

Reassessing the Long-term Risk of Suicide After a First Episode of Psychosis

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Context: The long-term risk of suicide after a first episode of psychosis is unknown because previous studies often have been based on prevalence cohorts, been biased to more severely ill hospitalized patients, extrapolated from a short follow-up time, and have made a distinction between schizophrenia and other psychoses.

Objective: To determine the epidemiology of suicide in a clinically representative cohort of patients experiencing their first episode of psychosis.

Design: Retrospective inception cohort.

Setting: Geographic catchment areas in London, England (between January 1, 1965, and December 31, 2004; n=2056); Nottingham, England (between September 1, 1997, and August 31, 1999; n=203); and Dumfries and Galloway, Scotland (between January 1, 1979, and December 31, 1998; n=464).

Participants: All 2723 patients who presented for the first time to secondary care services with psychosis in the 3 defined catchment areas were traced after a mean follow-up period of 11.5 years.

Main Outcome Measure: Deaths by suicide and open verdicts according to the *International Classification of Diseases* (seventh through tenth editions).

Results: The case fatality from suicide was considerably lower than expected from previous studies (1.9% [53/2723]); the proportionate mortality was 11.9% (53/444). Although the rate of suicide was highest in the first year after presentation, risk persisted late into follow-up, with a median time to suicide of 5.6 years. Suicide occurred approximately 12 times more than expected from the general population of England and Wales (standardized mortality ratio, 11.65; 95% confidence interval, 8.73-15.24), and 49 of the 53 suicides were excess deaths. Even a decade after first presentation—a time when there may be less intense clinical monitoring of risk—suicide risk remained almost 4 times higher than in the general population (standardized mortality ratio, 3.92; 95% confidence interval, 2.22-6.89).

Conclusions: The highest risk of suicide after a psychotic episode occurs soon after presentation, yet physicians should still be vigilant in assessing risk a decade or longer after first contact. The widely held view that 10% to 15% die of suicide is misleading because it refers to proportionate mortality, not lifetime risk. Nevertheless, there is a substantial increase in risk of suicide compared with the general population.

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THE LIFETIME RISK OF SUICIDE had been estimated at 10% for individuals with schizophrenia¹ and 15% for those with affective disorders² after 2 seminal meta-analyses in the 1970s. Such high rates were shown to be mathematically improbable for both types of illness using 2 different methods.^{3,4} More recently, data pertaining to suicide in patients with schizophrenia⁵ and individuals with affective disorder⁶ have been re-examined; caution has been advised concerning the concept of a lifetime risk for suicide because rates fluctuate over time and vary according to the stage of the illness. Palmer et al⁵ suggest proportionate mortality—the percentage of those who died within the follow-up period who com-

mitted suicide (10%-15%, as commonly cited)—should not be used. Instead, case fatality—the percentage of the original cohort who died of suicide—is a more accurate approximation of lifetime suicide risk. The meta-analysis by Palmer et al estimated a case fatality of approximately 5% for patients with schizophrenia.⁵

Cohorts studied to date have had several methodologic limitations. Relatively short follow-up periods inflate suicide estimates if proportionate mortality is used to estimate risk because suicide rates are high in the early stages of the illness.⁷ All published studies, to our knowledge, make a division between studies of schizophrenia and studies of affective disorder, whereas recent evidence, particularly from genetic studies, suggests that these are far from dis-

tinct disease entities^{8,9} and clinical diagnosis is known to vary over time.^{10,11} Moreover, within the affective disorder cohorts it is frequently difficult to ascertain which of the patients had psychotic symptoms.¹² For all diagnoses, many studies have not been true inception cohorts comprising first-episode cases and have been biased to more severe cases (eg, by restriction to inpatients¹³ or attendees of a specialist clinic beginning a particular treatment).¹⁴ Some studies have focused on first hospitalizations rather than including outpatients or community patients,^{15,16} whereas others have determined eligibility of cohort members on the basis of clinical judgment based on classification criteria¹⁷ or diagnosis from hospital admission registers¹⁸ rather than operational diagnoses.

For a true estimation of lifetime risk after a first episode of psychosis, a representative cohort of patients would need to be followed up until death, yet the feasibility of such an undertaking is debatable, not least because it would need to involve researchers during successive generations.¹⁹ A more practical option (which, to our knowledge, has not been used) is to investigate suicide among all patients with a first episode of psychosis, irrespective of diagnosis, ascertained from hospital and outpatient settings from well-defined geographic catchment areas in a defined time frame, with a long follow-up period. We used this approach and aimed to describe the epidemiology of suicide in a clinically representative incidence cohort and to compare the risk of death from suicide among patients with first-episode psychosis to that of the general population of England and Wales.

METHODS

STUDY POPULATION

Demographic and clinical data were collected with regard to all patients who presented to secondary care services with any psychotic phenomena during 4 decades (between January 1, 1965, and December 31, 2004) in Camberwell, a densely populated, urban, inner-city area, geographically aligned to the southern portion of the London borough of Southwark in England. For the period between January 1, 1965, and December 31, 1983, these data were compiled using the Camberwell Cumulative Psychiatric Case Register,^{20,21} and then for the period between January 1, 1984, and December 31, 2004, hospital computer records were used to generate a list of all patients admitted with any possible psychotic illness (*International Classification of Diseases, Ninth Revision [ICD-9]* codes 295, 295.6, 297, 296.0, 296.2, 296.4, 298, and 292.1 and *International Statistical Classification of Diseases, 10th Revision [ICD-10]* codes F20, F25, F22, F30, F31.3, F31.2, F31.6, F28, F29, F12.5, F16.6, F19.5, F16.75, and F19.75) in the catchment area. In addition, all case records of patients from the area were examined to identify those who made contact with services but were not admitted to the hospital. The records of those not admitted were of a similar quality to the records of those admitted. Patients who were admitted to hospitals outside the area would usually be transferred back to local hospitals or referred to local services for continuing care. These records were also identified in the comprehensive search of all case notes. All patients' records were checked to ensure that these were true incident cases (ie, patients had not had prior psychiatric treatment for a possible psychotic illness). Between January 1, 2000, and December 31, 2003, owing to resource limitations, the study was restricted to a smaller area consisting of the 9 most south-

ern contiguous electoral wards (approximately two-thirds of the original Camberwell population). The Joint South London and Maudsley and the Institute of Psychiatry Research Ethics Committee approved the London portion of the study.

The Nottingham cohort (from a mixture of urban, suburban, and rural environments) was that identified in the *Ætiology and Ethnicity in Schizophrenia and Other Psychoses (ÆSOP)* study²² (1997-1999), which aimed to investigate the cause of high rates of psychosis in certain minority ethnic populations in the United Kingdom. All those who presented for the first time as an inpatient or outpatient to any psychiatric service (including adult community mental health teams, inpatient units, adolescent mental health services, drug and alcohol units, forensic services, and learning disability services) because of psychotic phenomena were screened using a broadly inclusive psychosis screening instrument.²³ The search was broad to maximize the opportunity of identifying all incident cases and included a leakage study,²⁴ which was undertaken after the survey period closed to identify any overlooked cases in the local public and private health systems. Approval for this portion of the *ÆSOP* study was obtained from the Nottingham Research Ethics Committee.

The Dumfries and Galloway cohort was that identified for a study conducted in parallel with the London study.²⁵ Dumfries and Galloway is a relatively sparsely populated, mainly rural area of Scotland that comprises predominantly white residents (99.5%).²⁶ All residents who had come into first contact with psychiatric services with a psychotic disorder between January 1, 1979, and December 31, 1998, were included in the cohort. Cases were obtained from 2 main sources: (1) the data for inpatients held centrally in Edinburgh by the Information and Statistical Division of the Scottish Office and (2) locally held registers of outpatients, domiciliary visits, and after-hours referrals.²⁶ The case ascertainment procedures were the same as those described for London. Approval for this portion of the study was obtained from the Dumfries and Galloway Health Board Research Ethics Committee and the Privacy Committee of the Information and Statistical Division Scotland. Exclusion criteria in all 3 centers were not being a resident in the catchment area, having a clear organic cause for the symptoms, and onset before 16 years of age.

DIAGNOSTIC PROCEDURE

Case records of the patients, including medical, nursing, social work, and occupational therapy notes, together with all correspondence relating to the case were examined and then rated using the Operational Checklist for Psychotic Disorders (OPCRIT), version 3.4.²⁷ This is a well-validated symptom checklist based on the present state examination²⁸ and enabled operational research diagnostic criteria (RDC)²⁹ computer diagnoses to be made using the OPCRIT program²⁷ for the year after each patient's first presentation. Those patients with a broad RDC diagnosis of schizophrenia, schizoaffective disorder, psychotic mania or bipolar disorder, psychotic depression, or other (which included atypical psychosis and schizophreniform psychosis) were included in this analysis. Interrater reliability was monitored frequently and found to be strong for diagnostic categories (from January 1, 1965, through December 31, 1983, $\kappa=0.82^{30}$; from January 1, 1984, through December 31, 1997, $\kappa=0.79^{31}$; overall range of agreement, 0.75-0.94³²).

IDENTIFICATION OF SUICIDES

All deaths up to and including those that occurred on March 31, 2007, were identified by a case-tracing procedure with the Office for National Statistics (ONS) for England and Wales and the General Register Office (GRO) for Scotland using name, sex, date of birth, and last known address of each patient. The

ONS and GRO also provided information (including the date) for those who had emigrated or left the register for other reasons (eg, they had been removed from a family physician's list by the health authority because their whereabouts or status were unknown). Further tracing was done through the Central Services Agency in Northern Ireland.

Copies of death certificates were obtained for all those who had died. The method used to ascertain suicide was identical to that used for the generation of national statistics. Causes of death used in this study were the underlying conditions recorded on the death certificates as being the primary cause of death. The years studied in this analysis span 4 revisions of the ICD, and the codes used for a coroner's verdict of suicide were as follows: *International Classification of Diseases, Seventh Revision (ICD-7)*, E970 to E979; *International Classification of Diseases, Eighth Revision (ICD-8)*, E950 to E959; *ICD-9*, E950 to E959; and *ICD-10*, X60 to X84. In addition, from *ICD-8* onward, the new ICD category of 'undetermined deaths' (deaths given open verdicts by coroners) was included (ie, *ICD-8* and *ICD-9* codes E980 to E989; *ICD-10* codes Y10 to Y34, excluding the temporary codes E988.8 [*ICD-9*] and Y33.9 [*ICD-10*], both of which specify injury by other specified means, undetermined whether accidentally or purposely inflicted). Most such deaths are deemed to be suicides, and including this category is in accordance with official reporting of national suicide rates.³³⁻³⁶ Official death details were rechecked against case notes to ascertain whether there were any cases that were designated as "accidental poisoning," in which death may have been self-inflicted but was not proven beyond a reasonable doubt; there were no such cases. Unascertainable causes of deaths (*ICD-9* code 7999; *ICD-10* code R99) were reviewed in a similar manner, and the case notes revealed no strong reason to believe that these patients had committed suicide.

CENSORED OBSERVATIONS

Those people who had emigrated were treated as having left the study alive at the date of emigration. Those whose whereabouts became unknown (because they were removed from health authority listings) were treated as having left the study alive at a midpoint between the date of removal and the date they were last definitely known to be alive from information held on case records.

STATISTICAL ANALYSES

All statistical analyses were conducted using Stata statistical software, version 10 for Windows (StataCorp LP, College Station, Texas). Descriptive analyses and comparisons of patient characteristics were undertaken using independent *t* tests and Mann-Whitney tests as appropriate. All patients traced by ONS or GRO for any length of time from their first presentation were entered into a survival analysis with the end date being the date of death, the date the patient was last known to be alive, the censor date, or the end of follow-up (March 31, 2007), whichever came first. Risk of suicide was calculated by considering the number of patients who entered a study period for whom outcome was known at the end of that period. Kaplan-Meier curves were plotted and log-rank tests used to compare risk of suicide in males and females. A lexis expansion was used to take into account the differing lengths of follow-up and to generate rates of suicide in person-years according to sex, age group at first presentation, and geographic location of the cohort.³⁷

Poisson regression modeling was then used to estimate the effect of sex on suicide rate, checking for the confounding effect of age and calendar period. The effect of age group on suicide rate was also assessed, making the appropriate adjustments. A likelihood ratio test (LRT) was used to test for an interaction between age group and sex.

All-cause and suicide mortality rates specific for age (split into 10-year age groups of 16-25 years onward), sex, and calendar period (split into eight 5-year groups from 1965 to 2004 and a 3-year group from 2005 to 2007) in the general population of England and Wales were applied using the STATA *istdize* procedure to the study population to calculate the expected number of cases for each calendar period by sex. The overall all-cause mortality rate and suicide standardized mortality ratios (SMRs) were calculated by dividing the total number of observed cases by the total expected number. The 95% confidence intervals (CIs) of the SMRs were calculated by assuming that the observed number of deaths followed a Poisson distribution.³⁸ The number of excess deaths for each cause of death was calculated by subtracting the expected number of deaths from the observed number of deaths.

RESULTS

COHORT CHARACTERISTICS

Table 1 presents the number of patients, deaths, and suicides by geographic catchment area according to sex, age at first contact, broad RDC diagnosis, and ethnicity. Of the 2723 individuals identified with first-episode psychosis, 22 (0.8%) were known to have emigrated and 213 (7.8%) had to be censored before the final follow-up date because their whereabouts became unknown. Of all patients, 55.2% were male, and the age range at first contact was 16 to 86 years (mean age, 33.6 years). The broad RDC diagnostic categories from the OPCRIT criteria were 1460 (53.6%) with schizophrenia, 383 (14.1%) with schizoaffective disorder, 287 (10.5%) with psychotic mania or bipolar disorder, 171 (6.3%) with psychotic depression, and 422 (15.5%) in other diagnostic groups. The ethnic composition was 1406 white (51.6%), 1071 black African or Caribbean (39.3%), and 246 (9.0%) from other ethnic groups. The main difference among the catchment areas was that all patients in Dumfries and Galloway were white and there was a predominantly white cohort in Nottingham (77.8%), whereas in London, the black African or Caribbean group formed the largest proportion (50.8%).

The main difference in baseline characteristics for those censored compared with those who were completely followed up was that there were more "other" diagnoses in the censored group (30.5%) than in the completely followed-up group (14.1%). Sex, age at first contact, and ethnicity did not differ between the 2 groups. There was also no statistical difference in age at first contact, broad RDC diagnosis, or ethnicity between those who had committed suicide and those alive at follow-up.

SUICIDES IN THE COHORT

By March 31, 2007, 444 (16.3%) of the cohort had died, 53 of suicide, with a mean follow-up period of 11.5 years (169.7 per 100 000 person-years; 95% CI, 129.7-222.1). The overall case fatality was therefore 1.9% (53/2723), and the proportionate mortality was 11.9% (53/444). Five of the 53 suicides were in the undetermined death category. Forty suicides occurred among males (237.9 per 100 000 person-years; 95% CI, 174.5-324.3) and 13 among females (90.2 per 100 000 person-years; 52.4-

Table 1. Distribution of Patients, Deaths, and Suicides in the 3 Geographic Catchment Areas^a

Characteristic	London			Nottingham			Dumfries and Galloway		
	Patients	Deaths	Suicides	Patients	Deaths	Suicides	Patients	Deaths	Suicides
Total, No.	2056	299	41	203	12	3	464	133	9
Sex, No. (%)									
Male	1175 (57.1)	144 (48.2)	31 (75.6)	121 (59.6)	8 (66.7)	3 (100)	208 (44.8)	58 (43.6)	6 (66.7)
Female	881 (42.9)	155 (51.8)	10 (24.4)	82 (40.4)	4 (33.3)	0	256 (55.2)	75 (56.4)	3 (33.3)
Age at first contact, y									
<25	824 (40.1)	42 (14.0)	17 (41.5)	80 (39.4)	2 (16.7)	1 (33.3)	111 (23.9)	5 (3.8)	0
25-34	728 (35.4)	49 (16.4)	16 (39.0)	62 (30.5)	6 (50.0)	2 (66.7)	107 (23.1)	11 (8.3)	5 (55.6)
35-44	203 (9.9)	41 (13.7)	5 (12.2)	38 (18.7)	1 (8.3)	0	74 (15.9)	10 (7.5)	2 (22.2)
45-54	114 (5.5)	38 (12.7)	2 (4.9)	13 (6.4)	2 (16.7)	0	55 (11.9)	14 (10.5)	1 (11.1)
55-64	67 (3.3)	39 (13.0)	0	10 (4.9)	1 (8.3)	0	39 (8.4)	23 (17.3)	1 (11.1)
65-74	54 (2.6)	39 (13.0)	1 (2.4)	0	0	0	32 (6.9)	29 (21.8)	0
75-84	54 (2.6)	40 (13.4)	0	0	0	0	36 (7.8)	32 (24.1)	0
≥85	12 (0.6)	11 (3.7)	0	0	0	0	10 (2.2)	9 (6.8)	0
Diagnosis, broad RDC, No. (%)									
Schizophrenia	1182 (57.5)	182 (60.9)	18 (43.9)	67 (33.0)	5 (41.7)	1 (33.3)	211 (45.5)	67 (50.4)	4 (44.4)
Schizoaffective	221 (10.7)	26 (8.7)	8 (19.5)	41 (20.2)	4 (33.3)	1 (33.3)	121 (26.1)	20 (15.0)	3 (33.3)
Psychotic mania/bipolar	189 (9.2)	20 (6.7)	3 (7.3)	26 (12.8)	1 (8.3)	1 (33.3)	72 (15.5)	21 (15.8)	0
Psychotic depression	124 (6.0)	8 (2.7)	1 (2.4)	36 (17.7)	1 (8.3)	0	11 (2.4)	1 (0.8)	0
Other	340 (16.5)	63 (21.1)	11 (26.8)	33 (16.3)	1 (8.3)	0	49 (10.6)	24 (18.0)	2 (22.2)
Ethnicity, No. (%)									
White	784 (38.1)	197 (65.9)	18 (43.9)	158 (77.8)	11 (91.7)	3 (33.3)	464 (100)	133 (100)	9 (100)
Black African/Caribbean	1045 (50.8)	84 (28.1)	20 (48.8)	26 (12.8)	0	0	0	0	0
Other	227 (11.0)	18 (6.0)	3 (7.3)	19 (9.4)	1 (8.3)	0	0	0	0

Abbreviation: RDC, research diagnostic criteria.

^aPercentages may not total 100 because of rounding.

Table 2. Rate Ratios for Suicide According to Sex, Age of Onset, Calendar Period, and Geographic Center

	Rate Ratio (95% CI)					
	Crude	Sex Adjusted	Age Adjusted ^a	Calendar Period Adjusted ^b	Sex and Calendar-Period Adjusted ^b	Sex and Age Adjusted ^a
Sex						
Female	1 [Reference]	NA	1 [Reference]	1 [Reference]	NA	NA
Male	2.64 (1.41-4.93)	NA	2.48 (1.27-4.46)	2.64 (1.41-4.93)	NA	NA
Age at presentation, y						
<25	1 [Reference]	1 [Reference]	NA	1 [Reference]	1 [Reference]	NA
25-34	2.37 (0.82-6.84)	2.44 (0.85-7.05)	NA	2.40 (0.83-6.93)	2.45 (0.85-7.07)	NA
35-44	1.61 (0.53-4.84)	1.74 (0.58-5.24)	NA	1.62 (0.54-4.90)	1.75 (0.58-5.29)	NA
45-54	0.90 (0.24-3.34)	1.00 (0.27-3.74)	NA	0.91 (0.24-3.39)	1.02 (0.27-3.79)	NA
55-64	0.87 (0.19-3.88)	1.00 (0.22-4.49)	NA	0.89 (0.20-3.98)	1.02 (0.23-4.57)	NA
65-74	1.08 (0.20-5.88)	1.29 (0.24-7.07)	NA	1.10 (0.20-6.00)	1.30 (0.23-7.14)	NA
Calendar period						
1965-1974	2.88 (0.81-10.22)	3.04 (0.86-10.77)	2.88 (0.81-10.22)	NA	NA	2.96 (0.83-10.50)
1975-1984	0.80 (0.23-2.84)	0.86 (0.24-3.07)	0.82 (0.23-2.92)	NA	NA	0.87 (0.24-3.07)
1985-1994	0.91 (0.33-2.51)	0.96 (0.35-2.65)	0.94 (0.34-2.60)	NA	NA	0.98 (0.36-2.70)
1995-2004	1.42 (0.59-3.42)	1.45 (0.60-3.50)	1.44 (0.60-3.47)	NA	NA	1.46 (0.61-3.53)
≥2005	1 [Reference]	1 [Reference]	1 [Reference]	NA	NA	1.0 [Reference]
Center						
London	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]
Nottingham	0.98 (0.30-3.18)	0.93 (0.29-3.02)	0.88 (0.27-2.86)	0.87 (0.26-2.90)	0.84 (0.25-2.79)	0.84 (0.26-2.75)
Dumfries and Galloway	0.77 (0.38-1.60)	0.86 (0.41-1.77)	0.83 (0.40-1.72)	0.80 (0.38-1.68)	0.89 (0.42-1.86)	0.90 (0.44-1.86)

Abbreviations: CI, confidence interval; NA, not applicable.

^aAdjusted by 10-year age bands.

^bAdjusted by 10-year calendar periods from 1965 to end of study period.

155.3). The rate ratio for the crude effect of sex on risk of suicide, comparing males with females, was 2.64 (95% CI, 1.41-4.93; $P=.002$). There was no evidence of confounding by age or calendar period (see **Table 2** for main

Poisson regression results according to sex, age at presentation, calendar period, and geographic center).

There was no evidence in a Poisson regression model adjusted for sex and age group that there was any statis-

Table 3. Methods of Suicide in the Cohort^a

Method	Male, No. (%) (n=40)	Female, No. (%) (n=13)
Drowning	8 (20.0)	1 (7.7)
Hanging, strangulation, and suffocation	13 (32.5)	2 (15.4)
Poisoning and drugs or gas	4 (10.0)	6 (46.2)
Jumping from a high place	4 (10.0)	3 (23.1)
Jumping in front of a moving object	3 (7.5)	1 (7.7)
Burning	3 (7.5)	0
Firearms and explosives	2 (5.0)	0
Cutting or piercing	1 (2.5)	0
Other methods	2 (5.0)	0

^aPercentages may not total 100 because of rounding.

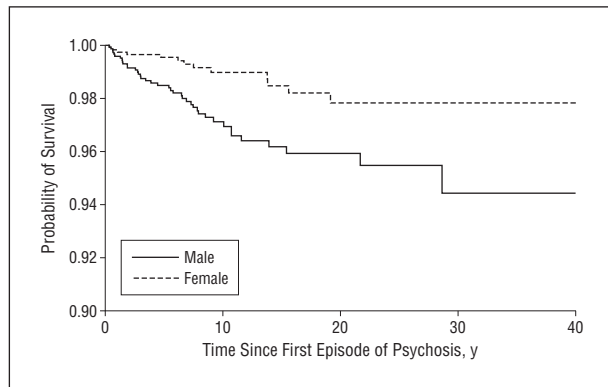


Figure. Kaplan-Meier survival curves showing risk of suicide according to sex.

tically significant difference in the rates of suicide after first-episode psychosis in each of the geographic catchment areas (LRT, $P=.66$) (London: 41 suicides; 184.4 per 100 000 person-years; 95% CI, 134.3-250.7; Nottingham: 3 suicides; 172.5 per 100 000 person-years; 55.6-535.0; and Dumfries and Galloway: 9 suicides; 145.9 per 100 000 person-years; 75.9-280.4). Therefore, the data sets were merged for further analysis.

Table 3 summarizes the method of suicide used according to 9 broad categories used in previous studies.³⁹ There was a marked difference between the sexes in the distribution of methods of suicide. For males, the most frequent methods were drowning, hanging, strangulation, or suffocation. However, among females, poisoning and jumping from a high place were the most common methods used.

There was only 1 suicide after the age of 65 years, in a man aged 72 years who committed suicide by drowning. The interquartile range for age at which suicide occurred was 29.3 to 41.2 years. The mean age at suicide for females (34.1 years) appeared slightly lower than that for males (37.1 years). However, a 2-group mean comparison t test indicated that there was no statistical difference in the mean age at suicide between the sexes ($t=0.72$, $P=.47$).

The highest rate of suicide occurred in the 25- to 34-year age group (23 suicides; 273.6 per 100 000 person-years; 95% CI, 183.4-408.2); however, the rate ratio comparing this group to the less-than-25-year age group encompassed unity (2.37; 95% CI, 0.82-6.84) (Table 2). A test for nonlinearity provided no evidence against a linear increase in the log (rate) of suicide from one age group

Table 4. Suicide Rates (per 100 000 Person-years) by Time Since First Episode of Psychosis

Time Since First Psychotic Episode ^a	Male	Female	Entire Cohort
<1 Year			
Total No. of patients followed up	1504	1219	2723
No. of patients with known outcome	1398	1124	2522
No. of suicides	6	2	8
Suicide rate (95% CI)	410.8 (184.6-914.4)	170.6 (42.7-682.0)	303.8 (151.9-607.5)
Cumulative risk at 1 year, % (95% CI)	0.42 (0.19-0.92)	0.17 (0.01-0.68)	0.31 (0.15-0.61)
1-5 Years			
No. of patients with known outcome	1049	876	1925
No. of suicides	14	3	17
Suicide rate (95% CI)	281.0 (166.4-474.4)	74.0 (23.9-229.5)	188.1 (117.0-302.7)
Cumulative risk at 5 years, % (95% CI)	1.51 (0.98-2.34)	0.46 (0.19-1.11)	1.04 (0.71-1.54)
5-10 Years			
No. of patients with known outcome	554	501	1055
No. of suicides	12	4	16
Suicide rate (95% CI)	281.7 (160.0-496.0)	111.0 (41.7-295.8)	203.5 (124.7-332.1)
Cumulative risk at 10 years, % (95% CI)	2.88 (2.02-4.10)	1.03 (0.52-2.00)	2.05 (1.50-2.79)
10-20 Years			
No. of patients with known outcome	267	241	508
No. of suicides	6	4	10
Suicide rate (95% CI)	145.9 (65.6-324.8)	106.9 (40.1-284.8)	127.3 (68.5-236.6)
Cumulative risk at 20 years, % (95% CI)	4.09 (2.90-5.74)	2.17 (1.18-3.98)	3.23 (2.38-4.36)

Abbreviation: CI, confidence interval.

^aTwo suicides occurred after greater than 20 years of follow-up and are not shown in this table.

to the next (LRT, $P=.69$). Therefore, age was treated as a continuous variable and resulted in a rate ratio of 0.972 (95% CI, 0.949-0.995; $P=.01$), suggesting that as a whole there was strong evidence of increasing age being associated with reduced risk of suicide death. There did not appear to be confounding by sex, calendar period, or sex and calendar period combined. There was no evidence of interaction between age group and sex (LRT, $P=.36$).

Time to suicide in the cohort ranged from 0.5 to 28.7 years, with a median value from Kaplan-Meier analysis of 5.6 years. For males the Kaplan-Meier median time to suicide was 5.4 years, and for females it was 7.5 years; however, this difference was not statistically significant (Mann-Whitney test=114.0; $P=.40$).

The **Figure** shows the Kaplan-Meier survival curves for suicide by sex. The risk of suicide in males was markedly higher than in females throughout the follow-up period (log-rank, $\chi^2=7.87$; $P=.005$). **Table 4** summarizes the cumulative risk of suicide (based on Kaplan-Meier estimates) after 1, 5, 10, and 20 years of follow-up. Although 8 of the total 53 suicides (15.1%) occurred within the year after first contact, 12 (22.6%) occurred a decade or more after first presentation, with 2 occurring

Table 5. Suicide Rates (per 100 000 Person-years) and Age- and Calendar Period–Adjusted SMRs by Time Since First Presentation With Psychosis

Time Since First Episode of Psychosis	Male	Female	Entire Cohort
1 Year			
Rate (95% CI)	221.4 (158.2-309.9)	83.1 (46.0-150.0)	157.4 (117.5-210.8)
SMR	11.01 (7.87-15.42)	11.36 (6.29-20.50)	11.10 (8.28-14.86)
5 Years			
Rate (95% CI)	192.8 (124.4-298.8)	87.1 (43.5-174.1)	143.1 (98.8-207.3)
SMR	6.72 (4.34-10.42)	8.57 (4.28-17.13)	7.16 (4.95-10.37)
10 Years			
Rate (95% CI)	130.9 (65.4-261.7)	71.6 (26.9-190.8)	102.6 (58.3-180.6)
SMR	3.49 (1.74-6.97)	5.19 (1.95-13.82)	3.92 (2.22-6.89)
20 Years			
Rate (95% CI)	99.9 (25.0-400.0)	NA ^a	52.0 (13.0-208.1)
SMR	1.41 (0.35-5.65)	NA ^a	1.04 (0.26-4.18)

Abbreviations: CI, confidence interval; NA, not applicable; SMR, standardized mortality ratio.

^aNo suicides occurred among females after 20 years of follow-up.

after more than 20 years of follow-up (at 21.7 and 28.7 years).

The suicide rate was 303.8 (per 100 000 person-years) in the first year of follow-up, 188.1 between 1 and 5 years, 203.5 between 5 and 10 years, and 127.3 between 10 and 20 years (Table 4). There was evidence that the crude rate declined over time ($\chi^2=5.93$, $P=.01$ from score test for trend).

COMPARISON WITH THE GENERAL POPULATION OF ENGLAND AND WALES

The all-cause mortality SMR was 2.07 (95% CI, 1.80-2.37) for males and 1.68 (1.47-1.90) for females. When standardized by age, sex, and calendar period, the SMR for all causes of death was 1.84 (95% CI, 1.67-2.02). The number of excess deaths (compared with the number that would have been expected if the mortality pattern for the general population of England and Wales for this period had applied) was 108 for males and 94 for females.

The SMRs for suicides among males and those among females were significantly increased and of a similar magnitude (males: SMR, 11.53; 95% CI, 8.24-15.70; females: SMR, 12.04; 6.41-20.58), with 37 excess deaths by suicide calculated for males and 12 for females (49 of the 53 suicides were, therefore, excess deaths). When data for both sexes were aggregated and standardized by age, sex, and calendar period, the overall SMR for suicide was 11.65 (95% CI, 8.73-15.24). The risk of suicide persists (Table 5) such that 1 year after first presentation the SMR remains at a similar magnitude of 11.10 (95% CI, 8.28-14.86). For those who survive 5 years, the SMR remains elevated at 7.16 (95% CI, 4.95-10.37), and even a decade after first presentation, the SMR is 3.92 (2.22-6.89). It is only 20 years after first pre-

sentation that the risk is not statistically significantly different from that of the general population (SMR, 1.04; 95% CI, 0.26-4.18).

COMMENT

To our knowledge, this is the most epidemiologically complete catchment area–based incidence study of suicide among patients presenting with first-episode psychosis. We had a long mean follow-up period of 11.5 years for these patients.

EPIDEMIOLOGY OF SUICIDE

The case fatality in this study (1.9%) was considerably lower than that generated for first admission and new-onset samples by Palmer et al⁵ using generalized estimating equations (4.9%; 95% CI, 4.3%-5.6%). Similarly, the proportionate mortality (11.9%) was lower than would be expected from their meta-analysis (30.6%; 95% CI, 19.0%-49.1%). One possible reason could relate to a restricted follow-up period for those patients forming the latter portion of our cohort, in whom suicides have not yet occurred. Another possibility is that some of the 235 (8.6%) of the cohort that were censored may have died by suicide in a foreign country or homeless and unidentifiable. This could have led to an underestimate of the suicide risk. The censored patients were more likely to have an “other” RDC diagnosis than the completely followed-up individuals, which might indicate that their illness type was less clearly defined.

Similar to most previous studies of schizophrenic illness (such as that by Hunt et al⁴⁰), the risk of suicide after first-episode psychosis was higher in males than in females. Males in particular used violent methods of suicide, as had been found by Heilä et al.⁴¹ The higher rate of suicide in younger patients was also in keeping with that reported by previous studies (as reviewed by Caldwell and Gottesman⁴²). Although young people in the early stages of their illness form a particularly high-risk group,^{43,44} suicide risk persisted even a decade after first presentation with psychosis, with the risk being almost 4 times higher than for the general population (SMR, 3.92; 95% CI, 2.22-6.89).

There is a tendency for health care professionals to be less mindful of this late risk even though our conclusions build on those reported in other first-contact studies. For example, in a much smaller incidence cohort of 82 patients with nonaffective psychosis followed up for 15 years, Wiersma et al⁴⁵ reported 2 of the 9 suicides occurring at 10 and 13 years, respectively, after first onset. Similarly, Lindelius and Kay⁴⁶ reported 4 of 11 suicides occurring after more than a decade (at 12, 13, 15, and 21 years, respectively) in their study of 187 male first-admission patients. Indeed, persistence of high risk of suicide over time was also shown in the case register study by Baxter and Appleby⁴⁷ and in the recalculation of lifetime risk of suicide by Inskip et al,⁴ which used curve fitting to extrapolate data to cohort extinction.

There are too few suicides in each category to be able to definitively say whether certain methods have become

more or less prevalent over time. In theory, deaths from poisoning may have decreased over time owing to a transition from tricyclic antidepressants to prescriptions of selective serotonin reuptake inhibitors (which are less toxic in overdose) among patients with psychosis who have been prescribed antidepressants and antipsychotics. However, Flanagan⁴⁸ found that antipsychotic-related deaths in England and Wales were higher in 2004 than at any time since 1993, and conclusions about the trends in suicide owing to poisoning cannot be drawn from the 10 cases found in this study. Low access to guns in the United Kingdom may explain the low use of firearms that was observed, as was also noted in a Swedish study.¹⁶

Our results are a significant contribution to the literature regarding suicide after psychosis because they are based on a cohort of all first episodes of psychosis, regardless of diagnosis, from 3 defined catchment areas within a 40-year period. The published cohort that most closely approximates ours is the Suffolk County, New York study,⁴⁹ but this only included first-admission patients during a 6-year period (1989-1995). There was also an upper age restriction of 60 years, and the patients had to speak English and give informed consent for participation, making the sample less complete than in this cohort. The Suffolk County study also had only one-fifth ($n=567$) of the number of participants included in this cohort. The fact that no significant difference in suicide rate was found among the 3 geographic centers suggests that the results we are reporting are not unique to 1 particular region of the United Kingdom but are consistent across regions, from the urban to the rural.

The mortality risk for suicide was almost 12 times more than would be expected compared with the general population and was similar to the random-effects SMR for schizophrenia calculated by Neeleman⁵⁰ in his meta-analysis involving 8 cohorts (SMR, 12.3; 95% CI, 8.6-17.6). Future analysis of this cohort will investigate deaths of natural causes and consider whether there are identifiable early risk factors for later suicide.

STRENGTHS AND LIMITATIONS

The strength of this study is that it was based on comprehensive case ascertainment of all first-episode psychoses with a long mean follow-up period from 3 strictly defined geographic areas. Including all psychiatric contacts with psychosis rather than restricting to admissions meant that a clinically representative cohort was compiled, and this also minimized the possibility of changes in service provision during the 40 years affecting case ascertainment. The possibility of losing cases owing to diagnostic or coding inaccuracies was minimal because case notes were individually checked to ensure that patients had not had previous contact elsewhere for psychosis and were part of a true incident cohort. This means that although the cohort is smaller than with population register-based studies,^{43,51,52} we can be much more confident about the quality of the diagnostic information. Diagnostic consistency was ensured by using OPCRIT-generated diagnoses rather than clinical diagnoses.

Inclusion of deaths from injuries and poisonings of undetermined intent, as well as official suicides, is a well-

accepted practice.⁵³ There were only 5 such deaths, and this would hardly affect the conclusions, especially because the rates for these undetermined causes were included in the national rates used in the SMR analysis, in which diagnostic consistency is most vital.

Although follow-up time was considerably longer than in other studies, with a mean of 11.5 years and ranging to 28.7 years, still only 16.3% of the cohort had died. There were insufficient numbers to study differences between those who committed suicide more than a decade after presentation and those who did so in the first year; there were insufficient numbers in each of the diagnostic groups to make valid comparisons.

If a person were only ever treated for psychosis in primary care, he or she would have been missed in this study, but in the United Kingdom nearly all patients with psychosis are seen in secondary services at some point.⁵⁴ The same argument applies for those seen only in private outpatient or inpatient facilities; however, in the United Kingdom this is a vanishingly small component of the mental health care sector.

The method of indirect standardization was used to obtain SMRs because a single summary measure for the study population was more easily compared than long lists of specific rates. Also, in this study the small numbers of people in certain strata meant that the associated rates were too imprecise for detailed comparisons. Because the absolute number of suicides is small, a variation of 1 or 2 deaths would make a relatively large difference to the SMR calculated. Therefore, high mortality ratios do not necessarily indicate a particularly poor mortality outcome relative to the general population of England and Wales and might just reflect small numbers.

CONCLUSION

Our study provides further and conclusive evidence that the widely discussed suicide risk of 10% in psychosis is an inflated estimate. There is an obvious danger of overestimating suicide risk in studies with a limited follow-up period and in those biased toward patients with more severe disease. From this study of a true incidence cohort, suicide appears to occur approximately 12 times more than expected in the general population and males are prone to use violent methods. Although the rates of suicide are highest in young patients in the early stages of their illness, suicide is not just a phenomenon of early psychosis. Of clinical importance is the consistently high risk in later years, with the risk of suicide remaining almost 4 times higher than that in the general population after a decade.

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REFERENCES

- Miles CP. Conditions predisposing to suicide. *J Nerv Ment Dis.* 1977;164(4):231-246.
- Guze SB, Robins E. Suicide and primary affective disorders. *Br J Psychiatry.* 1970; 117(539):437-438.
- Blair-West GW, Mellsoy GW, Eyeson-Annan ML. Down-rating lifetime suicide risk in major depression. *Acta Psychiatr Scand.* 1997;95(3):259-263.
- Inskip HM, Harris EC, Barraclough B. Lifetime risk of suicide for affective disorder, alcoholism and schizophrenia. *Br J Psychiatry.* 1998;172:35-37.
- Palmer BA, Pankratz VS, Bostwick JM. The lifetime risk of suicide in schizophrenia: a reexamination. *Arch Gen Psychiatry.* 2005;62(3):247-253.
- Bostwick JM, Pankratz VS. Affective disorders and suicide risk: a reexamination. *Am J Psychiatry.* 2000;157(12):1925-1932.
- Salokangas RK, Stengård E. Gender and short-term outcome in schizophrenia. *Schizophr Res.* 1990;3(5-6):333-345.
- Owen MJ, Craddock N, Jablensky A. The genetic deconstruction of psychosis. *Schizophr Bull.* 2007;33(4):905-911.
- Cardno AG, Rijdsdijk FV, Sham PC, Murray RM, McGuffin P. A twin study of genetic relationships between psychotic symptoms. *Am J Psychiatry.* 2002;159(4):539-545.
- Amin S, Singh SP, Brewin J, Jones PB, Medley I, Harrison G. Diagnostic stability of first-episode psychosis. *Br J Psychiatry.* 1999;175(6):537-543.
- Veen ND, Seltén J-P, Schols D, Laan W, Hoek HW, van der Tweel I, Kahn RS. Diagnostic stability in a Dutch psychosis incidence cohort. *Br J Psychiatry.* 2004; 185(6):460-464.
- Angst J, Angst F, Gerber-Werder R, Gamma A. Suicide in 406 mood-disorder patients with and without long-term medication. *Arch Suicide Res.* 2005;9(3):279-300.
- Angst F, Stassen HH, Clayton PJ, Angst J. Mortality of patients with mood disorders: follow-up over 34-38 years. *J Affect Disord.* 2002;68(2-3):167-181.
- Brodersen A, Licht RW, Vestergaard P, Olesen AV, Mortensen PB. Sixteen-year mortality in patients with affective disorder commenced on lithium. *Br J Psychiatry.* 2000; 176:429-433.
- Hoyer EH, Olesen AV, Mortensen PB. Suicide risk in patients hospitalised because of an affective disorder. *J Affect Disord.* 2004;78(3):209-217.
- Ösby U, Brandt L, Correia N, Ekbohm A, Sparén P. Excess mortality in bipolar and unipolar disorder in Sweden. *Arch Gen Psychiatry.* 2001;58(9):844-850.
- Limosin F, Loze JY, Philippe A, Casadebaig F, Rouillon F. Ten-year prospective follow-up study of the mortality by suicide in schizophrenic patients. *Schizophr Res.* 2007;94(1-3):23-28.
- Nordentoft M. Prevention of suicide and attempted suicide in Denmark. *Dan Med Bull.* 2007;54(4):306-369.
- Susser E, Terry MB. A conception-to-death cohort. *Lancet.* 2003;361(9360):797-798.
- Castle D, Wessely S, Der G, Murray RM. The incidence of operationally defined schizophrenia in Camberwell, 1965-84. *Br J Psychiatry.* 1991;159:790-794.
- Wing JK, Hailey AM. *Evaluating a Community Psychiatric Service: the Camberwell Register, 1964-1971.* London, England: Oxford University Press; 1972.
- Kirkbride JB, Fearon P, Morgan C, Dazzan P, Morgan K, Tarrant J, Lloyd T, Holloway J, Hutchinson G, Leff JP, Mallett RM, Harrison GL, Murray RM, Jones PB. Heterogeneity in incidence rates of schizophrenia and other psychotic syndromes: findings from the 3-center AESOP study. *Arch Gen Psychiatry.* 2006; 63(3):250-258.
- Jablensky A, Sartorius N, Ernberg G, Anker M, Korten A, Cooper JE, Day R, Bertelsen A. Schizophrenia: manifestations, incidence and course in different cultures. *Psychol Med Monogr Suppl.* 1992;20:1-97.
- Cooper JE, Goodhead D, Craig T, Harris M, Howat J, Korner J. The incidence of schizophrenia in Nottingham. *Br J Psychiatry.* 1987;151:619-626.
- Allardyce J, Boydell J, Van Os J, Morrison G, Castle D, Murray RM, McCreadie RG. Comparison of the incidence of schizophrenia in rural Dumfries and Galloway and urban Camberwell. *Br J Psychiatry.* 2001;179:335-339.
- Kirkpatrick B, Tek C, Allardyce J, Morrison G, McCreadie RG. Summer birth and deficit schizophrenia in Dumfries and Galloway, southwestern Scotland. *Am J Psychiatry.* 2002;159(8):1382-1387.
- McGuffin P, Farmer A, Harvey I. A polydiagnostic application of operational criteria in studies of psychotic illness. *Arch Gen Psychiatry.* 1991;48(8):764-770.
- Wing JK, Cooper JE, Sartorius N. *The Measurement and Classification of Psychiatric Symptoms.* New York, NY: Cambridge University Press; 1974.
- Spitzer RL, Endicott J, Robins E. Research diagnostic criteria: rationale and reliability. *Arch Gen Psychiatry.* 1978;35(6):773-782.
- Castle DJ, Wessely S, Van Os J, Murray RM. *Psychosis in the Inner City.* Maudsley monographs No. 40. London, England: Psychology Press; 1998.
- Boydell J, Van Os J, Lambri M, Castle D, Allardyce J, McCreadie RG, Murray RM. Incidence of schizophrenia in south-east London between 1965 and 1997. *Br J Psychiatry.* 2003;182:45-49.
- Dutta R, Boydell J, Kennedy N, Van Os J, Fearon P, Murray RM. Suicide and other causes of mortality in bipolar disorder. *Psychol Med.* 2007;37(6):839-847.
- Charlton J, Kelly S, Dunnell K, Evans B, Jenkins R, Wallis R. Trends in suicide deaths in England and Wales. *Popul Trends.* 1992;69:10-16.
- Kelly S, Bunting J. Trends in suicide in England and Wales, 1982-96. *Popul Trends.* 1998;92(92):29-41.
- Linsley KR, Schapira K, Kelly TP. Open verdict v. suicide—importance to research. *Br J Psychiatry.* 2001;178:465-468.
- Ohberg A, Lonnqvist J. Suicides hidden among undetermined deaths. *Acta Psychiatr Scand.* 1998;98(3):214-218.
- Clayton D, Hills M. *Statistical Models in Epidemiology.* New York, NY: Oxford University Press; 1993.
- Breslow NE, Day NE. *The Design and Analysis of Cohort Studies.* Lyon, France: International Agency for Research on Cancer; 1987.
- Hawton K, Zahl D, Weatherall R. Suicide following deliberate self-harm. *Br J Psychiatry.* 2003;182:537-542.
- Hunt IM, Kapur N, Windfuhr K, Robinson J, Bickley H, Flynn S, Parsons R, Burns J, Shaw J, Appleby L; National Confidential Inquiry into Suicide and Homicide by People with Mental Illness. Suicide in schizophrenia. *J Psychiatr Pract.* 2006;12(3):139-147.
- Heilä H, Isometsä ET, Henriksson MM, Heikkinen ME, Marttunen MJ, Lönnqvist JK. Suicide and schizophrenia. *Am J Psychiatry.* 1997;154(9):1235-1242.
- Caldwell CB, Gottesman II. Schizophrenics kill themselves too: a review of risk factors for suicide. *Schizophr Bull.* 1990;16(4):571-589.
- Mortensen PB, Juel K. Mortality and causes of death in first admitted schizophrenic patients. *Br J Psychiatry.* 1993;163:183-189.
- Rossau CD, Mortensen PB. Risk factors for suicide in patients with schizophrenia: nested case-control study. *Br J Psychiatry.* 1997;171:355-359.
- Wiersma D, Nienhuis FJ, Slooff CJ, Giel R. Natural course of schizophrenic disorders. *Schizophr Bull.* 1998;24(1):75-85.
- Lindeliur R, Kay DW. Some changes in the pattern of mortality in schizophrenia, in Sweden. *Acta Psychiatr Scand.* 1973;49(3):315-323.
- Baxter D, Appleby L. Case register study of suicide risk in mental disorders. *Br J Psychiatry.* 1999;175:322-326.
- Flanagan RJ. Fatal toxicity of drugs used in psychiatry. *Hum Psychopharmacol.* 2008;23(suppl 1):43-51.
- Craig TJ, Ye Q, Bromet EJ. Mortality among first-admission patients with psychosis. *Compr Psychiatry.* 2006;47(4):246-251.
- Neeleman J. A continuum of premature death. *Int J Epidemiol.* 2001;30(1):154-162.
- Ösby U, Correia N, Brandt L, Ekbohm A, Sparén P. Mortality and causes of death in schizophrenia in Stockholm county, Sweden. *Schizophr Res.* 2000;45(1-2):21-28.
- Tiihonen J, Wahlbeck K, Lönnqvist J, Klaukka T, Ioannidis JPA, Volavka J, Haukka J. Effectiveness of antipsychotic treatments in a nationwide cohort of patients in community care after first hospitalisation due to schizophrenia and schizoaffective disorder: observational follow-up study. *BMJ.* 2006;333(7561):224-227.
- Neeleman J, Wessely S. Changes in classification of suicide in England and Wales. *Psychol Med.* 1997;27(2):467-472.
- Prince MJ, Phelan MC. Invisible schizophrenia: a postal survey of the incidence and management of new cases of schizophrenia in primary care. *J Ment Health.* 1994; 3:91-98.