Schizophrenia and suicide: systematic review of risk factors

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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; Inskip *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), paraphrenia, delusional psychoses, paranoid psychosis, psychosis not otherwise specified, schizophreniform 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), PsycINFO (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 SCHIZOPHREN*, 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;

(b) family history: psychiatric disorder, depression, alcohol misuse, suicide;

(c) personal history: childhood broken home/parental loss, education, IQ, living circumstances, recent loss and life events;

(d) clinical history: positive symptoms of schizophrenia, delusions, hallucinations (command or other), paranoia, suspiciousness, negative symptoms of schizophrenia, flat affect, social withdrawal, agitation/motor restlessness, worthlessness/low self-esteem, hopelessness, sleep disturbance, insight, fear of mental disintegration, medication, adherence to treatment, compulsory admission, attempted suicide, suicide threats or ideation, depression (past and recent), alcohol misuse/dependence, drug misuse/dependence, substance misuse/dependence (drugs and/or alcohol), violence, impulsivity, hostility, suspiciousness, anxiety, social relationships and physical illness.

Two approaches to the extraction of study results were used. Where numbers of suicides and non-suicides were known for patients with and without the risk factor, a 2×2 table was created from these numbers and used in the meta-analysis. Otherwise, if an estimate of the odds ratio for an association with a risk factor was stated, together with a measure of its precision (e.g. a standard error, confidence interval or P value), these numbers were used in the analysis. If there were insufficient data to use either of these approaches the study was excluded from the review for that risk factor.

We only present meta-analyses on variables for which data were available from more than one study, where it is possible to ascertain results are repeatable. A full list of the variables examined only in single studies is available from the authors upon request. Meta-analyses are also only presented for variables for which there are dichotomous results. Where findings are based on continuous measures we provide details where these add further information to the results from dichotomous analyses.

Statistical analysis

Study results were combined using the DerSimmonian 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

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; Casadebaig & 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; Shaffer et al, 1974; Roy, 1982; Drake et al, 1984; Drake & Cotton, 1986; Law, 1986; Wolfersdorf et al, 1989; Cheng et al, 1990; Hu et al, 1991;

Modestin et al, 1992; Havaki-Kontaxaki et al, 1994; Taiminen & Kujari, 1994; Steblaj et al, 1999; Taiminen et al, 2001; Wolfersdorf & 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 & Ganesvaran, 1999; Funahashi et al, 2000).

Socio-demographic factors

Suicide risk was associated with male gender (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 association was not significant (OR=2.18, 95% CI 0.16–30.39; heterogeneity $P=0.22$). No association was found with religious denomination (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 0.45–1.04; heterogeneity $P=0.26$). Single 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, heterogeneity $P=0.36$). Similarly, the impact of having
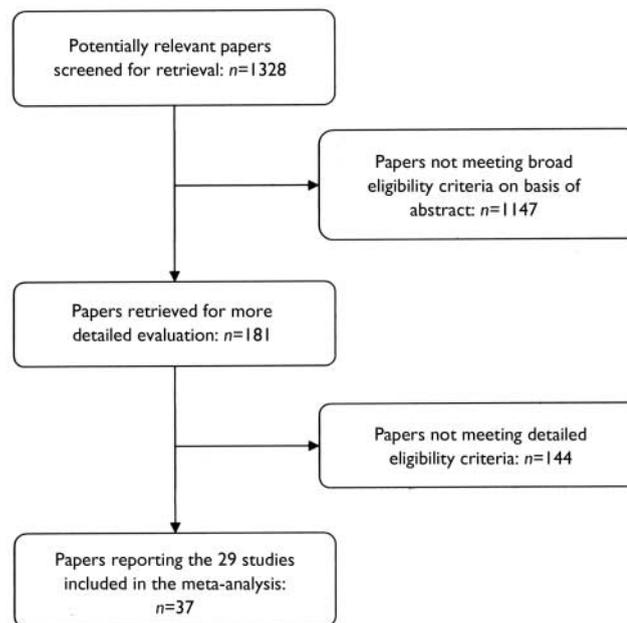

Fig. 1 Results of the search for relevant papers.

Table I Studies included in the review

References (country)	Study design[1]	Participant details	Diagnostic criteria[2]	Suicides n	Controls n
Allebeck et al, 1987 (Sweden)	3	Patients with schizophrenia discharged in 1971 (n=1190). Controls: 10% random sample from surviving cohort. Follow-up period 10 years	DSM–III	32	64
Breier & Astrachan, 1984 (USA)	5	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	DSM–III schizophrenia, schizoaffective or schizophreniform disorder	20	81
Casadebaig & Philippe, 1999a,b (France)	1	In- and out-patients with schizophrenia (aged 18–64 years) from 120 public psychiatric sectors (n=3470). Controls: living patients. Exclusions: patients hospitalised for >1 year, deaths from natural causes (n=97) or lost to follow-up (n=215). Follow-up period 4 years, from 1993	ICD–10	83	3075
Cheng et al, 1990 (Hong Kong)	4	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 ($\pm$5 years), gender and hospital number closest to that of the case	DSM–III	74	74
Cohen et al, 1964 (USA)	4	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	Not specified	40	40
Cohen et al, 1990 (USA)	1	Patients with schizophrenia aged 18–30 years, <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	RDC for schizophrenia or schizoaffective disorder	8	74
De Hert & Peuskens, 1995, 1997; Peuskens et al, 1997; De Hert et al, 1999, 2001 (Belgium)	3	Patients with schizophrenia aged <30 years, consecutive admissions hospitalised between 1973 and 1992 (n=870). In-patient suicides: 52%. Controls: matched for age admission, gender, year of index admission and diagnostic subtype. Mean follow-up period 11.4 years	DSM–III–R schizophrenia or schizoaffective disorder	63	63
Dingman & McGlashan, 1986; Fenton et al, 1997; Fenton, 2000 (USA)	2	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	DSM–III or Feighner criteria for schizophrenia or schizoaffective disorder	17	235
Drake et al, 1984; Drake & Cotton, 1986 (USA)	4	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 >65 years, admitted <2 weeks or >2 years, lost to follow-up (n=3) or death from other cause (n=1). Follow-up period 3–7 years	DSM–III	15	89
Funahashi et al, 2000 (Japan)	5	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	DSM–III–R schizophrenia, schizoaffective disorder or schizotypal personality disorder	80	80
Havaki-Kontaxaki et al, 1994 (Greece)	4	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 ($\pm$9.9)	ICD–9	22	60

(continued)

Table I Studies included in the review (*continued*)

References (country)	Study design[1]	Participant details	Diagnostic criteria[2]	Suicides *n*	Controls *n*
Hu *et al*, 1991 (Taiwan)	4	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	DSM–III	42	84
Law, 1986 (Hong Kong)	4	Patients attending open-door general hospital psychiatric unit during period July 1979 to March 1982. Controls: matched for age (±2 years) and gender	Not stated	23	23
Lim & Tsoi, 1991 (Singapore)	1	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	Similar to DSM–III–R	41	411
Modestin *et al*, 1992 (Switzerland)	4	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	RDC	53	53
Roos *et al*, 1992 (South Africa)	5	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.	DSM–III	33	33
Rossau & Mortensen, 1997 (Denmark)	3	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	ICD–8	508	5080
Roy, 1982 (Canada)	4	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	DSM–III	30	30
Roy & Draper, 1995 (Canada)	5	In-patient suicides 1970–1991. In-patient controls	ICD–8, ICD–9, ICD–10	28	13
Shaffer *et al*, 1974 (USA)	4	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	Not specified	12	75
Shah & Ganesvaran, 1999 (Australia)	5	In-patient suicides (on hospital premises, on leave <1 month, absent without leave or <1 month after discharge) between January 1973 and December 1993. Data reported separately for patients with schizophrenia. Controls: selected from non-suicide in-patients	ICD–9	62	21
Steblaj *et al*, 1999 (Slovenia)	4	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	ICD–9	36	36
Stephens *et al*, 1999 (USA)	2	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	Discharge diagnosis of schizophrenia, schizophrenic reaction type, parergasic reaction type, dementia praecox, catatonia and allied to schizophrenia	28	1184
Taiminen & Kujari, 1994 (Finland)	4	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	Not specified	28	28

(continued)

Table 1 Studies included in the review (*continued*)

References (country)	Study design[1]	Participant details	Diagnostic criteria[2]	Suicides n	Controls n
Taiminen *et al*, 2001 (Finland)	4	All patients with schizophrenia in Finland who died by suicide between April 1987 and March 1988 and who had contact with psychiatric services in the year before suicide. Subjects were investigated using psychological autopsy methodology. Controls: consecutive in- and out-patients aged ⩾18 years at Turku City Mental Health Centre in 1997, matched for treatment setting and age ± 10 years. The findings of the study were used to validate the Schizophrenia Suicide Risk Scale (SSRS)	DSM–IV	69	69
Warnes, 1968 (Canada)	5	In-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	Not specified	16	16
Wilkinson & Bacon, 1984 (UK)	5	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	ICD–8, ICD–9	17	17
Wolfersdorf & Neher, 2003 (Germany)	4	In-patients with schizophrenia who died by suicide between 1992 and 1993 at ten psychiatric hospitals in southern Germany. Controls: in-patients at one of the ten hospitals between 1992 and 1993, matched for age, gender and ICD–9 subgroup	ICD–9	80	80
Wolfersdorf *et al*, 1989 (Germany)	4	In-patients who died by suicide between January and December 1981. Controls: patients who had received in-patient treatment 1986–1987, matched for age (±3 years) and gender	ICD–9	115	115

RDC, Research Diagnostic Criteria.
1. 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.
2. Schizophrenia only unless stated.

children was examined in only two studies, although there was a trend toward a protective effect. Being employed had no impact on risk. Unemployment was not associated with risk. Difference in categorisation of social class precluded meta-analysis of the findings of four studies in which it was examined (Shaffer *et al*, 1974; Wilkinson & Bacon, 1984; Hu *et al*, 1991; Modestin *et al*, 1992).

Personal, social and family history

Suicide risk was not related to coming from a broken home or having lost a parent (Fig. 3). Limited education was unrelated to risk, but there was a non-significant trend for risk to be greater in those with higher education. When the study in design category 5 (Shah & Ganesvaran, 1999) was omitted there was a significant association of higher education with risk (OR=5.66, 95% CI 1.91–16.8; heterogeneity P=0.6), but this was based on just two studies. Two studies were identified that investigated the impact of IQ on suicide risk

(Fenton, 2000; De Hert *et al*, 2001) but dichotomous data from these studies could not be extracted for our meta-analyses. Both, however, showed a significant association of risk with higher IQ.

Participants living alone or not living with their families were at greater risk of suicide. Although the converse – living with family – was not significantly associated with reduced risk of suicide in the full analysis, it became so when the two studies in design category 5 (Brier & Astrachan, 1984; Wilkinson & Bacon, 1984) were omitted (OR=0.52, 95% CI 0.31–0.88; heterogeneity P=0.58). In the single study that examined it, number of friends was not associated with suicide risk (Cohen *et al*, 1990).

Suicide was associated with recent loss events. A family history of depression was correlated with suicide risk, although family history of any psychiatric disorder was not. There were insufficient data on family history of alcohol misuse for analysis. This also applied to family history of suicide, although a positive association

was found in the largest and methodologically robust study included in this analysis (De Hert *et al*, 2001; OR=7.39, 95% CI 2.04–26.8).

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 (Roos *et al*, 1992) was omitted, delusions appeared to be associated with lower risk (OR=0.48, 95% CI 0.24–0.94; heterogeneity P=0.04). In a

Study	Cases (n/N)	Controls (n/N)	Odds ratio (95% CI)	Design
Male gender				
Allebeck (1987)	15/32	31/64		3
Breier (1984)	18/20	48/81		5
Casadebaig (1999b)	65/83	1946/3075		1
Drake (1984, 1986)	15/15	48/89		4
Havaki-Kontaxaki (1994)	19/22	43/60		4
Lim (1991)	22/41	239/411		1
Rossau (1997)	*	*		3
Roy (1995)	20/28	9/13		5
Shaffer (1974)	12/12	36/75		4
Shah (1999)	39/62	9/21		5
Stephens (1999)	17/28	558/1184		2
Taiminen (2001)	48/69	36/69		4
OR=1.56 (95% CI 1.29–1.9)				
Heterogeneity: Q=11.7, P=0.38				
Ethnicity: White (v. non-White)				
Breier (1984)	18/20	46/81		5
Drake (1984, 1986)	15/15	72/89		4
Shaffer (1974)	12/12	74/75		4
OR=4.59 (95% CI 1.21–17.3)				
Heterogeneity: Q=2.14, P=0.34				
Married or cohabiting				
Allebeck (1987)	3/32	14/64		3
Breier (1984)	2/20	10/81		5
Cohen (1964)	15/40	12/40		4
Hu (1991)	2/42	21/84		4
Law (1986)	4/23	5/23		4
Lim (1991)	8/41	118/409		1
Roy (1982)	3/30	5/30		4
Roy (1995)	3/28	2/13		5
Shaffer (1974)	9/12	69/75		4
Shah (1999)	10/60	3/20		5
Steblaj (1999)	9/36	6/36		4
Taiminen (1994)	6/28	7/28		4
Taiminen (2001)	8/69	9/69		4
Warnes (1968)	5/16	3/16		5
Wilkinson (1984)	1/16	2/17		5
OR=0.75 (95% CI 0.54–1.04)				
Heterogeneity: Q=13.1, P=0.51				
Divorced				
Steblaj (1999)	6/36	2/36		4
Taiminen (1994)	5/28	1/28		4
Taiminen (2001)	10/69	8/69		4
Wilkinson (1984)	0/16	2/17		5
OR=1.79 (95% CI 0.65–4.89)				
Heterogeneity: Q=4.07, P=0.25				

Study	Cases (n/N)	Controls (n/N)	Odds ratio (95% CI)	Design
Single				
Breier (1984)	14/20	55/81		5
Cohen (1964)	23/40	25/40		4
Drake (1984, 1986)	15/15	83/89		4
Havaki-Kontaxaki (1994)	14/22	43/60		4
Law (1986)	19/23	18/23		4
Lim (1991)	33/41	291/409		1
Modestin (1992)	42/53	36/53		4
Roy (1982)	25/30	21/30		4
Roy (1995)	20/28	8/13		5
Shah (1999)	50/60	18/20		5
Steblaj (1999)	21/36	28/36		4
Stephens (1999)	22/28	864/1184		2
Taiminen (1994)	16/28	20/28		4
Taiminen (2001)	50/69	51/69		4
Warnes (1968)	11/16	13/16		5
Wilkinson (1984)	12/16	10/17		5
OR=1.05 (95% CI 0.8–1.38)				
Heterogeneity Q=13.1, P=0.59				
Has children				
Modestin (1992)	11/53	16/53		4
Shah (1999)	18/54	7/19		5
OR=0.69 (95% CI 0.34–1.38)				
Heterogeneity: Q=0.23, P=0.63				
Employed				
Steblaj (1999)	14/36	7/36		4
Taiminen (1994)	7/28	9/27		4
Taiminen (2001)	3/69	1/69		4
Wilkinson (1984)	3/15	3/16		5
OR=1.46 (95% CI 0.69–3.09)				
Heterogeneity: Q=3.43, P=0.33				
Unemployed				
Breier (1984)	16/20	67/81		5
Drake (1984, 1986)	14/15	83/89		4
Havaki-Kontaxaki (1994)	15/22	34/60		4
Hu (1991)	32/42	44/84		4
Roy (1982)	24/30	17/30		4
Roy (1995)	27/28	11/13		5
Shah (1999)	23/56	11/20		5
Steblaj (1999)	3/36	7/36		4
Taiminen (1994)	1/28	0/27		4
Taiminen (2001)	6/69	5/69		4
Wilkinson (1984)	9/15	10/16		5
OR=1.33 (95% CI 0.84–2.11)				
Heterogeneity: Q=13.2, P=0.21				

Odds ratio — 0.01 0.1 1 10 100 — Decreased risk / Increased risk

Fig. 2 Demographic 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. *Estimates based on reported incidence rate ratio (counts of cases and controls not available).

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

Study	Cases (n/N)	Controls (n/N)	Odds ratio (95% CI)	Design
Childhood broken home or parental loss				
Law (1986)	1/23	0/23		4
Modestin (1992)	17/53	11/53		4
Roy (1982)	11/30	14/30		4
Steblaj (1999)	12/35	18/36		4
OR=0.93 (95% CI 0.45–1.89)				
Heterogeneity: Q=4.53, P=0.21				
Limited education				
Lim (1991)	26/41	214/399		1
Modestin (1992)	19/53	18/53		4
Shah (1999)	1/52	2/15		5
Steblaj (1999)	15/36	14/36		4
OR=1.14 (95% CI 0.68–1.90)				
Heterogeneity: Q=3.65, P=0.30				
Higher education				
Drake (1984, 1986)	11/15	26/89		4
Shah (1999)	11/52	3/15		5
Steblaj (1999)	3/36	1/36		4
OR=2.91 (95% CI 0.85–9.88)				
Heterogeneity: Q=3.6, P=0.17				
Living alone				
Allebeck (1987)	10/32	17/64		3
Breier (1984)	6/20	21/81		5
Drake (1984, 1986)	9/13	24/64		4
Hu (1991)	4/42	1/84		4
Roy (1982)	14/30	14/30		4
Roy (1995)	20/28	6/13		5
Shaffer (1974)	2/12	8/75		4
Taiminen (1994)	16/26	11/27		4
Wilkinson (1984)	6/17	7/17		5
OR=1.64 (95% CI 1.09–2.47)				
Heterogeneity: Q=7.46, P=0.49				
Living with family				
Allebeck (1987)	22/32	47/64		3
Breier (1984)	7/20	24/81		5
Drake (1984, 1986)	4/13	40/64		4
Havaki-Kontaxaki (1994)	9/22	33/60		4
Taiminen (1994)	10/26	16/27		4
Wilkinson (1984)	8/17	7/17		5
OR=0.67 (95% CI 0.42–1.06)				
Heterogeneity: Q=5.2, P=0.39				
Not living with family				
Allebeck (1987)	10/32	17/64		3
Drake (1984, 1986)	9/13	24/64		4
Havaki-Kontaxaki (1994)	13/22	27/60		4
Taiminen (1994)	16/26	11/27		4
Wilkinson (1984)	9/17	10/17		5
OR=1.70 (95% CI 1.04–2.78)				
Heterogeneity: Q=3.42, P=0.49				

Odds ratio — 0.01   0.1   1   10   100
Decreased risk   Increased risk

Study	Cases (n/N)	Controls (n/N)	Odds ratio (95% CI)	Design
Recent loss				
De Hert (2001)	23/63	3/63		3
Drake (1984, 1986)	12/15	53/89		4
Shaffer (1974)	4/12	15/75		4
OR=4.03 (95% CI 1.37–11.8)				
Heterogeneity: Q=4.03, P=0.13				
Family history of psychiatric disorder				
Havaki-Kontaxaki (1994)	5/22	12/60		4
Law (1986)	5/23	5/23		4
Modestin (1992)	16/53	17/53		4
Roy (1982)	8/30	5/30		4
Shah (1999)	25/45	11/16		5
Steblaj (1999)	6/33	7/35		4
Warnes (1968)	4/16	4/16		5
OR=0.98 (95% CI 0.63–1.53)				
Heterogeneity: Q=1.86, P=0.93				
Family history of depression				
Havaki-Kontaxaki (1994)	1/22	2/60		4
Roy (1982)	2/30	2/30		4
Stephens (1999)	12/28	165/1184		2
OR=2.95 (95% CI 1.13–7.67)				
Heterogeneity: Q=2.53, P=0.28				
Family history of alcohol misuse				
Havaki-Kontaxaki (1994)	7/22	5/60		4
Modestin (1992)	9/53	7/53		4
Steblaj (1999)	8/31	9/35		4
OR=1.80 (95% CI 0.71–4.56)				
Heterogeneity: Q=3.91, P=0.14				
Family history of suicide				
De Hert (2001)	17/63	3/63		3
Drake (1984, 1986)	1/15	5/89		4
Havaki-Kontaxaki (1994)	0/22	2/60		4
Hu (1991)	1/42	3/84		4
Roy (1982)	1/30	1/30		4
OR=1.82 (95% CI 0.56–5.94)				
Heterogeneity: Q=5.85, P=0.21				

Odds ratio — 0.01   0.1   1   10   100
Decreased risk   Increased risk

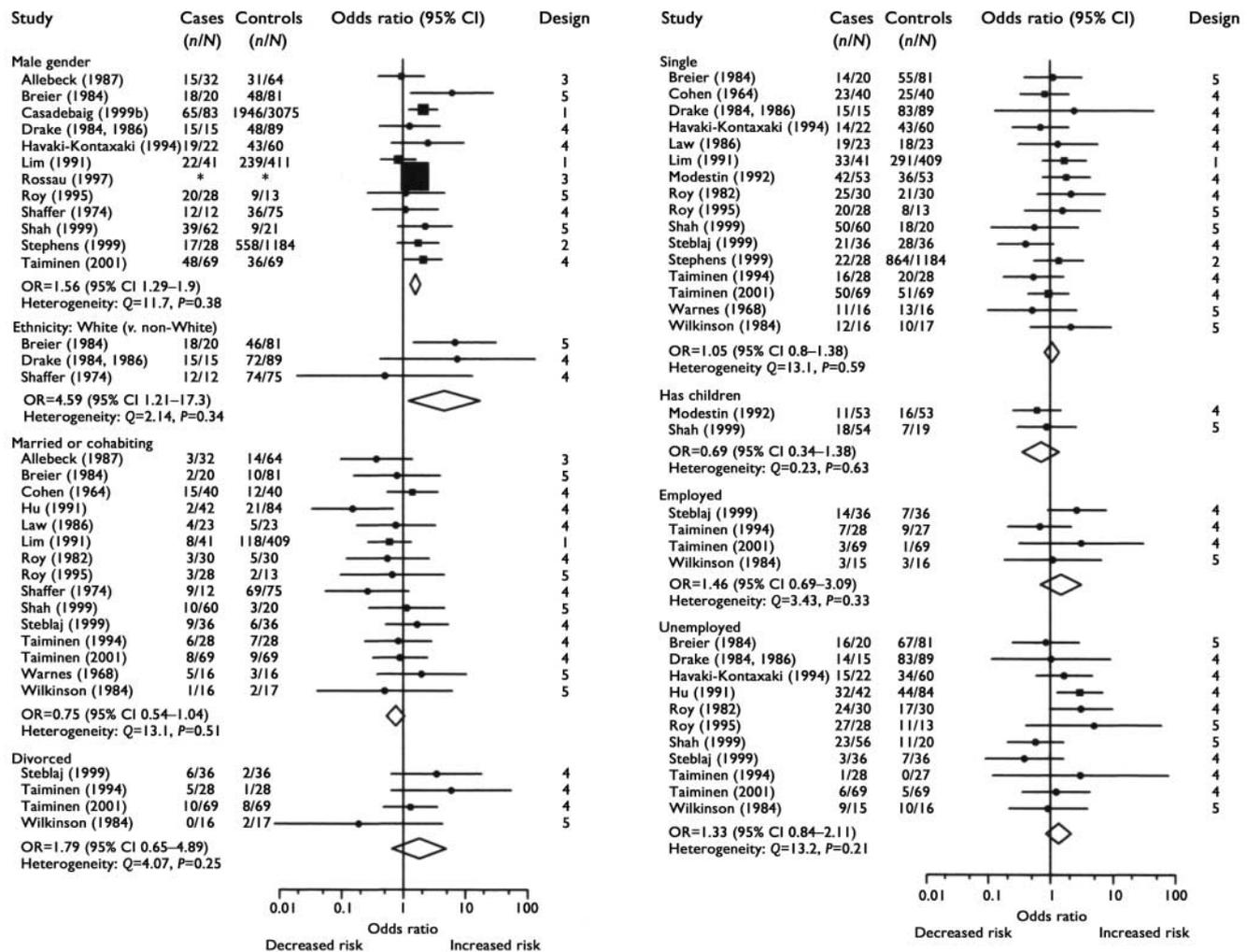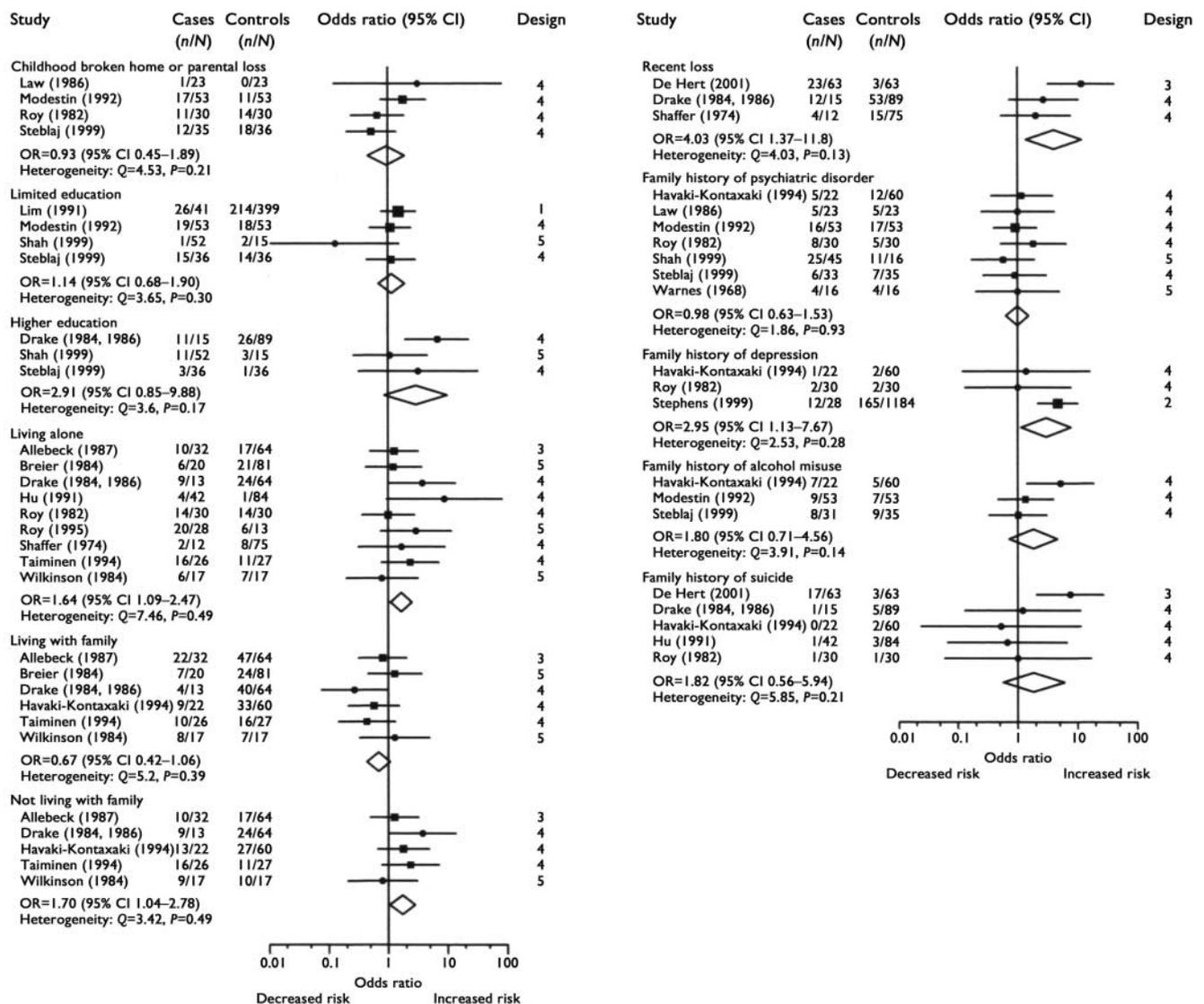**Fig. 3** Personal, social and family history characteristics. Studies identified by first-named author and year only. Study design: 1, prospective cohort; 2, retrospective cohort; 3, nested case–control; 4, case–control: controls equivalent (patient status, timing, etc.); 5, case–control: controls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

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 ($\geqslant 10$) 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
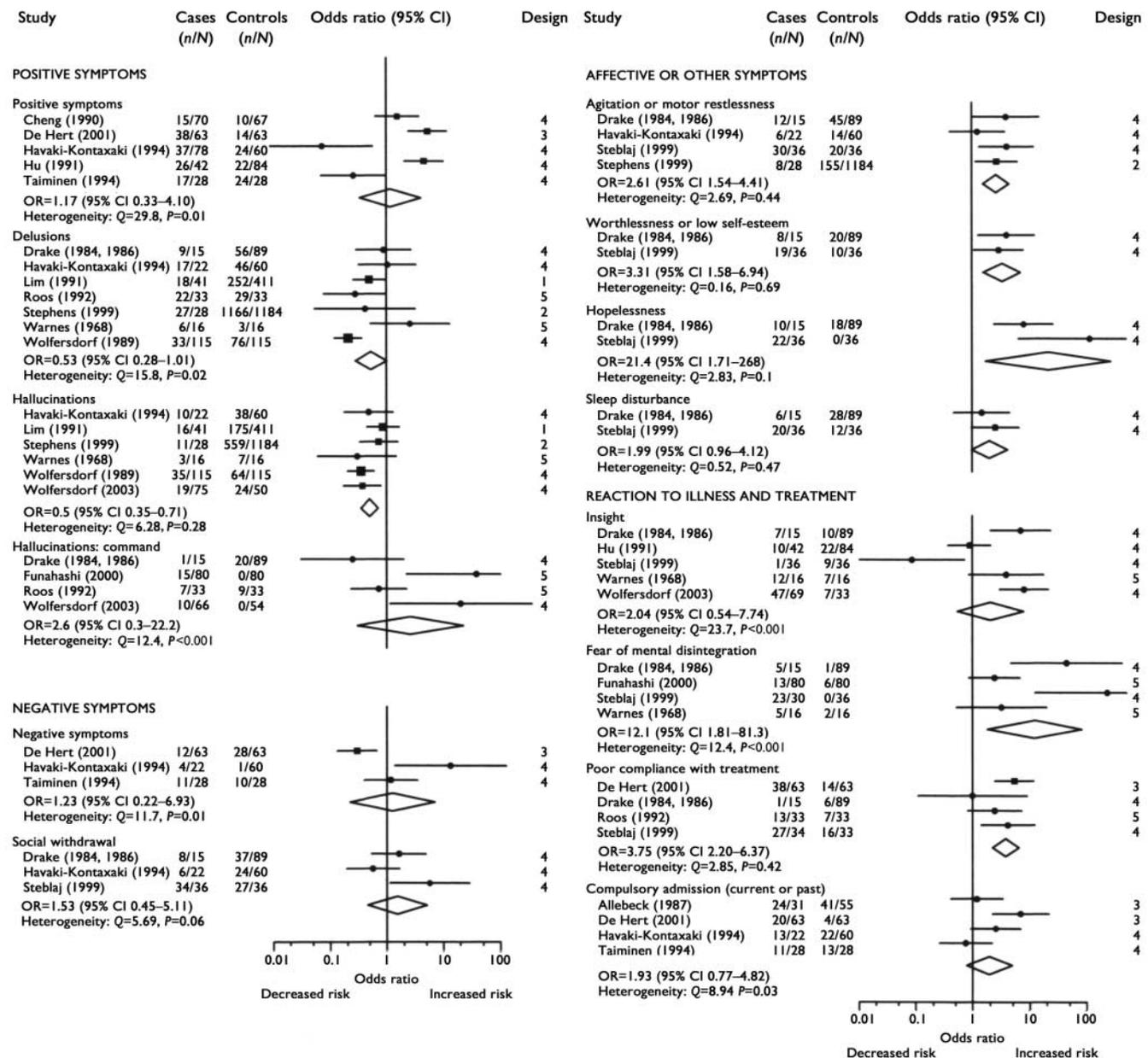
Study	Cases (n/N)	Controls (n/N)	Odds ratio (95% CI)	Design
POSITIVE SYMPTOMS				
Positive symptoms				
Cheng (1990)	15/70	10/67		4
De Hert (2001)	38/63	14/63		3
Havaki-Kontaxaki (1994)	37/78	24/60		4
Hu (1991)	26/42	22/84		4
Taiminen (1994)	17/28	24/28		4
OR=1.17 (95% CI 0.33–4.10)				
Heterogeneity: Q=29.8, P=0.01				
Delusions				
Drake (1984, 1986)	9/15	56/89		4
Havaki-Kontaxaki (1994)	17/22	46/60		4
Lim (1991)	18/41	252/411		1
Roos (1992)	22/33	29/33		5
Stephens (1999)	27/28	1166/1184		2
Warnes (1968)	6/16	3/16		5
Wolfersdorf (1989)	33/115	76/115		4
OR=0.53 (95% CI 0.28–1.01)				
Heterogeneity: Q=15.8, P=0.02				
Hallucinations				
Havaki-Kontaxaki (1994)	10/22	38/60		4
Lim (1991)	16/41	175/411		1
Stephens (1999)	11/28	559/1184		2
Warnes (1968)	3/16	7/16		5
Wolfersdorf (1989)	35/115	64/115		4
Wolfersdorf (2003)	19/75	24/50		4
OR=0.5 (95% CI 0.35–0.71)				
Heterogeneity: Q=6.28, P=0.28				
Hallucinations: command				
Drake (1984, 1986)	1/15	20/89		4
Funahashi (2000)	15/80	0/80		5
Roos (1992)	7/33	9/33		5
Wolfersdorf (2003)	10/66	0/54		4
OR=2.6 (95% CI 0.3–22.2)				
Heterogeneity: Q=12.4, P<0.001				
NEGATIVE SYMPTOMS				
Negative symptoms				
De Hert (2001)	12/63	28/63		3
Havaki-Kontaxaki (1994)	4/22	1/60		4
Taiminen (1994)	11/28	10/28		4
OR=1.23 (95% CI 0.22–6.93)				
Heterogeneity: Q=11.7, P=0.01				
Social withdrawal				
Drake (1984, 1986)	8/15	37/89		4
Havaki-Kontaxaki (1994)	6/22	24/60		4
Steblaj (1999)	34/36	27/36		4
OR=1.53 (95% CI 0.45–5.11)				
Heterogeneity: Q=5.69, P=0.06				

Odds ratio — Decreased risk / Increased risk (0.01, 0.1, 1, 10, 100)

Study	Cases (n/N)	Controls (n/N)	Odds ratio (95% CI)	Design
AFFECTIVE OR OTHER SYMPTOMS				
Agitation or motor restlessness				
Drake (1984, 1986)	12/15	45/89		4
Havaki-Kontaxaki (1994)	6/22	14/60		4
Steblaj (1999)	30/36	20/36		4
Stephens (1999)	8/28	155/1184		2
OR=2.61 (95% CI 1.54–4.41)				
Heterogeneity: Q=2.69, P=0.44				
Worthlessness or low self-esteem				
Drake (1984, 1986)	8/15	20/89		4
Steblaj (1999)	19/36	10/36		4
OR=3.31 (95% CI 1.58–6.94)				
Heterogeneity: Q=0.16, P=0.69				
Hopelessness				
Drake (1984, 1986)	10/15	18/89		4
Steblaj (1999)	22/36	0/36		4
OR=21.4 (95% CI 1.71–268)				
Heterogeneity: Q=2.83, P=0.1				
Sleep disturbance				
Drake (1984, 1986)	6/15	28/89		4
Steblaj (1999)	20/36	12/36		4
OR=1.99 (95% CI 0.96–4.12)				
Heterogeneity: Q=0.52, P=0.47				
REACTION TO ILLNESS AND TREATMENT				
Insight				
Drake (1984, 1986)	7/15	10/89		4
Hu (1991)	10/42	22/84		4
Steblaj (1999)	1/36	9/36		4
Warnes (1968)	12/16	7/16		5
Wolfersdorf (2003)	47/69	7/33		4
OR=2.04 (95% CI 0.54–7.74)				
Heterogeneity: Q=23.7, P<0.001				
Fear of mental disintegration				
Drake (1984, 1986)	5/15	1/89		4
Funahashi (2000)	13/80	6/80		5
Steblaj (1999)	23/30	0/36		4
Warnes (1968)	5/16	2/16		5
OR=12.1 (95% CI 1.81–81.3)				
Heterogeneity: Q=12.4, P<0.001				
Poor compliance with treatment				
De Hert (2001)	38/63	14/63		3
Drake (1984, 1986)	1/15	6/89		4
Roos (1992)	13/33	7/33		5
Steblaj (1999)	27/34	16/33		4
OR=3.75 (95% CI 2.20–6.37)				
Heterogeneity: Q=2.85, P=0.42				
Compulsory admission (current or past)				
Allebeck (1987)	24/31	41/55		3
De Hert (2001)	20/63	4/63		3
Havaki-Kontaxaki (1994)	13/22	22/60		4
Taiminen (1994)	11/28	13/28		4
OR=1.93 (95% CI 0.77–4.82)				
Heterogeneity: Q=8.94 P=0.03				

Odds ratio — Decreased risk / Increased risk (0.01, 0.1, 1, 10, 100)

Fig. 4 Characteristics of the disorder. 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 re-analysed 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.
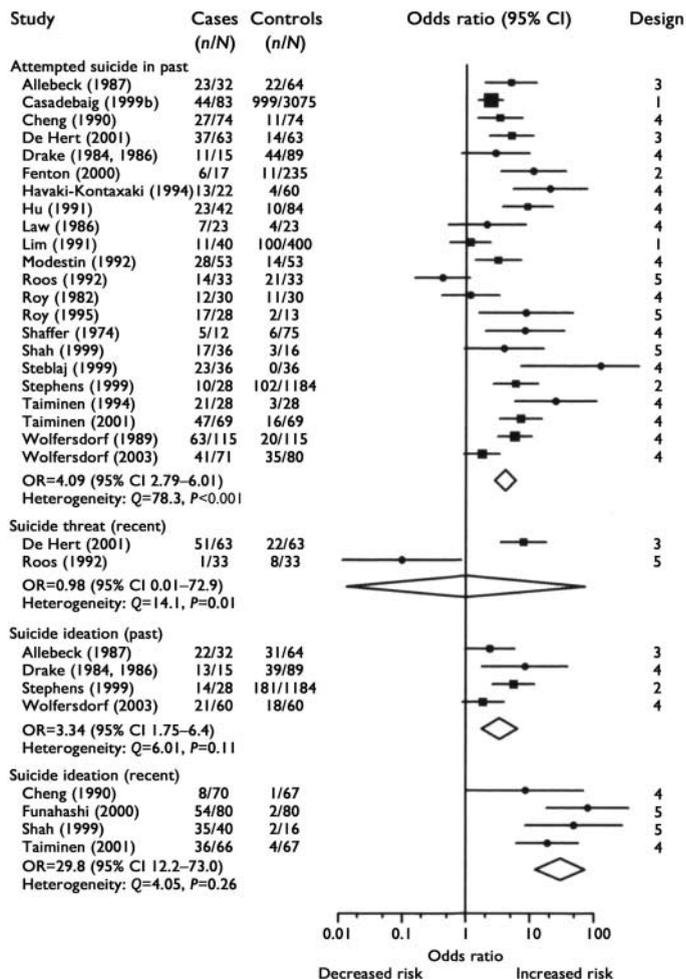
Study	Cases (n/N)	Controls (n/N)	Odds ratio (95% CI)	Design
Attempted suicide in past				
Allebeck (1987)	23/32	22/64		3
Casadebaig (1999b)	44/83	999/3075		1
Cheng (1990)	27/74	11/74		4
De Hert (2001)	37/63	14/63		3
Drake (1984, 1986)	11/15	44/89		4
Fenton (2000)	6/17	11/235		2
Havaki-Kontaxaki (1994)	13/22	4/60		4
Hu (1991)	23/42	10/84		4
Law (1986)	7/23	4/23		4
Lim (1991)	11/40	100/400		1
Modestin (1992)	28/53	14/53		4
Roos (1992)	14/33	21/33		5
Roy (1982)	12/30	11/30		4
Roy (1995)	17/28	2/13		5
Shaffer (1974)	5/12	6/75		4
Shah (1999)	17/36	3/16		5
Steblaj (1999)	23/36	0/36		4
Stephens (1999)	10/28	102/1184		2
Taiminen (1994)	21/28	3/28		4
Taiminen (2001)	47/69	16/69		4
Wolfersdorf (1989)	63/115	20/115		4
Wolfersdorf (2003)	41/71	35/80		4
OR=4.09 (95% CI 2.79–6.01)				
Heterogeneity: Q=78.3, P<0.001				
Suicide threat (recent)				
De Hert (2001)	51/63	22/63		3
Roos (1992)	1/33	8/33		5
OR=0.98 (95% CI 0.01–72.9)				
Heterogeneity: Q=14.1, P=0.01				
Suicide ideation (past)				
Allebeck (1987)	22/32	31/64		3
Drake (1984, 1986)	13/15	39/89		4
Stephens (1999)	14/28	181/1184		2
Wolfersdorf (2003)	21/60	18/60		4
OR=3.34 (95% CI 1.75–6.4)				
Heterogeneity: Q=6.01, P=0.11				
Suicide ideation (recent)				
Cheng (1990)	8/70	1/67		4
Funahashi (2000)	54/80	2/80		5
Shah (1999)	35/40	2/16		5
Taiminen (2001)	36/66	4/67		4
OR=29.8 (95% CI 12.2–73.0)				
Heterogeneity: Q=4.05, P=0.26				

Odds ratio scale: 0.01 0.1 1 10 100 — Decreased risk / Increased risk

Fig. 5 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 produces 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 – notably 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 synthesis 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 included studies in which some of the patients had schizoaffective disorder. The psychopathology of schizoaffective disorder overlaps 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 disorder 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 investigators in the definition of individual risk factors. This variability necessitates compromise 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 findings 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 summary data is that it not only allows the findings of a range of studies to be synthesised, but also greatly reduces the danger of findings from individual studies leading to spurious conclusions. The degree of heterogeneity 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 weaker research designs. A disadvantage of this approach is that it is not possible to adjust estimates of risk factors for effects of confounding 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 suicide in the general population, it has highlighted certain risk factors that are clearly specific to schizophrenia and its consequences. 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 finding, which was no longer positive when the sensitivity analysis was applied. We could not examine age as a risk factor because it was used as a matching factor in some of the case–control studies, and in other studies for which age data were supplied there were differences in manner of reporting. Married or cohabiting patients
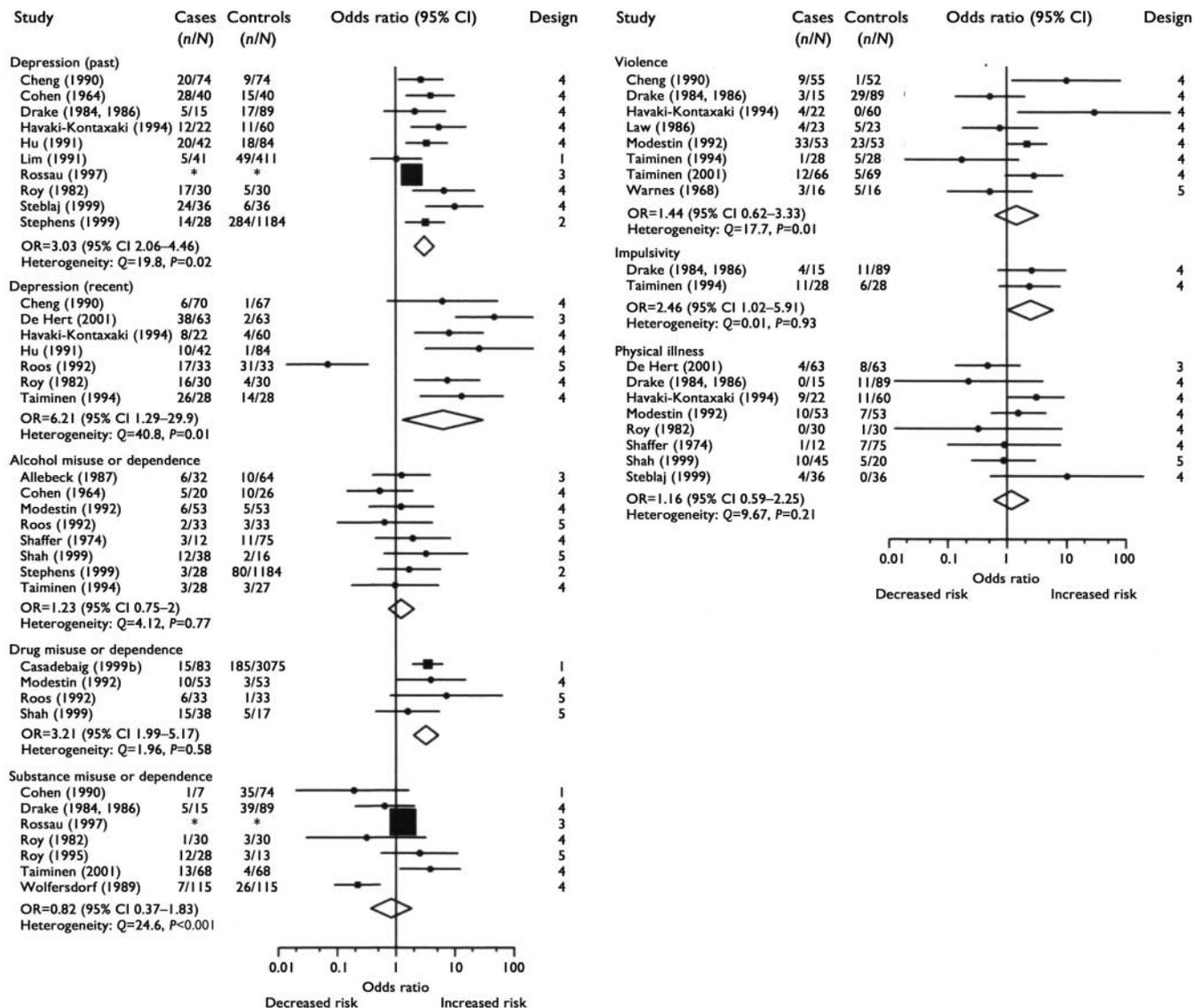
Left panel:

Study	Cases (n/N)	Controls (n/N)	Odds ratio (95% CI)	Design
Depression (past)				
Cheng (1990)	20/74	9/74		4
Cohen (1964)	28/40	15/40		4
Drake (1984, 1986)	5/15	17/89		4
Havaki-Kontaxaki (1994)	12/22	11/60		4
Hu (1991)	20/42	18/84		4
Lim (1991)	5/41	49/411		1
Rossau (1997)	*	*		3
Roy (1982)	17/30	5/30		4
Steblaj (1999)	24/36	6/36		4
Stephens (1999)	14/28	284/1184		2
OR=3.03 (95% CI 2.06–4.46)				
Heterogeneity: Q=19.8, P=0.02				
Depression (recent)				
Cheng (1990)	6/70	1/67		4
De Hert (2001)	38/63	2/63		3
Havaki-Kontaxaki (1994)	8/22	4/60		4
Hu (1991)	10/42	1/84		4
Roos (1992)	17/33	31/33		5
Roy (1982)	16/30	4/30		4
Taiminen (1994)	26/28	14/28		4
OR=6.21 (95% CI 1.29–29.9)				
Heterogeneity: Q=40.8, P=0.01				
Alcohol misuse or dependence				
Allebeck (1987)	6/32	10/64		3
Cohen (1964)	5/20	10/26		4
Modestin (1992)	6/53	5/53		4
Roos (1992)	2/33	3/33		5
Shaffer (1974)	3/12	11/75		4
Shah (1999)	12/38	2/16		5
Stephens (1999)	3/28	80/1184		2
Taiminen (1994)	3/28	3/27		4
OR=1.23 (95% CI 0.75–2)				
Heterogeneity: Q=4.12, P=0.77				
Drug misuse or dependence				
Casadebaig (1999b)	15/83	185/3075		1
Modestin (1992)	10/53	3/53		4
Roos (1992)	6/33	1/33		5
Shah (1999)	15/38	5/17		5
OR=3.21 (95% CI 1.99–5.17)				
Heterogeneity: Q=1.96, P=0.58				
Substance misuse or dependence				
Cohen (1990)	1/7	35/74		1
Drake (1984, 1986)	5/15	39/89		4
Rossau (1997)	*	*		3
Roy (1982)	1/30	3/30		4
Roy (1995)	12/28	3/13		5
Taiminen (2001)	13/68	4/68		4
Wolfersdorf (1989)	7/115	26/115		4
OR=0.82 (95% CI 0.37–1.83)				
Heterogeneity: Q=24.6, P<0.001				

Odds ratio: 0.01 0.1 1 10 100
Decreased risk — Increased risk

Right panel:

Study	Cases (n/N)	Controls (n/N)	Odds ratio (95% CI)	Design
Violence				
Cheng (1990)	9/55	1/52		4
Drake (1984, 1986)	3/15	29/89		4
Havaki-Kontaxaki (1994)	4/22	0/60		4
Law (1986)	4/23	5/23		4
Modestin (1992)	33/53	23/53		4
Taiminen (1994)	1/28	5/28		4
Taiminen (2001)	12/66	5/69		4
Warnes (1968)	3/16	5/16		5
OR=1.44 (95% CI 0.62–3.33)				
Heterogeneity: Q=17.7, P=0.01				
Impulsivity				
Drake (1984, 1986)	4/15	11/89		4
Taiminen (1994)	11/28	6/28		4
OR=2.46 (95% CI 1.02–5.91)				
Heterogeneity: Q=0.01, P=0.93				
Physical illness				
De Hert (2001)	4/63	8/63		3
Drake (1984, 1986)	0/15	11/89		4
Havaki-Kontaxaki (1994)	9/22	11/60		4
Modestin (1992)	10/53	7/53		4
Roy (1982)	0/30	1/30		4
Shaffer (1974)	1/12	7/75		4
Shah (1999)	10/45	5/20		5
Steblaj (1999)	4/36	0/36		4
OR=1.16 (95% CI 0.59–2.25)				
Heterogeneity: Q=9.67, P=0.21				

Odds ratio: 0.01 0.1 1 10 100
Decreased risk — Increased risk

Fig. 6 Comorbid disorders and behaviour. 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. *Estimates based on reported incidence rate ratio (counts of cases and controls not available).

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; Barraclough *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.

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