# Thirty-Day Mortality After Infection Among Persons With Severe Mental Illness: A Population-Based Cohort Study in Denmark

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**Objective:** Persons with severe mental illness die 15–20 years earlier on average than persons without severe mental illness. Although infection is one of the leading overall causes of death, no studies have evaluated whether persons with severe mental illness have a higher mortality after infection than those without.

**Method:** The authors studied mortality rate ratios and cumulative mortality proportions after an admission for infection for persons with severe mental illness compared with persons without severe mental illness by linking data from Danish national registries.

**Results:** The cohort consisted of all persons hospitalized for infection during the period 1995–2011 in Denmark (N=806,835), of whom 11,343 persons had severe mental illness. Within 30 days after an infection, 1,052 (9.3%) persons with a history of severe mental illness and 58,683 (7.4%) persons without a history of severe mental illness died. Thirty-day mortality after any infection was 52% higher in persons with severe mental illness than in persons without (mortality rate ratio=1.52, 95% CI=1.43–1.61). Mortality was increased for all infections, and the mortality rate ratios ranged from 1.27 (95% CI=1.15–1.39) for persons hospitalized for sepsis to 2.61 (95% CI=1.69–4.02) for persons hospitalized for CNS infections. Depending on age, 1.7 (95% CI=1.2–2.2) to 2.9 (95% CI=2.0–3.7) more deaths were observed within 30 days after an infection per 100 persons with a history of severe mental illness compared with 100 persons without such a history.

**Conclusions:** Persons with severe mental illness have a markedly elevated 30-day mortality after infection. Some of these excess deaths may be prevented by offering individualized and targeted interventions.

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Persons with severe mental illness, defined as those with schizophrenia and bipolar affective disorder, have a life expectancy gap of 15–20 years, which is mostly explained by natural causes of death (1, 2). The underlying causes of this excess mortality are not completely understood, but previous research has pointed to higher prevalences of noncommunicable physical diseases (e.g., diabetes and cardiovascular disease) (2–4), poor quality of medical health care (5–7), dysregulation of stress response systems (8), and adverse health behaviors (e.g., smoking and substance abuse) (9, 10).

Although infections are common conditions and leading causes of death (11), it remains unclear whether poor prognosis after infection contributes to the excess mortality among persons with severe mental illness. Identification of higher mortality after infection among persons with severe mental illness may lead to health care interventions that could reduce the inequality in health outcomes for this group of patients. Deaths due to infections are unnecessary and are potentially preventable by affordable and readily available treatment. Three studies have shown that persons with severe mental illness have three to seven times the risk of having an infection-related cause of death compared with persons without severe mental illness (2, 12, 13), but the quality of routinely collected information on causes of death is known to be poor (14). Furthermore, studies of causes of death cannot help us understand whether persons with severe mental illness are more prone to catching an infection or to dying when they have an infection. Distinction between these two types of risks is important, as they call for different clinical interventions.

The aim of this study was to investigate the relative risk and the absolute risk of dying within 30 days after hospitalization for an infection among persons with severe mental illness as compared with persons without severe mental illness in a large population-based cohort between 1995 and 2011.

## METHOD

We conducted a population-based cohort study using data from nationwide Danish registries. These registries contain information on Danish citizens, and all data are recorded with reference to a 10-digit civil registration number, a unique personal identification number assigned to all residents of Denmark. This number provides accurate linkage of information at the individual level (15). All diagnoses in the Danish national registers are classified according to the Danish-language version of ICD-8 before 1994, and according to ICD-10 starting January 1, 1994.

### Procedures

*Study population and all-cause mortality.* We used the Danish Civil Registration System (15) and the Danish National Patient Register (16) to establish our study cohort. The Civil Registration System includes information on gender, date of birth, and continuously updated information on vital status and migration since 1968. Our study population consisted of all persons who were born in Denmark, were at least 15 years old, and had a first-time hospitalization for infection between 1995 and 2011. All deaths occurring within 30 days or 12 months after the date of a first-time hospitalization for an infection were identified from the Civil Registration System between 1995 and 2011.

*Psychiatric illness.* Information on psychiatric disorders was obtained from the Danish Psychiatric Central Register (17), which contains information on all admissions to psychiatric hospitals in Denmark since 1969 and outpatient mental health contacts (comprising all contacts with psychiatric ambulatory care) since 1995. All psychiatric admissions in Denmark with a diagnosis of severe mental illness (defined as those with schizophrenia and bipolar affective disorder) recorded between 1969 and 2011 were identified. Outpatient contacts (excluding psychiatric emergency contacts) from 1995 onward were also included.

*Infections.* Information on hospitalizations for infections was obtained from the National Patient Register (16), which contains information on all Danish medical inpatient hospital contacts since 1977 and outpatient contacts since 1995. All first-time inpatient hospitalizations for infections (i.e., primary and secondary discharge diagnoses of infection) between 1994 and 2011 were identified and categorized according to the type of infection causing the hospitalization (see the appendix in the data supplement that accompanies the online edition of this article). To avoid including rehospitalizations, we excluded persons admitted with an infection during the year preceding the start of follow-up.

*Deaths due to infectious causes.* Information on causes of death was obtained from the Danish Register of Causes of Death (14), which contains information on all deaths of Danish citizens and residents between 1970 and 2010. Causes of death due to infections were divided into the same categories as the hospital contacts for infections. All deaths due to infectious causes within 30 days after admission for an infection were identified between 1995 and 2010.

*Potential moderators.* Information on diabetes was obtained from the Danish National Diabetes Register (18) between 1995 and 2011. The applied algorithm for identifying individuals with diabetes has been shown to have a sensitivity of 86% and a positive predictive value of 89% (18); it has been described in detail elsewhere (4, 18). All contacts based on a diagnosis of cardiovascular disease and all contacts based on diagnoses of chronic diseases included in the Charlson comorbidity index (19) were identified from the National Patient Register between 1977 and 2011. All contacts based on a diagnosis of substance abuse (i.e., alcohol-related or drug-related substance abuse, excluding tobacco abuse) were identified from the Psychiatric Central Register or the National Patient Register between 1969 and 2011. Information on education level was obtained from Statistics Denmark (20), which maintains a data bank with socioeconomic information on all citizens in Denmark from 1980 onward. As education level was unknown for a substantial proportion of individuals over age 70, we adjusted for education level in a sensitivity analysis among those under age 70.

### Statistical Analysis

We included persons over age 15 in the study cohort when they were admitted with a first-time infection during the study period, and these individuals were censored 30 days after the admission, on the date of death, on the date of emigration, or on April 30, 2011, whichever came first.

Mortality rate ratios were calculated for the all-cause 30-day mortality after any infection and for different categories of infections for persons with severe mental illness as compared with persons without. We also performed several sensitivity analyses. First, we evaluated the 30-day mortality rate ratio among the subpopulation that was over age 18 at the time of infection diagnosis. Second, we evaluated the 30-day mortality rate ratios for the periods before and after discharge from the hospital. Third, we evaluated separate effects of infection on persons with schizophrenia and bipolar affective disorder. Fourth, we evaluated the mortality rate ratios for the all-cause mortality for each month of the first year after an admission for infection. Finally, we evaluated the mortality rate ratios for death due to infectious causes, as stated in the death certificate, within 30 days after a hospitalization for infection. All mortality rate ratios were adjusted for age, gender, and calendar period.

We fitted three models of survival analysis to the all-cause mortality outcome after admission for any infection and evaluated them for four different time periods during the 30 days after admission for an infection: 0–30 days, 0–7 days, 8–14 days, 15–21 days, and 22–30 days. The first model included demographic characteristics (age and gender) and calendar period, and we additionally included education level

as a sensitivity analysis. The second model added clinical comorbidity (diabetes, cardiovascular disease, and Charlson comorbidity index score), and the third added substance abuse.

All-cause mortality was analyzed with time since infection diagnosis as a time scale, and cumulative mortality proportions for up to 30 days after the date of admission were estimated by Kaplan-Meier curves. The risk of dying within 30 days after admission for any infection was estimated for persons with and without severe mental illness. In addition, we calculated risk differences (i.e., cumulative mortality proportion differences) between persons with and without severe mental illness for each age category.

Data were analyzed by using log-linear Poisson regression analysis, with the logarithm of the person-years as an offset variable, using Stata, version 13 (StataCorp, College Station, Tex.). All variables except gender were treated as time-dependent variables. Adjustments for age and calendar period were performed using 5-year age bands and 4-year time bands, respectively. The assumption of piecewise constant intensity for the Poisson regression model was checked. The p values and 95% confidence intervals were based on likelihood ratio tests.

## RESULTS

### Thirty-Day All-Cause Mortality After a Hospital Admission for Infection

During the study period, 806,835 persons were hospitalized because of an infection, of whom 11,343 had severe mental illness (7,388 with schizophrenia and 3,955 with bipolar affective disorder) (Table 1).

Admission for infection was followed by a markedly increased mortality, not only for persons with severe mental illness, but also for those without (Figure 1). A total of 59,735 persons died within 30 days after admission for infection, of whom 1,052 (9.3%) had severe mental illness (654 with schizophrenia and 398 with bipolar affective disorder).

The overall mortality rate ratio for all-cause mortality within 30 days after admission for any infection for persons with severe mental illness as compared with those without was 1.52 (95% CI=1.43–1.61) (Figure 2). This estimate did not differ when evaluated in the subpopulation of persons over age 18 (results not shown). The mortality rate ratio tended to be marginally higher for the period after discharge compared with the period before discharge (before discharge, mortality rate ratio=1.37, 95% CI=1.27–1.49; after discharge, mortality rate ratio=1.60, 95% CI=1.45–1.76). The mortality rate ratio was significantly lower for persons with bipolar affective disorder (mortality rate ratio=1.27, 95% CI=1.15–1.40) than for persons with schizophrenia (mortality rate ratio=1.71, 95% CI=1.58–1.85) ($p<0.001$) when compared with persons without severe mental illness (see Figures S1 and S2 in the online data supplement).

The mortality rate ratios for persons with severe mental illness as compared with those without were virtually the same for women and men, but decreased with age. In addition, the mortality rate ratios among persons with severe mental illness compared with those without were lower for those with comorbid diabetes, cardiovascular disease, or substance abuse and decreased with increasing number of comorbidities (i.e., increasing Charlson comorbidity index score). The mortality rate ratios were higher after all types of infections among persons with severe mental illness compared with those without severe mental illness, ranging from 1.27 (95% CI=1.15–1.39) for sepsis to 2.61 (95% CI=1.69–4.02) for CNS infections (Figure 2).

Adjusting all-cause mortality rate ratio after any infection for comorbidity and substance abuse did not change the estimate significantly (Table 2). Adjusting for education level in a subanalysis did not change the estimate significantly either (results not shown). The excess mortality rate ratios for persons with severe mental illness were similar for different time periods within the 30 days after admission (Table 2).

The absolute risks of dying within 30 days after admission for any infection (i.e., the cumulative mortality proportion) for persons with and without severe mental illness were 2.3% (95% CI=1.9–2.9) and 0.6% (95% CI=0.6–0.7), respectively, for those under age 50; 8.9% (95% CI=8.1–9.8) and 6.1% (95% CI=5.9–6.2), respectively, for those 50–70 years of age, and 16.8% (95% CI=15.6–18.1) and 14.2% (95% CI=14.1–14.3), respectively, for those over age 70 (Figure 3). This corresponds to a cumulative mortality proportion risk difference of 1.7 percentage points (95% CI=1.2–2.2), 2.9 percentage points (95% CI=2.0–3.7), and 2.6 percentage points (95% CI=1.3–3.9) for persons with severe mental illness compared with those without in these three age groups, respectively.

### All-Cause Mortality Within 12 Months After Admission for Infection

Overall mortality rates after an admission for infection were particularly increased during the first 30 days for persons with severe mental illness as well as for those without (Figure 1). The mortality rate ratio for persons with severe mental illness compared with those without tended to be particularly high during the first 30 days, during which period the underlying mortality rate was also high. The mortality after admission for infection remained higher for persons with severe mental illness than for those without for up to 12 months after hospitalization (at 12 months, mortality rate ratio=1.31, 95% CI=1.03–1.66), although the difference was not always statistically significant (Figure 1). The estimates did not change when the mortality rate ratios within the 12-month period after an infection admission were adjusted for comorbidity and substance abuse (results not shown).

### Infectious Causes of Death Within 30 Days After Admission for Infection

In a sensitivity analysis, we restricted the study period to 1995–2010, during which information on causes of death was

**TABLE 1. Patient Characteristics at First-Time Hospitalization for Any Infection, as Registered in the Danish National Patient Register for Persons With and Without a History of Severe Mental Illness in a Population-Based Cohort From Denmark, 1995–2011 (N=806,835)[a]**

| | Without Severe Mental Illness | | | With Severe Mental Illness | | |
|---|---|---|---|---|---|---|
| Measure | N | % | Person-Years at Risk[b] | N | % | Person-Years at Risk[b] |
| Hospitalizations for any infection | 795,492 | | 62,200 | 11,343 | | 881 |
| Age (years) | | | | | | |
| <50 | 283,704 | 35.7 | 23,137 | 3,468 | 30.6 | 282 |
| 50–69 | 192,569 | 24.2 | 15,168 | 4,470 | 39.4 | 347 |
| ≥70 | 319,219 | 40.1 | 23,895 | 3,405 | 30.0 | 252 |
| Gender | | | | | | |
| Female | 432,535 | 54.4 | 34,042 | 6,158 | 54.3 | 479 |
| Male | 362,957 | 45.6 | 28,158 | 5,185 | 45.7 | 402 |
| Calendar period | | | | | | |
| 1995–1998 | 187,380 | 23.6 | 14,571 | 2,160 | 19.0 | 163 |
| 1999–2002 | 194,141 | 24.4 | 15,225 | 2,640 | 23.3 | 205 |
| 2003–2006 | 198,194 | 24.9 | 15,518 | 3,056 | 26.9 | 237 |
| 2007–2011 | 215,777 | 27.1 | 16,886 | 3,487 | 30.8 | 275 |
| Diabetes | | | | | | |
| No | 713,909 | 89.7 | 55,556 | 9,673 | 85.3 | 743 |
| Yes | 81,583 | 10.3 | 6,644 | 1,670 | 14.7 | 138 |
| Cardiovascular disease | | | | | | |
| No | 528,004 | 66.4 | 38,290 | 7,839 | 69.1 | 562 |
| Yes | 267,488 | 33.6 | 23,910 | 3,504 | 30.9 | 318 |
| Charlson comorbidity index score | | | | | | |
| 0 | 433,469 | 54.5 | 31,059 | 5,882 | 51.9 | 391 |
| 1 | 129,673 | 16.3 | 10,784 | 2,094 | 18.4 | 182 |
| 2 | 109,269 | 13.7 | 9,102 | 1,734 | 15.3 | 151 |
| ≥3 | 123,081 | 15.5 | 11,255 | 1,633 | 14.4 | 157 |
| Substance abuse disorder | | | | | | |
| No | 733,543 | 92.2 | 57,263 | 7,290 | 64.3 | 561 |
| Yes | 61,949 | 7.8 | 4,937 | 4,053 | 35.7 | 320 |

[a] Persons with severe mental illness comprised persons with schizophrenia and bipolar affective disorder. With the exception of gender distribution, the groups with and without severe mental illness differed significantly in all baseline characteristics (p values <0.001).
[b] Person-years at risk=person-years at risk of dying within 30 days after an infection.

available, and examined infection as a cause of death. Within 30 days after an infection admission, 247 (25.7%) deaths among persons with severe mental illness and 9,565 (17.9%) deaths among persons without were classified as infectious deaths on the death certificates (see Table S1 in the online data supplement). Correspondingly, the mortality rate ratio was 2.61 (95% CI=2.30–2.96) for death due to infection when comparing persons with severe mental illness to persons without.

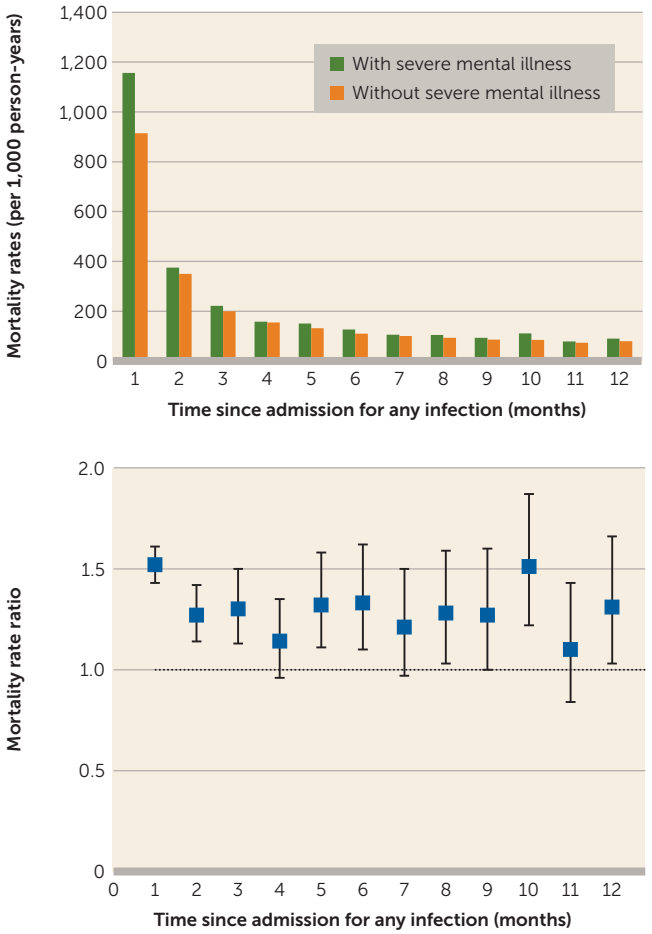
## DISCUSSION

This large population-based study showed that the mortality was high after hospitalization for infection for everyone, but it was substantially (52%) higher during the 30 days after admission for an infection for persons with severe mental illness than for those without. The excess risk of death after infection depended on the type of infection, with the increase in risk ranging from 27% after admission for sepsis to 161% after admission for a CNS infection. Depending on age, 1.7 to 2.9 more deaths were observed per 100 persons with a history of severe mental illness within 30 days after admission for infection when compared with 100 persons without such a history.

Our study has several strengths, including the large population-based cohort, which was followed without loss to follow-up. Bias due to selection of study subjects, loss to follow-up, and nonresponse is therefore unlikely to explain our findings. The data we used on psychiatric hospital contacts, hospitalizations for infection, and all-cause mortality have high validity and completeness, which minimizes any potential information bias. The diagnosis of schizophrenia has been shown to have a sensitivity of 93% and a positive predictive value of 87% in the Danish Psychiatric Central Register (21). The diagnosis of infection has been shown to have a positive predictive value of 95% in the National Patient Register (22), and the completeness of registration of death is considered to be close to 100% in the Civil Registration System (15).

This study was, however, limited by the lack of some important clinical information. For example, we had access to information only on persons who were treated for their infection in a hospital setting. Our results therefore may not apply to persons with less severe infections who were treated in primary care settings or in psychiatric wards or were left untreated. We did adjust for several potential intermediate variables, and these analyses did not change the results

**FIGURE 1. All-Cause Mortality Rates and All-Cause Mortality Rate Ratios for the 12 Months After First-Time Hospitalization for Infections Among Persons With Severe Mental Illness Compared With Those Without in Denmark, 1995–2011 (N=806,835)[a]**




[a] Mortality rate ratios were adjusted for age, gender, and calendar period.

significantly. However, substance abuse and comorbid physical diseases may be underdiagnosed among persons with severe mental illness (23, 24), which could lead to an underestimation of the excess mortality accounted for by these intermediate variables. We were unable to include information on adverse health risk factors that could potentially be associated with mortality, such as body mass index, smoking, sedentary lifestyle, and low socioeconomic status, as these data either were not available or were substantially affected by missing information. Consequently, residual confounding cannot be excluded. This study was conducted in a country with free and equal access to health care, and therefore our results may be generalizable only to countries with similar health care systems. Because receipt of care among persons with severe mental illness may be somewhat lower in countries in which access to health care depends on health insurance (25), our results may represent conservative estimates of the excess mortality after an infection for persons with severe mental illness.

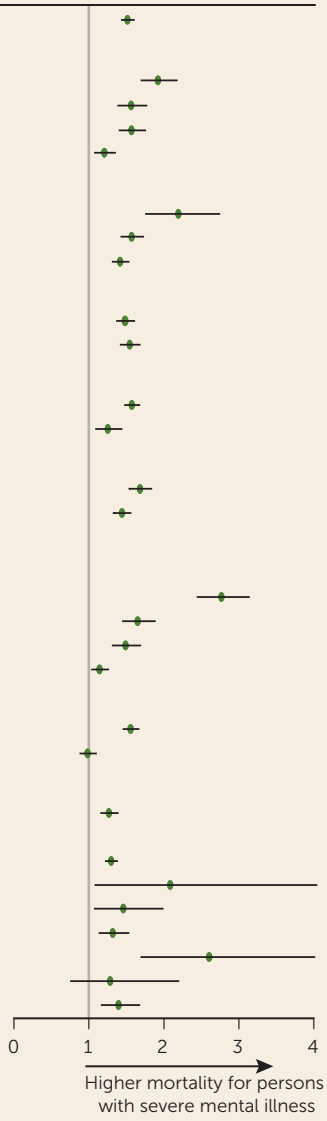
Although previous studies have shown that infections are a predictor for subsequent development of severe mental illness (26–28) and that severe mental illness is a risk factor for infections (12, 13), to our knowledge no studies have been published in the psychiatric literature on prognosis after admission for infections. A few studies have reported that the risk of death from pneumonia (12, 13) and from any infection (2) is three to seven times higher in persons with severe mental illness than in those without. However, these studies evaluated the mortality rate ratios exclusively on the basis of information from death certificates. The quality of cause-of-death registrations is known to vary on death certificates (14), which makes the cause-specific mortality prone to bias if the certificate registrations vary between persons with and without severe mental illness. Also, the significance of infection for the risk of premature death is likely to be underestimated when considering death certificates only, since infection may contribute to fatal conditions other than infection that may be recorded as the cause of death.

Our study is the first to show, on the basis of highly valid data on all-cause mortality from the Civil Registration System, that all-cause mortality is increased after hospitalization for any infection in persons with severe mental illness. We also conducted a sensitivity analysis using data from the Danish Register of Causes of Death to evaluate the risk of infectious death as stated in death certificates in our hospitalized cohort. Persons with severe mental illness had a 2.6-fold higher risk of infectious causes of death than those without severe mental illness. This ratio is lower than that previously reported in a Nordic study of persons with recent onset of psychiatric illness, which found that the risk of death due to infectious causes was two to five times higher for persons with a psychiatric disorder than those without (2). Yet the Nordic study included a younger cohort and studied the long-term outcome for persons with severe mental illness, whereas our study was restricted to a 30-day period after admission for infection among persons with severe mental illness. Thus, these estimates are hardly comparable.

The presence of medical comorbidities is associated with poorer outcome for persons from the general population hospitalized for an infection (29, 30), and persons with severe mental illness generally have higher rates of all types of chronic physical illnesses (31). Also, severe mental illness is known to be associated with substance abuse (9), which is also independently associated with poorer outcome after infections (32). However, adjusting for these variables in our analyses decreased the risk only slightly, which suggests that other explanations for this excess mortality are more likely. Persons with severe mental illness could potentially have received suboptimal care for their infection or could have experienced treatment delays within the health care system, leading to greater severity of the infection. Several studies have shown that persons with severe mental illness generally receive suboptimal treatment for medical diseases, although this has only been documented for noncommunicable diseases (5–7). It has also been shown that persons with severe

**FIGURE 2. Mortality Rate Ratios for All-Cause Mortality up to 30 Days After First-Time Hospitalization for Infections Among Persons With Severe Mental Illness Compared With Those Without in Denmark, 1995–2011 (N=806,835)[a]**

| Measure | Deaths: Without Severe Mental Illness | Deaths: With Severe Mental Illness | Mortality Rate Ratio | 95% CI |
|---|---|---|---|---|
| Any infection | 58,683 | 1,052 | 1.52 | 1.43–1.61 |
| Calendar period | | | | |
| 1995–1998 | 12,685 | 241 | 1.92 | 1.69–2.19 |
| 1999–2002 | 13,978 | 245 | 1.57 | 1.38–1.78 |
| 2003–2006 | 15,165 | 292 | 1.57 | 1.40–1.76 |
| 2007–2011 | 16,855 | 274 | 1.21 | 1.07–1.36 |
| Age | | | | |
| <50 years | 1,797 | 79 | 2.20 | 1.75–2.75 |
| 50–69 years | 11,593 | 400 | 1.57 | 1.42–1.73 |
| ≥70 years | 45,293 | 573 | 1.42 | 1.31–1.54 |
| Gender | | | | |
| Women | 27,680 | 553 | 1.48 | 1.36–1.61 |
| Men | 31,003 | 499 | 1.55 | 1.41–1.69 |
| Diabetes | | | | |
| No | 48,968 | 864 | 1.57 | 1.47–1.68 |
| Yes | 9,715 | 188 | 1.25 | 1.08–1.45 |
| Cardiovascular disease | | | | |
| No | 18,328 | 474 | 1.68 | 1.54–1.84 |
| Yes | 40,355 | 578 | 1.44 | 1.33–1.57 |
| Charlson comorbidity index score | | | | |
| 0 | 7,696 | 245 | 2.77 | 2.44–3.15 |
| 1 | 11,468 | 213 | 1.65 | 1.44–1.89 |
| 2 | 12,922 | 232 | 1.49 | 1.31–1.70 |
| ≥3 | 26,597 | 362 | 1.14 | 1.03–1.27 |
| Substance abuse | | | | |
| No | 52,317 | 752 | 1.56 | 1.45–1.67 |
| Yes | 6,366 | 300 | 0.98 | 0.88–1.11 |
| Type of infection | | | | |
| Sepsis | 19,881 | 431 | 1.27 | 1.15–1.39 |
| Respiratory | | | | |
| Pneumonia | 49,467 | 897 | 1.30 | 1.21–1.39 |
| Other respiratory | 453 | 9 | 2.15 | 1.11–4.16 |
| Gastrointestinal | 3,044 | 40 | 1.46 | 1.07–2.00 |
| Urinary tract | 10,014 | 168 | 1.32 | 1.13–1.54 |
| CNS | 1,158 | 21 | 2.61 | 1.69–4.02 |
| HIV and hepatitis | 330 | 14 | 1.28 | 0.75–2.20 |
| Other | 6,608 | 112 | 1.40 | 1.16–1.68 |




[a] The figure shows the mortality rate ratios for all-cause mortality after a hospitalization for different categories of infections among persons with a history of severe mental illness compared with persons without such a history.

mental illness are likely to be discriminated against (33) and to experience "diagnostic overshadowing" (i.e., misattribution of physical illness signs and symptoms to concurrent mental disorders), leading to poorer-quality physical health care (34). It is notable that our study includes only persons who have already been identified, diagnosed, and hospitalized for their infection by the health care system. Consequently, the health care contact has already been established and antibiotic treatment and supportive care are presumably available and do not depend on whether the patient has a history of severe mental illness.

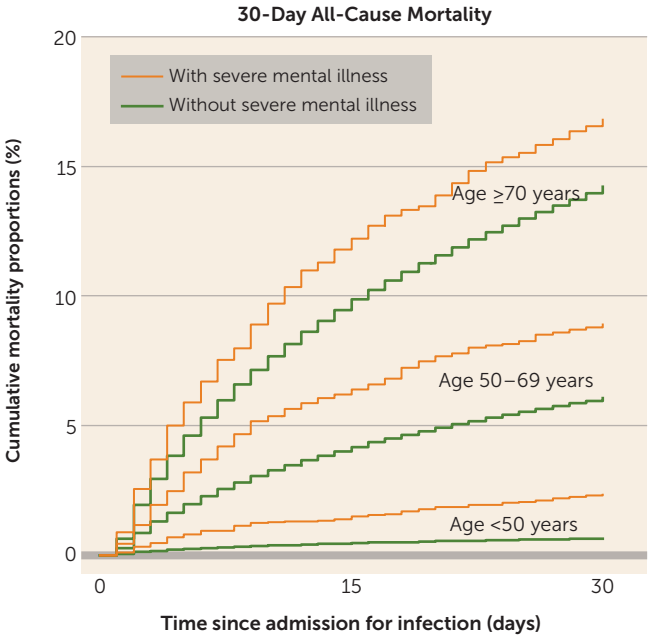
Nevertheless, treatment of persons with severe mental illness can pose a difficult challenge for clinicians, and discrimination and suboptimal delivery of in-hospital and follow-up care may therefore play an important role in the inequality in outcome (5–7, 33). In addition, many persons with schizophrenia have cognitive and social dysfunctions that could hamper self-care, engagement in treatment, and adherence (35). Thus, persons with severe mental illness may have a higher risk of premature death if they present to health care professionals with symptoms of infection late in the disease course, self-discharge

**TABLE 2. Mortality Rate Ratios for All-Cause Mortality up to 30 Days After First-Time Hospital Admission for Any Infection (N=59,735) Among Persons With Severe Mental Illness Compared With Those Without in Denmark, 1995–2011 (N=806,835)**

| | Deaths (N) | | Model 1[a] | | Model 2[b] | | Model 3[c] | |
|---|---|---|---|---|---|---|---|---|
| Interval | Without Severe Mental Illness | With Severe Mental Illness | Mortality Rate Ratio | 95% CI | Mortality Rate Ratio | 95% CI | Mortality Rate Ratio | 95% CI |
| 0–30 days | 58,683 | 1,052 | 1.52 | 1.43–1.61 | 1.59 | 1.50–1.69 | 1.52 | 1.43–1.61 |
| 0–7 days | 24,788 | 475 | 1.60 | 1.46–1.75 | 1.66 | 1.52–1.82 | 1.56 | 1.42–1.71 |
| 8–14 days | 14,366 | 252 | 1.49 | 1.32–1.69 | 1.58 | 1.39–1.79 | 1.50 | 1.32–1.70 |
| 15–21 days | 9,925 | 175 | 1.49 | 1.29–1.74 | 1.58 | 1.36–1.84 | 1.54 | 1.32–1.79 |
| 22–30 days | 9,604 | 150 | 1.32 | 1.12–1.55 | 1.40 | 1.19–1.65 | 1.37 | 1.17–1.62 |

[a] Adjusted for age, gender, and calendar period.
[b] Additionally adjusted for diabetes, cardiovascular disease, and Charlson comorbidity index score (excluding diabetes and cardiovascular disease).
[c] Additionally adjusted for substance abuse.

**FIGURE 3. Age-Stratified Cumulative Mortality Curves for All-Cause Mortality Within 30 Days After First-Time Hospitalization for Any Infection Among Persons With and Without Severe Mental Illness During Follow-Up, 1995–2011 (N=806,835)[a]**




[a] Estimated cumulative mortality curves for the all-cause mortality by the Kaplan-Meier estimator for up to 30 days after a hospitalization for any infection, plotted by applying hazard ratios for death from any cause (specific for age at risk) from this study's analyses.

prematurely from hospital, or fail to follow up appropriately after hospitalization.

Interestingly, this study showed that the highest excess risk appears after admission for a CNS infection. This may be explained by delayed detection of CNS infections among persons with severe mental illness because recognition of deviations in neurological behaviors in this group may be confounded by baseline cognitive status, psychotic symptoms, or abnormal behavior.

Finally, increased vulnerability or even familial liability to infection has been suggested to exist among those with severe mental illness (36). Such vulnerability could possibly lead to more severe and treatment-resistant infections (36) and thereby increase the risk of dying after an infection. In line with this hypothesis, we found that the mortality among persons with severe mental illness tended to remain significantly elevated in the year after admission for an infection compared with the mortality among persons without severe mental illness, even after adjusting for potential intermediate variables. This suggests that persons with severe mental illness who have an infection or are hospitalized for one constitute a vulnerable group with a persistently high risk of premature death, independent of co-occurring noncommunicable physical illnesses. Because we studied only first-time hospitalizations, we do not know whether persons with severe mental illness and a first-time hospitalization for an infection are in fact susceptible to repeated hospitalizations for infections and subsequent premature death.

## CONCLUSIONS

Persons with severe mental illness have a markedly elevated risk of dying within 30 days after a hospital admission for any type of infection. As infections are common and treatment is affordable and available, some of these excess deaths may be prevented by offering individualized and targeted interventions. Further research should identify which steps on the pathway between infection and death, such as physician delay, patient delay, underdiagnosis, or undertreatment, may account for this excess mortality.

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