

Suicide in patients with schizophrenia: a nested case control study

Denmark's former high suicide rate has fallen in the general population. **Leanne Tite** explains how a nested case-control study was used to investigate whether there was also a fall in people with schizophrenia

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Abstract

Objective—To study the change in risk of suicide among patients with schizophrenia and related disorders.

Design—Nested case-control design with linked data.

Setting—4 longitudinal Danish registers.

Participants—18 744 people aged up to 75 years who committed suicide in 1981-97 individually matched with 20 controls.

Results—Over the time studied the reduction in suicide rate among patients with schizophrenia and schizophrenia spectrum disorder was similar to that seen in the general population (incidence rate ratio 1.00, 95% confidence interval 0.98 to 1.03). The reduction among patients with other psychosis in the schizophrenia spectrum was faster than the reduction seen in the general population. Among people admitted to hospital with schizophrenia the risk of suicide was highest in the first year after first admission, and the excess risk was largest in the younger age groups—that is, the risk decreased per year for every additional year of age.

Conclusion—The suicide rate among patients with a diagnosis of schizophrenia and related disorders has fallen. This may be due to better psychiatric treatment, reduced access to means of suicide, or improvements in treatment after suicide attempts.

alongside the marked decrease in the overall suicide rate. Given that suicide rates seemed to have actually increased in young women with schizophrenia during this period, the researchers thought it likely that, compared with the general population, the suicide risk for schizophrenic patients would have increased in this time.

What is a nested case-control study?

A nested case-control study is a type of observational study. That means that the researcher studies something that has happened or is happening in the real world. This is different to an experimental study, in which a researcher purposefully sets up a controlled situation to look at the effect of one variable on another. In an experimental study, because the researcher has more control over the environment in which the study takes place, causal explanations are possible. But because the real world is far more complex, observational studies do not allow for this level of specificity. Nevertheless, they are widely used and are indispensable in epidemiological research, in which the aim is to study naturally occurring associations between the presence of a disease and another factor of interest.

Nested case-control studies use retrospective data collected for the purpose of the study about past events. The design of a nested case-control study has four core elements—cases, controls, disease, and exposure. Cases comprise all the people in the study group of interest, and a person counts as a case if he or she has the disease that the researcher wishes to find out about. Controls are people who share some important defining characteristics with the cases but who do not have the disease under study. Finally, data about exposure to another factor, called the explanatory variable are collected for everyone in the study (both the cases and the controls). The researchers then look to see how many of the cases and how many of the controls have been exposed in the past to the explanatory variable to see if exposure differs between the two groups. From this a comparison can be made between the two groups of the relative risk, or size of the association between the presence and the absence of the disease and past exposure to the explanatory variable. Remember that what you end up with is an estimate of the relative risk—the difference in risk between cases and controls—not an actual risk estimate for either group.

In this study, the cases were people who had committed suicide, so here suicide is the disease of interest (although it may be more helpful to think of it as an outcome) and schizophrenia (or exposure to inpatient treatment for schizophrenia) is the explanatory variable.

What data did the researchers use for the study?

Nested case-control studies often use self reported data, usually from interviews with every case and control to try

This month's paper is Nordentoft M, Laursen TM, Agerbo E, Qin P, Høyer EH, Mortensen PB. Change in suicide rates for patients with schizophrenia in Denmark, 1981-97: nested case-control study. *BMJ* 2004;329:261. You can read it by going to studentbmj.com and clicking on the link.

Why do the study?

In 1980, Denmark had one of the highest suicide rates in the world, at 34 suicides for every 100 000 inhabitants. About half of those people committing suicide had had a previous admission to a psychiatric hospital due to mental illness, and about half of these people had been admitted during the year before their suicide. Research from several different countries has shown that patients with schizophrenia are at particular risk of suicide, with a 5.6% lifetime risk of suicide for a patient treated in hospital for schizophrenia. Since 1980, Denmark's suicide rate for the general population has begun to fall, and by 1997 incidence had reduced by 56% to 15 suicides per 100 000 inhabitants. But the decrease in suicides in the general population was accompanied by an increase in the suicide rate in young women diagnosed as having schizophrenia. The researchers wished to find out whether the risk of suicide for all patients with schizophrenia, relative to that of the general population, had changed in 1980-97

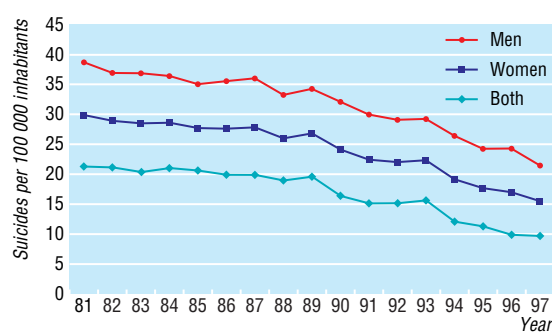


Fig 1 Number of suicides per 100 000 inhabitants in Denmark, 1981-97

to find out about their past exposure to the explanatory variable. In this study, however, objective data from national records were used to select the cases and controls and to check for previous inpatient treatment for schizophrenia and related disorders (the exposure or explanatory variable). One vital point about this study, and all case-control studies worth reading, is that it was a nested case-control study. This means that the data about the cases and controls used in the study were nested within, or taken from, a cohort study. Importantly, a cohort study involves collecting data about every single person from a predefined cohort, or group of people, usually of the same age or era. In this study, a time cohort was used matching the years during which the suicide rates had decreased in Denmark's general population (1981-97). This means that the cases studied were every single person in Denmark whose death was recorded as suicide on national registers during the years 1981-97 (a total of 18 744 cases); the controls were taken from a random selection of 5% of the remainder of Denmark's population. For every case, 20 controls matched for birth year, sex, and calendar time were selected, giving a total of 374 880 controls. So why is this point so important? Given that the objective of a case-control study is to look at the relative exposure-disease risk between cases and controls, the meaningfulness of the comparison depends entirely on what the relationship is between cases and controls. In this study, the researchers simply wanted to look at people who committed suicide versus those who did not, making anyone who lived in Denmark in 1981-97 and did not commit suicide an eligible control. For the data to have any meaning then, it was vital that the controls were drawn from exactly this group of people, and so from the same cohort as the cases. The researchers achieved this by randomly selecting their control sample from national registers listing everyone in the Danish population.

What does the study show?

The study found that the cases were 20 times more likely to have been treated for schizophrenia and related disorders than those in the control group. The increased risk of suicide in this group, however, remained consistent in 1981-97, meaning that although the suicide rate in the general population had decreased during this period, the suicide rate among people treated for schizophrenia also fell in line with this decrease. The only exception was cases diagnosed as having "other psychoses in the schizophrenia spectrum," for whom the suicide rate fell at a faster rate than for the other schizophrenia case categories and the controls. The researchers also looked at suicide risk for different subcategories of cases and found the risk highest during, and in the first month after, an inpatient stay, but gradually decreasing the longer the duration since discharge.

One of the problems of nested case-control studies is the issue of confounding. It is easy to assume that because the exposure variable is evidently associated with the disease, in this case suicide, that the exposure variable is therefore in some way instrumental in the increased risk. But the risk associated with the explanatory variable may in fact be caused by a third confounding factor, which is associated with both exposure and the disease under study. In this study, factors that are associated with both a diagnosis of schizophrenia and suicide risk include some social and demographic factors (for example, lower socio-economic status is associated with increased suicide risk but is also often an outcome of schizophrenic breakdown). To deal with this problem the researchers reanalysed the data, adjusting for the sociodemographic status of the cases versus the controls. When these factors were levelled out between the groups, the data showed that the increased relative risk of suicide in the case group fell from 20 times to 12 times greater, suggesting that unfavourable socio-demographic factors also contribute considerably to the increased risk of suicide in people treated for schizophrenia. Although in this instance the researchers were able to identify and statistically control for the effect of socio-demographic factors on suicide risk, confounding factors cannot always be anticipated. This would not necessarily invalidate the findings of a study, but if left unacknowledged could result in some misleading conclusions.

Was it a good study?

Nested case-control studies can help us to understand the different factors that can put people at greater risk of disease and the times when an individual might be at most risk. This study was able to show that at certain points after an individual is diagnosed as having schizophrenia they are particularly at risk and that extra care should be taken at these times. By studying a period during which the suicide rates for the general population were falling, the researchers could also look to see if positive changes affecting the general population or other changes to psychiatric care might be having a positive effect on suicide rates in schizophrenic individuals.

As nested case-control studies are observational studies, however, causal inference is limited and is at best speculative. Recall bias (or people recalling information about their past inaccurately) is often a problem with nested case-control studies in which self reported data is used. Use of national records and attention to confounding variables, however, make this a good example of a nested case-control study.

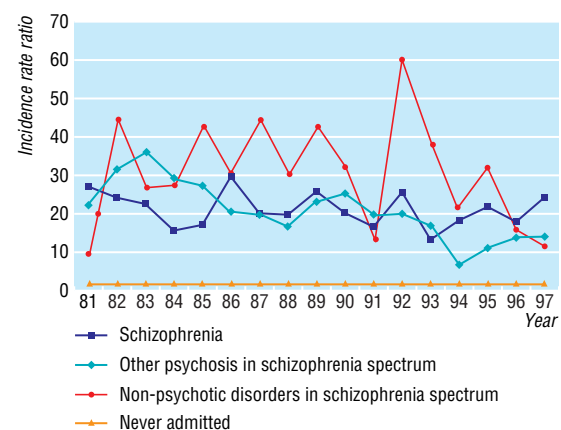


Fig 2 Incidence rate ratio for suicide in patients with schizophrenia and related disorders, relative to general population. Adjusted for age and sex