Assessment of Functioning (GAF). Treatment non-compliance and frequent hospitalisations were also common in males. At discharge, males had significantly lower levels of functioning compared to FEP females.

As noted above, Levine et al. (2010) found that FEP patients admitted as a result of a suicide attempt (8.5% of the total FEP admissions) were more often college educated, female and not married.

Cognitive deficits seem to be protective factors (De Hert, et al., 2001). An association between insight and increased suicidal behaviour has been reported (Crumlish, et al., 2005; Kim et al., 2003; Schwartz and Smith, 2004), but evidence for this association during the pre-treatment phase is weak. For the majority of patients, in the first months after FEP when negative symptoms remain prevalent and psychosocial functioning is impaired, more insight into the disorder may develop which, along with persistent dysfunctions and reduced quality of life, may contribute to increased hopelessness and depression (Kim, et al., 2003; Pompili, et al., 2007). In a sample of 107 patients with FEP, Foley et al. (2008) found that a higher insight score at first presentation was significantly associated with a history of suicide attempts.

3.3.3. Suicidal risk in the first months of treatment

In a retrospective analysis of 696 patients treated between 2002 and 2005 from an Early Psychosis Prevention and Intervention Centre, Fedyszyn et al. (2010) found that 94 individuals met the criterion for being a high suicide risk (based on the Brief Psychiatric Rating Scale) during the follow-up (of up to 24 months). The suicide risk was highest in the first month of treatment, decreased rapidly over the next 6 months and declined slightly thereafter. Fluctuations around the trend did not reach statistical significance. The authors suggested that intensive suicide screening across the course of treatment may facilitate identification and early management of FEP patients who are at high risk for suicide.

3.3.4. Suicide attempts after the first hospitalization

In a retrospective analysis of data from a 48-month of follow-up in 44 participants of the Suffolk County Mental Health Project, Bakst et al. (2010) found that 33.0% of patients with poor or declining premorbid functioning had a history of suicide attempts compared to 23.5% with good premorbid functioning. Among the 126 patients with a history of attempting suicide, poor premorbid functioning was significantly associated with an increased likelihood of additional attempts during the 4 years after the first hospitalization.

4. Meta-analytic and review studies

4.1. Completed suicide rates

In a meta-analytic study, Palmer et al. (2005) reviewed follow-up studies, dividing them into two groups (32 studies of 25,578 schizophrenics recruited at various illness points and 29 studies of 22,598 schizophrenics identified at illness onset or first admission). They calculated that the lifetime prevalence of completed suicide in patients identified at first admission or illness onset was 5.6%. Mixed

samples showed a rate of 1.8% (95% confidence interval, 1.4%–2.3%). They estimated that 4.9% of patients with schizophrenia commit suicide during their lifetimes, most often near illness onset.

5. Limitations of the present review

The present review should be considered in the light of some limitations. First, we did not carry out a meta-analysis because data from most of the studies that were focused on the main topic did not permit it. Specifically, samples included different measurements and different outcomes, and they assessed patients at different time points. Moreover, we did not score papers for the quality of the research, but we indirectly ranked studies by grouping them according to their main design which is indicative of the quality of the research according to evidence-based medicine (Greenhalgh, 2006; Sackett et al., 1996).

Although, the current review adequately summarizes the research in this field, focusing on relevant issues related to the phenomenon, and attempts to present key topics in order to offer an easy tool when facing suicide risk in FEP patients, the inclusion and exclusion of papers cited in this paper may reflect the authors' choice, both on the basis of their expertise and the consultations that they engaged with experts in the field.

Despite the fact that we tried to analyse the most relevant suicidal risk factors, it appeared difficult to distinguish between risk factors for suicide attempts and completed suicide because there are no studies, to our knowledge, which can be used for that purpose.

The studies attempting to identify risk factors for suicide in FEP have a number of shortcomings. First, some studies had small sample sizes and small numbers of suicides that reduces the power of the research. Second, a number of methodological problems often made

the results difficult to interpret (e.g., not all studies included specific follow-up periods and, additionally, not all studies mention the exact number of suicide attempts and completions so that the rate of suicide among subjects cannot be calculated). Some of the studies included in the present review were retrospective designs, and the absence of strategies to ensure both inter-rater reliability and the validity of the data need to be considered.

The present review includes only suicides explicitly reported, excluding accidental deaths and other deaths of uncertain causes. Excluding these ambiguous cases of death may result in an underestimation of suicide rates. In addition, although the samples usually met the diagnostic criteria for the inclusion in the studies, the diagnostic criteria differ in the different samples.

Most of the studies investigated a mixture of age groups, and future research should take the age of FEP patients into account. Most of the studies were carried out in heterogeneous samples, mixing patients at different stages of their illness (Yung et al., 2004). This did not permit clarification of whether there is an association between age of onset of psychotic symptoms and the age at suicide. A relatively younger age of onset may expose subjects to a longer period of higher suicidal risk. Palmer et al. (2005) suggested that, given that schizophrenia is typically diagnosed in the third decade of life, the preponderance of suicides soon after diagnosis in this subgroup is skewed toward a younger age.

Although most of the studies analysed were based on retrospective data, risk factors such as age, gender, marital status and employment status can be assessed reliably. If the information, collected retrospectively, is reliable, a retrospective design is adequate and not hampered by recall bias. On the other hand, clinical variables are not easily measured reliably in retrospective designs. Some studies considered only inpatients, studied only a few variables, and did not include a control group (Caldwell and Gottesman, 1990; De Hert,

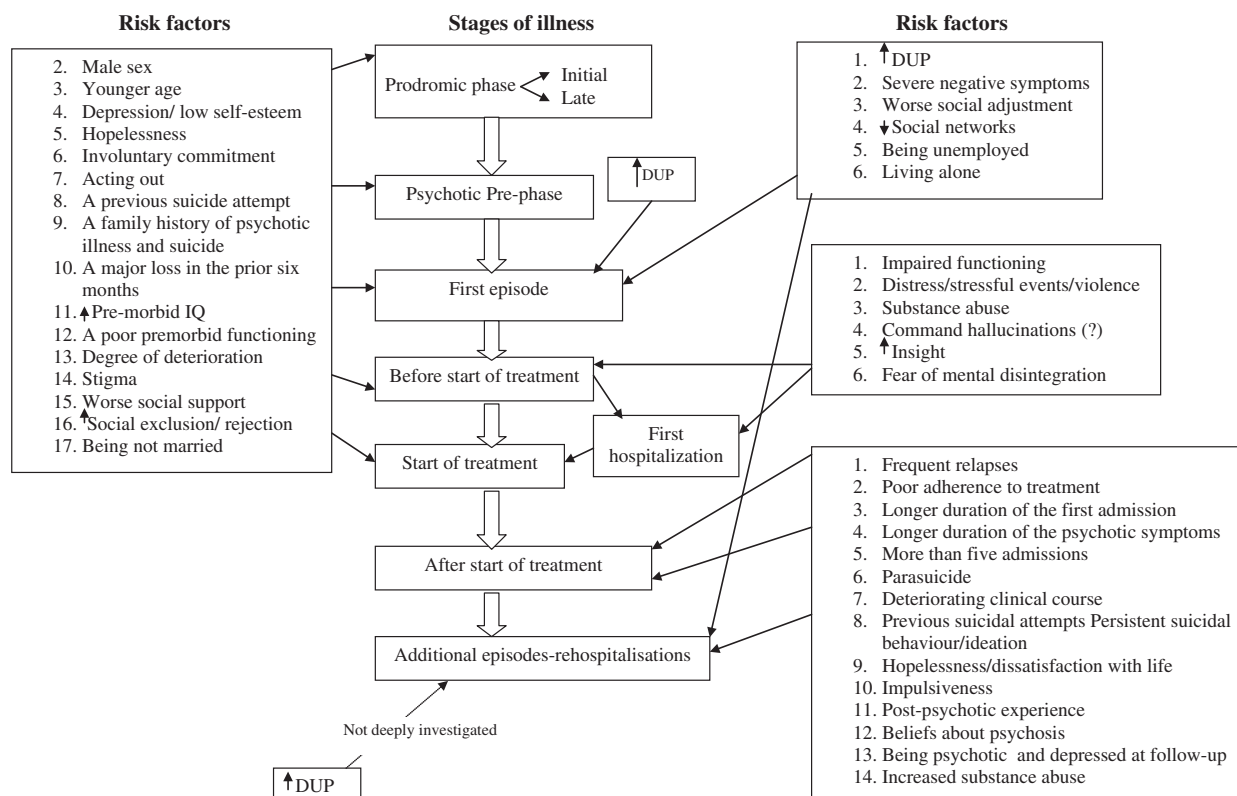


Fig. 2. Flow diagram of stages of illness and increased suicidal risk by risk factors.

1995; De Hert and Peuskens, 1998, 2000; Drake et al., 1985; Roy et al., 1986; Westermeyer et al., 1991).

6. Conclusions

Suicide accounts for a large percentage of deaths in patients with FEP and other psychotic disorders and is an important health concern. Early intervention and correct management in FEP patients is critical to minimize their suicidality.

The rigorous assessment of the suicidal risk aiming to identify both the protective and the risk factors (see Fig. 2) in FEP patients with particular regard to previous suicidal attempts and current suicidality is of paramount importance. Clinicians should assess suicidal risk in the initial prodromal phases of psychosis as well as during the period of treatment and finally along the course of the illness.

Particular attention should be given to the presence of depression and hopelessness at the start of the treatment and then during the follow-up period. Being depressed for more than half of the initial psychotic episode was a relevant indicator of future suicidal risk.

The impact of the substance abuse, another relevant risk factor in FEP patients, should not be neglected as it is acknowledged that attempters among FEP patients were more likely to have substance abuse compared to non-attempters. Assessing the impact of substance abuse as risk factor for suicidal behaviour should be considered crucial in FEP patients.

Although standard treatment may yield some benefit, further prospective studies may reveal which aspects of the intervention are salient. Specific medications and adequate psychosocial interventions may play a role, offering complementary benefits, but this needs to be examined further.

One limitation for identifying which aspects of treatment are effective in reducing the suicide rate in FEP patients is that suicide is a rare outcome, and we will never presumably have a Randomized Control Trial (RCT) with sufficient power to detect differences in the effectiveness of different treatments on suicidal behaviour. Focusing on suicide attempts may be an alternative outcome measure, but even that will require large very large samples.

Further longitudinal studies are required to better clarify the complex issue of suicide in FEP. One of the most relevant challenges is to carry out longitudinal studies with complete or representative populations, including thorough examination of both risk factors and fatal and non-fatal suicidal acts. Here, for instance, the studies conducted by Melle et al. (2010) and Robinson et al. (2010) during the 7.4 years of follow up periods were excellent in prospectively defining the whole range of suicidal behaviours; the first investigates the differences between completed suicides and suicide attempts with particular regard to severe suicidality (plans and attempts) in two groups of patients with FEP spectrum, where one group was recruited through an early detection program and the second, respectively, the differences between single vs. multiple suicide attempters.

Finally, the prediction and prevention of suicidal behaviour is still a difficult challenge for clinicians at the individual level and should include a sound clinical strategy for identifying every patient with recent onset psychosis who is at elevated risk for suicidal behaviour.

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Contributors

Drs. Pompili, Serafini, and Innamorati designed the study and provided preliminary review; Dr. Shrivastava provided supervision and consultation. Drs. Girardi, Lester, and Nordentoft provided the intellectual impetus for the research. All authors contributed to drafting the manuscript and in reviewing selected papers.

Conflict of interest

None.

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