

Suicide and schizophrenia: a systematic review of rates and risk factors

Kahyee Hor and Mark Taylor

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Abstract

Risk assessment is a core skill in psychiatry. Risk prediction for suicide in schizophrenia is known to be complex. We undertook a systematic review of all original studies concerning suicide in schizophrenia published since 2004. We found 51 data-containing studies (from 1281 studies screened) that met our inclusion criteria, and ranked these by standardized quality criteria. Estimates of rates of suicide and risk factors associated with later suicide were identified, and the risk factors were grouped according to type and strength of association with suicide. Consensus on the lifetime risk of suicide was a rate of approximately 5%. Risk factors with a strong association with later suicide included being young, male, and with a high level of education. Illness-related risk factors were important predictors, with number of prior suicide attempts, depressive symptoms, active hallucinations and delusions, and the presence of insight all having a strong evidential basis. A family history of suicide, and comorbid substance misuse were also positively associated with later suicide. The only consistent protective factor for suicide was delivery of and adherence to effective treatment. Prevention of suicide in schizophrenia will rely on identifying those individuals at risk, and treating comorbid depression and substance misuse, as well as providing best available treatment for psychotic symptoms.

Keywords

Schizophrenia, suicide, systematic review

Introduction

People with schizophrenia are known to die much earlier (Saha et al., 2007) than expected. Up to 40% (Bushe et al., 2010) of this excess premature mortality can be attributed to suicide and unnatural deaths, with one authoritative review (Palmer et al., 2005) estimating a lifetime suicide risk of 4.9% for people with schizophrenia. Detection of those at risk is clinically important, but risk prediction is known to be imprecise (Goldney, 2000).

An earlier systematic review (Hawton et al., 2005) of risk factors for suicide in schizophrenia identified 29 high-quality data-containing studies which were analysed for individual risk factors. Hawton et al. (2005) found, perhaps unsurprisingly, that many of the important risk factors for suicide in schizophrenia were similar to those in the general population, including mood disorder, recent loss, previous suicide attempts, and drug misuse. However, some other factors they identified as associated with high suicide risk in schizophrenia, such as fear of mental disintegration, agitation or restlessness, and poor adherence with treatment, are not immediately self-evident. Interestingly, Hawton et al. (2005) also observed a reduced risk of suicide associated with the presence of hallucinations. Since that time, Tiihonen et al. (2006) have confirmed, in a nationwide follow-up of individuals discharged from hospital after a first episode of schizophrenia, that not taking any regular antipsychotic medication was associated with a 12-fold increase in the relative risk of all-cause death and a worrying 37-fold increase in death by suicide.

Risk assessment and risk management remain core skills in clinical psychiatry. Since the 2005 review of Hawton et al., which examined data published up until June 2004, a large number of studies examining the rates and correlates of suicide in schizophrenia have been produced. For example, a recent non-systematic review by Carlborg et al. (2010) found many of the risk factors listed above to be important, as well as some disease-specific factors such as high suicide risk in the first year of illness and associations with a high premorbid function and high IQ, but also noted the low predictive specificity of these factors. We undertook a systematic review of all relevant studies published after June 2004 which provided new data on risk factors for suicide in schizophrenia to better inform clinical practice. We decided to only include studies likely to provide valid estimates of risk factors, namely randomized controlled trials, prospective and retrospective cohort studies, and case-control studies. As part of our systematic review we decided to rank the quality of the evidence, and hence assessed the quality of the included studies, according to standardized criteria.

NHS Scotland, Ballenden House, Edinburgh, UK.

Corresponding author:

Dr Taylor, Ballenden House, 28 Howden St, Edinburgh EH8 9HL, UK
Email: marktaylor2@nhs.net

Methods

Search strategy and study eligibility

This systematic review included literature published between June 2004 and January 2010. An electronic search on the following databases were carried out – EMBASE, PsychINFO and OVID Medline (R). The subject headings used included:

- (a) Catatonic Schizophrenia or Paranoid Schizophrenia or Schizophrenia or Disorganized Schizophrenia or Childhood Schizophrenia or schizophrenia.mp., Psychotic Disorders or schizoaffective psychosis.mp., and
- (b) Suicide.mp. or Suicide, and
- (c) Risk factor.mp. or Risk Factors, and
- (d) Cohort Studies.mp. or Cohort Studies, Case Control Studies.mp. or Case-Control Studies, Cohort Analysis.mp. or Cohort Studies, Follow Up Studies.mp. or Follow-Up Studies

The results of the search were screened for suitability independently by both investigators. These studies were further screened for eligibility based on the inclusion criteria:

- (a) Literature published in English
- (b) Case-control, cohort or follow-up studies
- (c) Patient diagnosis of schizophrenia (including all subtypes), psychosis and schizoaffective disorder

Data extraction

The shortlisted studies were then analysed and the following data were extracted:

- (a) Rate of suicide
- (b) Socio-demographic information: age, gender, ethnicity, marital status, employment, education, social class, rural/urban
- (c) Genetic/biological information: genetics, family history of suicidal behaviour, biological markers
- (d) Illness-related: age of onset, duration of disease, physical illness, affective disorder, thought disorder, depression, psychopathology, insight
- (e) Life events
- (f) Previous suicide attempts/ideation
- (g) Substance misuse/abuse/dependence: alcohol, smoking, drugs

Quality of studies

The studies included in this systematic review were assessed for quality. A score was given for study design: 4, randomized controlled trials; 3, prospective cohort/follow-up study; 2, retrospective cohort study; 1, case-control study. The studies were also assessed for the following characteristics: explicit aims, definition and size of population investigated, demographic details of subjects, explicit risk factors (if study looked at risk factors), validity and reliability of methods, response and drop-out rate specified, justification of response

or drop-out rate, discussion of generalizability and discussion of limitations. Each of these criteria was allocated 1 point and the total score for each article was calculated. The six studies which provided data on over 100 subjects and had the highest quality scores were extracted and analysed in more detail, in order to ascertain recurrent findings or themes.

Results

Data extraction

A total of 1281 articles were initially identified by the search strategy. Of the 1281 studies identified, 12 papers were not written in English and were therefore excluded from the study. Some 71 papers (out of 1269) were shortlisted for detailed analyses based on the abstracts; 20 of these papers were not included as they did not address the objectives of this study. A final total of 51 studies were identified as relevant to this study and were reviewed, as depicted in Figure 1.

All 51 papers were further analysed for risk factors for suicide. The risk factors were grouped into six main categories – Demographics, Illness-Related Factors, Insight, Suicide Attempt/Ideation, Life Events and Genetics.

The following studies provided new data on the rates of suicide in schizophrenia, which we have presented in Table 1.

The new data on risk factors for suicide in schizophrenia were grouped into the six main themes noted above. Individual demographic characteristics identified as risk factors for suicide are depicted in Table 2.

Risk factors for later suicide that were identified from systematic review and were related to the individual's illness are shown in Table 3.

Those familial or genetic characteristics studied, and elicited by our systematic review, in individuals with schizophrenia who later committed suicide are contained in Table 4.

The other three specific domains of risk factors associated with later suicide in people with schizophrenia are separated below:

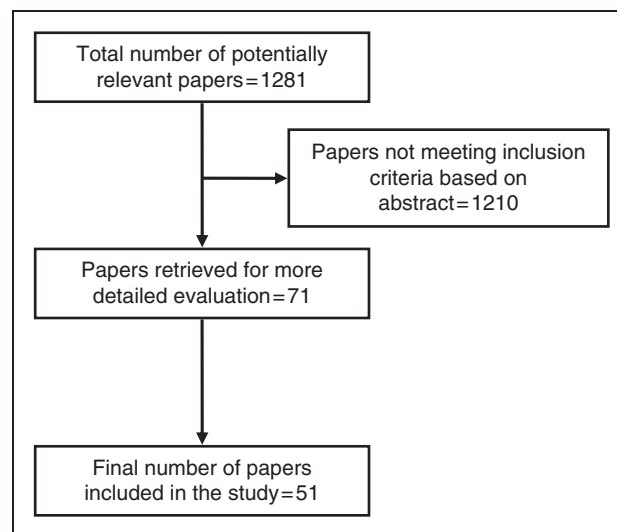


Figure 1. Flow chart showing the article-identification process.

Table 1. Rates of suicide

Study	Details of study	Population	Conclusion on suicide rates
Phillips et al. (2004)	Retrospective observational study in China. Data for 1995–99 were extrapolated from data obtained from 1993	Annual estimate of 4.25 million people with schizophrenia and 284,614 total suicides – of which 28,737 suicides are by people with schizophrenia	10.1% of all suicides had schizophrenia. Suicide rate in adults with schizophrenia was 6.8/1000 people/year. RR of suicide in those with schizophrenia vs. those without is 23.8.
Silverton et al. (2008)	43 year prospective longitudinal Danish cohort study	208 children in 'high-risk' group (based on mother's diagnosis of schizophrenia), 11 committed suicide	Suicide was 14 times more likely in 'high-risk' subjects diagnosed with schizophrenia, compared with other mental disorders or no mental disorders
Craig et al. (2006)	Prospective cohort study. 5- and 10-year survival; absolute and relative mortality rates among first-admission patients with psychotic disorder	235 patients with schizophrenia, 12 deaths due to all causes (four natural deaths, seven unnatural death, one unknown)	1.7% of all patients with schizophrenia died by suicide
Ran et al. (2007)	10-year prospective follow-up study in rural China	500 patients with schizophrenia; 21 died by suicide	Suicide rate was 477/100000 person-years. SMR was 32.0. Risk of suicide during the follow-up period was 4.5%.
Osborn et al. (2008)	Retrospective cohort study in general practices in UK from 1987–2002	46,136 patients with severe mental illness (40.2% with schizophrenia) included, matched with 300,426 controls	48 (0.26%) patients with schizophrenia committed suicide; adjusted hazard ratio = 7.00
Healy et al. (2006)	Retrospective cohort study, North Wales, UK. Compared lifetime suicide rates in treated schizophrenia between cohorts from 1875–1924 and 1994–1998	1875–1924: 594 patients with schizophrenia, three suicides 1994–1998: 85 patients, four suicides	1875–1924: 16/100000 patient-years, lifetime suicide rate of 0.46% 1994–1998: 752/100000 patient-years
Nordentoft et al. (2004)	Case-control study using four Danish longitudinal registers from 1981–1997	18,744 individuals committed suicide in total, including 756 people with schizophrenia	Suicide rates were found to decline from 1981–1997 by >50%. Incidence rate ratio for suicide among patients with schizophrenia was about 20 times higher than the general population
Carlborg et al. (2008)	Follow-up study in Sweden from 1973–2006	385 inpatients (153 men, 232 women) with schizophrenia spectrum psychoses	Rate of suicide during the follow-up period was 6.8%. Incidence rate ratio for suicide was 1.01
Bhatia et al. (2006)	Retrospective cohort study with Indian and American samples	460 Indians and 424 Americans	More attempted suicides in US (205/424 in US vs. 107/460 in India cohorts)
Limosin et al. (2007)	10-year prospective follow-up study in France	3470 patients with schizophrenia, 141 suicides	Prevalence of suicide (global SMR) was 16.2. Mortality due to suicide especially high during the first 4 years of follow-up
Barak et al. (2004a)	10-year case-control study in Israel	692 elderly patients with schizophrenia, 30 patients attempted suicide	Rate of suicide attempts was ~5%, somewhat less than that reported for younger patients
Laursen et al. (2007)	Retrospective cohort study using two population-based cohorts in Denmark	Schizophrenia: 17,660 first admissions and 3942 deceased. Schizoaffective: 4055 first admissions and 1261 deaths	Mortality rate ratio for suicide among male and female patients with schizophrenia was 34.51 and 58.81, respectively. Schizophrenia highest mortality rate ratio in the age groups 55–79 and 80+.

RR, relative risk; SMR, standardised mortality ratio.

Suicide attempt/ideation. Of the 51 studies, 10 evaluated history of suicide attempt/ideation as a risk factor for suicide in patients with schizophrenia. All 10 studies identified a positive correlation between suicide attempt/ideation and suicide.

Substance abuse. Of the seven studies that looked into substance misuse, four studies identified alcohol as a predisposing factor to increased suicides among patients with schizophrenia, while three studies identified substance abuse and one study identified smoking only. Only one study found

Table 2. Patient demographics

Characteristic	Number of studies	Positive association	No association	Conclusion on risk factors
Age	10	7/10 identified young age as a predisposing risk factor for increased suicide. One study noted higher risk among patients >50y/o, and another identified higher mean age of suicide among females, but not in males	Young age not replicated in one study	Young age
Gender	16	Two studies identified females having a higher risk of suicide. Eleven studies found that males have a higher risk of suicide	One study did not replicate findings on male gender as a predisposing factor for suicide. Two studies found no difference in suicide between gender	Males
Ethnicity	2	One study showed that whites have higher suicide rate, another found that being born in Sweden predisposes to suicide	–	Inconclusive
Marital status	3	Two studies found that being single predisposes to suicide	One study found that there was no difference in suicide	Single
Employment	3	Two studies found unemployment and inability to work, respectively, as increasing risk of suicide. One study identified minimal lost work potential amongst the suicide group	–	Unemployment
Education	6	All six studies identified higher levels of education as a predisposing risk factor for suicide. One of the studies only found this amongst the Americans but not Indian subjects	–	Higher levels of education
Social class	4	One study identified higher suicide rate in those from higher social class, and two studies identified homelessness and living alone, respectively, as positive risk factors	One study found no difference in economic status	Inconclusive
Rural/urban	1	Rural >urban by 3.18 times	–	Rural

no difference in current substance abuse in those who committed suicide.

Life events. Only two studies looked at life events as a risk factor for suicide. One of the studies looked at childhood trauma and found that patients who committed suicide had higher scores on the Childhood Trauma Questionnaire. Another study found that those with schizophrenia had a higher number of life events compared with a normal control group, but people with schizophrenia who were suicidal had fewer incidences of life events than those who were non-suicidal.

Our systematic quality analysis of all available included studies, using the scoring criteria noted above, yielded the following results (Table 5):

The top six articles (percentage of maximum quality score=92%) were extracted for more detailed analysis. Table 6 summarizes the details on methods, risk factors investigated and conclusions of each of these six studies.

Discussion

This systematic review included findings from 51 articles published from June 2004 to January 2010. The main findings from this review are as follows:

Suicide rate in schizophrenia

Studies so far have not come to an agreement on suicide rates amongst patients with schizophrenia. The most widely cited lifetime suicide rate is 10%, as estimated by a review by Miles (1977). However, a recent study by Palmer et al. (2005) has challenged this and has proposed that the lifetime suicide risk in schizophrenia is approximately 4.9%. The current review analysed contemporary data on suicide rates amongst patients with schizophrenia, and we conclude that an accurate estimated suicide rate is 579/100,000 person-years (477–680/100,000 person-years). However, two other studies that investigated the proportion of people who died due to suicide who also had schizophrenia reported a rate of 10.1% (Philips et al., 2004) and 22.3% (Osborn et al., 2008), but proportionate mortality should not be confused with lifetime risk.

It is perhaps not surprising that different studies, using different populations and methodologies, return varying estimates of the suicide rate in schizophrenia. Also, the 'true' suicide rate will fluctuate over time, depending on numerous complex variables including the period over which the studies were carried out. In addition, many suicides may be misclassified as 'unnatural' or 'undetermined' deaths. However, most studies seem to indicate that the earlier consensus figure of 10% lifetime risk is an overestimate (perhaps due to confusion with proportionate

Table 3. Illness-related factors

Characteristic	Number of studies	Positive association	No association	Conclusion
Age of illness onset	5	Three studies identified later age of onset as a predisposing factor to increased suicide. One study found younger age of onset associated with suicide	One study found no difference	Later age of onset
Duration of illness	6	One study: ≥ 10 years, two studies: acute/shorter duration of illness, two studies: within first 3–5 years, one study: long illness with exacerbations	–	Inconclusive
Physical illness	2	Both studies found positive correlation	–	Presence of physical illness
Affective disorder	23	Seven studies found positive correlation between affective disorders and increased suicide. Fifteen studies identified a positive relationship between the presence of depression and increased risk of suicide	Only one study found no difference in level of depression between attempters and non-attempters	Hopelessness, negative self-thoughts. Presence of depression
Psychotic symptoms	16	Ten studies identified a positive correlation between positive psychotic symptoms and suicide in schizophrenia. Low levels of negative symptoms also showed a strong relationship with increased suicide in three studies. Also positive: higher level of baseline mental suffering (one study) and mental disintegration and agitation/restlessness (one study)	One study found no relationship between suicide and lifetime occurrence of hallucinations or delusions. One study showed no difference in suicidality by mean number of negative symptoms	Increased positive symptoms, particularly auditory hallucinations and delusions, but lower levels of negative symptoms
Insight	5	Four studies showed a positive correlation between suicide and insight	One study found no difference in suicide rates between groups with insight and without	Presence of insight
Treatment	11	Two studies identified increased suicide risk with current use of antidepressants and being treated by male psychiatrists. One study identified higher number of hospitalizations amongst those with who committed suicide. Protective factors include CBT, SGAs and deinstitutionalization	One study found no difference in suicide rates between those who have been treated and those who have not. Another study identified no difference between groups treated with CBTp, supportive counselling or usual treatment	Inconclusive. Studies suggest that second-generation antipsychotics are protective

CBT, cognitive behavioural therapy; SGA, second generation antipsychotic.

Table 4. Genetics

Characteristic	Number of studies	Positive association	No association	Conclusion
Family history	4	Three studies identified a positive correlation between family history of suicide (behaviour/attempt) and suicide	One study found no difference	Positive family history
Biological markers	1	–	No difference in CSF 5-HIAA levels and CSF HVA levels between suicide attempters and non-attempters	No association between CSF 5-HIAA and HVA levels, and suicide
Genetics	2	One study: COMT Del Allele confers susceptibility to suicide attempters. One study: difference in mean ratios, with the 'C' alleles showing lower cDNA levels in the suicide group; decreased total 5-HT2A receptor mRNA in suicide victims	–	Genes identified to be associated with suicide – COMT Del Allele, "C" alleles and 5-HT2A receptor

Table 5. Quality analysis of all included original studies

Study	Study design	Percentage of maximum quality score (%)
Crumlish et al. (2005)	Prospective Cohort Study	92
Fialko et al. (2006)	Randomized Controlled Trial	92
Ran et al. (2007)	Follow-Up/Cohort Study	92
Ran et al. (2009)	Prospective Cohort Study	92
Montross et al. (2008)	Randomized Controlled Trial	92
Ran et al. (2008)	Prospective Cohort Study	92
Sevincok et al. (2007)	Prospective Case-Control Study	85
Alaräisänen et al. (2006)	Retrospective Cohort Study	85
Kuo et al. (2005)	Follow-up Cohort Study	85
Pompili et al. (2009)	Retrospective Cohort Study	85
Loas et al. (2009)	Prospective Cohort Study	85
Bhatia et al. (2006)	Retrospective Cohort Study	85
Limosin et al. (2007)	Prospective Follow-up Study	85
McGirr et al. (2008)	Retrospective Cohort Study	85
Bickley et al. (2006)	Retrospective Cohort Study	85
Bateman et al. (2007)	Randomized Controlled Trial	85
Silverton et al. (2008)	Prospective Cohort Study	77
Carlborg et al. (2008)	Follow-Up/Cohort Study	77
Tidemalm et al. (2008)	Follow-Up/Cohort Study	77
Healy et al. (2006)	Retrospective Cohort Study	77
Bertelsen et al. (2007)	Randomized Controlled Trial	77
Laursen et al. (2007)	Retrospective Cohort Study	77
Kelly et al. (2004)	Retrospective Cohort Study	77
Haukka et al. (2008)	Retrospective Cohort Study	77
Barak et al. (2004a)	Retrospective Case-Control Study	77
Sinclair et al. (2004)	Retrospective Case-Control Study	77
Reutfors et al. (2009)	Retrospective Case-Control Study	77
Carlborg et al. (2009)	Prospective Cohort Study	77
Preti et al. (2009)	Prospective Cohort Study	77
Barak et al. (2004b)	Retrospective Case-Control Study	77
Tarrier et al. (2006)	Prospective Randomized Controlled Trial	77
Strauss et al. (2006)	Retrospective Cohort Study	77
Altamura et al. (2007)	Retrospective Cohort Study	77
Alaräisänen et al. (2009)	Prospective Cohort Study	77
Rantanen et al. (2009)	Follow-up Study	77
Niehaus et al. (2004)	Case-Control Study	77
Ran et al. (2005)	Retrospective Cohort Study	77
Lewine and Shriner (2009)	Retrospective Cohort Study	69
Barak et al. (2008)	Case-Control Study	69
Lee et al. (2009)	Case-Control Study	69
McGirr et al. (2006)	Case-Control Study	69
Osborn et al. (2008)	Retrospective Cohort Study	69
Harkavy-Friedman et al. (2004)	Retrospective Cohort Study	69
Roy (2005)	Retrospective Case-Control Study	69
Li et al. (2008)	Case-Control Study	69
De Luca et al. (2007)	Case-Control Study	62
Bourgeois et al. (2004)	Follow-Up/Cohort Study	62
De Luca et al. (2006)	Case-Control Study	62
Karvonen et al. (2007)	Retrospective Cohort Study	62
Phillips et al. (2004)	Retrospective Cohort Study	62
Fennig et al. (2005)	Case-Control Study	46

mortality), with a lifetime risk of around 5% being more representative, and compatible with various studies we analysed (Barak et al., 2004a; Carlborg et al., 2008; Ran et al., 2007; Limosin et al., 2007). This 5% figure remains

significantly higher than the general population risk of suicide.

We decided it would be clinically relevant and helpful to classify the data on risk factors for suicide in schizophrenia,

Table 6. Summary of the highest-quality studies of risk factors for suicide in schizophrenia

Study	Title of paper	Details of participants	Conclusions re increased suicide risk
Crumlish et al. (2005)	Early insight predicts depression and attempted suicide after 4 years in first-episode schizophrenia	101 participants, suicide attempts was used as a measurement	Insight is associated with increased risk of suicide attempts. Insight is also associated with depression
Fialko et al. (2006)	Understanding suicidal ideation in psychosis: findings from the Psychological Prevention of Relapse in Psychosis (PRP) trial	290 patients	Younger age and male gender not replicated Whites Anxiety, negative beliefs and depression Auditory hallucinations Daily alcohol consumption
Ran et al. (2007)	Mortality in people with schizophrenia in rural China: 10-year cohort study	500 patients	>50 y/o, male gender and inability to work associated with increased risk Age of onset > 45 y/o, duration of disease \geq 10 years, physical illness Reduced risk with treatment
Ran et al. (2009)	Differences in mortality and suicidal behaviour between treated and never-treated people with schizophrenia in rural China	500 patients, 132 never received antipsychotic and 368 reported having received antipsychotic treatment	Suicide rates were not significantly different between treated and non-treated schizophrenic patients. Overall mortality rates in patients are high when compared with general population (>6.5 times)
Montross et al. (2008)	Suicidal ideation and attempts among middle-aged and older patients with schizophrenia spectrum and concurrent subsyndromal depression.	132 patients	Male gender Hopelessness, depression, higher PANSS general psychopathology subscale scores
Ran et al. (2008)	Mortality of geriatric and younger patients with schizophrenia in the community	500 patients	History of suicidal ideation Patients from the younger age group had higher suicide rates

PANSS, positive and negative syndrome scale

according to the strength of the findings in the data reviewed. Thus we produced Table 7, which summarizes those risk factors which have a strong association, and those with a weaker (or negative) association for later suicide.

What have we learnt since 2005?

This systematic review has replicated some of the key findings found in Hawton et al. (2005), including identifying a strong association with later suicide in schizophrenia and earlier depression, history of suicide attempts, and drug misuse. Depression is one of the major risk factors for suicide among individuals with schizophrenia. A randomized controlled trial (OPUS Trial) (Bertelsen et al., 2007) investigated suicidal thoughts and plans, depressive symptoms and drug misuse in predicting suicidal attempts at 1- and 2-year follow-up. This trial has shown that suicidal thoughts and plans, previous suicide attempts and depressive symptoms are among the strongest predictors of suicidality in patients presenting with first-episode psychosis. One of our top-scoring articles (Fialko et al., 2006) used the Beck Depression Inventory as a measure of the severity of depression and its association with the risk of committing suicide. This study has shown that the likelihood of patients with scores equal or greater than 2 on Suicide Item (9) committing suicide increases by seven-fold.

A history of prior suicide attempts elevates risk of completed suicide threefold according to both Reutfors et al. (2009) and Sinclair et al. (2004), who found that individuals who were admitted for an attempted suicide had the highest risk (of all variables studied) of committing suicide (Odds Ratio (OR) = 8.10).

In addition to drug misuse, we also identified alcohol misuse as a key risk factor for suicide. The WHO Mental Health Surveys (Nock et al., 2009) aimed to identify mental disorders associated with suicidal behaviour and have shown that alcohol (OR = 2.6) and drug (OR = 2.0) abuse or dependency are strong predictive factors for suicide. However, one of the studies included in this review (McGirr and Turecki, 2008) has shown that substance abuse does not increase risk of suicide amongst patients with schizophrenia (alcohol abuse and lifetime suicide risk OR = 0.29, drug abuse and lifetime suicide risk OR = 0.94), although this study used data from interviews with family members of the deceased patients, which may not be the most accurate source of information.

Hawton et al. (2005) found that poor adherence to treatment is associated with increased risk of suicide (OR = 3.75). Some of the studies included in this review have shown that individuals who underwent treatment had a smaller risk of committing suicide (Barak et al., 2008; Preti et al., 2009; Ran et al., 2007), but one particular study (Ran et al., 2009) found no significant difference between suicide rates

Table 7. Summary of risk factors associated with suicide in schizophrenia

Risk factor	Strong association with suicide	Weak association with suicide
Demographic factors	Young, male, unemployment, with higher levels of education	Single (not married), rural
Illness-related factors	Presence of depression, hopelessness, negative self-thoughts, anxiety, insomnia, self-devaluation, low self-esteem, guilty thoughts and PTSD	Treatment (in particular, second-generation antipsychotic) may be a protective factor against suicide
	Increased positive symptoms, in particular auditory hallucinations and delusions; low negative symptoms; higher level of mental suffering at baseline; mental disintegration and agitation/motor restlessness	Later age of onset The impact of duration of disease on suicide risk is inconclusive
	Presence of insight Presence of physical illnesses	
Genetics	Positive family history	
Previous suicide attempt/ideation	Strong correlation with history of suicide attempt/ideation	
Substance abuse	Alcohol and drug abuse	Smoking
Life events		Potentially increased risk with history of increased childhood trauma

PTSD, post-traumatic stress disorder

between the treated and non-treated group, although Ran et al. (2009) found that the non-treated group had more severe symptoms.

An interesting finding in this study is the association between the presence of positive symptoms, in particular auditory hallucinations and delusions, and an increased risk of suicide among patients with schizophrenia. This is in contrast with the findings reported by Hawton et al. (2005). This difference may be due to the heterogeneity of the data in Hawton et al. (2005) which resulted in a relatively weak association between hallucinations and reduced risk of suicide. While our study has identified a positive association, further studies are required to confirm this.

Conventional wisdom suggests that increased risk of suicide in schizophrenia is associated with young age. However, some of the studies (Fialko et al., 2006; Kuo et al. 2005; Ran et al., 2007; Reutfors et al., 2009) included in this review have challenged this association, with both Reutfors et al. (2009) and Kuo et al. (2005) finding that a later age of illness onset is associated with an increased risk of suicide. Ran et al. (2007) identified that age (>50 years old, hazard ratio = 4.8) and age at illness onset (>45 years old, hazard ratio = 9.2) are independent predictors of mortality in the population studied, but this study did not define the causes of death or investigate specific predictors of suicide. The difference in conclusions about age as a risk factor for suicide in patients with schizophrenia may be a result of the design of the study, with shorter-term studies having a tendency of identifying younger patients as a higher risk group. Further studies are needed to identify if older age and later age of onset are indeed strong predictors of suicide, and such studies should take into account the severity of psychotic symptoms, chronicity of illness, and other co-morbidities including affective disorders. Until then, the weight of evidence supports a younger age as a risk factor.

Some of the risk factors identified in this systematic review may be similar or may oppose those observed in the general population, as Agerbo (2007) has pointed out. However, for the purposes of this study, the risk factors identified are in relation to patients with schizophrenia and are not compared with risk factors in the general population. This systematic review looked at studies that identified either suicide or suicide ideation as an outcome. This may potentially affect our findings, although a history of suicide attempt or ideation has a strong positive correlation with completed suicide among patients with schizophrenia. Therefore, we feel that inclusion of studies with suicide ideation or attempt as an outcome in this study is justified.

Limitations

We did not attempt to perform a meta-analysis, which would allow a quantitative analysis of predictors of suicide for schizophrenia. However, differing study designs of studies included in this systematic review mean that not all data are amenable to meta-analysis. We only reviewed papers that were published in English.

Conclusions

Since an earlier systematic review conducted by Hawton et al. (2005), there have been numerous studies published concerning suicide in schizophrenia. We included 51 new data-containing studies in this critical systematic review, and found that the factors with the strongest association with later suicide (in schizophrenia) included being young and male, with a higher level of education. Illness-related factors were also important predictors, namely depressive symptoms, a history of suicide attempts, active hallucinations (contrary to Hawton et al., 2005) and delusions, the presence of insight,

and comorbid chronic physical illness. Lastly, a family history of suicide and co-existing alcohol and drug misuse were also factors with a strong association with later suicide. Adequate treatment for schizophrenia and related comorbid problems was the only protective factor identified.

Prevention of suicide in schizophrenia would thus rely on identifying those individuals with the risk factors noted above, and actively treating any comorbid depressive illness and positive psychotic symptoms, as well as addressing any co-existent substance misuse. However, suicide prediction in those with schizophrenia is complex, and efforts at prevention should also focus on optimizing adherence to medication, and possible earlier use of clozapine, as the only antipsychotic medication with demonstrated efficacy (and a licence in the USA) for the management of suicidality in schizophrenia.

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