Schizophrenia and suicide: systematic review of risk factors

KEITH HAWTON, LESLEY SUTTON, CAMILLA HAW, JULIA SINCLAIR and JONATHAN J. DEEKS

Background Suicide risk is greatly increased in schizophrenia. Detection of those at risk is clinically important.

Aims To identify risk factors for suicide in schizophrenia.

Method The international literature on case–control and cohort studies of patients with schizophrenia or related conditions in which suicide was reported as an outcome was systematically reviewed. Studies were identified through searching electronic databases and reference lists, and by consulting experts.

Results Twenty-nine eligible studies were identified. Factors with robust evidence of increased risk of suicide were previous depressive disorders (OR = 3.03, 95% CI 2.06–4.46), previous suicide attempts (OR = 4.09, 95% CI 2.79–6.01), drug misuse (OR = 3.21, 95% CI 1.99–5.17), agitation or motor restlessness (OR = 2.61, 95% CI 1.54–4.41), fear of mental disintegration (OR = 12.1, 95% CI 1.89–81.3), poor adherence to treatment (OR = 3.75, 95% CI 2.20–6.37) and recent loss (OR = 4.03, 95% CI 1.37–11.8). Reduced risk was associated with hallucinations (OR = 0.50, 95% CI 0.35–0.71).

Conclusions Prevention of suicide in schizophrenia is likely to result from treatment of affective symptoms, improving adherence to treatment, and maintaining special vigilance in patients with risk factors, especially after losses.

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Schizophrenia is associated with a significant risk of suicide (Harris & Barraclough, 1997; Inskipp et al., 1998). Risk factors for suicide in schizophrenia are similar to those in the general population. There are, however, other risk factors that are specific to the disorder (Siris, 2001). Prediction of risk of suicide in general is difficult, owing to the low base rate of suicide and the relative imprecision of risk factors (Goldney, 2000; Powell et al., 2000). As with other disorders, however, careful identification of risk factors is important to assist clinicians caring for patients with schizophrenia, as the former often have to make crucial decisions based on risk assessment. Risk factors have been investigated in several studies. Several reviews summarising the studies of risk factors in schizophrenia are available, but these are largely descriptive and have usually not taken account of the designs of the investigations. Systematic review procedures offer the best means of aggregating and summarising findings from individual studies. We conducted a systematic review of the international literature on studies of risk factors for suicide in schizophrenia, focusing entirely on studies most likely to provide valid estimates of risk factors (cohort and case-control studies).

METHOD

Study eligibility Studies were selected for inclusion in this review if they met the following criteria:

(a) patient diagnosis of schizophrenia (including its subtypes), paranoia, delusional psychoses, paranoid psychosis, psychosis not otherwise specified, schizophrenia disorder, schizotypal disorder or schizoaffective disorder;

(b) at least 90% of the participants aged 16 years or over;

(c) cohort studies, with a minimum follow-up period of 1 year, and case-control studies;

(d) specific risk factors for suicide were investigated.

Search strategy A broad search strategy for potential articles was used in order to include all relevant studies. Electronic searches of Medline (1966 to June 2004), Embase (1980 to June 2004), PsychINFO (1872 to June 2004) and Biological Abstracts (1985 to June 2004) were made with subject headings including SCHIZOPHRENIA, SCHIZOAFFECTIVE PSYCHOSIS, SUICIDE, with COHORT ANALYSIS, CASE CONTROL STUDIES, COHORT STUDIES, RISK FACTORS, FOLLOW UP STUDIES; and text words including SCHIZOPHRENIA*, SUICID* with RISK*, FOLLOW UP STUD*, CASE CONTROL STUD*, COHORT STUD* and COHORT ANALYSIS. No language restrictions were applied to the search. We hand-searched the journal Schizophrenia Research (1991, 1993, 1995–1999, 2001). A total of 1329 articles were identified from searching the electronic databases. Identified studies were screened for suitability independently by two investigators. Where a study was reported in more than one article, data were extracted from the most recent report. Bibliographies of eligible papers were checked for possible relevant studies. We consulted international experts in the field to check whether there were any omissions from our identified studies. Where there were uncertainties about the data in studies we approached authors for clarification.

Design of studies The identified studies were categorised using the following order to reflect strength of study design (Sackett et al., 1991): 1, prospective cohort study; 2, retrospective cohort study; 3, nested case-control study; 4, case–control study, with similar patient groups; 5, case–control study in which the status of the controls was unclear or different.

Data extraction Data were extracted from the reports independently by two members of the research team using a structured pro forma. Data were extracted on the following variables:

(a) socio-demographic: gender, ethnicity, religion, civil status, children, employment, social class;
was performed including only the strongest
designs, to determine whether the
magnitude and significance of risk factors
was dependent on including results from
studies of less robust design.

RESULTS

We identified 29 studies that met the review
criteria (Fig. 1; Table 1). The main reasons
for excluding studies identified in the original
search were: risk factors not reported;
case-control or cohort study design not used;
or no extractable data provided. In some
of the included studies the diagnoses
had been updated to modern criteria by the
original authors. The numbers of studies in
each design category were as follows:

(a) prospective cohort studies: n = 3 (Cohen
et al, 1990; Lim & Tsoi, 1991; Casade-
baig & Philippe, 1999a,b);
(b) retrospective cohort studies: n = 2
(Dingman & McGlashan, 1986;
Fenton et al, 1997; Stephens et al,
1999; Fenton, 2000);
(c) nested case-control studies: n = 3
(Allebeck et al, 1987; De Hert & Peuskens,
1995, 1997; Peuskens et al, 1997;
Rossau & Mortensen, 1997; De Hert
et al, 1999, 2001);
(d) case-control studies with similar
controls: n = 14 (Cohen et al, 1964;
Shafer et al, 1974; Roy, 1982; Drake
et al, 1984; Drake & Cotton, 1986;
Law, 1986; Woltersdorf et al, 1989;
Modestin et al, 1992; Havaki-
Kontaxaki et al, 1994; Taiminen
& Kujari, 1994; Steblaj et al, 1999;
Taiminen et al, 2001; Woltersdorf
& Neher, 2003);
(e) case-control studies with different or
unclear controls: n = 7 (Warnes, 1968;
Wilkinson & Bacon, 1984; Breier
& Astrachan, 1984; Roos et al, 1992;
Roy & Draper, 1995; Shah & Ganes-
varan, 1999; Funahashi et al, 2000).

Socio-demographic factors

Suicide risk was associated with male gen-
der (Fig. 2). White people were more at risk
than non-White people, but this finding
was based on only three studies; when the
study in design category 5 (Breier
& Astrachan, 1984) was omitted, the associa-
tion was not significant (OR = 2.18, 95% CI
0.16–30.39; heterogeneity P = 0.22). No asso-
ciation was found with religious denomina-
tion (data not shown). Those who were
married or cohabiting were at somewhat
lower risk, although this finding, based on
15 studies, was not statistically significant.
Omitting the four studies in design category
5 did not affect the result (OR = 0.68, 95% CI
0.43–1.04; heterogeneity P = 0.26). Sin-
gle marital status was not a risk factor. This
appears to be a robust finding, having been
investigated in 16 studies. Being divorced
did not appear to influence suicide risk,
even when the study in design category 5
(Wilkinson & Bacon, 1984) was omitted
(OR = 1.97, 95% CI 0.88–4.43, heterogene-
ity P = 0.36). Similarly, the impact of having

Statistical analysis

Study results were combined using the
DerSimonian and Laird random effects
method of meta-analysis (Deeks et al,
2001). Risk factors were expressed as
odds ratios because of the inclusion of
case-control studies in the analysis.
Between-study heterogeneity was tested
using Cochran’s Q. A sensitivity analysis

Fig. 1 Results of the search for relevant papers.
Table 1  Studies included in the review

<table>
<thead>
<tr>
<th>References</th>
<th>Study design</th>
<th>Participant details</th>
<th>Diagnostic criteriaa</th>
<th>Suicides n</th>
<th>Controls n</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allebeck et al., 1987 (Sweden)</td>
<td>3</td>
<td>Patients with schizophrenia discharged in 1971 (n = 1190). Controls: 10% random sample from surviving cohort. Follow-up period 10 years</td>
<td>DSM-III</td>
<td>32</td>
<td>64</td>
</tr>
<tr>
<td>Breier &amp; Astrachan, 1984 (USA)</td>
<td>5</td>
<td>Patients with schizophrenia who died by suicide between 1970 and 1981 while registered at Connecticut Mental Health Centre. Controls: selected from patients discharged between July 1980 and December 1981. Data from a gender-matched control group (n = 20) were not used in this review</td>
<td>DSM-III schizophrenia, schizoaffective or schizoaffective disorder</td>
<td>20</td>
<td>81</td>
</tr>
<tr>
<td>Casadebaig &amp; Philippe, 1999a,b (France)</td>
<td>1</td>
<td>In- and out-patients with schizophrenia (aged 18–64 years) from 120 public psychiatric sectors (n = 3470). Controls: living patients. Exclusions: patients hospitalised for &gt; 1 year, deaths from natural causes (n = 97) or lost to follow-up (n = 215). Follow-up period 4 years, from 1993</td>
<td>ICD-10</td>
<td>83</td>
<td>3075</td>
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<tr>
<td>Cheng et al., 1990 (Hong Kong)</td>
<td>4</td>
<td>Out-patients with chronic or sub-chronic schizophrenia who died by suicide between 1981 and 1985. Controls: attending same out-patient clinic, matched for age (± 5 years), gender and hospital number closest to that of the case</td>
<td>DSM-III</td>
<td>74</td>
<td>74</td>
</tr>
<tr>
<td>Cohen et al., 1964 (USA)</td>
<td>4</td>
<td>Patients with schizophrenia on Veterans Administration hospital rolls between 1955 and 1960. Controls: matched for age, gender, ethnicity, years of hospitalisation, religion, diagnostic subtype and geographic location</td>
<td>Not specified</td>
<td>40</td>
<td>40</td>
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<tr>
<td>Cohen et al., 1990 (USA)</td>
<td>1</td>
<td>Patients with schizophrenia aged 18–30 years, &lt; 1 year of total prior time spent in psychiatric or penal institutions (n = 122). Controls: matched for gender (only male data reported). Sample recruited to study between 1978 and 1986. Patients randomly assigned to Training in Community Living Programme (n = 75) or to usual system of care (n = 47). Suicide rate did not differ between the two groups, which were combined for analysis. Mean follow-up period 8.3 years</td>
<td>RDC for schizophrenia or schizoaffective disorder</td>
<td>8</td>
<td>74</td>
</tr>
<tr>
<td>Dingman &amp; McGlashan, 1986; Fenton et al., 1997; Fenton, 2000 (USA)</td>
<td>2</td>
<td>Chestnut Lodge Follow-Up Study of patients with schizophrenia discharged between 1950 and 1975 (n = 274). Controls: surviving patients from same cohort. Follow-up period 19 years</td>
<td>DSM-III or Feighner criteria for schizophrenia or schizoaffective disorder</td>
<td>17</td>
<td>235</td>
</tr>
<tr>
<td>Drake et al., 1984; Drake &amp; Cotton, 1986 (USA)</td>
<td>4</td>
<td>Patients with schizophrenia admitted to hospital between 1976 and 1980. In-patient suicides: 33%. Controls: patients in hospital during same period and alive at follow-up. Exclusions: age &gt; 65 years, admitted &lt; 2 weeks or &gt; 2 years, lost to follow-up (n = 3) or death from other cause (n = 1). Follow-up period 3–7 years</td>
<td>DSM-III</td>
<td>15</td>
<td>89</td>
</tr>
<tr>
<td>Funahashi et al., 2000 (Japan)</td>
<td>5</td>
<td>In- and out-patients with schizophrenia from 3 hospitals, who died by suicide between 1967 and 1992. Controls: randomly selected in- and out-patients from same 3 hospitals, with no past history of attempted suicide, alive in June 1993, matched for gender and duration of illness</td>
<td>DSM-III–R schizophrenia, schizoaffective disorder or schizotypal personality disorder</td>
<td>80</td>
<td>80</td>
</tr>
<tr>
<td>Havski-Kontaxaki et al., 1994 (Greece)</td>
<td>4</td>
<td>In-patients with schizophrenia between 1959 and 1987 who died by suicide during hospitalisation. Controls: from random sampling of non-suicide in-patients, matched for time of hospitalisation. Follow-up period 13.5 years (± 9.9)</td>
<td>ICD-9</td>
<td>22</td>
<td>60</td>
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(continued)
<table>
<thead>
<tr>
<th>References (country)</th>
<th>Study design</th>
<th>Participant details</th>
<th>Diagnostic criteria</th>
<th>Suicides ( n )</th>
<th>Controls ( n )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hu et al, 1991 (Taiwan)</td>
<td>4</td>
<td>Patients 1972–1984. In-patient suicides 31%. Controls: alive at time of study, matched for age ± 5 years, gender, date of admission and length of out-patient care. Data from a second control group assessed in 1982 within 1 year of symptom onset (( n=60 )) were not used in this review</td>
<td>DSM–III</td>
<td>42</td>
<td>84</td>
</tr>
<tr>
<td>Law, 1986 (Hong Kong)</td>
<td>4</td>
<td>Patients attending open-door general hospital psychiatric unit during period July 1979 to March 1982. Controls: matched for age (± 2 years) and gender</td>
<td>Not stated</td>
<td>23</td>
<td>23</td>
</tr>
<tr>
<td>Lim &amp; Tsoi, 1991 (Singapore)</td>
<td>1</td>
<td>Patients with schizophrenia first admitted and discharged in 1975 (( n=482 )). Controls: living patients. Excluded from analysis: death from natural causes (( n=30 )). Follow-up period 15 years</td>
<td>Similar to DSM–III–R</td>
<td>41</td>
<td>411</td>
</tr>
<tr>
<td>Modestin et al, 1992 (Switzerland)</td>
<td>4</td>
<td>In-patients diagnosed with ICD–9 schizophrenia at two institutions 1973–1987. Cases: in-patient suicides (including on hospital premises, on leave and absent without leave). Controls: selected from patients who had not completed suicide, matched for gender and date of admission</td>
<td>RDC</td>
<td>53</td>
<td>53</td>
</tr>
<tr>
<td>Roos et al, 1992 (South Africa)</td>
<td>5</td>
<td>In- and out-patients with schizophrenia who died by suicide between 1979 and 1989. Controls: patients with high risk of suicide, scoring ≥ 10 on Beck Hopelessness Scale, matched for age, gender and duration of illness.</td>
<td>DSM–III</td>
<td>33</td>
<td>33</td>
</tr>
<tr>
<td>Rossau &amp; Mortensen, 1997 (Denmark)</td>
<td>3</td>
<td>Danish Case Register study of all patients with schizophrenia first admitted to any Danish psychiatric hospital or department between April 1970 and December 1987 (( n=9156 )). Controls: 10 per case, schizophrenia diagnosed before data of suicide case, alive at date of case suicide. Follow-up period 18 years</td>
<td>ICD–8</td>
<td>508</td>
<td>5080</td>
</tr>
<tr>
<td>Roy, 1982 (Canada)</td>
<td>4</td>
<td>Patients with chronic (( n=26 )) and sub-chronic (( n=4 )) schizophrenia who died by suicide between July 1968 and June 1979. In-patient suicides: 23%. Controls: from same patient population, matched for gender, age (± 7 years), type of schizophrenia and date of admission to the unit</td>
<td>DSM–III</td>
<td>30</td>
<td>30</td>
</tr>
<tr>
<td>Shaffer et al, 1974 (USA)</td>
<td>4</td>
<td>Suicides from cohort of psychiatric patients with final diagnosis of schizophrenia hospitalised at some time between 1947 and 1960 (( n=361 )). Controls: selected using random number table from non-suicide cases. Follow-up period ≥ 5 years</td>
<td>Not specified</td>
<td>12</td>
<td>75</td>
</tr>
<tr>
<td>Shah &amp; Ganesvaran, 1999 (Australia)</td>
<td>5</td>
<td>In-patient suicides (on hospital premises, on leave &lt; 1 month, absent without leave or &lt; 1 month after discharge) between January 1973 and December 1993. Data reported separately for patients with schizophrenia. Controls: selected from non-suicide in-patients</td>
<td>ICD–9</td>
<td>62</td>
<td>21</td>
</tr>
<tr>
<td>Steblaj et al, 1999 (Slovenia)</td>
<td>4</td>
<td>All in-patient suicides (on hospital premises, on leave, outing, trial discharge or stay in another hospital) at unit between 1984 and 1993. Schizophrenia results reported separately. Controls selected from current in-patients 1993–1995</td>
<td>ICD–9</td>
<td>36</td>
<td>36</td>
</tr>
<tr>
<td>Stephens et al, 1999 (USA)</td>
<td>2</td>
<td>Follow-up study of cohort of discharged patients with schizophrenia hospitalised between 1913 and 1940 (( n=1357 )). Data available for 1212 patients. Controls included patients dying from natural causes (( n=116 )). Follow-up period mean 10.5 years</td>
<td>Discharge diagnosis of schizophrenia, schizophrinic reaction type, parergasic reaction type, dementia praecox, catatonia and allied to schizophrenia</td>
<td>28</td>
<td>1184</td>
</tr>
<tr>
<td>Taiminen &amp; Kujari, 1994 (Finland)</td>
<td>4</td>
<td>All in-patient suicides with diagnosis of schizophrenia or paranoid psychosis between August 1967 and March 1993. Controls: matched for gender, age (± 5 years) and year of hospitalisation</td>
<td>Not specified</td>
<td>28</td>
<td>28</td>
</tr>
</tbody>
</table>

(continued)
Two studies were identified that investi-gated the impact of IQ on suicide risk.

- Warnes, 1968 (Canada) identified patients with schizophrenia and former in-patients who died by suicide between November 1962 and September 1966. Controls: patients with chronic schizophrenia, matched for gender and age, who had shown suicidal behaviour in the past. Omitted (OR was not associated with suicide risk (Cohen was not associated with suicide risk (Cohen et al, 1994).)
- Wilkinson & Bacon, 1984 (UK) identified patients with a history of parasuicide who died by suicide between 1968 and 1981 (n = 16) plus undetermined deaths (n = 3); in-patient suicides: 35%. Controls: with or without a history of parasuicide, matched for age, gender and year of admission. Omitted (OR was not associated with suicide risk (Cohen et al, 1994).)

**Characteristics of the disorder**

**Positive symptoms of schizophrenia**

The results of the studies of positive symptoms of schizophrenia (Fig. 4) were conflicting (heterogeneity P < 0.001): two studies reported a statistically significant positive association and two reported a significant negative association. In a further study, which recorded symptoms on a continuous scale, there was an association of total number of positive symptoms and risk (Fenton, 2000). Delusions and hallucinations were also investigated separately. Delusions were not associated with suicide risk, although again there was significant heterogeneity (P = 0.02). When the study in design category 5 reported a positive association (OR = 0.48, 95% CI 0.24–0.94; heterogeneity P = 0.04). In a
single study a scaled measure of paranoid ideation was associated with suicide risk (Cohen et al., 1990) and in another similar study a measure of suspiciousness was also associated with risk (Fenton, 2000). Hallucinations were associated with a lower risk of suicide. The finding for the three studies of command hallucinations showed significant heterogeneity ($P=0.006$). Although there was no overall association with suicide risk, this was based on relatively few data, and two of the studies were in design category 5.

**Negative symptoms of schizophrenia**

There were conflicting data on negative symptoms in general (heterogeneity $P=0.003$), with no overall association with suicide risk (Fig. 4). A protective association was found in a single study using a negative symptom scale, which also found a protective association for flat affect (Fenton, 2000). There were limited data on social withdrawal, but the result of the meta-analysis did not show an association with suicide.

**Affective symptoms**

Agitation (or motor restlessness) was associated with suicide (Fig. 4). The same was true for both a sense of worthlessness (or low self-esteem) and hopelessness. There was a trend towards an association with sleep disturbance, but the data were very limited. No study examined anxiety as a dichotomous variable; however, no association with suicide was found in a study using a continuous measure of anxiety (Cohen et al., 1990).

**Reaction to illness and treatment**

Insight into the nature of the illness was not associated with suicide, but there was considerable heterogeneity in the result (Fig. 4). This finding did not change when the study in design category 5 (Warnes, 1968) was omitted from the analysis (OR=1.70, CI 0.33–8.75; heterogeneity $P<0.001$). Fear of mental disintegration was associated with risk, but again there was considerable heterogeneity in this finding. This result remained positive when the two studies in design category 5 were omitted from the analysis, but the confidence intervals were very wide (OR=81, CI 13.8–481). Suicide risk was considerably increased in participants with poor adherence to treatment (defined as failure to take medication as prescribed or to attend follow-up). Patients who had been compulsorily admitted to hospital were not at greater risk of suicide, although there was significant heterogeneity ($P=0.03$).

**Suicidal phenomena**

Previous suicidal phenomena were assessed in a variety of ways in the studies, all but...
one of which were significantly associated with suicide in the meta-analyses (Fig. 5). On the basis of the results of 22 studies, a history of attempted suicide strongly increased the risk of suicide, a finding that was largely unaffected when the studies in design category 5 were omitted from the analysis (OR = 4.44, 95% CI 3.06–6.45). Suicide risk was also associated with both attempted suicide being a reason for the last admission (OR = 2.87, 95% CI 1.66–4.95) and an attempt during that admission (OR = 8.91, 95% CI 3.40–23.4) (data not shown in Fig. 5). The findings for suicide threats were contradictory; this may be due to one study selecting controls from among patients with high scores (≥ 10) on the Beck Hopelessness Scale (Roos et al., 1992), whereas the other study, which involved a more robust design (De Hert et al., 2001), showed a strong association. Suicide was linked to both past and recent suicidal ideation.

**Comorbid disorders and behaviour**

**Depression**

Both a history of depression and recent depression were associated with suicide (Fig. 6). The different result for recent depression in one study may be explained by the selection of high-risk controls (Roos et al., 1992). Omitting this study from the analysis resulted in an even stronger association (OR = 12.7, 95% CI 6.72–24.1), with little heterogeneity (P = 0.43).

**Alcohol and drug misuse**

Suicide risk was not associated with alcohol misuse or dependence (Fig. 6), a finding that was unaffected by omission of the studies in design category 5 (Roos et al., 1992; Shah & Ganesvaran, 1999) (OR = 1.17, 95% CI 0.69–1.99; heterogeneity P = 0.81). On the other hand, suicide risk was considerably increased in the presence of drug misuse or dependence, a finding again unaffected by omitting the two studies in design category 5 (Roos et al., 1992; Shah & Ganesvaran, 1999) (OR = 3.51, 95% CI 2.06–5.97; heterogeneity P = 0.88). Where authors did not define the substance of misuse there was no association with suicide risk, although this result showed considerable heterogeneity and may reflect the fact that the majority

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**Fig. 3** Personal, social and family history characteristics. Studies identified by first-named author and year only. Study design: 1, prospective cohort; 2, retrospective cohort; 3, nested case-control; 4, case-control: controls equivalent (patient status, timing, etc.); 5, case-control: controls unclear or different.
of patients in this category could have been alcohol misusers.

Violence, impulsivity and physical illness

There was considerable variation in the findings for violence between individual studies, although the overall result did not indicate an association (Fig. 6). Omitting the study in design category 5 (Warnes, 1968) did not alter this finding (OR = 1.66, 95% CI 0.67–4.14; heterogeneity P = 0.015). Impulsivity was associated with increased risk, although this finding was based on the results of only two studies. Suicide was not associated with physical illness, a finding unaffected by omitting the study in design category 5 (Shah & Ganesvaran, 1999) (OR = 1.22, 95% CI 0.54–2.72; heterogeneity P = 0.16).

DISCUSSION

We adopted a thorough and systematic approach to searching the world literature for studies of risk factors for suicide in schizophrenia, including searching for studies in any language. Some authors reanalysed their original data for us, or supplied us with additional data. This is therefore the most comprehensive review of risk factors for suicide in schizophrenia that has been conducted to date. Its findings indicate that suicide risk in patients with schizophrenia is related less to the core psychotic symptoms of the disorder and more to affective symptoms, agitation or motor restlessness, and to awareness that the illness is affecting mental functioning.

Previous suicidal behaviour is a strong risk factor. Drug misuse and loss events also appear to increase risk. Treatment compliance is important. Hallucinations are associated with decreased risk.
Currently published information.

esis of the evidence that is available from

attention. However, the approach we have

Also, some potential risk factors have been

cohort studies – examine relatively few

fact that some investigations – especially

meta-analysis. Reviews of this type are also

duces non-significant associations, since

Authors to provide little or no data when

bias is increased by the tendency among

As with all systematic reviews based on

Small. Small.

Suicidal phenomena. Studies identified by first-named author and year only. Study design: 1,

prospective cohort; 2, retrospective cohort; 3, nested case–control; 4, case–control: controls equivalent

(patient status, timing, etc.); 5, case–control: controls unclear or different.

Limitations of the study

As with all systematic reviews based on

published studies, the findings of our

review are subject to publication bias. This

bias is increased by the tendency among

authors to provide little or no data when

investigation of potential risk factors pro-

duces non-significant associations, since

this results in their exclusion from the

meta-analysis. Reviews of this type are also

subject to potential bias resulting from the

fact that some investigations – especially

cohort studies – examine relatively few

potential risk factors, whereas others – no-

tably case–control studies – include more.

Also, some potential risk factors have been

examined in a fairly large number of

studies, whereas others have received less

attention. However, the approach we have

used in this review provides the best syn-

thesis of the evidence that is available from

currently published information.

We only included investigations that

met the criteria of being either cohort or

case–control studies. The patients could

have any of the diagnoses within the broad

spectrum of schizophrenia. We also in-

cluded studies in which some of the patients

had schizoaffective disorder. The psycho-

pathology of schizoaffective disorder over-

laps with that of schizophrenia and this

disorder also has a high suicide risk (Fenton

et al., 1997). It was not possible to analyse

risk according to specific diagnoses because

the numbers of cases of schizoaffective dis-

order were either not supplied or were small.

One of the main drawbacks of a meta-

analytical study of this kind is that there is

considerable variation between investiga-

tors in the definition of individual risk

factors. This variability necessitates com-

promise on the specificity of definitions

in order to allow inclusion of the largest

possible number of studies.

Specific criteria were used to group

the studies according to research design. Cohort studies are likely to yield the most

robust findings, followed by nested case–

control studies, and then case–control

studies with similar patient groups (Sackett

et al., 1991). Relatively few of the studies

were in the former categories. However, their

findings did not differ markedly from those of other categories of study for most

variables. We have re-examined all the find-
ings excluding studies with the least robust

design (case–control studies with controls

that differed from those of the cases or where

their status was unclear). This resulted in

changes to some of the findings.

The advantage of meta-analysis of sum-

mary data is that it not only allows the find-
ings of a range of studies to be synthesised,

but also greatly reduces the danger of find-
ings from individual studies leading to spurious conclusions. The degree of hetero-
geneity in the analyses of some factors is
testimony to how much findings can vary

between studies and how misleading single

studies can be, especially when based on

small numbers of participants and/or weak-

er research designs. A disadvantage of this

approach is that it is not possible to adjust

estimates of risk factors for effects of con-

founding factors, since this would

require access to individual patient data.

Factors associated with risk

of suicide

Although this meta-analysis has shown that

some of the risk factors for suicide in

schizophrenia are similar to those for sui-

cide in the general population, it has high-

lighted certain risk factors that are clearly

specific to schizophrenia and its conse-

quences. The odds ratio for suicide in men

compared with women of 1.57 is somewhat

less than the ratio observed in the general

populations of most countries (Cantor,

2000). The excess risk in White patients is

in keeping with the situation in the general

populations of multiracial countries at the

time the studies examining this factor were

conducted. It was, however, a weak find-

ing, which was no longer positive when the

sensitivity analysis was applied. We

could not examine age as a risk factor be-

cause it was used as a matching factor in

some of the case–control studies, and in

other studies for which age data were sup-

plied there were differences in manner of

reporting. Married or cohabiting patients
did not appear to be at markedly lower risk. This is perhaps surprising, as being married might reflect less severe illness or later-onset disorders, which tend to be less damaging (Eaton et al., 1992). In contrast, to the risk in the general population, being single or divorced was not associated with greater risk. The living circumstances of patients appeared to be important, in that those living alone or not living with their families were at increased risk; again, this might reflect severity of the disorder. Life events in the form of recent losses appear to be associated with suicide risk, in keeping with their role in suicide risk in general.

The most robust findings were of risk of suicide being strongly associated with comorbid affective disorders, specific affective symptoms (agitation, sense of worthlessness and hopelessness) and a history of suicidal thinking, threats and (especially) non-fatal suicidal acts. It was not possible to distinguish between depressive symptoms that were part of the schizophrenic illness, occurred after an episode of illness or represented a separate disorder. Further support for the importance of depression as a risk factor came from the positive association of risk with a family history of affective disorders. Although family history of suicide did not emerge from the meta-analysis as a factor, perhaps because it is a relatively rare phenomenon, it was a risk factor in the largest study that examined this factor (De Hert et al., 2001).

With regard to the characteristics of schizophrenia, we could not examine age at onset or duration of the disorder as potential risk factors because of considerable variation in the way this was recorded in different studies, and because of matching for this factor in some studies. Using a different study design to address this problem has shown that the majority of suicides in cases of schizophrenia occur early in the course of the illness (Palmer et al., 2005). Active psychotic symptoms were not associated with increased risk; indeed, hallucinations were associated with a reduced risk of suicide, as were delusions when the...
studies of more robust design were examined. Also, command hallucinations were not associated with increased risk, although some authors have cited command hallucinations as causing patients with schizophrenia to complete suicide (Planansky & Johnston, 1973; Barracough et al., 1974). In separate single studies, paranoid ideation (Cohen et al., 1990) and suspiciousness (Fenton, 2000) were associated with risk. Suicide risk was not associated with negative symptoms, although there was significant heterogeneity in the result. Findings based on a scale of negative symptoms (Fenton, 2000) suggest that risk is probably inversely related to such symptoms.

Developing schizophrenia after having achieved academically has been claimed to be associated with particular risk of suicide (Drake et al., 1984). Meta-analysis provides some support for this. The results of two studies also indicated increased risk associated with higher IQ. Fear of mental disintegration was significantly associated with suicide risk, although there was considerable variation between studies regarding the possible role of insight into the nature of the illness. Surprisingly, given the significance of alcohol misuse as a major risk factor for suicide in the general population (Murphy, 2000), it does not appear to be a risk factor in schizophrenia. On the other hand, drug misuse or dependence was strongly associated with suicide risk. Drug misuse is twice as common in people with schizophrenia as in the general population (Bühler et al., 2002).

We were unable to examine treatments in this review, partly because it is difficult to compare these across studies and partly because medication was often referred to in general terms, such as ‘antipsychotics’ or ‘antidepressants’. However, our review has shown that suicide risk is considerably increased in patients who adhere poorly to treatment. Although akathisia is often cited by clinicians as a risk factor for suicide, the association is based on case reports only (Shear et al., 1983; Drake & Ehrlich, 1985). No study in this review provided data on akathisia as a possible risk factor and so the association was not confirmed.

Limitations in predicting risk

A further methodological issue, which needs to be borne in mind when considering the findings of this review, is that evaluation of potential risk factors (e.g. symptoms) often took place a long time before death occurred, and these factors might have changed in the intervening period. Another issue is that suicide is a relatively uncommon event, even in a disorder such as schizophrenia, which is characterised by relatively high risk. The prediction of suicide both in the general population (Goldney, 2000) and in psychiatric patients (Powell et al., 2000), using risk factors that are by their nature somewhat crude and are often present in a sizeable proportion of the patient population, is always going to be difficult.

Clinical implications

The main factors to be taken into account when assessing risk of suicide in patients with schizophrenia are affective symptoms or syndromes, suicidal thoughts, threats or behaviour, poor adherence to treatment, fears of the impact of the illness on mental functioning, and drug misuse. The nature of the schizophrenic disorder seems to be less important and, in the case of positive symptoms, may be misleading. Prevention of suicide is thus likely to result from active treatment of affective symptoms and syndromes, improving adherence to treatment, use of medication that may have special anti-suicidal effects, and maintaining special vigilance in patients with risk factors, especially when faced with significant loss events.

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**CLINICAL IMPLICATIONS**

- Risk of suicide in people with schizophrenia is strongly associated with depression, previous suicide attempts, drug misuse, agitation or motor restlessness, fear of mental disintegration, poor adherence to treatment and recent loss.

- Active psychotic features have less predictive value.

- Prevention of suicide in schizophrenia may be best addressed through treatment of affective symptoms, improving adherence to treatment and maintaining special vigilance in patients with risk factors, especially after loss events.

**LIMITATIONS**

- The findings may be subject to the influences of publication bias and differential attention to risk factors between the studies.

- Relatively few of the included studies were of robust cohort design.

- It was not possible to adjust the findings for the potential influence of confounding factors.