Review

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Clinical and epidemiological aspects of suicide in patients with schizophrenia

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Suicide is a major cause of death among patients with schizophrenia. Suicide phenomenon's characterization is the best available approach for improved prediction and prevention of suicide. Patients at high risk for suicide need a more intensive monitoring and intervention. The aim of this review is to characterize, from a clinical-epidemiological point of view, the phenomenon of completed suicide in schizophrenia. We performed a systematic review to identify the most relevant studies published between 1994 and 2009, by searching on the international database Medline and among previous reviews references.

Patients with schizophrenia experience higher mortality rates than the general population, especially due to the suicide. Most patients with schizophrenia who commit suicide are likely to be young and males, with a higher risk around illness onset and hospitalization periods. Previous suicide attempts are an important risk factor for completed suicide. Suicide risk is associated to psychotic positive symptoms, affective symptoms, depression and substance abuse. Treatment adherence is as protective factor. Patients with schizophrenia are likely to commit suicide by violent means.

Suicide prevention should focus on treating affective symptoms and syndromes, improving treatment compliance and providing intensive monitoring to those patients at high risk of suicide, specially aroung hospitalization periods. Further studies are needed to clarify differential characteristics between suicide behaviour and completed suicide.

Key words: Schizophrenia, Suicide, Mortality, Causes, Risk factors

Actas Esp Psiquiatr 2012;40(6):333-45

Aspectos clínico-epidemiológicos del suicidio consumado en pacientes con esquizofrenia

El suicidio es una de las principales causas de muerte entre los pacientes con esquizofrenia, siendo la caracterización del fenómeno del suicidio la mejor aproximación que puede realizarse para predecir y prevenir el acto suicida. Los pacientes identificados como de alto riesgo precisan una monitorización y una intervención más intensivas. El objetivo de esta revisión es caracterizar desde el punto de vista clínico-epidemiológico el fenómeno del suicidio consumado en la esquizofrenia. Presentamos una revisión sistemática de los estudios más relevantes publicados entre 1994 y 2009, identificados mediante una búsqueda en la base de datos internacional Medline y en las referencias bibliográficas de las revisiones previas.

Las tasas de mortalidad en la esquizofrenia son más elevadas que en la Population general, especialmente debido al suicidio. Los sujetos que se suicidan son principalmente varones y jóvenes, con un riesgo mayor al inicio de la enfermedad y en torno a la hospitalización. Los intentos autolíticos previos son un importante factor de riesgo. El riesgo de suicidio también se asocia a síntomas psicóticos positivos, síntomas afectivos, depresión y abuso de sustancias. Un adecuado cumplimiento terapéutico actúa como factor protector. El método de suicidio utilizado es frecuentemente violento.

La prevención del suicidio debería centrarse en el abordaje de los síntomas y síndromes afectivos, en la mejora de la adherencia al tratamiento y en la vigilancia intensiva de los pacientes con más factores de riesgo, especialmente en torno a los ingresos hospitalarios. Se recomienda proseguir el estudio específico del suicidio consumado por sus características diferenciales con otras conductas suicidas.

Palabras clave: Esquizofrenia, Suicidio, Mortalidad, Causas, Factores de riesgo

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INTRODUCTION

Suicide is a major international public health problem, and psychiatric patients are in special risk. Schizophrenia is considered a life-shortening disease and excess of mortality in schizophrenic patients is a well-known fact, especially due this unnatural cause of death.[1] Hawton pointed a 30-40 times higher risk compared to general population and that a high proportion of schizophrenic patients commit suicide (4-10 %).[2]

Nevertheless, although much attention has been paid to the suicidal behaviour in schizophrenia, just a few studies currently focus on the phenomenon of completed suicide. Characterization of the suicidal phenomenon in schizophrenia can help offering an overall treatment of this disorder, based on an adjusted suicidal risk assessment and a better management of suicidal behaviour.

We consider suicidal behaviour and completed suicide intimately related but differential phenomena and conducted a systematic review of the international literature on studies of epidemiological and clinical issues of completed suicide in schizophrenia in the last 15 years.

METHODS

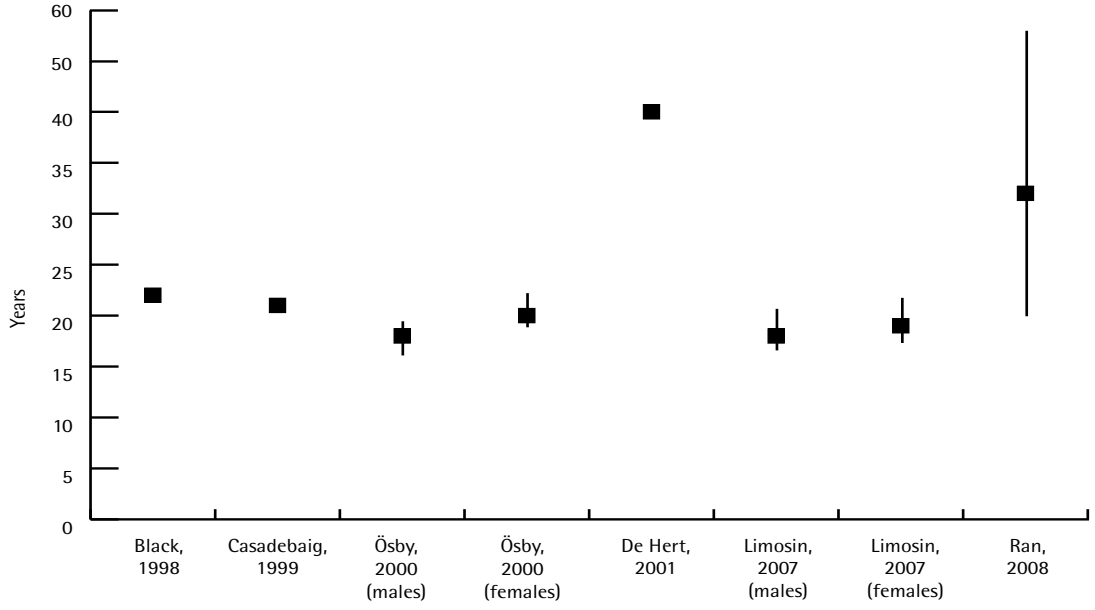
Electronic searches of Medline were made with the terms "schizophrenia" and "suicide" in the title or abstract, limiting the research to studies published in the last 15 years, between years 1994 and 2009, in Spanish, English, Italian or French. The 103 papers meeting broad eligibility criteria on basis of the abstract were selected out of the 623 iniatially identified and a more detailed evaluation was made according to the complete paper. Furthermore, bibliographies of eligible papers and latest reviews were checked for possible relevant studies, and selected ones were evaluated. 69 studies (Table 1) were selected for inclusion in this review according to the following criteria: studies that investigate the clinical-demographic aspects of the committed suicidal phenomenon in schizophrenia; cohort studies and case-control studies with participants older than 15 years with a diagnosis of schizophrenia. If the sample included a broader spectrum of pathologies, only data concerning schizophrenia subgroup were registered. Epidemiological, sociodemographic and clinical data, as well as data concerning the suicidal act were recorded.

RESULTS

Epidemiological and sociodemographical data

Since Earle's study in 1994,[3] many others have reported a higher proportion of mood disorders among their analyzed suicides.[4-13] However, other authors identified a higher proportion of schizophrenia, mainly in in-patient samples.[14-22]

Studies also differ with respect to risk of suicide associated to the different psychiatric pathologies,



* The Standard Mortality Rates soared in two of the studies selected (Menezes et al. in 1996 indicated a SMR of 317.9 and Hiroeh et al. in 2001, a SMR 1073-1080), so they were excluded from the figurew

Figure 1 | *Standardized mortality rates*

Table 1 Studies selected

Author	Design	Participants	Diagnostic Criteria	Suicides (n)	Controls (n)
Earle, 1994.[3] (USA)	IV	93 of 104 out-patients who committed suicide between 1988 and 1991.	NS	93	16139
King, 1994.[4] (UK)	IV	245 suicides and 41 undetermined deaths occurred between 1974 and 1981.	ICD-9	245	Population NS
Roy, 1995.[14] (Canada)	III	37 in-patients who committed suicide compared with 37 matched sex and age controls next admitted to the same hospital.	ICD	37	37
Menezes, 1996.[66] (Brasil)	I	124 psychiatric patients admitted in 1991, 18 to 44 years old, with a diagnosis of schizophrenia, paranoid psychosis or other functional psychoses, followed until 1993.	ICD-9	5	
Wieselgren, 1996.[48] (Sweden)	I	120 schizophrenic patients admitted to a special ward for young psychotic patients. 5-year follow-up.	DSM-III y III-R	7	
Fenton, 1997.[61] (USA)	I	295 patients with schizophrenia or schizophrenia spectrum disorders. 6 to 23-year follow-up.	DSM-III or Feighner	19	
Proulx, 1997.[5] (Canada)	II	3079 suicides over a 5-year period.	DSM	3079	
Rossau, 1997.[38] (Denmark)	III	From the cohort of 9156 patients admitted to psychiatric hospitals and diagnosed as schizophrenics, the 508 who committed suicide were individually matched to 10 controls.	ICD-8	508	5080
Heilä, 1997.[39] (Finland)	II	92 schizophrenic patients from 1397 suicide victims during 1 year in Finland. Psychological autopsies.	DSM-III-R ICD-8	92	
Shah, 1997.[15] (UK)	IV	60 psychiatric inpatients who committed suicide compared with a matched control group.	ICD-9	60	60
Sharma, 1998.[6] (UK)	III	44 in-patients who committed suicide during their hospital stay from 1969 to 1995, were compared with a group of inpatient controls matched.	DSM-IV	44	44
Wiersma, 1998.[49] (Holland)	I	Incident cohort between 1978 and 1979 of 82 recent "first-ever" onset of non-affective psychosis with positive symptoms, 15-year follow-up.	ICD-10 y DSM-IV	9	
Ruschena, 1998.[24] (Australia)	II	188 psychiatric patients who committed suicide.	ICD-9	188	Population
Lecomte, 1998.[7] (France)	I	392 suicides involving young people occurred between 1989 and 1996.	NS	392	
Lee, 1998.[60] (China)	II	100 patients with first onset of schizophrenia in 1977-78 randomly selected from a pool of 797 patient files. 15-year follow-up.	ICD-9	10	
Black, 1998.[50] (USA)	II	356 schizophrenic patients admitted from 1972 until 1981.	ICD-9	NS	Population
Heilä, 1998.[67] (Finland)	II	Suicide victims during 1 year in Finland. Psychological autopsies. Comparing the 86 victims with a schizophrenia diagnosis with 1109 victims without evidence for psychosis.	DSM-III-R	86	1109
Stephens, 1999.[51] (USA)	II	From 1357 schizophrenics discharged they study 1212 cases with follow-up data available (follow up from 4 months to 26 years).	NS	28	
Häfner, 1999.[62] (Alemania)	II y I	232 first schizophrenia-episode cases studied retrospectively from onset to first admission. 115 of them studied prospectively over a 5-year period and compared with 114 age and sex- matched controls.	DSM-III	8	114
Casadebaig, 1999.[34] (France)	I	3470 schizophrenic patients, followed during three years.	ICD-10	60-71	Population

Table 1 Continuation

Author	Design	Participants	Diagnostic Criteria	Suicides (n)	Controls (n)
Steblaj, 1999.[16] (Slovenia)	III	32548 psychiatric inpatients, 79 suicides. The 59 patients with schizophrenia or affective psychosis were compared to an age, sex and diagnosis control group.	ICD-9	36	36
Baxter, 1999.[25] (UK)	II	7921 psychiatric patients, maximum follow-up of 18 years.	ICD-8 and 9	171	Population
Heilä, 1999.[53] (Finland)	III	From 1397 suicide victims during 1 year in Finland, they study 72 schizophrenic patients with available life event data and 216 nonschizophrenia subjects with life event available data paired with the schizophrenia cases. Psychological autopsies.	DSM-III-R ICD-8	72	216
Heilä, 1999.[54] (Finland)	II	88 psychological autopsies of schizophrenics who died by suicide between 1987 and 1988 with a known treatment: 25 inpatients, 28 discharged in the last 3 months and 3 outpatients.	ICD-9	88	
Saarinen, 1999.[43] (Finland)	II	17 cases from 108 suicides committed in the province of Kuopio from 1987 to 1988. Psychological autopsies.	DSM-III-R	108	
Funahashi, 2000.[52] (Japan)	III	80 in and out-patients diagnosed with schizophrenia, schizoaffective disorder and schizotypal personality disorder, who committed suicide and 80 matched living patients.	DSM-II-R	80	80
Ösby, 2000.[30] (Sweden)		7784 individuals discharged with a first schizophrenia diagnosis between 1973 and 1995.	NS	380	Population
Martin, 2000. [8] (USA)	II	276 psychiatric patients who committed suicide between 1966 and 1997.	NS	276	
Deisenhammer, 2000.[9] (Austria)	II	44 deaths due to suicide with a psychiatric diagnosis, 8-year observation period.	ICD-9	44	
Bralet, 2000.[68] (France)	I	150 chronic schizophrenic patients followed during 8 years.	*Critères Spitzer*	3	
De Hert, 2001.[46] (Belgium)	III	63 schizophrenics that committed suicide, matched with 63 patients who had not.	DSM III-R	63	63
Hiroeh, 2001.[10] (UK)	II	72208 psychiatric patients admitted between 1973 and 1993, who died before 1994.	ICD-8 y 10	12977	Population
Spieß, 2002.[17] (Germany)	II	21062 psychiatric in-patients, investigated over a period of 11 years.	ICD-9/10	30	
Kreyenbuhl, 2002.[57] (USA)	IV	115 suicides, 15 with a schizophrenia diagnosis and 100 without it.	DSM-IV	15	100
Kua, 2003.[37] (Singapore)	I	402 patients, 20-year follow-up (revaluations every 5 years).	ICD-9	39	
Yim, 2004.[18] (China)	III	73 psychiatric patients discharged between 1996 and 1999 and died by suicide during the same period, age, sex and diagnostic matched with 73 surviving discharged patients.	NS	73	73
Jarbin, 2004.[23] (Sweden)	I	88 subjects with adolescent-onset psychotic disorders were followed up 10.6 +/- 3.6 years.	DSM-IV	4	Population
Kim, 2004.[65] (Canada)	II	115 male suicide completers were evaluated for psychiatric disorders, and assessed for seasonal differences.	DSM-IV	115	
Kelly, 2004.[58] (USA)	II	Psychological autopsy of 97 schizophrenics who died between 1989 and 1998 (unnatural and natural causes).	DSM-IV	15	82

Table 1 Continuation

Author	Design	Participants	Diagnostic Criteria	Suicides (n)	Controls (n)
Philips, 2004.[32] (China)		19223 Chinese residents, 892 suicides between 1995 and 1999. 74 suicides with a schizophrenia diagnosis.	ICD-9 and DSM-IV	892	
Sinclair, 2004.[55] (UK)	III	Patients who committed suicide within the 12-months of discharge between 1988 and 1997, matched with up to two controls.	ICD-9 and 10	59	114
Kuo, 2005.[42] (Taiwan)	III	4237 schizophrenic inpatients admitted from 1985 to 2000, followed through 2001 by linkage to the Death Certification System. 78 subjects who died from suicide matched with living controls (age, sex, year of admission).	DSM-III, II-R and IV	78	78
Heilä, 2005.[33] (Finland)	II	811920 deaths, 16940 schizophrenic subjects, period from 1980 until 1996.	ICD-8, 9 y 10	2042	
Qin, 2005.[56] (Denmark)	III	21169 suicides committed in Denmark from 1981 to 1997 and 423128 matched population control subjects.	ICD-8, ICD-10	21169	423128
Dong, 2005.[19] (China)	III	In-patients who committed suicide between 1997 and 1999, compared with admission-sex-matched controls.	ICD-10	93	92
McGirr, 2006.[47] (Canada)	III	81 subjects diagnosed with schizophrenia or a chronic psychotic disorder. 45 suicide completers and 36 matched controls. Psychological autopsy method.	DSM-IV	45	36
Bickley, 2006.[28] (UK)	II	131 homeless who committed suicide within 12 months of contact with mental health services, compared to the rest of suicides from 1996-2000.	ICD-10	131	
Hunt, 2006.[11] (UK)	II	England and Wales 4859 suicide deaths registered 1996-2000	ICD-10	4859	
Ward, 2006.[63] (Canada)	I	41754 y 3291 schizophrenics who filled at least 1 prescription for risperidone, olanzapine or quetiapine, compliance was assessed and different variables examined. Followed from 1999 to 2004.	ICD-9		
Kan, 2007.[20] (China)	III	97 suicides within 60 days of psychiatric hospitals discharges from 1997 to 1999, matched with controls.	ICD-10	97	97
Pirkola, 2007.[12] (Finland)	II	Psychiatric patients who committed suicide within one year of discharge, a group control of discharged patients, during two periods: 1985-1991 and 1995-2001.	ICD-10	1978 - 1863	163236 - 191764
Shields, 2007.[40] (USA)	II	2864 cases of suicide during the period from 1993 to 2002.	NS	29	
Karvonen, 2007.[59] (Finland)	II	1877 deaths due to suicide during the years 1988-2003.	ICD-8, 9 and 10	1877	
Limosin, 2007.[41] (France)	I	3470 schizophrenic patients followed during 10 years. 443 died, 141 by suicide.	ICD-10	141	
Rockett, 2007.[13] (USA)	IV	District of Columbia´s suicides and unintentional injury decedents between 1999 and 2003.	ICD-10	151183	488574
Bertelsen, 2007.[45] (Denmark)	I	547 individuals with first-episode schizophrenia spectrum psychosis, 5-year follow-up.	ICD-10	7	
Ran, 2007.[26] (China)	I	500 schizophrenic patients, 10-year follow-up. Community sample in rural China.	ICD-10	21	
McGirr, 2008.[44] (Canada)	II	527 consecutive suicides. Psychological autopsy method.	DSM-IV	527	
Capasso, 2008.[35] (USA)	II	319 residents with a schizophrenia or a schizoaffective disorder diagnosis followed for a median of 23.5 years.	DSM-IV-TR	4	

Table 1 Continuation

Author	Design	Participants	Diagnostic Criteria	Suicides (n)	Controls (n)
Osborn, 2008.[27] (UK)	II	Cohort of 46136 with Severe Mental Illness (SMI) patients and 300426 without, from the general practice research database, between 1987 and 2002, a median follow-up of 4.7 years.	NS	215	
Silverton, 2008.[29] (USA)	I	208 children of schizophrenic women, 43-year follow-up.	"broad definition"	7	
Haukka, 2008.[69] (Finland)	II	18199 in-patients with a diagnosis of attempted suicide between 1996 and 2003.	ICD-10	1021	
Thong, 2008. [21] (Singapore)	III	123 psychiatric patients who committed suicide between 2003 and 2004, compared with 123 surviving matched controls.	DSM-IV	123	123
Loas, 2008.[36] (France)	I	150 chronic schizophrenics included between 1991 and 1995, revaluated in 2005. 14-year follow-up.	*Spitzer research diagnostic criteria*	8	
Li, 2008.[22] (China)	III	During the period of 1956-2005 77 inpatients died by suicide during hospitalization. 64 in-patients with schizophrenia who died by suicide were compared with a matched 64 controls. China.	ICD-10	64	64
Reisch, 2008.[64] (Switzerland)	II	17482 suicides between 1990 and 2003; 1830 had died by jumping (283 from bridges).	ICD-10	17482	
Tidemalm, 2008.[70] (Sweden)	II	713 schizophrenic patients admitted to hospital for a suicide attempt during 1973-1982 and followed to 2003. Controls: Without psychiatric diagnosis within one year after a suicide attempt.	ICD-8	229	27004
Ran, 2008.[31] (China)	I	A 10-year follow-up among a 1994 cohort of 500 patients with schizophrenia, comparing geriatric and young subjects. China.	ICD 10	21	
Carlborg, 2008.[71] (Sweden)	I	385 inpatients between 1973 and 1987 with schizophrenia spectrum psychoses according to DSM-III-R. Median follow-up 26 years.	DSM-III-R and IV	26	

Studies identified by first-named author and year only
Study design: I (prospective cohort study), II (retrospective cohort study), III (nested case-control study), IV (case-group control study)
ICD (International Classification of Diseases), DSM (Diagnostic and Statistical Manual of Mental Disorders). NS (not specified)

highlighting the importance of either affective psychosis[23] or schizophrenia[14, 24-46] or not finding significant differences. King in 1994[4] found a higher risk of suicide in males with a schizophrenia diagnosis, whereas among females risk was higher for affective psychosis. Osborn[27] (2008) found the highest risk among subjects with a bipolar disorder diagnosis of his sample of 215 suicides, however for the age category of 18 to 30 years old, risk was higher for schizophrenia. Some of the selected studies focus on concrete subgroups of patients with schizophrenia. Bickley[28] (2006), in his suicide sample of patients who have had contact with mental health services in the year before, found a higher proportion of schizophrenia diagnosis among the homeless group and of affective disorders among the non-homeless group, with a overall higher proportion of affective disorder. In a high risk group conformed by offspring of mothers with a schizophrenia diagnosis, Silverton[29] (2008) found a higher risk of suicide in schizophrenic subjects than in other pathologies or subjects without a psychiatric diagnosis.

Mortality rates in subjects with schizophrenia diagnosis, exceeds widely that of the general population, especially mortality rates due to suicide (Figure 1), and suicide is the largest single cause of excess mortality in this illness, as every study selected pointed out.[3-71] Standardized Mortality Rates (SMR) showed an increase if focused on young subsamples; Ösby[30] (2000) found a SMR of 102,7 for young males and 175,6 for young females and Ran[31] found a large variation in the risk of suicide among age groups with an SMR of 10.1 (6.6 to 18.2) for geriatric patients, 52.2 (40.2 to 84.1) for middle-aged subjects and 94.5 (82.1 to 185.5) in the range of 14-40 years. Other studies reported Relative Risk (RR) data (King[4] in 1994 registered a RR of 44 and Phillips[32] in 2004, a RR of 23,8, Casadebaig et al.[34] double RR in patients under 35 years old) or Adjusted Relative Risk (Heilä[33] in 2005 found an age-adjusted RR of 9,9), invariably high. In Spain, the age of death by suicide in schizophrenia is around late twenties (Figure 2), this being lower than in other diseases or in general population.[34, 35]

Lifetime percentage of people with schizophrenia that commit suicide varies considerably among the studies. If we review those studies with a longer follow-up period, Loas et

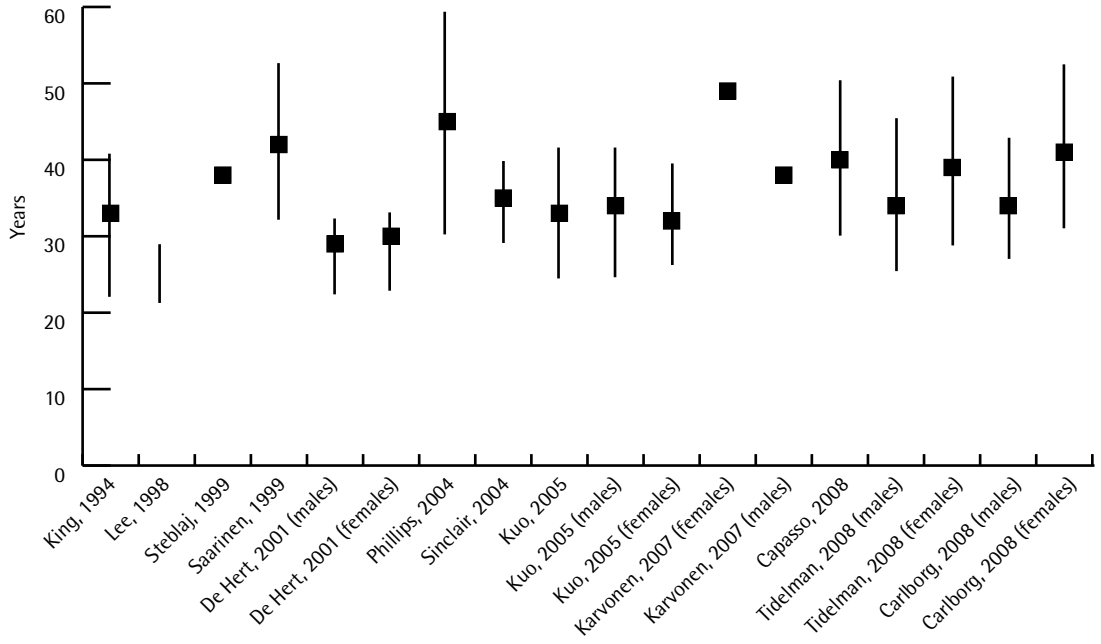


Figure 2 | *Age at time of suicide*

al.[36] recorded a 5.3 % in their sample of 14-year follow-up in France and Kua[37] (2003) found a 9.7% in his sample of 20-year follow-up in Singapore.

Suicide risk in schizophrenia has been repeatedly associated to male sex.[8, 17, 23, 31, 34, 38-40] Limosin[41] (2007) identified male sex as an independant risk factor for suicide in his simple of subjects with a schizophrenia diagnosis, with an Hazard Ratio of 2.03 (95% CI 1.34-3.07). Among the reviewed studies, the ones conducted in Asian population show contradictory data. Phillips[32] (2004) found a higher proportion of females (70 %) in his suicide sample of subject with a schizophrenia diagnosis and Kuo[42] (2005) registered a 51 % of women in his study.

Traditionally, a higher risk for suicide in young, unmarried and unemployed males has been accepted, and different studies reproduce this profile in their suicide samples.[4] Hunt[11] in 2006 found a higher proportion of unmarried subjects. Other factors, such as unsatisfying family relationships,[23] unemployment[39] or incapacity[4, 43] have also been related with a higher risk of suicide. However, Phillips[32] (2004) studied a wide simple of suicides in Asia and found different characteristics: a 9% of the subjects with a schizophrenia diagnosis lived alone and 54% were married.

McGirr[44] (2008) reported that people with schizophrenia that commit suicide, were more likely to have attended university than general population. On the other hand, Kua[37] (2003) in Asian population found a higher risk for complete suicide for those with primary education or less.

Clinical data

Bertelsen et al.[45] in 2007 did not find significant associations for clinical factors and complete suicide in schizophrenia. Nevertheless, the rest of the studies identified show interesting findings about suicide in schizophrenia. Family history of schizophrenia is, according to Kua (2003), De Hert et al. y McGirr et al. a risk factor for suicide.[37, 46-47] De Hert[46], in a sample of young subjects with a schizophrenia diagnosis, found a CI, evaluated by the WAIS (Wechsler Adult Intelligence Scale), higher than the one found in the schizophrenia control group. The onset of the disease has a particular high risk of suicide, being the period with the higher percentage of cases.[5, 30, 33, 37, 39, 48-51] Funahashi[52] and De Hert et al.[46] found significant differences in having suffered a recent loss or life events in relation with the control group, whereas Heilä et al.[53] did not find significant differences in life events within the last 3 months in comparison with the matched controls of their sample. The number of previous admissions and the number of admissions by year is considered a risk factor.[22, 38, 39, 46, 54] Heilä[39] in 1997 pointed a significantly higher number of admissions among females than among males with a schizophrenia diagnosis that commit suicide. De Hert[46] found a 17 times-folds risk among in-patients compulsorily admitted. Sinclair[55] in 2004 reported as an independent risk factor the police involvement at admission and highlighted that patients with schizophrenia who commit suicide were more likely to have police involvement at their admission, to have been detained under the Mental Health Act and to have gone AWOL (Away

Table 2 Suicide method used

Author	Jumping	Submersion	Hanging	Drug overdose/ poisoning	Firearms	Bladed instruments	Others/	Total
Unknown	Total	3	1	1	0	0	1	10
Stephens, 1999.	10	1	-	9	6	1	1	28
Casadebaig, 1999.	14	1	12	13	10	-	10	60
Funahashi, 2000.	25	1	27	5	-	3	18	79
Spieβl, 2002.	13	-	8	-	-	-	-	21
Kreyenbuhl & Kelly, 2002, 2004.	6	2	1	4	1	1	0	15
Phillips, 2004.	-	-	22	4	-	-	48	74
Kuo, 2005.	25	10	16	18	0	6	3	78
McGirr, 2006.	5	3	23	-	-	5	9	45
Shields, 2007.	1	2	4	6	14	-	2	29
Limosin, 2007.	32	8	27	39	20		15	141
Loas, 2008.	-	3	1	2	1	-	1	8
Carlborg, 2008.	6	4	3	10	0	0	3	26
Total	**141**	**38**	**145**	**111**	**32-52**	**16-36**	**111**	**614**

- Without specifications regarding number of deaths by this method

Without Licence) at some time during their admission, compared to the one with another diagnosis.

When the patient is out of the hospital's ward during an hospitalization, with or without licence, the risk of suicide increases.[38, 46] As well as immediately after discharge from hospital.[16, 24, 46, 52] In a sample of 1,658 suicides in subjects with schizophrenia Qin et al.[56] found that the risk of suicide increases after admission and after discharge (6 months), and declines rapidly after treatment and recovery. Heilä[39] in 1997 reported that, among the subjects that completed suicide, a high proportion have contacted a Mental Health Service recently (51% in the last 4 days) and in Saarinen's sample[43] one third of the subjects had contacted a therapist the day of their death. The paranoid subtype of schizophrenia has been associated with a higher risk of suicide than the other subtypes. Heilä (1999) sldo found this association but only in out-patients.

Previous suicide attempts have been reported as a risk factor repeatedly.[16, 17, 22, 34, 41, 42, 46, 55, 57, 58] Karvonen[59] in 2007 found a higher proportion of previous suicide attempts in females than in males with a schizophrenia diagnosis who committed suicide.

De Hert[46] and Kreyenbuhl[57] registered previous suicide threats as a risk factor, but King[4] found a lower proportion of patients that threat to kill themselves among suicide completers with a schizophrenia diagnosis than among the rest of diagnosis. Kreyenbuhl et al.[57] found in his sample of subjects with schizophrenia that commit suicide a coger proportion of planned acts than in the other psychiatric pathologies. Heilä[54] found a greater proportion of subjects with schizophrenia with previous suicide attempts or threats, suicide plans or ideation compared to the control subjects without psychosis, but proportions were similar during the last three months, even though finding of this study did not reach statistical significance after the logistic regression analysis.

There is a higher risk of suicide during the active phase of illness.[32, 39, 46, 60] Mc Girr[47] in 2006 reported that severe or moderate psychotic symptoms are a risk factor for suicide in schizophrenia. Heilä[54] in 1999 found a high risk of suicide associated with the presence of prominent positive schizophrenia symptoms (OR 6.6; CI 95% 1.9-22.7). Loas[36] in 2008 reported a significantly higher proportion of subjects classified as "positives" according to the PANSS (The Positive and Negative Syndrome Scale) among subjects with schizophrenia who completed suicide, whereas the score for negative symptoms was lower but did not reach statistical significance. Negative symptoms and deficitary sindrome has been related with a lower risk of suicide in schizophrenia.[46, 61] Fenton[61] associated positive symptoms with a higher risk of suicide, especially suspiciousness and delusions, in addition, in the study conducted by Saarinen[43] in 88% of the sample, paranoid symptoms represented the dominant clinical feature of the illness. Paranoid subtype has been

associated with a higher risk of suicide,[16, 61] but Heilä et al.[53] (1999) found this association only in non hospitalized patients. Funahashi[52] associated the risk of suicide with a worst course of illness, with significant association with the presence of suicidal ideation, anxiety with fear of mental disintegration and auditory hallucination demanding suicide. Funahashi[52] (1999) identified in his sample a significant association with some items of the PANSS: hostility, anxiety, guilt feeling, tension, depression and poor impulse control, and three items showed significantly lower scores: blunted affect, emotional withdrawal and disturbance of volition. The presence of depressive symptoms (guilty feelings, suicidal ideation, hopelessness…) or a present or past diagnosis of depression are considered risk factors for schizophrenia. De Hert[46] pointed a tendency to "acting out" in subject with schizophrenia whot committed suicide.

McGirr[47] in 2006 considered the presence of comorbid diagnosis of axis I as a risk factor in schizophrenia, but two years later in the study conducted in 2008 the same author reports a lower percentage of comorbid disorders in subjects with a schizophrenia diagnosis than the rest of suicides (n=527)[44]. Depressive symptoms (guilty feelings, suicide ideation, hopelessness…) and comorbid depressive disorders, are considered a risk factor for suicide in schizophrenia.[16, 21, 32, 38, 39, 42, 43, 46, 47, 49, 54, 55, 57, 60, 62] Karvonen[59] in 2007 reported a higher percentage of depressive symptoms in females than in males with a schizophrenia diagnosis who committed suicide, but considered that depressive symptoms could be a diferential factor among males, with a tendency to immediate suicide after discharge among males with a comorbid depressive disorder. Guilty feelings have been pointed as a risk factor for suicide and Li et al.[22] in 2008 reported a OR of 11.095 (CI 95% 1.429-86.163) in their nested case-control study, as well as a OR of 4.788 (CI 95% 1.591-14.414) for depressed mood. The only study that yields data against depressive symptoms relationship with suicide was done by McGirr et al.[44] in 2008, in which subjects with schizophrenia less frequently met criteria for current or past depressive disorder (OR 0.2, 95% CI 0.09-0.449 and OR 0.18, 95% CI 0.08-0.40 respectively).

The alcohol abuse or drugs abuse have been reported as risk factors for suicide in schizophrenia.[11, 34, 39, 41] However Heila[54] did not found significant differences regarding alcohol consumption with control group. Karvonen et al.[59] reported that alcohol abuse was more frequent in males with schizophrenia that committed suicide than in women.

Only two studies reported data about personality traits in relation to the suicidal phenomenon in schizophrenia. McGirr[47] in 2006 reported a lower proportion of subjects with cluster A and C personality traits, and considered having cluster C traits as a protective factor. Again McGirr[44] in 2008, pointed a lower prevalence of cluster B and C traits among subjects with a schizophrenia diagnosis that committed suicide compared to the rest of suicide completers and scored higher on the harm avoidance subscale and lower on the persistence subscale of the TCI ("Temperament and Character Inventory").

In regards to treatment, De Hert[46] considers the ambulatory based treatment and a functional daily activity as protective factors. Hunt[11] in 2006, compared to other psychiatric diagnosis, reported a longer time of illness without assistance in suicide completers with a schizophrenia diagnosis and reported that suicides in schizophrenia relates with a worse adherence to treatment. Among suicide completers with schizophrenia Loas[36] reported a more intensive neuroleptic treatment. Whereas Heilä[54] in 1999 found that a 57% of those suicide completers with schizophrenia were not taking their treatment or were not prescribed adequate neuroleptic treatment, in this same group inpatients showed a high proportion of negative or indifferent treatment attitudes. Ward[63] (2006), in the biggest sample he studied, identified a good adherence to treatment as a protective factor for suicide, but in his smaller sample which he considered more representative, results showed only a tendency that could not reach statistical significance.

Suicidal act

De Hert[46] in 2001 reported that patients with schizophrenia were more likely to have used a highly lethal method and considered that the history of previous attempts with highly lethal methods multiplies by 11 the risk of completing suicide.

In Spiebl's sample[17] of in-patients, all suicides were completed using violent methods. Karvonen[59] pointed that men with schizophrenia more often used violent suicide method in comparison with women. Heilä[39] in 1997 registered that young patients with schizophrenia tended to use a violent method, but the most frequent method of suicide in their sample was drug overdose, especially in women, what was later on reproduced by Saarinen[43] in 1999.

Jumping from a height is a violent method of suicide repeatedly reported as frequent among subjects with schizophrenia.[17, 51, 58, 60] Hunt[11] in 2006 confirmed a higher proportion of jumping among patients with schizophrenia. Kreyenbuhl[57] reported that a higher proportion of persons with schizophrenia jumped from a height compared with those without the disorder, whereas a smaller proportion used firearms, in comparison with general population. Reisch[64] in a study focused on jumping from a height reported that subjects who jumped were 2-6 times more likely to suffer from schizophrenia, compared with those who used other methods. Ösby[30] in 2000 reported that hanging was the most common method in males and poisoning in women, just as in general population, but identified a higher proportion of jumping in both sexes

Table 3 Elements characteristic of the completed suicide cases in subjects with schizophrenia

Special risk	Protective factors
Males	Predominance of negative symptoms or deficit syndrome
Young persons	Adequate adherence and therapeutic compliance
Predominance of paranoid subtype	Cluster C personality
At onset of the disease	
Near-hospital admission	
Presence of active symptoms, predominance of positive psychotic symptoms	
Comorbidity, especially depressive symptoms or disorders	
Poor treatment adherence, high number of hospitalizations	

compared with the general population. In the Asian sample of Phillips,[32] the most common method was ingestion of pesticides, followed by hanging with a high proportion reported as "other methods". Proportions reported by the different studies are listed in Table 2.

In regards to seasonal variations in suicide, just two of the studies reviewed considered directly this variable, and both reported a lower rate of suicide in spring. Kim[65] studied males exclusively and found a significant difference with Mayor Depressive Disorder: 87.5% of suicides in schizophrenia occurred in fall/winter. Shields[40] reported a 55% of suicides in fall/winter and only 13.7% in spring.

DISCUSSION

This review provides important data on the phenomenon of suicide in schizophrenia, although the findings presented are subject to regular publication bias and limited by the heterogeneity of the studies in the number and types of variables analyzed, the diagnostic criteria used, the in-patient or out-patient condition, the different time of evolution, the original population (cultural biases, western and oriental studies differ substantially), the way of inclusion (when admitted to a psychiatric hospital, selected from a Coroner´s Register, including as suicide concrete lethal acts those that did not finally cause the subject´s death…) or the possible misclassification of the cause and mechanism of death through several sources (death certificate, forensic consulting, national records, psychological autopsies…).

Thus, Phillips (2004) stated that suicides in individuals with schizophrenia were more likely to be misclassified as non-suicide deaths on the death certificate than were suicides in people without the illness (20% vs 6%; $p<0.0001$).

Retrospective investigations prevail, with particularly notable methodological limitations inherent in the study of certain variables such as personality traits.

We also believe that the different variables interact with each other in their relationship with suicide making highly recommendable the statistically adjust for potential confounders, which is not true in many of the studies reviewed.

Furthermore, it is noteworthy that suicide is a relatively uncommon event, so prediction of suicide is always going to be difficult and the identification of risk factors require big samples; therefore, some of them might not be identified because of lack of statistical power.

Despite the variability between studies and the consequent difficulties in comparing results, we found consistent findings regarding certain variables and all the studies reviewed reported suicide as the most important independent factor regarding the excess of mortality in patients with schizophrenia. However, there are variations in the risk of suicide depending on the age of subjects, their sex, the time course of the disease, the symptoms or the condition of inpatient or outpatient.

Estimating lifetime suicide risk is very complicated and also susceptible to change along with improvements in the treatment offered to the patient and in the general features of society but it seems reasonable to conclude that case fatality due to suicide does not reach as high as the 9.7 % reported by Ran et al.[31]

Studies in European population reported repeatedly a higher proportion of males among their suicides. Studies conducted in Asia reported a higher proportion of women, what may implicate a culturally based gender difference.[32]

Age of death was reported to be younger than for other psychiatric illnesses and around thirty years old,[34, 42] in relation with the tendency to commit suicide in the onset of illness. Nevertheless, the data on this variable are difficult to assess because many studies use it as a factor to match cases with controls and the age groups classification differs between studies. Age could not be examined broadly as a risk factor because of these.

Family history of suicide and of schizophrenia was reported by several studies as risk factors but after a global evaluation did not emerge as a risk factor, perhaps because it was a rarely studied variable.[37, 46]

However, we did find consistency between studies regarding the relationship with the suicide of the active symptoms or comorbidity with affective disorders.

Different variables that reflect a poor outcome of illness have been reported as risk factor for suicide (being unmarried, unemployed or disabled) but this aspect could be mediated by the severity of schizophrenia itself and did not show strong evidence.

Thus, other clinical variables considered as risk factors for suicide, such as a high number of previous admissions,[22, 38, 39, 46, 54] compulsory admissions, policy participation in the admissio[46, 55] or suicide during AWOL,[38, 46] could also be explained by the strong presence of positive symptoms (hostility and impulsivity, suspiciousness, delusions and mandatory hallucinations)[38, 43, 52, 54] and the predominance of paranoid subtype of schizophrenia.[16, 38,54]

On the other hand, a higher IQ and educational level were reported,[46, 47] what can lead to depressive symptoms depending on the awareness of illness and subsequent fear of deterioration.

An association alcohol misuse-suicide can be established in schizophrenia according to this review, as well as for drug misuse or dependence,[11, 34, 39, 41] although it was a insufficiently studied variable.

Finally, jumping from a height is a violent method of suicide repeatedly reported as frequent among subjects with schizophrenia.[17] This finding is consistent with the findings of a lower proportion of previous threats and planning for the event than in other diseases, and greater impulsivity in patients with schizophrenia who commit suicide,[4, 44, 46, 47, 52, 57] although higher scores have been described in avoidance of damage to them[44, 47].

Schizophrenia showed a different seasonal fluctuation than affective disorders.[40, 65] This could be interpreted as a weaker dependence on affective symptoms than initially supposed or as a specific characteristic of subjects with schizophrenia and depression who committed suicide.

CONCLUSIONS

Review´s findings indicate that schizophrenic patients had a mortality rate higher than that of the general population, so their assessment should include this aspect specifically and the evaluation of the various factors identified in this review (Table 3). We should be extremely cautious with patients with demographic risk factors, particularly during periods of significant life events. We strongly recommend the assessment of autolytic risk prior to the authorization of leaves and ensure a continuum of care for patients after discharge.

We should pay attention to the diagnosis and treatment of depression in schizophrenia[72] and perform a differential diagnosis between negative symptoms, which could be a protective factor, and depressive symptoms as a risk factor. Suicide prevention in schizophrenia involves improving adherence, so we must work with the patient's insight and consider the use of long-acting depot antipsychotics.[11, 54, 63]

Drug abuse in these patients should not be considered as an exclusion criterion for certain programs, highlighting the importance of a comprehensive treatment of dual diagnosis also in relation to suicide risk.

Finally, we must emphasize the need for a better coordination between healthcare institutions and the Institutes of Legal Medicine,[73, 74] given the importance of forensic data sources[75] in achieving long-term prospective studies which would make possible the research of the entire spectrum of suicidal behavior, identifying distinctive features of completed suicide.

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