

# Somatic Hospital Contacts, Invasive Cardiac Procedures, and Mortality From Heart Disease in Patients With Severe Mental Disorder

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**Context:** Excess mortality from heart disease is observed in patients with severe mental disorder. This excess mortality may be rooted in adverse effects of pharmacological or psychotropic treatment, lifestyle factors, or inadequate somatic care.

**Objectives:** To examine whether persons with severe mental disorder, defined as persons admitted to a psychiatric hospital with bipolar affective disorder, schizoaffective disorder, or schizophrenia, are in contact with hospitals and undergoing invasive procedures for heart disease to the same degree as the nonpsychiatric general population, and to determine whether they have higher mortality rates of heart disease.

**Design, Setting, and Participants:** A population-based cohort of 4.6 million persons born in Denmark was followed up from 1994 to 2007. Rates of mortality, somatic contacts, and invasive procedures were estimated by survival analysis.

**Main Outcome Measures:** Incidence rate ratios of heart disease admissions and heart disease mortality as well as probability of invasive cardiac procedures.

**Results:** The incidence rate ratio of heart disease contacts in persons with severe mental disorder compared with the rate for the nonpsychiatric general population was only slightly increased, at 1.11 (95% confidence interval, 1.08-1.14). In contrast, their excess mortality rate ratio from heart disease was 2.90 (95% confidence interval, 2.71-3.10). Five years after the first contact for somatic heart disease, the risk of dying of heart disease was 8.26% for persons with severe mental disorder (aged <70 years) but only 2.86% in patients with heart disease who had never been admitted to a psychiatric hospital. The fraction undergoing invasive procedures within 5 years was reduced among patients with severe mental disorder as compared with the nonpsychiatric general population (7.04% vs 12.27%, respectively).

**Conclusions:** Individuals with severe mental disorder had only negligible excess rates of contact for heart disease. Given their excess mortality from heart disease and lower rates of invasive procedures after first contact, it would seem that the treatment for heart disease offered to these individuals in Denmark is neither sufficiently efficient nor sufficiently intensive. This undertreatment may explain part of their excess mortality.

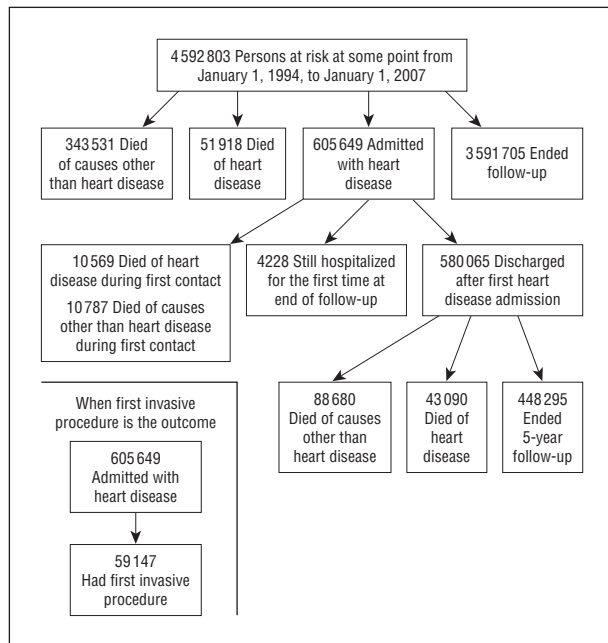
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**H**EART DISEASE IS THE LEADING cause of death in Denmark, where it accounted for at least 31% of all deaths from 1970 to 2002.<sup>1</sup> During the 1990s and 2000s, the mortality from heart disease in Denmark and the United States declined owing mainly to improved treatment, such as the use of new pharmacological treatment of myocardial infarction, and to a lesser degree because of improvement in primary prevention.<sup>2-5</sup>

Patients with severe mental disorder, including schizophrenia, schizoaffective disorder, and bipolar affective disorder, have particularly high mortality from heart disease.<sup>6</sup> Suicide in psychiatric patients has received much attention because it is a ma-

ajor cause of “years of life lost,” but excess mortality from heart disease is responsible for an even larger share of the total of years of life lost in this patient group.<sup>6,7</sup> The reasons proposed to explain this excess mortality from heart disease include adverse effects of pharmacological treatment<sup>8</sup>; unhealthy diets potentially causing obesity, hyperlipidemia, hypertension, and diabetes mellitus<sup>9</sup>; high rates of cigarette smoking<sup>10,11</sup>; and negative social consequences of having a mental disorder.<sup>12</sup> Primary prevention aimed, for instance, at reducing smoking is important, but somatic monitoring including screening for lipid-lowering pharmacotherapy, invasive cardiac procedures, or other potential life-prolonging steps are also crucial elements in countering this excess mortality.<sup>2</sup>

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**Figure 1.** Number of cohort members, heart disease contacts, invasive procedures, and deaths by heart disease.

Health care in Denmark is free of charge; therefore, Danish citizens should in principle have equal access to somatic and psychiatric health care. The question is, however, whether equal access also implies equal and sufficient treatment and care.

The principal aim of this article was to use the Danish registers to examine whether individuals with severe mental disorder, defined as persons previously admitted to a psychiatric hospital with schizophrenia, schizoaffective disorder, or bipolar affective disorder, are sufficiently evaluated and monitored by health professionals in somatic departments. This question is addressed by comparing rates of heart disease contacts, rates of subsequent invasive cardiac procedures, and rates of mortality from heart disease in 2 groups: individuals who have never been admitted to a psychiatric hospital, and individuals with severe mental disorder. As individuals with severe mental disorder have a much higher mortality than the general population and are subject to multiple risk factors for heart disease, we expected to find much higher rates of contacts with diagnoses of heart disease and much higher rates of invasive cardiac procedures in this group. Failing to do so could indicate insufficient somatic monitoring and surveillance of individuals with severe mental disorder.

## METHODS

### STUDY POPULATION AND FOLLOW-UP

We identified all persons born in Denmark before January 1, 1994, and still residing in Denmark on that date using the Danish Civil Registration System.<sup>13</sup> The Danish Civil Registration System was established in 1968, at which time all persons alive and living in Denmark were registered and assigned a 10-digit personal identification number used in all registers. The register records information on sex, date of birth, place of birth,

and vital status (eg, date of death and migration out of Denmark). The follow-up of the cohort began on January 1, 1994, or on the cohort member's 15th birthday, whichever came last. Follow-up ended on January 1, 2007, the date of death (including death by heart disease), the date of first contact with heart disease, or the date of emigration, whichever came first. The cohort members who were admitted or had an outpatient contact to a hospital with a heart disease diagnosis during the follow-up period formed the study population for follow-up on death or invasive procedure after heart disease contact (**Figure 1**). Follow-up of these patients started on the date of discharge from the first heart disease contact (the date of first contact, when an invasive procedure was the outcome) and ended after 5 years, on January 1, 2007, the date of death (or the date of operation, when an invasive procedure was the outcome), or the date of emigration, whichever came first. Cohort members admitted to a psychiatric hospital for the first time after first contact with heart disease were censored at the date of the psychiatric admission.

### ASSESSMENT OF PSYCHIATRIC ADMISSION, HEART DISEASE, AND CAUSE OF DEATH

The Danish Psychiatric Central Register<sup>14</sup> includes data on all psychiatric inpatient admissions in Denmark since April 1, 1969, and we identified all persons with severe mental disorder in this register. Only patients admitted to a psychiatric hospital bed were included. Thus, we did not include psychiatric patients receiving only outpatient treatment. Three diagnostic categories were included in the categorization of severe mental disorder: bipolar disorder (*International Classification of Diseases, Eighth Revision [ICD-8]* code<sup>15</sup> 296.19 or 296.39; *ICD-10* code<sup>16</sup> F30 or F31), schizoaffective disorder (*ICD-8* code 295.79 or 296.8; *ICD-10* code F25), and schizophrenia (*ICD-8* code 295 [excluding 295.79]; *ICD-10* code F20).

All persons with hospital contacts with any diagnosis of heart disease were identified from the Danish National Hospital Register,<sup>17</sup> which was established in 1977 and covers information on all Danish somatic inpatient hospital contacts; outpatient contacts were included from January 1, 1995. Two categories were defined, using all diagnostic codes: a broad definition of heart disease (*ICD-10* codes I00-I25, I27, I30-I52; *ICD-8* codes 390-429) and a narrow definition including myocardial infarction (MI) only (*ICD-10* code I21; *ICD-8* code 410). Invasive procedures were defined as coronary artery bypass graft (codes 300.09-302.41), and KFNA-KFNF or percutaneous transluminal coronary angioplasty (codes 303.50, 303.54, 303.59, KFNG02, KFNG05). The Nordic Medico-Statistical Committee classification of surgical procedures was used from 1996.<sup>17</sup> From 1994 to 1996, a national classification system was used.<sup>18</sup> We excluded all persons admitted with heart disease during the 17-year period from 1977 to 1994 preceding the study period. This minimized the mixing of prevalent and incident cases in the follow-up period (1994-2007). After the 17-year wash-out period, we assumed all cases to be incident.

The underlying cause of death was identified from the Cause of Death Register.<sup>19</sup> We used the same definitions for death by heart disease and MI as listed earlier.

### STATISTICAL ANALYSES

In the prospective cohort study, rates of heart disease mortality and heart disease contacts were analyzed using Poisson regression with the GENMOD procedure in SAS version 9.1 statistical software (SAS Institute, Inc, Cary, North Carolina). Outcome measures were denoted as incidence rate ratios (IRRs), where first contact was the end point, and mortality rate ratios

**Table 1. Incidence Rates of Contact and Mortality of Heart Disease by Age Group<sup>a</sup>**

Age, y	Contact With Diagnosis of Heart Disease				Mortality From Heart Disease			
	Never Admitted		Severe Mental Disorder		Never Admitted		Severe Mental Disorder	
	Cases, No.	Rate <sup>b</sup>	Cases, No.	Rate <sup>b</sup>	Cases, No.	Rate <sup>b</sup>	Cases, No.	Rate <sup>b</sup>
≤49	92 265	3.20	1034	6.25	1521	0.05	72	0.44
50-59	101 413	13.48	1185	16.24	2964	0.39	125	1.71
60-69	119 406	24.33	1220	28.67	5809	1.18	153	3.60
70-79	137 323	42.90	1000	39.18	10 862	3.39	237	9.29
≥80	115 664	68.14	558	53.06	25 813	15.21	287	27.29
<b>Total</b>	<b>566 071<sup>c</sup></b>	<b>12.26</b>	<b>4997<sup>c</sup></b>	<b>15.76</b>	<b>46 969<sup>d</sup></b>	<b>1.02</b>	<b>874<sup>d</sup></b>	<b>2.76</b>

<sup>a</sup>Never admitted indicates never admitted to a psychiatric hospital; severe mental disorder, previously admitted to a psychiatric hospital with bipolar disorder, schizoaffective disorder, or schizophrenia.

<sup>b</sup>The rate measures the incidence rate, that is, the number of new cases per 1000 person-years under risk.

<sup>c</sup>A total of 34 437 persons with a psychiatric diagnosis other than bipolar disorder, schizoaffective disorder, or schizophrenia were admitted with heart disease.

<sup>d</sup>A total of 4075 persons with a psychiatric diagnosis other than bipolar disorder, schizoaffective disorder, or schizophrenia died of heart disease.

(MRRs), where death was the end point of interest. All IRRs and MRRs were adjusted for or stratified by sex, calendar time, and age. The IRRs and MRRs were calculated by log-likelihood estimation, and Wald 95% confidence intervals (CIs) were used.

To take the high mortality from all causes into account, we used the Aalen-Johansen method to estimate the probability (cumulative incidence) of dying of heart diseases or being subject to invasive procedures, after discharge from the first hospital contact. The more frequently used Kaplan-Meier product-limit estimator corresponds to the hypothetical situation where individuals who die of other causes are censored, whereas the Aalen-Johansen curves estimate the probability of dying of heart disease (or having an invasive procedure) by taking competing causes of death into account.<sup>20</sup> Aalen-Johansen survival curves were obtained using the SAS macro presented by Rosthøj et al.<sup>21</sup>

## RESULTS

### FIRST SOMATIC HEART DISEASE CONTACT

Among the 4 592 803 cohort members, 605 649 had a diagnosis of heart disease during the follow-up period from 1994 to 2007. Among these, the first heart disease diagnosis was the main diagnosis in 53.05%, an auxiliary diagnosis in 40.11%, and a referral diagnosis in 5.71%; 1.13% had another diagnosis type or a missing diagnosis type. The diagnosis type was distributed almost identically to these percentages among the 4997 persons with severe mental disorder prior to their contact with a diagnosis of heart disease.

The overall incidence rate of first hospital contact with a diagnosis of heart disease was higher for older cohort members than for younger cohort members and higher for men than for women. Persons admitted with severe mental disorder who were younger than 70 years had a higher heart disease contact incidence than persons who had no mental disorder. In the groups aged 70 years or older, persons with severe mental disorder had lower rates than those with no mental disorder (**Table 1**).

These differences in heart disease contact rates between persons admitted with severe mental disorder and persons who had never been admitted to a psychiatric

hospital (reference group) were negligible when we adjusted for age, sex, and calendar period in a Poisson regression: overall IRR, 1.11 (95% CI, 1.08-1.14). As indicated by the incidence rates in Table 1, an effect measure modification by age was present as individuals with severe mental disorder in the groups younger than 70 years had an excess heart disease contact rate, whereas the oldest patients had rates significantly below those of the matching reference groups (**Table 2**).

The group with severe mental disorder was slightly heterogeneous, and patients with schizophrenia had lower rates of somatic contacts with heart disease (IRR=1.04; 95% CI, 1.00-1.08) than those with bipolar disorder (IRR=1.19; 95% CI, 1.14-1.24). As there was no overlap between the CIs, we assumed this difference to be statistically significant. Cohort members with schizoaffective disorder had an IRR of 1.31 (95% CI, 1.23-1.40) for contact with heart disease.

### MORTALITY FROM HEART DISEASE WITHOUT A PRIOR SOMATIC CONTACT WITH HEART DISEASE

In the follow-up period from 1994 to 2007, a total of 51 918 persons (1.13%) died of heart disease (Figure 1) without previous hospital contact with heart disease. Among these, 874 had had a prior admission with a severe psychiatric disorder.

In contrast to the IRR of heart disease contact, we found that the MRR of heart disease for individuals previously admitted with severe mental disorder was highly elevated, at 2.90 (95% CI, 2.71-3.10) compared with persons who had never been admitted to a psychiatric hospital (Table 2). No effect measure modification (interaction) in the overall MRR was observed between sex and psychiatric status. The excess mortality was higher in the younger groups than in the older groups, and it tended to be highest among young women.

Persons with schizophrenia experienced a higher mortality (overall MRR=3.52; 95% CI, 3.22-3.84) than persons with bipolar disorder (MRR=2.50; 95% CI, 2.26-2.78). As there was no overlap between the CIs, we assumed this difference to be statistically significant. The

**Table 2. Incidence and Mortality Rate Ratios of Heart Disease and Myocardial Infarction in Patients Previously Admitted to a Psychiatric Hospital With a Severe Mental Disorder Compared With Patients Never Admitted to a Psychiatric Hospital<sup>a</sup>**

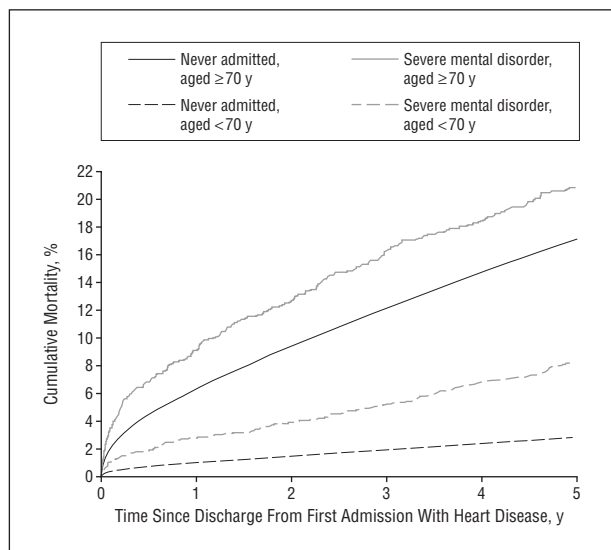
Age, y	Contact		Mortality	
	Patients, No.	IRR (95% CI) <sup>b</sup>	Patients, No.	MRR (95% CI) <sup>c</sup>
<b>Heart disease</b>				
≤49	1034	1.40 (1.32-1.49)	72	5.38 (4.24-6.81)
50-59	1185	1.19 (1.13-1.26)	125	4.52 (3.78-5.41)
60-69	1220	1.20 (1.14-1.27)	153	3.25 (2.77-3.81)
70-79	1000	0.94 (0.89-1.00)	237	2.98 (2.62-3.39)
≥80	558	0.81 (0.74-0.88)	287	2.15 (1.92-2.42)
Overall rate ratio	4997	1.11 (1.08-1.14)	874	2.90 (2.71-3.10)
<b>Myocardial infarction</b>				
≤49	62	0.99 (0.77-1.28)	25	4.29 (2.88-6.40)
50-59	112	1.05 (0.87-1.27)	47	3.86 (2.88-5.16)
60-69	139	1.16 (0.98-1.38)	60	3.03 (2.35-3.92)
70-79	123	1.05 (0.88-1.26)	86	2.92 (2.36-3.61)
≥80	72	1.05 (0.83-1.32)	62	1.93 (1.50-2.48)
Overall rate ratio	508	1.07 (0.98-1.17)	280	2.81 (2.50-3.17)

Abbreviations: CI, confidence interval; IRR, incidence rate ratio; MRR, mortality rate ratio.

<sup>a</sup>All IRRs and MRRs were adjusted for calendar year. The reference group was cohort members never admitted to a psychiatric hospital. Heart disease was also adjusted for sex, with an MRR of 0.56 (95% CI, 0.55-0.57) and an IRR of 0.75 (95% CI, 0.75-0.76) in women compared with men. Myocardial infarction was also adjusted for sex, with an MRR of 0.48 (95% CI, 0.46-0.49) and an IRR of 0.44 (95% CI, 0.43-0.45) in women compared with men.

<sup>b</sup>Incidence rate ratio of somatic heart disease admission between cohort members previously admitted with severe mental disorder and cohort members never admitted to a psychiatric hospital.

<sup>c</sup>Mortality rate ratio of death by heart disease between cohort members previously admitted with severe mental disorder and cohort members never admitted to a psychiatric hospital.



**Figure 2.** Overall cumulative mortality from heart disease after discharge from the first heart disease contact. The y-axis shows cumulative mortality rates measuring the risk of dying of heart disease, taking into account other causes of death. Never admitted indicates never admitted to a psychiatric hospital; severe mental disorder, previously admitted to a psychiatric hospital with schizophrenia, bipolar disorder, or schizoaffective disorder.

MRR for schizoaffective disorder was 3.05 (95% CI, 2.57-3.61).

### MI SUBGROUP

Examination of the subgroup with MI revealed a similar pattern, with an excess MRR of MI in individuals with severe mental disorder. However, the IRR of contact with MI was the same as in individuals without mental disorder (Table 2).

### MORTALITY AFTER FIRST HEART DISEASE CONTACT

The 605 649 cohort members with heart disease contact during the first follow-up period formed the cohort, which was used to examine the mortality following discharge after the first contact with heart disease.

A total of 25 584 individuals died during their first contact or were still admitted at the end of follow-up, leaving 580 065 persons to follow up (Figure 1). Mortality rates increased with age. Rates of heart disease mortality in the group of individuals with severe mental disorder and the nonpsychiatric group were calculated as survival curves with time since discharge from the first heart disease contact as the underlying time axis (up to 1825 days, or 5 years). **Figure 2** shows the curves for all 5 years of follow-up. The mean durations of follow-up were 3.23 years for cohort members never admitted to a psychiatric hospital and 2.94 years for those previously admitted with severe mental disorder. A total of 43 090 individuals (437 persons previously admitted with severe mental disorder) died of heart disease during the 5-year follow-up period. A total of 88 680 individuals, of whom 938 persons had previously been admitted with severe mental disorder, died of other causes. We stratified the analysis by age, and the curves are displayed separately for the 2 age groups (aged <70 years and ≥70 years at the time of first heart disease contact). Taking into account that cohort members should be alive and should not have died of another competing cause, we found that for cohort members aged 70 years or older, the risk of dying of heart disease within 1 year after discharge was 9.08% for individuals with severe mental disorder but only 6.33% for individuals who had never been admitted with severe mental disorder. The corresponding numbers af-

ter 5 years were 21.00% and 17.13%, respectively (Figure 2). As expected, for patients with heart disease, the mortality from heart disease during the 5-year follow-up period was much lower for those younger than 70 years than among the older cohort members, but we observed the same tendency: persons younger than 70 years who were previously admitted with severe mental disorder had a higher risk of dying of heart disease than persons younger than 70 years who had never been admitted to a psychiatric hospital (1-year mortality risk, 2.80% and 1.00% respectively; 5-year mortality risk, 8.26% and 2.86%, respectively) (Figure 2). Survival curves for the 3 separate psychiatric disorders were similar, but mortality tended to be higher among persons with schizophrenia than among persons with bipolar disorder or schizoaffective disorder (data not shown).

### INVASIVE PROCEDURES

The 605 649 cohort members with a heart disease contact during the first follow-up period formed the cohort, which was used to examine the rates of invasive cardiac procedures following the first contact with heart disease. Probabilities of invasive procedures were calculated to be similar to those of heart disease mortality; however, follow-up began on the date of first contact, not the date of first discharge.

In all, 59 147 of the 605 649 persons with a first heart disease contact had an invasive procedure performed within the 5-year follow-up period. **Table 3** shows the probability of having an invasive procedure within 1 month, 1 year, and 5 years after the first heart disease contact, taking into account the competing risk from death. Separate analyses were made for cohort members aged 70 years and older and cohort members younger than 70 years at the time of the first heart disease contact. After 5 years, the probability of having an invasive procedure performed was 7.04% among cohort members (aged <70 years) with severe mental disorder, while there was a substantially larger probability, 12.27%, of cohort members never admitted to a psychiatric hospital having an invasive procedure performed. The same pattern applied for all age groups and all 3 periods (Table 3).

When we examined only cohort members admitted with MI, the differences between psychiatric and non-psychiatric patients were even larger. After 5 years, the probability of cohort members younger than 70 years having an invasive procedure was 28.18% among those with severe mental disorder, whereas it was 41.54% in the comparison group. For cohort members aged 70 years or older, the probability of having an invasive procedure was 10.51% among those with severe mental disorder and 18.70% in the comparison group.

### COMMENT

#### KEY FINDINGS

The IRRs of somatic heart disease contacts were almost similar in individuals with and without severe mental disorder. By contrast, an almost 3-fold increased MRR of heart

**Table 3. Probability of Having an Invasive Procedure After First Contact With Heart Disease in 605 649 Patients<sup>a</sup>**

Time of Invasive Procedure	Probability, %	
	No Mental Disorder Prior to Heart Disease Contact	Severe Mental Disorder Prior to Heart Disease Contact
Aged <70 y at time of first heart disease contact		
Within 1 mo	2.96	1.60
Within 1 y	7.90	3.76
Within 5 y	12.27	7.04
Aged ≥70 y at time of first heart disease contact		
Within 1 mo	1.57	0.90
Within 1 y	4.21	2.16
Within 5 y	6.48	3.29

<sup>a</sup>Invasive procedures were coronary artery bypass graft or percutaneous transluminal coronary angioplasty. A total of 566 071 patients had no prior psychiatric contact and 4997 had a severe mental disorder. A total of 34 581 patients had a prior mental disorder other than severe mental disorder (not included in this table). All probabilities were calculated by the Aalen-Johansen method taking competing risk from death into account.

disease without a prior somatic heart disease contact was found in psychiatric patients with severe mental disorder compared with the nonpsychiatric general population. Furthermore, rates of invasive cardiac procedures after the first heart disease contact in patients with severe mental disorder were approximately only half of those in the comparison group. Patients with severe mental disorder continued to have an excess mortality from heart disease following the first somatic heart disease contact.

### DANISH DATA VS DATA FROM OTHER COUNTRIES

The results in this study are based on the entire Danish population. In Denmark, hospital treatment is offered to all citizens regardless of socioeconomic status because treatment is paid for via the tax system. The Danish setting therefore offers a unique and singular opportunity to address the issue of equality of treatment for people with and without mental disorder. Similar data can be obtained in very few countries. We speculate that the discrepancy between somatic contact, invasive procedure, and death by heart disease among patients with severe mental disorder compared with the nonpsychiatric part of the population may be even more marked in countries where medical services are not fully tax financed.

### HIGH RATES OF MORTALITY

The excess mortality in persons with bipolar disorder, schizoaffective disorder, and especially schizophrenia (under different names) has been reported since the 1800s.<sup>22</sup> In the start of the 1900s, Kraepelin found excess mortality in psychiatric patients compared with the general population, an observation that was also made by Bleuer in the 1950s.<sup>22</sup> More recent studies have also shown that persons with severe psychiatric disorders have a higher

mortality from natural causes and especially from heart disease.<sup>6,23-25</sup>

The onset of bipolar disorder and schizophrenia may result in a cascade of unhealthy lifestyle behaviors such as heavy smoking,<sup>10,11</sup> social decline,<sup>12</sup> unhealthy diets,<sup>9</sup> and adverse effects of pharmacological or psychotropic treatment,<sup>8</sup> which are probably all pieces of a large puzzle explaining the excess mortality. However, a more direct link between the psychiatric disorders and the excess mortality has also been proposed. This link suggests the existence of a common genetic liability to somatic illness and schizophrenia or bipolar disorder.<sup>26,27</sup> Furthermore, bipolar disorder has been suspected to be linked to metabolic syndromes, and this association could also explain part of the excess mortality from heart disease.<sup>28</sup>

In light of the earlier evidence from the literature, the excess mortality found in our study is hardly surprising, even if we found higher excess mortality rates than other studies simultaneously exploring somatic contact and mortality.<sup>29,30</sup> A recent systematic review of schizophrenia<sup>31</sup> calculated an average standardized mortality ratio of 2 from cardiovascular diseases, which is lower than the MRRs found in our study. It should be noted that the MRRs from our study are not directly comparable to the standardized mortality ratios reported in the literature, first because we examined mortality from heart disease without a prior heart disease contact and second because we chose persons who had never been admitted to a psychiatric hospital as the reference group as opposed to using the entire population. Our approach gives higher MRRs because persons admitted with other psychiatric illnesses in general form a large group with high mortality affecting the total mortality in the population.<sup>25</sup>

Persons with severe mental disorder often belong to lower social classes whose mortality is higher than that of higher social classes. If we had compared the persons with severe mental disorder only with persons from similar socioeconomic strata, we probably would have found smaller mortality discrepancies. However, mental disorder often involves social decline; such a comparison would therefore not estimate the correct magnitude of the excess mortality associated with severe mental disorder.

#### LOW RATES OF CONTACT AND INVASIVE PROCEDURES

Rates of heart disease contact with somatic hospitals for persons with bipolar disorder, schizoaffective disorder, or schizophrenia were similar to those of the nonpsychiatric part of the Danish population. This pattern of equal rates of somatic contact was also found in studies from Canada<sup>29</sup> and Australia.<sup>30</sup> Several studies have found that risk factors for cardiovascular disorders were more common in patients with severe mental disorders<sup>2,32</sup> than in patients without such disorders and that persons with these psychiatric disorders had a higher prevalence of chronic medical conditions.<sup>33,34</sup> These observations, along with the higher mortality in psychiatric patients, indicate that persons with severe mental disorder are at high risk for heart disease and thus should have higher rates of somatic care and invasive cardiac procedures. However, we found only the same level of heart disease con-

tact; even more surprisingly, the rates of invasive procedures after the first contact were much lower. One possible explanation for these findings could be that symptoms of heart disease are not found owing to the severity and symptoms of the mental disorder. However, a similar pattern emerged when we examined a more specific subgroup of patients with heart disease, those with MI, in whom more severe symptoms are generally anticipated. Hence, our findings seem to suggest that psychiatric patients are not examined sufficiently enough by general practitioners or internal specialists. The same conclusion was suggested in a recent review of somatic health in persons with bipolar disorder: these patients were more likely to receive suboptimal somatic treatment.<sup>35</sup>

#### DISCREPANCY BETWEEN HIGH MORTALITY RATES AND LOW SOMATIC CONTACT RATES

The excess mortality found in this study is comparable in magnitude to that of other severe physical diseases, eg, diabetes.<sup>22</sup> This emphasizes the need for initiatives aimed at lowering the excess mortality. Most risk factors for the excess heart disease mortality are irresolvably linked to the psychiatric disorders, and the single most important target for prevention would be to intensify the somatic care of psychiatric patients. The excess mortality and the reduced survival after treatment in combination with the low somatic contact and invasive procedure rates invite the question of whether psychiatric patients receive the amount of care that corresponds to their clinical need. Evaluation on a more regular basis by clinicians specializing in somatic diseases would therefore seem to be one way to reduce the excess mortality of psychiatric patients.

The origin of the excess mortality is not fully understood, but the effect of unhealthy lifestyles (smoking, physical inactivity, poor diet, obesity, etc), reduced access to somatic primary care, medical comorbidities, and antipsychotic medication have all been proposed as possible causative factors.<sup>2,36-38</sup> In this study, we have suggested that the insufficiency of physical health care for persons with severe mental disorder may contribute to the excess mortality. However, we were not able to measure the effect of the other factors, and we cannot exclude the notion that they have a significant effect on the excess mortality as well.

#### STRENGTHS AND LIMITATIONS

In our estimates of the risk of death from heart disease and invasive procedures, we took into account the competing risk from other causes of death. This aids the interpretation of our results because we calculated the actual probability of dying of heart disease (or receiving an invasive procedure) after somatic contact and not a hypothetical probability that does not involve death by other causes. Danish persons with severe mental disorder have a high rate of mortality from unnatural causes, for instance, suicide,<sup>6</sup> especially in the younger groups. This affects the risk of mortality from heart disease because persons who commit suicide evidently will not die of heart disease or receive an invasive cardiac procedure. The

Aalen-Johansen method used in this study takes these competing causes of death into account.

We examined psychiatric inpatients. Thus, interpretation of the results should be evaluated with the notion that we have examined the most severe cases.

Diagnostic information, for example, on the severity of the somatic illness, in the registers is probably not as accurate as the information in more structured research settings. Validations of the Danish National Hospital Register and Cause of Death Register have shown high sensitivity and specificity for MI.<sup>39</sup> Furthermore, studies have shown high agreement between the psychiatric clinical diagnoses in the registers and research criteria diagnoses.<sup>14,40,41</sup> Some of the older persons in the cohort who were in contact with the psychiatric system before April 1, 1969, and had no later contact might have been misclassified as having no psychiatric diagnosis. The Psychiatric Central Register started in 1969, and the cases entered into the register at this time were a mix of incident and prevalent cases. Some of the older patients might have shown their first signs of mental disorder years before the start of the register. Thus, a "healthy survivor" effect could be present in these persons. When we censored persons with severe mental disorder from 1969 to 1993 from the cohort and thus included only incident cases (in the sense that they had not had a psychiatric hospitalization for  $\geq 24$  years), we found very similar results with only very slightly elevated IRRs for contact with heart disease, but again, mortality in persons with severe mental disorder was almost 3-fold as high as that in nonpsychiatric patients. This suggests that the possible mixing of prevalent and incident cases does not affect the results of this study.

We examined both inpatient and outpatient heart disease contacts. However, in the 17-year washout period from 1977 to 1994, we had information only on inpatient stays. A mix of first outpatient contact and prevalent outpatient contact could therefore be observed in the start of the follow-up period. We have repeated all analyses examining cohort members having only inpatient heart disease contact and found 20% fewer heart disease cases. The IRR and MRR in this setup were almost identical to the results presented in Table 2. Mortality and rates of invasive procedures after first admission were slightly higher in the group with severe mental disorder as well as in the comparison group.

## CONCLUSIONS

Persons with bipolar affective disorder, schizoaffective disorder, or schizophrenia had only negligible excess contact rates for heart disease or MI compared with the part of the population who had no psychiatric disorder. Inversely, psychiatric patients without a prior contact for heart disease or MI had a substantial excess mortality from these diseases. Furthermore, rates of invasive procedures were considerably lower and survival after the first contact for heart disease was reduced. Given this, it would seem that the treatment for heart disease offered to these individuals in Denmark is neither sufficiently efficient nor sufficiently intensive. This situation could possibly

be addressed by drawing on clinicians specialized in somatic disease for the examination of psychiatric patients.

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## REFERENCES

1. Laursen TM. *A Register-Based Epidemiological Description of Risk Factors and Outcomes for Major Psychiatric Disorders, Focusing on a Comparison Between Bipolar Affective Disorder and Schizophrenia* [PhD thesis]. Aarhus, Denmark: Aarhus University; 2006.
2. Newcomer JW, Hennekens CH. Severe mental illness and risk of cardiovascular disease. *JAMA*. 2007;298(15):1794-1796.
3. Johnsen SP, Videbaek J, Pedersen L, Steffensen R, Videbaek R, Niemann T, Nielsen TT, Sorensen HT. Survival trends among Danish patients undergoing coronary angiography for known or suspected ischaemic heart disease: a population based follow up study, 1992-2000. *Heart*. 2006;92(1):27-31.
4. Lichtenstein AH, Appel LJ, Brands M, Carnethon M, Daniels S, Franch HA, Franklin B, Kris-Etherton P, Harris WS, Howard B, Karanja N, Lefevre M, Rudel L, Sacks F, Van Horn L, Winston M, Wylie-Rosett J; American Heart Association Nutrition Committee. Diet and lifestyle recommendations revision 2006: a scientific statement from the American Heart Association Nutrition Committee. *Circulation*. 2006;114(1):82-96.
5. Hennekens CH, Albert CM, Godfried SL, Gaziano JM, Buring JE. Adjunctive drug therapy of acute myocardial infarction: evidence from clinical trials. *N Engl J Med*. 1996;335(22):1660-1667.
6. Laursen TM, Munk-Olsen T, Nordentoft M, Mortensen PB. Increased mortality among patients admitted with major psychiatric disorders: a register-based study comparing mortality in unipolar depressive disorder, bipolar affective disorder, schizoaffective disorder, and schizophrenia. *J Clin Psychiatry*. 2007;68(6):899-907.
7. Colton CW, Manderscheid RW. Congruencies in increased mortality rates, years of potential life lost, and causes of death among public mental health clients in eight states. *Prev Chronic Dis*. 2006;3(2):A42.
8. Allison DB, Mentore JL, Heo M, Chandler LP, Cappelleri JC, Infante MC, Weiden PJ. Antipsychotic-induced weight gain: a comprehensive research synthesis. *Am J Psychiatry*. 1999;156(11):1686-1696.
9. Brown S, Birtwistle J, Roe L, Thompson C. The unhealthy lifestyle of people with schizophrenia. *Psychol Med*. 1999;29(3):697-701.
10. Itkin O, Nemets B, Einat H. Smoking habits in bipolar and schizophrenic outpatients in southern Israel. *J Clin Psychiatry*. 2001;62(4):269-272.
11. Dalack GW, Healy DJ, Meador-Woodruff JH. Nicotine dependence in schizophrenia: clinical phenomena and laboratory findings. *Am J Psychiatry*. 1998;155(11):1490-1501.
12. Agerbo E, Byrne M, Eaton WW, Mortensen PB. Marital and labor market status in the long run in schizophrenia. *Arch Gen Psychiatry*. 2004;61(1):28-33.
13. Pedersen CB, Gotzsche H, Møller JO, Mortensen PB. The Danish Civil Registration System: a cohort of eight million persons. *Dan Med Bull*. 2006;53(4):441-449.
14. Munk-Jørgensen P, Mortensen PB. The Danish Psychiatric Central Register. *Dan Med Bull*. 1997;44(1):82-84.
15. World Health Organization. *Klassifikation af sygdomme: Udvidet dansk-latinske udgave af verdenssundhedsorganisationens internationale klassifikation af sygdomme, Eighth Revision, 1965 [Classification of Diseases: Extended Danish-*

- Latin Version of the World Health Organization International Classification of Diseases, Eighth Revision, 1965*. Copenhagen, Denmark: Danish National Board of Health; 1971.
16. World Health Organization. *World Health Organization ICD-10: Psykiske lidelser og adfærdsmæssige forstyrrelser: Klassifikation og diagnostiske kriterier [World Health Organization International Statistical Classification of Diseases, 10th Revision: Mental and Behavioural Disorders: Classification and Diagnostic Criteria]*. Copenhagen, Denmark: Munksgaard; 1994.
  17. Andersen TF, Madsen M, Jørgensen J, Mellemkjøer L, Olsen JH. The Danish National Hospital Register: a valuable source of data for modern health sciences. *Dan Med Bull.* 1999;46(3):263-268.
  18. Danish National Board of Health. *Classification of Surgical Procedures and Therapies*. Copenhagen, Denmark: Danish National Board of Health; 1988.
  19. Juel K, Helweg-Larsen K. The Danish registers of causes of death. *Dan Med Bull.* 1999;46(4):354-357.
  20. Andersen PK, Borgan Ø, Gill RD, Keiding N. *Statistical Models Based on Counting Processes*. New York, NY: Springer-Verlag; 1993.
  21. Rosthøj S, Andersen PK, Abildstrom SZ. SAS macros for estimation of the cumulative incidence functions based on a Cox regression model for competing risks survival data. *Comput Methods Programs Biomed.* 2004;74(1):69-75.
  22. Brown S. Excess mortality of schizophrenia: a meta-analysis. *Br J Psychiatry.* 1997;171:502-508.
  23. Osby U, Brandt L, Correia N, Ekbohm A, Sparen P. Excess mortality in bipolar and unipolar disorder in Sweden. *Arch Gen Psychiatry.* 2001;58(9):844-850.
  24. Osby U, Correia N, Brandt L, Ekbohm A, Sparen P. Mortality and causes of death in schizophrenia in Stockholm County, Sweden. *Schizophr Res.* 2000;45(1-2):21-28.
  25. Harris EC, Barraclough B. Excess mortality of mental disorder. *Br J Psychiatry.* 1998;173:11-53.
  26. Eaton WW, Byrne M, Ewald H, Mors O, Chen CY, Agerbo E, Mortensen PB. Association of schizophrenia and autoimmune diseases: linkage of Danish national registers. *Am J Psychiatry.* 2006;163(3):521-528.
  27. Gough SC, O'Donovan MC. Clustering of metabolic comorbidity in schizophrenia: a genetic contribution? *J Psychopharmacol.* 2005;19(6)(suppl):47-55.
  28. Taylor V, MacQueen G. Associations between bipolar disorder and metabolic syndrome: a review. *J Clin Psychiatry.* 2006;67(7):1034-1041.
  29. Kisely S, Smith M, Lawrence D, Cox M, Campbell LA, Maaten S. Inequitable access for mentally ill patients to some medically necessary procedures. *CMAJ.* 2007;176(6):779-784.
  30. Lawrence DM, Holman CD, Jablensky AV, Hobbs MS. Death rate from ischaemic heart disease in Western Australian psychiatric patients 1980-1998. *Br J Psychiatry.* 2003;182:31-36.
  31. Saha S, Chant D, McGrath J. A systematic review of mortality in schizophrenia: is the differential mortality gap worsening over time? *Arch Gen Psychiatry.* 2007;64(10):1123-1131.
  32. Birkenaes AB, Opjordsmoen S, Brunborg C, Engh JA, Jonsdottir H, Ringen PA, Simonsen C, Vaskinn A, Birkeland KI, Friis S, Sundet K, Andreassen OA. The level of cardiovascular risk factors in bipolar disorder equals that of schizophrenia: a comparative study. *J Clin Psychiatry.* 2007;68(6):917-923.
  33. Carney CP, Jones L, Woolson RF. Medical comorbidity in women and men with schizophrenia: a population-based controlled study. *J Gen Intern Med.* 2006;21(11):1133-1137.
  34. Carney CP, Jones LE. Medical comorbidity in women and men with bipolar disorders: a population-based controlled study. *Psychosom Med.* 2006;68(5):684-691.
  35. McIntyre RS, Soczynska JK, Beyer JL, Woldeyohannes HO, Law CW, Miranda A, Konarski JZ, Kennedy SH. Medical comorbidity in bipolar disorder: re-prioritizing unmet needs. *Curr Opin Psychiatry.* 2007;20(4):406-416.
  36. Auquier P, Lancon C, Rouillon F, Lader M, Holmes C. Mortality in schizophrenia. *Pharmacoepidemiol Drug Saf.* 2006;15(12):873-879.
  37. Brown S, Inskip H, Barraclough B. Causes of the excess mortality of schizophrenia. *Br J Psychiatry.* 2000;177:212-217.
  38. Jeste DV, Gadsjo JA, Lindamer LA, Lacro JP. Medical comorbidity in schizophrenia. *Schizophr Bull.* 1996;22(3):413-430.
  39. Madsen M, Davidsen M, Rasmussen S, Abildstrom SZ, Osler M. The validity of the diagnosis of acute myocardial infarction in routine statistics: a comparison of mortality and hospital discharge data with the Danish MONICA registry. *J Clin Epidemiol.* 2003;56(2):124-130.
  40. Kessing LV. Validity of diagnoses and other register data in patients with affective disorder. *Eur Psychiatry.* 1998;13(8):392-398. doi:10.1016/S0924-9338(99)80685-3.
  41. Jakobsen KD, Frederiksen JN, Hansen T, Jansson LB, Parnas J, Werge T. Reliability of clinical ICD-10 schizophrenia diagnoses. *Nord J Psychiatry.* 2005;59(3):209-212.