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, 1979, 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% [33/2723]); 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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distinct disease entities and clinical diagnosis is known to vary over time. Moreover, within the affective disorder cohorts it is frequently difficult to ascertain which of the patients had psychotic symptoms. For all diagnoses, many studies have noted the true inception cohorts comprising first-episode cases and have been biased to more severe cases (e.g., by restriction to inpatients or attendees of a specialist clinic beginning a particular treatment).

Some studies have focused on first hospitalizations rather than including outpatients or community patients, whereas others have determined eligibility of cohort members on the basis of clinical judgment based on classification criteria or diagnosis from hospital admission registers 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. 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 9 decades (between January 1, 1905, 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, 1905, and December 31, 1983, these data were compiled using the Camberwell Cumulative Psychiatric Case Register, 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, F21.5, 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 (i.e., 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 southern 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 identified in the Epidemiology and Ethnicity in Schizophrenia and Other Psychoses (ESOP) study (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. The search was broad to maximize the opportunity of identifying all incident cases and included a leakage study, 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 ESOP 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. Dumfries and Galloway is a relatively sparsely populated, mainly rural area of Scotland that comprises predominantly white residents (99.5%). 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. 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. This is a well-validated symptom checklist based on the present state examination and enabled operational research diagnostic criteria (RDC) computer diagnoses to be made using the OPCRIT program 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 schizoaffective disorder) 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, k=0.82; from January 1, 1984, through December 31, 1997, k=0.70; overall range of agreement, 0.75-0.94).

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
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 stvdize 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. 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 OPCRT criteria were I 460 (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-
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-
cording to 9 broad categories used in previous studies.39 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 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 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, 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).

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, χ² = 7.87; P = .003). 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 3. Methods of Suicide in the Cohort

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

*Percentages may not total 100 because of rounding.*

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

<table>
<thead>
<tr>
<th>Time Since First Psychotic Episode</th>
<th>Male</th>
<th>Female</th>
<th>Entire Cohort</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;1 Year</td>
<td>1504</td>
<td>1219</td>
<td>2723</td>
</tr>
<tr>
<td>No. of patients with known outcome</td>
<td>1398</td>
<td>1124</td>
<td>2522</td>
</tr>
<tr>
<td>Suicide rate (95% CI)</td>
<td>281.0</td>
<td>74.0</td>
<td>188.1</td>
</tr>
<tr>
<td>Cumulative risk at 1 year, % (95% CI)</td>
<td>(166.4-474.4)</td>
<td>(23.9-229.5)</td>
<td>(117.0-302.7)</td>
</tr>
<tr>
<td>1-5 Years</td>
<td>1049</td>
<td>876</td>
<td>1925</td>
</tr>
<tr>
<td>No. of patients with known outcome</td>
<td>14</td>
<td>3</td>
<td>17</td>
</tr>
<tr>
<td>Suicide rate (95% CI)</td>
<td>281.0</td>
<td>74.0</td>
<td>188.1</td>
</tr>
<tr>
<td>Cumulative risk at 5 years, % (95% CI)</td>
<td>(9.89-2.34)</td>
<td>(0.19-1.11)</td>
<td>(0.71-1.54)</td>
</tr>
<tr>
<td>5-10 Years</td>
<td>554</td>
<td>501</td>
<td>1055</td>
</tr>
<tr>
<td>No. of patients with known outcome</td>
<td>12</td>
<td>4</td>
<td>16</td>
</tr>
<tr>
<td>Suicide rate (95% CI)</td>
<td>281.7</td>
<td>111.0</td>
<td>203.5</td>
</tr>
<tr>
<td>Cumulative risk at 10 years, % (95% CI)</td>
<td>(160.0-496.0)</td>
<td>(41.7-295.8)</td>
<td>(124.7-332.1)</td>
</tr>
<tr>
<td>10-20 Years</td>
<td>554</td>
<td>501</td>
<td>1055</td>
</tr>
<tr>
<td>No. of patients with known outcome</td>
<td>12</td>
<td>4</td>
<td>16</td>
</tr>
<tr>
<td>Suicide rate (95% CI)</td>
<td>281.0</td>
<td>74.0</td>
<td>188.1</td>
</tr>
<tr>
<td>Cumulative risk at 20 years, % (95% CI)</td>
<td>(9.89-2.34)</td>
<td>(0.19-1.11)</td>
<td>(0.71-1.54)</td>
</tr>
</tbody>
</table>

Abbreviation: CI, confidence interval.

a Two suicides occurred after greater than 20 years of follow-up and are not shown in this table.
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 even a decade 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 presentation that the risk is not statistically significantly different from that of the general population (SMR, 1.04; 95% CI, 0.26-4.18).

### 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 al 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 al), 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. The higher rate of suicide in younger patients was also in keeping with that reported by previous studies (as reviewed by Caldwell and Gottesman). Although young people in the early stages of their illness form a particularly high-risk group, 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 al reported 2 of the 9 suicides occurring at 10 and 13 years, respectively, after first onset. Similarly, Lindelius and Kay 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 Appleby and in the recalculations of lifetime risk of suicide by Inskip et al, 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, Flanagan\(^4^8\) 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.\(^1^6\)

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,\(^1^9\) 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 Neeleman\(^5^0\) 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,\(^4^3,5^1,5^2\) 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.\(^5^3\) 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.\(^4^9\) 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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**Author Contributions:** All authors had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

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