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Complete List of Authors:	Björkenstam, Emma; Karolinska Institutet, Department of Public Health Sciences, Division of Social Medicine Ljung, Rickard; Karolinska Institutet, Department of Public Health Sciences, Division of Social Medicine Burström, Bo; Karolinska Institutet, Department of Public Health Sciences, Division of Social Medicine Mittendorfer-Rutz, Ellenor; Karolinska Institutet, Department of Clinical Neuroscience, Division of Insurance Medicine Hallqvist, Johan; Karolinska Institutet, Department of Public Health Sciences, Division of Public Health Epidemiology; Uppsala University, Department of Public Health and Caring Sciences Ringbäck Weitoft, Gunilla; National Board of Health and Welfare, Department of Statistics, Monitoring and Evaluation
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Quality of medical care and excess mortality in psychiatric patients – a nationwide register-based study in Sweden

Emma Björkenstam BSc^{1,2}, Rickard Ljung M.D., MPH, PhD ^{1,2,3}, Bo Burström M.D., PhD¹, Ellenor Mittendorfer-Rutz PhD⁴, Johan Hallqvist M.D., PhD ^{5,6}, Gunilla Ringbäck Weitoft PhD²

Corresponding author: Emma Björkenstam

National Board of Health and Welfare, SE-106 30 Stockholm, Sweden

Telephone: +46 75 247 31 93, fax: +46 75 247 32 52

E-mail: emma.bjorkenstam@socialstyrelsen.se

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¹ Department of Public Health Sciences, Division of Social Medicine, Karolinska Institutet, Stockholm, Sweden

² Department of Statistics, Monitoring and Evaluation, National Board of Health and Welfare, Stockholm, Sweden

³ Upper Gastrointestinal Research, Department of Molecular Medicine and Surgery, Karolinska Institutet, Stockholm, Sweden

⁴ Department of Clinical Neuroscience, Division of Insurance Medicine, Karolinska Institutet, Stockholm, Sweden

⁵ Department of Public Health Sciences, Division of Public Health Epidemiology, Karolinska Institutet, Stockholm, Sweden

⁶ Department of Public Health and Caring Sciences, Uppsala University, Uppsala, Sweden

ARTICLE SUMMARY

Article focus:

- To investigate whether psychiatric patients have higher overall and cause-specific mortality
- To study whether the quality of somatic care for psychiatric patients is different from the care provided to patients with no concurrent mental disorder.

Key messages:

- This study shows a marked increase in excess mortality in mentally ill men and women.
- The findings suggest a lower quality of health care in the treatment of somatic disorders in psychiatric patients regarding the indicators studied.
- Careful medical examination of psychiatric patients together with efforts to promote a
 healthier life style may be of great importance in order to prevent, detect, and treat
 somatic disease.

Strengths and limitations:

- The strengths of the study include the population-based design, using national registers with high completeness
- We were unable to study the effects of health-related behaviors such as excessive alcohol consumption or tobacco smoking, which is a limitation.

ABSTRACT

Objective: To assess overall and cause-specific mortality, and the quality of somatic care among psychiatric patients.

Design: A register-based cohort study

Setting: All individuals aged 20-79 in Sweden in 2005.

Participants: In total 6 294 339 individuals.

Primary outcome measure: The individuals were followed for mortality in 2006 and 2007, generating 72 187 deaths. Psychiatric patients were grouped according to their diagnosis in the National Patient Register. Mortality risk of psychiatric patients was compared to that of non-psychiatric patients. Estimates of relative risk of mortality were calculated as incidence rate ratios (IRRs) with 95% confidence intervals (CIs) using Poisson regression analysis. Psychiatric patients were compared with non-psychiatric patients for three health care quality indicators: the proportion of avoidable hospitalisations, case fatality rate after myocardial infarction, and statin use among diabetic patients.

Results: Compared to individuals with no episodes of treatment for mental disorder, psychiatric patients had a substantially increased risk of all studied death-causes as well as death from conditions considered amenable to intervention by the health service, i.e. avoidable mortality. The highest mortality was found among those with another mental disorder, predominantly substance abuse (for women, an IRR of 4.7 (95% CI 4.3 to 5.0), and for men an IRR of 4.8 (95% CI 4.6 to 5.0)).

The analysis of quality of somatic care revealed lower levels of health care quality for psychiatric patients, signalling failures in public health and medical care.

Conclusion: This study shows a marked increase in excess mortality, suggesting a lower quality of somatic health care in psychiatric patients.

INTRODUCTION

 Psychiatric patients have been reported to have higher mortality rates and shorter life expectancy compared to the general population.¹⁻⁶ This applies especially to patients with severe psychiatric diseases, such as schizophrenia⁷⁻¹⁰ and bipolar disorder.^{11,12} The highest risks have been found among patients with substance abuse.^{3,5,13,14}

Psychiatric patients have a particularly pronounced risk of suicide. ¹⁵⁻¹⁸ Cardiovascular disease is also a major cause of excess deaths, partly due to a higher prevalence of smoking, obesity and hypertension. ¹⁹⁻²¹ There are conflicting data on cancer incidence and mortality in psychiatric patients, although most studies suggest that while cancer mortality is higher, incidence is no different from that of the general population. ^{22,23} Other potential explanations for the excess mortality are differences in access, provision and quality of somatic health care. ²⁴ For instance, it has been shown that people with a diagnosis of a mental disorder have less access to primary health care. ²⁵ Lower quality of diabetes care ²⁶ and cardiovascular procedures ^{19,27} have also been documented. In Sweden, different indicators are often used as measures reflecting health care quality. ²⁸

The concept of avoidable mortality was introduced in 1976 as an indicator of quality of health care.²⁹ Avoidable mortality measures deaths that could be argued to have been avoidable either by the health care system or by public health interventions, and has been applied in comparisons between regions, populations and over time. Psychiatric patients have been shown to have higher avoidable mortality rates than the general population,^{13,30} and questions have been raised as to whether the medical care of physical disorders provided to psychiatric patients is less adequate than for the population in general.³¹

The aim of this study was to investigate whether psychiatric patients have higher overall and cause-specific mortality, and whether the quality of somatic care for psychiatric patients is different from the care provided to patients with no concurrent mental disorder.

Results are reported with regard to age, sex, mental disorder, and comorbid substance abuse disorders.

METHOD

Study population

The study population comprised individuals alive and registered in Sweden in 2004 and 2005, aged 20-79 i.e. those born between 1926 and 1985. After excluding individuals diagnosed with mental retardation (as defined by the International Classification of Diseases, tenth revision (ICD-10): F70-F79) the study population comprised 6 294 339 individuals. The cohort was followed from January 1, 2006 until December 31, 2007. We used the unique personal identity number assigned to each Swedish citizen or permanent resident to link information from four population-based registers.³²

Types of mental disorder

We identified all individuals recorded with a principal psychiatric diagnostic code as defined by the ICD-10 F04-F99 (i.e. dementia excluded, besides mental retardation) in inpatient care or specialised outpatient care in 2004 or 2005 in the National Patient Register. The National Patient Register covers all inpatient care in Sweden since 1987 (psychiatric inpatient care since 1973) and all specialised outpatient care since 2001. If a patient had more than one discharge or outpatient visit, the principal diagnoses from all discharges and outpatient visits were kept to further categorise patients. Five mutually exclusive exposure groups were created according to a hierarchy of diagnoses: *i*) schizophrenia and other non-affective psychoses (diagnosis codes F20-F29), *ii*) affective disorder (F30-F39), *iii*) anxiety disorder (F40-F48), *iv*) other psychiatric diagnoses, (F04-F99 except for diagnoses above)), *v*) persons without inpatient and outpatient care due to mental disorder served as the reference group. Psychiatric in- or outpatient care due to substance abuse disorder was also studied in a subanalysis and was divided into categories according to whether the substance abuse was attributed to alcohol (F10), narcotic-related drugs (F11-F19), or both.

As certain mental disorders, e.g. bipolar disorder and schizophrenia are highly comorbid with alcohol and other substance abuse, ³³ schizophrenia/other non-affective psychoses, affective or anxiety disorder were analysed with and without a coexisting substance abuse disorder (attributed to either alcohol or narcotics-related drugs). In these analyses, persons without inpatient and outpatient care due to mental disorder served as the reference group.

Causes of death

The underlying cause of death, coded according to the ICD-10, was obtained from the Causes of Death Register. This register contains information on all deceased Swedish residents since 1952 and has a very high coverage. Since 1997 all deceased have been included, though for 0.5% there is a lack of medical information.

Causes of death were grouped as follows: ischemic heart disease (IHD) (diagnosis codes I20-I25), cancer (C00-C97), suicide and death with undetermined intent (X60-X84 and Y10-Y34), and external causes of death (suicide excluded) (V01-Y89 (except for X60-X84, Y10-Y34)). The indicators of avoidable mortality were divided into causes of death reflecting the outcome of medical care, and causes reflecting the effect of the national health policy. The following diseases were included as medical care indicators: typhoid (A01.0), tetanus (A35), tuberculosis (A15-A19 and B90), malignant neoplasm of cervix uteri (C53), Hodgkin's disease (C81), diabetes (E10-E14), chronic rheumatic heart disease (I05-I09), hypertensive disease (I10-I15), stroke (I60-I69), asthma (J45-J46), appendicitis (K35-K38), abdominal hernia (K40-K45), cholelithiasis and cholecystitis (K80-K81 and K83.0), maternal deaths (O00-O99), and osteomyelitis (M86-M87). Malignant neoplasms of the oesophagus (C15), malignant neoplasms of the trachea, bronchus or lung (C34), cirrhosis of the liver (K70 and K73-K74), and motor vehicle accidents (V00-V99) were included as national health policy indicators.

Health care quality indicators

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In analyses of indicators presumably reflecting aspects of health care quality, the age-span was restricted to individuals aged 40-79, because the studied outcomes are rare in younger individuals. The indicator regarding avoidable hospitalisation is based on the assumption that unnecessary hospitalisation can be avoided if patients with selected conditions receive proper outpatient care. This indicator includes hospitalisations for some chronic conditions (anaemia, asthma, diabetic complications, heart failure, hypertension, chronic obstructive lung disease, and angina pectoris), and hospitalisations for some acute conditions (bleeding ulcers, diarrhoea, epileptic seizures, inflammatory diseases of the female pelvic organs, pyelitis, and ear, nose and throat infection). The indicator regarding 28-day case fatality rate after myocardial infarction is an internationally established indicator of how well the health care system handles acute care after myocardial infarction. As a third indicator, the proportion on treatment with lipid lowering drugs was measured among patients receiving diabetes drugs. This treatment ought to be especially important for diabetes patients, due to the many risk factors in this population. All three indicators have been described elsewhere.²⁸

Statistical analysis

Poisson regression analyses, adjusted for age, were used to evaluate the association between mental disorder, mortality, and indicators of quality of health care. As a measure of the relative occurrence of death we used the incidence rate ratio (IRR). We assessed person-years at risk by adding up the years the individuals were alive and living in Sweden during the follow-up period. SAS Genmod procedure was used to calculate IRRs with 95% confidence intervals (CI). SAS Enterprise Guide 4.2 (SAS Institute Inc. Cary, NC, USA) was used. Agestandardised percentages were calculated when analysing differences regarding health care quality.

RESULTS

Cohort characteristics for the 6 294 339 individuals, (3 141 454 women and 3 152 885 men) are presented in table 1. In total, 101 500 women and 90 946 men were treated for mental disorder in 2004 or 2005. About 11% of mentally ill women had a diagnosis of schizophrenia and other non-affective psychoses, 37% affective disorders, 32% anxiety disorder, and 20% other psychiatric diagnoses, and for men 13%, 26%, 23%, and 37% respectively. Almost three quarters of the men (73%) included in the group for other mental disorders were treated for substance abuse.

Among all psychiatric patients, 5 498 (2.9% in all, 2% in women, and 4% in men respectively) died during the follow-up period, compared to 66 689 (1.1% in all, 0.9% in women, and 1.3% in men) among persons without episodes of treatment for mental disorder.

The IRRs for different causes of death and by mental disorder for both sexes are shown in table 2. When compared to the general population, mortality was considerably higher among all categories of mental disorder and for all causes of death. The highest excess mortality was found among individuals in the category comprised of having another mental disorder, predominantly substance abuse, (for women, an IRR of 4.7 (95 % CI 4.3 to 5.0), and for men an IRR of 4.8 (95% CI 4.6 to 5.0)).

The IRRs for different causes of death presented in table 3 show that, regardless of mental disorder, those with comorbid substance abuse disorders had the highest mortality risk.

Women treated for both alcohol-related and drug-related substance abuse had the highest risk for premature death, except for cancer and avoidable mortality (table 4). Except for cancer, men treated for both alcohol-related and drug-related substance abuse had the highest risk for premature death in all studied causes of death.

Separate analyses of different age groups 20-44, 45-64, and 65-79, showed that the younger the patient, the more pronounced increased risk for premature death (data not shown). This was true for all categories of mental disorder and for all studied causes of death, except for suicide.

The majority of patients (78% of women and 77% of men) with affective and anxiety disorders had been treated in outpatient care only. For the other disorders, around half of the patients had been treated in outpatient care only. Mortality rates were higher among those hospitalised than those treated in outpatient care. This was true for all categories of mental disorders and for all causes of death (data not shown).

The different health care quality indicators are presented in table 5. The percentage of avoidable admissions was higher among people treated for mental disorder, for women spanning from 2.4% to 4.1% (compared to 1.1% for those without episodes of treatment for mental disorder), and for men spanning from 3.4% to 5.4% (compared to 1.6%). Psychiatric patients had a higher 28-day case fatality rate for myocardial infarction, especially those treated for schizophrenia and other non-affective psychoses (women 53.5% (42.0-65.0) and men 51.4% (40.4-62.3)), compared to 26.5% of women (25.7-27.3) and 28.1% (27.5-28.6) of men not treated for mental disorder. The indicator on lipid lowering drug therapy shows that psychiatric patients with diabetes were given lipid lowering drugs to a lesser extent than diabetic patients without a concurrent mental disorder; this was particularly evident among both women and men with schizophrenia and other non-affective psychoses.

DISCUSSION

Our study of more than 6 million women and men shows that psychiatric patients had a substantially increased risk of death compared to individuals with no episodes of treatment for mental disorder, regardless of cause of death. Overall, people with schizophrenia and other non-affective psychoses, and people treated for substance abuse disorder had the highest risk for premature death. Psychiatric patients also had higher rates of potentially avoidable hospitalisations, higher case fatality rate after myocardial infarction, and lower use of lipid lowering therapy in diabetes.

The strengths of the study include the population-based design, using national registers with high completeness. The validity in the Causes of Death Register is very high, where information of cause of death is lacking in only 0.5% of the deceased.³⁴ The National Patient Register has close to complete coverage of all inpatient care. However in 2005 around 40% of psychiatric outpatient visits were not included, hence some patients who were treated in outpatient care are classified as unexposed, as there is no record of their outpatient visit. We were unable to study the effects of health-related behaviours such as excessive alcohol consumption or tobacco smoking, which is a limitation.

We found that psychiatric patients were at higher risk of premature death from IHD, particularly among those treated for schizophrenia and other non-affective psychoses. This has previously been shown in other settings, ^{10,11,19,20} and recently a study showed that the excess cardiovascular mortality among schizophrenia patients has increased over the past 25 years.⁷ We also found an elevated risk for cancer mortality, although to a lesser extent, in particular in patients treated for schizophrenia and other non-affective psychoses and substance abuse disorders. Studies evaluating cancer incidence and mortality at the same time have shown that, while individuals with mental disorder did not show any increased incidence rate for many types of cancer, they did have higher cancer mortality, which might be

explained by delays in detection,^{23,35} disparities in screening for cancer,²² and treatment compliance.³⁶

Psychiatric patients had an elevated risk of premature death from conditions considered amenable to intervention by the health service, i.e. avoidable mortality, compared to those not treated in psychiatric care. In particular, those treated for schizophrenia with comorbid substance abuse disorder had a higher risk, which has been shown by others. ^{13,30}

In line with previous studies, we found psychiatric patients to have significantly higher suicide risk, in particular those treated for schizophrenia and other non-affective psychosis, and affective disorder, and especially those treated with a comorbid substance abuse disorder.¹⁷

Mentally ill patients also had substantially increased risk of deaths from external causes when suicide was excluded. Studies have shown that people with mental illness are at greater risk of accidental and violent death, particularly when alcohol and drug comorbidities are involved.³⁷ As mentioned earlier, our results showed that mentally ill individuals with a coexisting substance abuse disorder have significantly higher risk for premature death. When we excluded those with a coexisting substance abuse disorder, the increased mortality risk remained for all diagnosis groups except for schizophrenia and other non-affective psychosis, but with lower estimates (data not shown).

Consistent with previous research, substance abuse disorders strongly contributed to premature death among both female and male psychiatric patients, especially for those with both alcohol and drug abuse.

When studying a set of indicators aimed to reflect the outcome of health care quality, we found that patients with a mental disorder had higher rates of potentially avoidable hospitalisations. Under some circumstances hospitalization is necessary and well motivated, but for most studied diseases, it is a failure. A recent study on avoidable hospitalisation

demonstrated that the quality of physical health care received by patients with schizophrenia was poorer than that of the general population, signalling failures in public health and medical care³³.

The indicator of 28-day case fatality rate after myocardial infarction showed worse outcome for those with a mental disorder. In a Danish study, ¹⁹ less somatic hospitalisation than needed, and less use of invasive heart disease procedures among persons with severe mental disorder than among the general population were suggested as additional reasons for their excess mortality in IHD.

Another finding was the low percentage of lipid lowering drugs given to diabetic patients with a concurrent mental disorder. As drug therapy against lipid disorders is particularly important in diabetic patients,³⁸ this is a clear indication of inequality in health care.

Disparities in access to and utilisation of health care, as well as the quality of health care provision may contribute to inequalities in health.³⁹ One reason for these disparities could be that a person with mental disorder may not be able to effectively communicate and express concerns because of cognitive disturbance. Also, psychiatrists and other mental health providers may prioritise psychiatric issues and neglect physical problems.⁴⁰ There is also some evidence of inequalities in case recognition and quality of medical care for psychiatric patients, where general practitioners might minimise the clinical significance of physical complaints when assessing and treating patients with a mental disorder; a process known as diagnostic overshadowing.⁴¹ As there is excess mortality across a wide range of mental disorders, somatic care should be improved for all psychiatric patients, regardless of the severity of the mental disorder.

In addition to inequalities in utilisation and quality of health care, there are many factors that contribute to poor physical health in people with a mental disorder, including health-related behaviours and medication side-effects. The increased morbidity and mortality seen in this

Conclusion

This study shows a marked increase in excess mortality in mentally ill men and women. This was especially evident in individuals with a comorbid substance abuse disorder. The findings also suggest a lower quality of health care in the treatment of somatic disorders in psychiatric patients. Careful medical examination of psychiatric patients together with efforts to promote a healthier life style may be of great importance in order to prevent, detect, and treat somatic disease.

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CONPETING INTERESTS

There are no competing interests.

CONTRIBUTORSHIP STATEMENT

EB, GWR and RL originated the idea. EB analyzed the data and wrote the manuscript draft.

All authors contributed the interpretation of the results and to the writing of the final manuscript.

DATA SHARING

There is no additional data available.

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Table 1. Cohort characteristics

5		V	Women				Men				
6	Schizophrenia and other	Affective	Anxiety	Other mental	No mental	Schizophrenia and other	Affective	Anxiety	Other mental	No mental	-
7	non-affective psychoses	disorder	disorder	disorder	disorder	non-affective psychoses	disorder	disorder	disorder	disorder	
8 N	11 165	37 245	32 690	20 400	3 039 954	11 993	23 762	21 209	33 982	3 061 939	6 29
9%	0.2	0.6	0.5	0.3	48.3	0.2	0.4	0.3	0.5	48.6	
10° Mean age (SD)	50.1 (13.6)	46.1 (15.6)	42.4 (14.3)	43.8 (16.4)	48.1 (16.0)	45.8 (13.0)	46.9 (14.9)	42.0 (13.4)	47.2 (15.2)	47.2 (15.6)	47.6
11 Person-years 12	21 923	73 620	64 788	40 039	6 017 464	23 463	46 604	41 790	65 925	6 042 510	12 43
13 Causes of death											
All-cause mortality	344 (3.1 %)	669 (1.8%)	413 (1.3 %)	638 (3.1 %)	27 421 (0.9 %)	459 (3.8 %)	764 (3.2 %)	389 (1.8 %)	1 822 (5.4 %)	39 268 (1.3 %)	72 187 (
Avoidable mortality: Medical Care Indicators	34 (0.3 %)	68 (0.2 %)	36 (0.1 %)	54 (0.3 %)	3 125 (0.1 %)	30 (0.3 %)	78 (0.3 %)	28 (0.1 %)	140 (0.4 %)	3 904 (0.1 %)	7 497 (
1-Avoidable mortality: National Health Policy Indicators	22 (0.2 %)	57 (0.2 %)	43 (0.1 %)	89 (0.4 %)	2 859 (0.1 %)	34 (0.3 %)	41 (0.2 %)	38 (0.2 %)	226 (0.7 %)	4 062 (0.1 %)	7 471 (
18 schemic heart disease	42 (0.4 %)	68 (0.2 %)	47 (0.1 %)	72 (0.4 %)	3 279 (0.1 %)	79 (0.7 %)	117 (0.5 %)	68 (0.3 %)	280 (0.8 %)	7 878 (0.3 %)	11 930 (
Cancer (all types)	83 (0.7 %)	163 (0.4 %)	129 (0.4 %)	111 (0.5 %)	12 369 (0.4 %)	65 (0.5 %)	136 (0.6 %)	71 (0.3 %)	247 (0.7 %)	13 636 (0.4 %)	27 010 (
2 Suicide	42 (0.4 %)	117 (0.3 %)	71 (0.2 %)	73 (0.4 %)	439 (0.0 %)	79 (0.7 %)	167 (0.7 %)	69 (0.3 %)	174 (0.5 %)	1 259 (0.0 %)	2 490 (
2 Peaths from external causes (suicide excluded)	15 (0.1 %)	44 (0.1 %)	27 (0.1 %)	47 (0.2 %)	652 (0.0 %)	39 (0.3 %)	67 (0.3 %)	48 (0.2 %)	232 (0.7 %)	1 867 (0.1 %)	3 038 (
22 23 ^{Health} care quality indicators*	8 413	22 833	17 078	11 171	1 961 968	7 864	15 502	11 126	22 762	1 931 860	4 01
24. Avoidable inpatient medical care											!
25 Number treated in 2006	234	521	409	445	22 433	235	474	341	1 189	29 159	
26. Myocardial infarction - 28-day case fatality											
27 AMI in 2006 or 2007	77	164	134	118	10 993	105	244	140	410	23 786	
28 Dead within 28 days	36	62	45	53	3 108	50	88	42	171	6 467	
29. Lipid lowering drug therapy											
30 Number receiving diabetes drug therapy in 2006	722	1 200	726	596	80 453	744	1 185	680	1 744	116 270	2
31 Of these, number who were given lipid lowering	292	618	385	280	45 193	318	631	367	743	65 440	
32 drugs in 2006											

^{*} Individuals aged 40-79

Table 2. Relative risk of death in psychiatric patients compared with a population with no episode of treatment for mental disorder (incidence rate ratios* with 95% confidence intervals)

Mental disorder group	All-cause mortality	Ischemic heart disease	Cancer (all types)	Avoidable mortality: Medical Care Indicators	Avoidable mortality: National Health Policy Indicators	Suicide	Death from external causes (suicide excluded)
<u>Females</u>							
No mental disorder	1 (REF)	1 (REF)	1 (REF)	1 (REF)	1 (REF)	1 (REF)	1 (REF)
Schizophrenia and other non-affective psychoses	3.8 (3.4-4.2)	4.1 (3.1-5.6)	1.9 (1.5-2.4)	3.5 (2.5-4.9)	2.1 (1.4-3.2)	24.9 (18.1-34.2)	6.7 (4.0-11.1)
Affective disorder	2.4 (2.2-2.6)	2.1 (1.7-2.7)	1.3 (1.1-1.5)	2.2 (1.7-2.8)	1.9 (1.5-2.5)	22.3 (18.1-27.3)	6.1 (4.5-8.3)
Anxiety disorder	2.6 (2.3-2.8)	2.9 (2.1-3.8)	1.7 (1.4-2.0)	2.2 (1.6-3.0)	2.4 (1.8-3.2)	16.0 (12.5-20.6)	5.3 (3.6-7.8)
Other mental disorder (including substance abuse disorder)	4.7 (4.3-5.0)	4.6 (3.6-5.8)	1.8 (1.5-2.2)	3.5 (2.7-4.6)	6.2 (5.0-7.6)	26.7 (20.8-34.3)	12.6 (9.4-17.0)
Males							
No mental disorder	1 (REF)	1 (REF)	1 (REF)	1 (REF)	1 (REF)	1 (REF)	1 (REF)
Schizophrenia and other non-affective psychoses	4.6 (4.2-5.0)	4.3 (3.4-5.3)	1.9 (1.5-2.5)	3.4 (2.4-4.9)	3.0 (2.1-4.1)	16.1 (12.9-20.3)	6.2 (4.5-8.6)
Affective disorder	2.8 (2.7-3.1)	2.2 (1.9-2.7)	1.5 (1.2-1.7)	3.0 (2.4-3.8)	1.4 (1.1-2.0)	17.2 (14.6-20.2)	4.9 (3.8-6.2)
Anxiety disorder	2.8 (2.5-3.0)	2.7 (2.1-3.5)	1.5 (1.2-2.0)	2.3 (1.6-3.4)	2.3 (1.7-3.2)	8.3 (6.5-10.6)	4.5 (3.4-6.1)
Other mental disorder (including substance abuse disorder) * Adjusted for age	4.8 (4.6-5.0)	3.7 (3.3-4.2)	1.9 (1.6-2.1)	3.9 (3.3-4.6)	5.5 (4.8-6.3)	12.6 (10.8-14.8)	11.8 (10.3-13.6)
					5.5 (4.8-6.3)		

^{*} Adjusted for age

Table 3. Associations of mental disorder and substance abuse in relation to mortality (incidence rate ratios* with 95% confidence intervals)

Mental disorder group	N	All-cause mortality	Ischemic heart disease	Cancer (all types)	Avoidable mortality: Medical Care Indicators	Avoidable mortality: National Health Policy Indicators	Suicide	Death fro
<u>Females</u>								
No mental disorder	3 039 954	1 (REF)	1 (REF)	1 (REF)	1 (REF)	1 (REF)	1 (REF)	
Schizophrenia and other non-affective psychoses with substance abuse disorder	502	10.8 (7.1-16.6)	5.7 (0.8-40.4)	5.2 (2.2-12.6)	-	21.5 (8.9-51.8)	44.6 (14.3-138.8)	
Schizophrenia and other non-affective psychoses without substance abuse disorder	10 663	3.6 (3.2-4.0)	4.1 (3.0-5.6)	1.8 (1.5-2.3)	3.5 (2.5-5.0)	1.7 (1.0-2.7)	24.2 (17.4-33.6)	
Affective disorder with substance abuse disorder	1 919	6.4 (4.9-8.3)	3.5 (1.1-10.9)	2.7 (1.5-4.8)	3.4 (1.1-10.6)	6.5 (3.1-13.6)	61.1 (37.1-100.6)	
Affective disorder without substance abuse disorder	35 326	2.3 (2.1-2.5)	2.1 (1.6-2.7)	1.2 (1.1-1.4)	2.2 (1.7-2.8)	1.8 (1.3-2.3)	20.3 (16.3-25.2)	
Anxiety disorder with substance abuse disorder	1 551	7.3 (5.4-9.8)	10.9 (4.9-24.3)	2.0 (0.9-4.4)	1.7 (0.2-12.2)	6.8 (2.8-16.4)	63.1 (36.3-109.7)	
Anxiety disorder without substance abuse disorder	31 139	2.4 (2.2-2.7)	2.6 (1.9-3.5)	1.7 (1.4-2.0)	2.2 (1.6-3.0)	2.2 (1.6-3.0)	13.8 (10.5-18.2)	
Other mental disorder with substance abuse disorder	387	17.0 (10.4-27.7)	-	-	11.3 (1.6-80.4)	-	171.6 (85.1-346.0)	
Other mental disorder without substance abuse disorder	10 773	2.6 (2.3-3.0)	2.9 (2.0-4.1)	1.4 (1.1-1.8)	2.6 (1.8-3.8)	0.9 (0.4-1.8)	10.0 (5.9-17.0)	
Substance abuse disorder without a psychiatric diagnosis	9 240	7.9 (7.1-8.7)	8.4 (6.2-11.4)	2.4 (1.9-3.1)	5.3 (3.6-7.8)	13.4 (10.7-16.7)	39.8 (29.8-53.2)	
Males								
No mental disorder	3 061 939	1 (REF)	1 (REF)	1 (REF)	1 (REF)	1 (REF)	1 (REF)	
Schizophrenia and other non-affective psychoses with substance abuse disorder	1 088	12.5 (9.8-15.9)	4.9 (1.9-13.2)	3.8 (1.7-8.4)	5.3 (1.3-21.1)	11 (5.2-23.1)	41.3 (25.6-66.7)	
Schizophrenia and other non-affective psychoses without substance abuse disorder	10 905	4.2 (3.8-4.6)	4.3 (3.4-5.3)	1.8 (1.4-2.4)	3.4 (2.3-4.9)	2.5 (1.7-3.6)	13.9 (10.7-17.9)	
Affective disorder with substance abuse disorder	2 237	6.7 (5.6-8.1)	5.4 (3.4-8.6)	1.6 (0.9-3.0)	5.8 (3.0-11.2)	5.3 (2.9-9.5)	43.7 (31.8-60.2)	
Affective disorder without substance abuse disorder	21 525	2.6 (2.4-2.8)	2 .0 (1.6-2.4)	1.5 (1.2-1.7)	2.8 (2.2-3.6)	1.1 (0.8-1.6)	14.5 (12.1-17.4)	
Anxiety disorder with substance abuse disorder	1 900	9.7 (7.9-11.8)	7.7 (4.5-13.2)	2.5 (1.2-4.9)	2.5 (0.6-10.2)	8.9 (4.9-16.1)	27.7 (17.8-43.1)	
Anxiety disorder without substance abuse disorder	19 309	2.2 (2.0-2.5)	2.4 (1.8-3.1)	1.5 (1.2-1.9)	2.3 (1.6-3.4)	1.8 (1.2-2.6)	6.5 (4.9-8.6)	
Other mental disorder with substance abuse disorder	380	9.8 (6.7-14.4)	21.0 (11.3-39.0)	2.3 (0.6-9.1)	8.7 (2.2-35.0)	-	47.6 (22.6-100.1)	
Other mental disorder without substance abuse disorder	9 298	2.5 (2.2-2.8)	1.7 (1.3-2.2)	1.4 (1.1-1.8)	3.5 (2.7-4.7)	1.2 (0.7-2.0)	5.4 (3.5-8.4)	
Substance abuse disorder without a psychiatric diagnosis	24 304	6.1 (5.8-6.4)	4.8 (4.2-5.5)	2.1 (1.8-2.4)	4.0 (3.3-5.0)	7.7 (6.7-8.8)	14.8 (12.5-17.6)	
* Adjusted for age								

^{*} Adjusted for age

29.3 (19.6-43.9)

	N	All-cause mortality	Ischemic heart disease	Cancer (all types)	Avoidable mortality: Medical Care Indicators	Avoidable mortality: National Health Policy Indicators	Suicide	Death from external causes (suicide excluded)
<u>Females</u>								
No substance abuse disorder	3 127 855	1 (REF)	1 (REF)	1 (REF)	1 (REF)	1 (REF)	1 (REF)	1 (REF)
Substance abuse disorder, alcohol	8 185	7.7 (6.9-8.5)	4.1 (0.6-29.3)	2.3 (1.8-3.0)	4.8 (3.2-7.2)	13.8 (11.1-17.2)	29.5 (22.1-39.4)	22.6 (16.0-32.0)
Substance abuse disorder, drug abuse	4 589	6.6 (5.5-8.0)	4.7 (2.3-9.4)	2.7 (1.8-4.1)	3.9 (1.9-8.2)	6.1 (3.5-10.8)	36.9 (25.8-52.8)	22.9 (13.9-37.6)
Substance abuse disorder, both alcohol and drug abuse	825	11.2 (8.0-15.7)	8.7 (6.4-11.8)	2.6 (1.0-6.9)	3.7 (0.5-26.5)	7.8 (2.5-24.1)	54.4 (28.1-105.1)	65.8 (32.7-132.4)
Males								
No substance abuse disorder	3 122 976	1 (REF)	1 (REF)	1 (REF)	1 (REF)	1 (REF)	1 (REF)	1 (REF)
Substance abuse disorder, alcohol	20 429	5.5 (5.3-5.9)	4.8 (4.2-5.5)	2.0(1.7-2.4)	3.8 (3.1-4.7)	7.5 (6.6-8.7)	12.5 (10.4-14.9)	12.8 (10.8-15.0)
Substance abuse disorder, drug abuse	7 753	9.4 (8.4-10.6)	5.8 (3.9-8.7)	2.7 (1.7-4.1)	4.9 (2.6-9.1)	4.1 (2.4-7.0)	22.4 (17.7-28.4)	22.5 (18.0-28.3)

2.5 (1.2-5.2)

(122-17.2) D.O.V...

8.7 (3.9-19.4)

16.0 (10.0-25.4)

35.2 (24.2-51.2)

Substance abuse disorder, both alcohol and drug abuse

1 727

14.5 (12.2-17.2)

6.8 (3.7-12.7)

^{*} Adjusted for age

Table 5. Age-standardised percentage (with 95% confidence intervals) as measures of health care quality indicators for individuals aged 40-79, 2006

Mental disorder group	N	Avoidable inpatient medical care	Myocardial infarction - 28-day case fatality	Lipid lowering drug therapy
		% (95% CI)	% (95% CI)	% (95% CI)
<u>Females</u>				
No mental disorder	1 961 968	1.1 (1.1-1.1)	26.5 (25.7-27.3)	56.1 (55.7-56.4)
Schizophrenia and other non-affective psychoses	8 413	2.9 (2.6-3.3)	53.5 (42.0-65.0)	40.9 (36.8-45.1)
Affective disorder	22 833	2.4 (2.2-2.6)	34.8 (26.5-43.2)	51.9 (49.0-54.8)
Anxiety disorder	17 078	3.0 (2.7-3.3)	36.1 (28.8-43.4)	54.9 (50.9-58.8)
Other mental disorder (including substance abuse disorder)	11 171	4.1 (3.7-4.5)	45.0 (35.8-54.3)	49.0 (44.8-53.1)
Males				
No mental disorder	1 931 860	1.6 (1.5-1.6)	28.1 (27.5-28.6)	56.2 (55.9-56.5)
Schizophrenia and other non-affective psychoses	7 864	3.8 (3.3-4.4)	51.4 (40.4-62.3)	41.9 (37.2-46.5)
Affective disorder	15 502	3.4 (3.1-3.7)	39.2 (32.6-45.7)	53.8 (50.8-56.8)
Anxiety disorder	11 126	4.4 (3.9-4.9)	32.5 (23.1-42.0)	56.4 (51.9-60.8)
Other mental disorder (including substance abuse disorder)	22 762	5.4 (5.1-5.7)	43.9 (38.6-49.1)	44.2 (41.7-46.7)

bmjopen-2011-000778 - Quality of medical care and excess mortality in psychiatric patients - a nationwide register-based study in Sweden STROBE Statement—Checklist of items that should be included in reports of *cohort studies*

	Item No	Recommendation
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract Page 1
		(b) Provide in the abstract an informative and balanced summary of what was done
		and what was found
		Page 3
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported Page 4
Objectives	3	State specific objectives, including any prespecified hypotheses Page 5
Methods		
Study design	4	Present key elements of study design early in the paper
study design		Page 6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment,
C		exposure, follow-up, and data collection
		Page 6
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of
		participants. Describe methods of follow-up
		Page 6
		(b) For matched studies, give matching criteria and number of exposed and
		unexposed
		N/A
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect
		modifiers. Give diagnostic criteria, if applicable
		Page 6 - 8
Data sources/	8*	For each variable of interest, give sources of data and details of methods of
measurement		assessment (measurement). Describe comparability of assessment methods if there is
		more than one group
		Page 6 - 8
Bias	9	Describe any efforts to address potential sources of bias
		N/A
Study size	10	Explain how the study size was arrived at
		Page 6
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable,
		describe which groupings were chosen and why
		N/A
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding
		Page 8 - 9
		(b) Describe any methods used to examine subgroups and interactions
		N/A
		(c) Explain how missing data were addressed
		N/A
		(d) If applicable, explain how loss to follow-up was addressed N/A
		4

		(e) Describe any sensitivity analyses
Results		
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed Page 10 and page 20
		(b) Give reasons for non-participation at each stage
		N/A
		(c) Consider use of a flow diagram
		N/A
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and
Descriptive data		information on exposures and potential confounders
		Page 20
		(b) Indicate number of participants with missing data for each variable of interest
		N/A
		(c) Summarise follow-up time (eg, average and total amount)
		Page 20
Outcome data	15*	Report numbers of outcome events or summary measures over time
		Page 10 and page 20
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and
		their precision (eg, 95% confidence interval). Make clear which confounders were
		adjusted for and why they were included
		Page 10-11 and page 21-23
		(b) Report category boundaries when continuous variables were categorized
		N/A
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a
		meaningful time period
		N/A
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and
		sensitivity analyses
		Page 11 and page 24
Discussion		
Key results	18	Summarise key results with reference to study objectives
		Page 2 and page 12 – 16
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or
		imprecision. Discuss both direction and magnitude of any potential bias
		Page 2 and page 12
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations,
		multiplicity of analyses, results from similar studies, and other relevant evidence
		Page 12 – 16
Generalisability	21	Discuss the generalisability (external validity) of the study results
		Page 15
Other information		
Funding	22	Give the source of funding and the role of the funders for the present study and, if
		applicable, for the original study on which the present article is based
		Page 16

^{*}Give information separately for exposed and unexposed groups.



Quality of medical care and excess mortality in psychiatric patients – a nationwide register-based study in Sweden

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Quality of medical care and excess mortality in psychiatric patients – a nationwide register-based study in Sweden

Emma Björkenstam BSc^{1,2}, Rickard Ljung M.D., MPH, PhD ^{1,2,3}, Bo Burström M.D., PhD¹, Ellenor Mittendorfer-Rutz PhD⁴, Johan Hallqvist M.D., PhD ^{5,6}, Gunilla

Ringbäck Weitoft PhD²

Corresponding author: Emma Björkenstam

National Board of Health and Welfare, SE-106 30 Stockholm, Sweden

Telephone: +46 75 247 31 93, fax: +46 75 247 32 52

E-mail: emma.bjorkenstam@socialstyrelsen.se

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¹ Department of Public Health Sciences, Division of Social Medicine, Karolinska Institutet, Stockholm, Sweden

² Department of Statistics, Monitoring and Evaluation, National Board of Health and Welfare, Stockholm, Sweden

³ Upper Gastrointestinal Research, Department of Molecular Medicine and Surgery, Karolinska Institutet, Stockholm, Sweden

⁴ Department of Clinical Neuroscience, Division of Insurance Medicine, Karolinska Institutet, Stockholm, Sweden

⁵ Department of Public Health Sciences, Division of Public Health Epidemiology, Karolinska Institutet, Stockholm, Sweden

⁶ Department of Public Health and Caring Sciences, Uppsala University, Uppsala, Sweden

ARTICLE SUMMARY

Article focus:

- To investigate whether psychiatric patients have higher overall and causespecific mortality
- To study whether the quality of somatic care for psychiatric patients is different from the care provided to patients with no concurrent mental disorder.

Key messages:

- This study shows a marked increase in excess mortality in mentally ill men and women.
- The findings suggest a lower quality of health care in the treatment of somatic disorders in psychiatric patients regarding the indicators studied.
- Careful medical examination of psychiatric patients together with efforts to promote a healthier life style may be of great importance in order to prevent, detect, and treat somatic disease.

Strengths and limitations:

- The strengths of the study include the population-based design, using national registers with high completeness
- We were unable to study the effects of health-related behaviors such as excessive alcohol consumption or tobacco smoking, which is a limitation.

ABSTRACT

Objective: To assess overall and cause-specific mortality, and the quality of somatic care among psychiatric patients.

Design: A register-based cohort study

Setting: All individuals aged 20-79 in Sweden in 2005.

Participants: In total 6 294 339 individuals.

Primary outcome measure: The individuals were followed for mortality in 2006 and 2007, generating 72 187 deaths. Psychiatric patients were grouped according to their diagnosis in the National Patient Register. Mortality risk of psychiatric patients was compared to that of non-psychiatric patients. Estimates of relative risk of mortality were calculated as incidence rate ratios (IRRs) with 95% confidence intervals (CIs) using Poisson regression analysis. Psychiatric patients were compared with non-psychiatric patients for three health care quality indicators: the proportion of avoidable hospitalisations, case fatality rate after myocardial infarction, and statin use among diabetic patients.

Results: Compared to individuals with no episodes of treatment for mental disorder, psychiatric patients had a substantially increased risk of all studied death-causes as well as death from conditions considered amenable to intervention by the health service, i.e. avoidable mortality. The highest mortality was found among those with another mental disorder, predominantly substance abuse (for women, an IRR of 4.7 (95% CI 4.3 to 5.0), and for men an IRR of 4.8 (95% CI 4.6 to 5.0)).

The analysis of quality of somatic care revealed lower levels of health care quality for psychiatric patients, signalling failures in public health and medical care.

Conclusion: This study shows a marked increase in excess mortality, suggesting a lower quality of somatic health care in psychiatric patients.

INTRODUCTION

Psychiatric patients have been reported to have higher mortality rates and shorter life expectancy compared to the general population. ¹⁻⁶ This applies especially to patients with severe psychiatric diseases, such as schizophrenia ⁷⁻¹⁰ and bipolar disorder. ^{11,12} The highest risks have been found among patients with substance abuse. ^{3,5,13,14} Psychiatric patients have a particularly pronounced risk of suicide. ¹⁵⁻¹⁸ Cardiovascular disease is also a major cause of excess deaths, partly due to a higher prevalence of smoking, obesity and hypertension. ¹⁹⁻²¹ There are conflicting data on cancer incidence and mortality in psychiatric patients, although most studies suggest that while cancer mortality is higher, incidence is no different from that of the general population. ^{22,23} Other potential explanations for the excess mortality are differences in access, provision and quality of somatic health care. ²⁴ For instance, it has been shown that people with a diagnosis of a mental disorder have less access to primary health care. ²⁵ Lower quality of diabetes care ²⁶ and cardiovascular procedures ^{19,27,28} have also been documented. In Sweden, different indicators are often used as measures reflecting health care quality. ²⁹

The concept of avoidable mortality was introduced in 1976 as an indicator of quality of health care.³⁰ Avoidable mortality measures deaths that could be argued to have been avoidable either by the health care system or by public health interventions, and has been applied in comparisons between regions, populations and over time. Psychiatric patients have been shown to have higher avoidable mortality rates than the general population, ^{13,31} and questions have been raised as to whether the medical care of physical disorders provided to psychiatric patients is less adequate than for the population in general.³²

The aim of this study was to investigate whether psychiatric patients have higher overall and cause-specific mortality, and whether the quality of somatic care for psychiatric patients is different from the care provided to patients with no concurrent mental disorder.

Results are reported with regard to age, sex, mental disorder, and comorbid substance abuse disorders.

METHOD

Study population

The study population comprised individuals alive and registered in Sweden in 2004 and 2005, aged 20-79 i.e. those born between 1926 and 1985. After excluding individuals diagnosed with mental retardation (as defined by the International Classification of Diseases, tenth revision (ICD-10): F70-F79) the study population comprised 6 294 339 individuals. The cohort was followed from January 1, 2006 until December 31, 2007. We used the unique personal identity number assigned to each Swedish citizen or permanent resident to link information from four population-based registers.³³

Types of mental disorder

We identified all individuals recorded with a principal psychiatric diagnostic code as defined by the ICD-10 F04-F99 (i.e. dementia excluded, besides mental retardation) in inpatient care or specialised outpatient care in 2004 or 2005 in the National Patient Register. The National Patient Register covers all inpatient care in Sweden since 1987 (psychiatric inpatient care since 1973, where both alcohol and drugs services are included) and all specialised outpatient care since 2001. If a patient had more than one discharge or outpatient visit, the principal diagnoses from all discharges and outpatient visits were kept to further categorise patients. Five mutually exclusive exposure groups were created according to a hierarchy of diagnoses: *i*) schizophrenia and other non-affective psychoses (diagnosis codes F20-F29), *ii*) affective disorder (F30-F39), *iii*) anxiety disorder (F40-F48), *iv*) other psychiatric diagnoses, (F04-F99 except for diagnoses above)), *v*) persons without inpatient and outpatient care due to mental disorder served as the reference group.

Psychiatric in- or outpatient care due to substance abuse disorder was also studied in a sub-analysis and was divided into categories according to whether the substance abuse was attributed to alcohol (F10), narcotic-related drugs (F11-F19), or both.

As certain mental disorders, e.g. bipolar disorder and schizophrenia are highly comorbid with alcohol and other substance abuse,³⁴ schizophrenia/other non-affective psychoses, affective or anxiety disorder were analysed with and without a coexisting substance abuse disorder (attributed to either alcohol or narcotics-related drugs). In these analyses, persons without inpatient and outpatient care due to mental disorder served as the reference group.

Causes of death

The underlying cause of death, coded according to the ICD-10, was obtained from the Causes of Death Register. This register contains information on all deceased Swedish residents since 1952 and has a very high coverage. Since 1997 all deceased have been included, though for 0.5% there is a lack of medical information.

Causes of death were grouped as follows: ischemic heart disease (IHD) (diagnosis codes I20-I25), cancer (C00-C97), suicide and death with undetermined intent (X60-X84 and Y10-Y34), and external causes of death (suicide excluded) (V01-Y89 (except for X60-X84, Y10-Y34)). The indicators of avoidable mortality were divided into causes of death reflecting the outcome of medical care, and causes reflecting the effect of the national health policy. The following diseases were included as medical care indicators: typhoid (A01.0), tetanus (A35), tuberculosis (A15-A19 and B90), malignant neoplasm of cervix uteri (C53), Hodgkin's disease (C81), diabetes (E10-E14), chronic rheumatic heart disease (I05-I09), hypertensive disease (I10-I15), stroke (I60-I69), asthma (J45-J46), appendicitis (K35-K38), abdominal hernia (K40-K45), cholelithiasis and cholecystitis (K80-K81 and K83.0), maternal deaths (O00-

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O99), and osteomyelitis (M86-M87). Malignant neoplasms of the oesophagus (C15), malignant neoplasms of the trachea, bronchus or lung (C34), cirrhosis of the liver (K70 and K73-K74), and motor vehicle accidents (V00-V99) were included as national health policy indicators.

Health care quality indicators

In analyses of indicators presumably reflecting aspects of health care quality, the agespan was restricted to individuals aged 40-79, because the studied outcomes are rare in younger individuals. The indicator regarding avoidable hospitalisation is based on the assumption that unnecessary hospitalisation can be avoided if patients with selected conditions receive proper outpatient care. This indicator includes hospitalisations for some chronic conditions (anaemia, asthma, diabetic complications, heart failure, hypertension, chronic obstructive lung disease, and angina pectoris), and hospitalisations for some acute conditions (bleeding ulcers, diarrhoea, epileptic seizures, inflammatory diseases of the female pelvic organs, pyelitis, and ear, nose and throat infection). The indicator regarding 28-day case fatality rate after myocardial infarction is an internationally established indicator of how well the health care system handles acute care after myocardial infarction. As a third indicator, the proportion on treatment with lipid lowering drugs was measured among patients receiving diabetes drugs. This treatment ought to be especially important for diabetes patients, due to the many risk factors in this population. All three indicators have been described elsewhere.²⁹

Statistical analysis

Poisson regression analyses, adjusted for age, were used to evaluate the association between mental disorder, mortality, and indicators of quality of health care. As a measure of the relative occurrence of death we used the incidence rate ratio (IRR).

We assessed person-years at risk by adding up the years the individuals were alive and living in Sweden during the follow-up period. SAS Genmod procedure was used to calculate IRRs with 95% confidence intervals (CI). SAS Enterprise Guide 4.2 (SAS Institute Inc. Cary, NC, USA) was used. Age-standardised percentages were calculated when analysing differences regarding health care quality.

RESULTS

Cohort characteristics for the 6 294 339 individuals, (3 141 454 women and 3 152 885 men) are presented in table 1. In total, 101 500 women and 90 946 men were treated for mental disorder in 2004 or 2005. About 11% of mentally ill women had a diagnosis of schizophrenia and other non-affective psychoses, 37% affective disorders, 32% anxiety disorder, and 20% other psychiatric diagnoses, and for men 13%, 26%, 23%, and 37% respectively. Almost three quarters of the men (73%) included in the group for other mental disorders were treated for substance abuse. Among all psychiatric patients, 5 498 (2.9% in all, 2% in women, and 4% in men respectively) died during the follow-up period, compared to 66 689 (1.1% in all, 0.9% in women, and 1.3% in men) among persons without episodes of treatment for mental disorder.

The IRRs for different causes of death and by mental disorder for both sexes are shown in table 2. When compared to the general population, mortality was considerably higher among all categories of mental disorder and for all causes of death. The highest excess mortality was found among individuals in the category comprised of having another mental disorder, predominantly substance abuse, (for women, an IRR of 4.7 (95 % CI 4.3 to 5.0), and for men an IRR of 4.8 (95% CI 4.6 to 5.0)).

The IRRs for different causes of death presented in table 3 show that, regardless of mental disorder, those with comorbid substance abuse disorders had the highest mortality risk.

Women treated for both alcohol-related and drug-related substance abuse had the highest risk for premature death, except for cancer and avoidable mortality (table 4).

Except for cancer, men treated for both alcohol-related and drug-related substance abuse had the highest risk for premature death in all studied causes of death.

Separate analyses of different age groups 20-44, 45-64, and 65-79, showed that the younger the patient, the more pronounced increased risk for premature death (data not shown). This was true for all categories of mental disorder and for all studied causes of death, except for suicide.

The majority of patients (78% of women and 77% of men) with affective and anxiety disorders had been treated in outpatient care only. For the other disorders, around half of the patients had been treated in outpatient care only. Mortality rates were higher among those hospitalised than those treated in outpatient care. This was true for all categories of mental disorders and for all causes of death (data not shown).

The different health care quality indicators are presented in table 5. The percentage of avoidable admissions was higher among people treated for mental disorder, for women spanning from 2.4% to 4.1% (compared to 1.1% for those without episodes of treatment for mental disorder), and for men spanning from 3.4% to 5.4% (compared to 1.6%). Psychiatric patients had a higher 28-day case fatality rate for myocardial infarction, especially those treated for schizophrenia and other non-affective psychoses (women 53.5% (42.0-65.0) and men 51.4% (40.4-62.3)), compared to 26.5% of women (25.7-27.3) and 28.1% (27.5-28.6) of men not treated for mental disorder. The indicator on lipid lowering drug therapy shows that psychiatric patients with diabetes were given lipid lowering drugs to a lesser extent than diabetic patients without a concurrent mental disorder; this was particularly evident among both women and men with schizophrenia and other non-affective psychoses.

DISCUSSION

Our study of more than 6 million women and men shows that psychiatric patients had a substantially increased risk of death compared to individuals with no episodes of treatment for mental disorder, regardless of cause of death. Overall, people with schizophrenia and other non-affective psychoses, and people treated for substance abuse disorder had the highest risk for premature death. Psychiatric patients also had higher rates of potentially avoidable hospitalisations, higher case fatality rate after myocardial infarction, and lower use of lipid lowering therapy in diabetes.

The strengths of the study include the population-based design, using national registers with high completeness. The validity in the Causes of Death Register is very high, where information of cause of death is lacking in only 0.5% of the deceased. The National Patient Register has close to complete coverage of all inpatient care. However in 2005 around 40% of psychiatric outpatient visits were not included, hence some patients who were treated in outpatient care are classified as unexposed, as there is no record of their outpatient visit. Also, as the National Patient Register does not cover primary care we were not able to study all levels of psychiatric care. Hence, patients treated for mental health problems solely in primary care are classified as unexposed. Assuming a similar effect for patients in primary care as for psychiatric patients in our study selected by a more strict definition of mental health problems, i.e. patients who have seen a psychiatrist, this misclassification will dilute our results towards the null. We were unable to study the effects of health-related behaviours such as excessive alcohol consumption or tobacco smoking, which is a limitation.

We found that psychiatric patients were at higher risk of premature death from IHD, particularly among those treated for schizophrenia and other non-affective psychoses.

This has previously been shown in other settings, ^{10,11,19,20} and recently a study showed that the excess cardiovascular mortality among schizophrenia patients has increased over the past 25 years.⁷ We also found an elevated risk for cancer mortality, although to a lesser extent, in particular in patients treated for schizophrenia and other non-affective psychoses and substance abuse disorders. Studies evaluating cancer incidence and mortality at the same time have shown that, while individuals with mental disorder did not show any increased incidence rate for many types of cancer, they did have higher cancer mortality, which might be explained by delays in detection, ^{23,36} disparities in screening for cancer, ²² and treatment compliance.³⁷

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Psychiatric patients had an elevated risk of premature death from conditions considered amenable to intervention by the health service, i.e. avoidable mortality, compared to those not treated in psychiatric care. In particular, those treated for schizophrenia with comorbid substance abuse disorder had a higher risk, which has been shown by others. ^{13,31}

In line with previous studies, we found psychiatric patients to have significantly higher suicide risk, in particular those treated for schizophrenia and other non-affective psychosis, and affective disorder, and especially those treated with a comorbid substance abuse disorder.¹⁷

Mentally ill patients also had substantially increased risk of deaths from external causes when suicide was excluded. Studies have shown that people with mental disorder are at greater risk of accidental and violent death, particularly when alcohol and drug comorbidities are involved.³⁸ As mentioned earlier, our results showed that mentally ill individuals with a coexisting substance abuse disorder have significantly higher risk for premature death. When we excluded those with a coexisting substance abuse disorder, the increased mortality risk remained for all diagnosis groups except

for schizophrenia and other non-affective psychosis, but with lower estimates (data not shown).

Consistent with previous research, substance abuse disorders strongly contributed to premature death among both female and male psychiatric patients, especially for those with both alcohol and drug abuse.

When studying a set of indicators aimed to reflect the outcome of health care quality, we found that patients with a mental disorder had higher rates of potentially avoidable hospitalisations. Under some circumstances hospitalization is necessary and well motivated, but for most studied diseases, it is a failure. A recent study on avoidable hospitalisation demonstrated that the quality of physical health care received by patients with schizophrenia was poorer than that of the general population, signalling failures in public health and medical care³⁴.

The indicator of 28-day case fatality rate after myocardial infarction showed worse outcome for those with a mental disorder. In a Danish study, ¹⁹ less somatic hospitalisation than needed, and less use of invasive heart disease procedures among persons with severe mental disorder than among the general population were suggested as additional reasons for their excess mortality in IHD.

Another finding was the low percentage of lipid lowering drugs given to diabetic patients with a concurrent mental disorder. As drug therapy against lipid disorders is particularly important in diabetic patients,³⁹ this is a clear indication of inequality in health care.

Disparities in access to and utilisation of health care, as well as the quality of health care provision may contribute to inequalities in health.⁴⁰ One reason for these disparities could be that a person with mental disorder may not be able to effectively communicate and express concerns because of cognitive disturbance. Also,

psychiatrists and other mental health providers may prioritise psychiatric issues and neglect physical problems.⁴¹ There is also some evidence of inequalities in case recognition and quality of medical care for psychiatric patients, where general practitioners might minimise the clinical significance of physical complaints when assessing and treating patients with a mental disorder; a process known as diagnostic overshadowing.⁴² As there is excess mortality across a wide range of mental disorders, somatic care should be improved for all psychiatric patients, regardless of the severity of the mental disorder.

In addition to inequalities in utilisation and quality of health care, there are many factors that contribute to poor physical health in people with a mental disorder, including health-related behaviours and medication side-effects. The increased morbidity and mortality seen in this population are largely due to a higher prevalence of modifiable risk factors, many of which are related to health-related behaviours. The use of alcohol and illicit drugs is more common among psychiatric patients. It is also known that psychiatric patients smoke to a larger extent, 3,43 which could be an explanation for the increased mortality in IHD and cancer. Regardless of the kind of mental disorder, we found psychiatric patients to have an increased risk of dying in smoking-related cancer (data not shown). An unhealthy diet may also elevate the risk of various somatic diseases and thus increase the risk of death. The effects of these health-related behaviours have all been proposed as possible causative factors for excess mortality.⁴⁴ Also, medications used to treat severe mental disorder may increase the risk of diabetes and cardiovascular disease, as most mood stabilisers are associated with weight gain. 12,45 However, these factors make careful monitoring of the physical health status of patients with mental disorders even more important.

Conclusion

This study shows a marked increase in excess mortality in mentally ill men and women. This was especially evident in individuals with a comorbid substance abuse disorder. The findings also suggest a lower quality of health care in the treatment of somatic disorders in psychiatric patients. Careful medical examination of psychiatric patients together with efforts to promote a healthier life style may be of great importance in order to prevent, detect, and treat somatic disease.

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COMPETING INTERESTS

There are no competing interests.

CONTRIBUTORSHIP STATEMENT

EB, GWR and RL originated the idea. EB analyzed the data and wrote the manuscript draft. All authors contributed the interpretation of the results and to the writing of the final manuscript.

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Table 1. Cohort characteristics

8		v	/omen					N			
9	Schizophrenia and other non-affective psychoses	Affective disorder	Anxiety disorder	Other mental disorder	No mental disorder	Schizophrenia and other non-affective psychoses	Affective disorder	Anxiety disorder	Other mental disorder	No mental disorder	
10											
1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	11 165	37 245	32 690	20 400	3 039 954	11 993	23 762	21 209	33 982	3 061 939	6 294 339
12	0.2	0.6	0.5	0.3	48.3	0.2	0.4	0.3	0.5	48.6	
1% Mean age (SD)	50.1 (13.6)	46.1 (15.6)	42.4 (14.3)	43.8 (16.4)	48.1 (16.0)	45.8 (13.0)	46.9 (14.9)	42.0 (13.4)	47.2 (15.2)	47.2 (15.6)	47.6 (15.8)
13 _{erson-years}	21 923	73 620	64 788	40 039	6 017 464	23 463	46 604	41 790	65 925	6 042 510	12 438 126
14											
1 5 auses of death											
1 6 Il-cause mortality	344 (3.1 %)	669 (1.8 %)	413 (1.3 %)	638 (3.1 %)	27 421 (0.9 %)	459 (3.8 %)	764 (3.2 %)	389 (1.8 %)	1 822 (5.4 %)	39 268 (1.3 %)	72 187 (1.1 %)
1 Avoidable mortality: Medical Care Indicators	34 (0.3 %)	68 (0.2 %)	36 (0.1 %)	54 (0.3 %)	3 125 (0.1 %)	30 (0.3 %)	78 (0.3 %)	28 (0.1 %)	140 (0.4 %)	3 904 (0.1 %)	7 497 (0.1 %)
Avoidable mortality: National Health Policy Indicators	22 (0.2 %)	57 (0.2 %)	43 (0.1 %)	89 (0.4 %)	2 859 (0.1 %)	34 (0.3 %)	41 (0.2 %)	38 (0.2 %)	226 (0.7 %)	4 062 (0.1 %)	7 471 (0.1 %)
Ischemic heart disease	42 (0.4 %)	68 (0.2 %)	47 (0.1 %)	72 (0.4 %)	3 279 (0.1 %)	79 (0.7 %)	117 (0.5 %)	68 (0.3 %)	280 (0.8 %)	7 878 (0.3 %)	11 930 (0.2 %)
19 Cancer (all types)	83 (0.7 %)	163 (0.4 %)	129 (0.4 %)	111 (0.5 %)	12 369 (0.4 %)	65 (0.5 %)	136 (0.6 %)	71 (0.3 %)	247 (0.7 %)	13 636 (0.4 %)	27 010 (0.4 %)
2Quicide	42 (0.4 %)	117 (0.3 %)	71 (0.2 %)	73 (0.4 %)	439 (0.0 %)	79 (0.7 %)	167 (0.7 %)	69 (0.3 %)	174 (0.5 %)	1 259 (0.0 %)	2 490 (0.0 %)
21 eaths from external causes (suicide excluded)	15 (0.1 %)	44 (0.1 %)	27 (0.1 %)	47 (0.2 %)	652 (0.0 %)	39 (0.3 %)	67 (0.3 %)	48 (0.2 %)	232 (0.7 %)	1 867 (0.1 %)	3 038 (0.0 %)
22											
ാ Health care quality indicators*	8 413	22 833	17 078	11 171	1 961 968	7 864	15 502	11 126	22 762	1 931 860	4 010 577
24 Avoidable inpatient medical care											55 440
	234	521	409	445	22 433	235	474	341	1 189	29 159	
25 Nyocardial infarction - 28-day case fatality											36 171
AIVII IN 2006 OF 2007	77	164	134	118	10 993	105	244	140	410	23 786	10 122
27 _{Dead within 28 days}	36	62	45	53	3 108	50	88	42	171	6 467	
28 Lipid lowering drug therapy											
29Number receiving diabetes drug therapy in 2006	722	1 200	726	596	80 453	744	1 185	680	1 744	116 270	204 320
Of these, number who were given lipid lowering	292	618	385	280	45 193	318	631	367	743	65 440	114 267
31 drugs in 2006 * Individuals aged 40-79											

* Individuals aged 40-79

Table 2. Relative risk of death in psychiatric patients compared with a population with no episode of treatment for mental disorder (incidence rate ratios* with 95% confidence intervals)

Mental disorder group	All-cause mortality	Ischemic heart disease	Cancer (all types)	Avoidable mortality: Medical Care Indicators	Avoidable mortality: National Health Policy Indicators	Suicide	Death from external causes (suicide excluded)
<u>Females</u>							
No mental disorder	1 (REF)	1 (REF)	1 (REF)	1 (REF)	1 (REF)	1 (REF)	1 (REF)
Schizophrenia and other non-affective psychoses	3.8 (3.4-4.2)	4.1 (3.1-5.6)	1.9 (1.5-2.4)	3.5 (2.5-4.9)	2.1 (1.4-3.2)	24.9 (18.1-34.2)	6.7 (4.0-11.1)
Affective disorder	2.4 (2.2-2.6)	2.1 (1.7-2.7)	1.3 (1.1-1.5)	2.2 (1.7-2.8)	1.9 (1.5-2.5)	22.3 (18.1-27.3)	6.1 (4.5-8.3)
Anxiety disorder	2.6 (2.3-2.8)	2.9 (2.1-3.8)	1.7 (1.4-2.0)	2.2 (1.6-3.0)	2.4 (1.8-3.2)	16.0 (12.5-20.6)	5.3 (3.6-7.8)
Other mental disorder (including substance abuse disorder)	4.7 (4.3-5.0)	4.6 (3.6-5.8)	1.8 (1.5-2.2)	3.5 (2.7-4.6)	6.2 (5.0-7.6)	26.7 (20.8-34.3)	12.6 (9.4-17.0)
<u>lales</u>							
No mental disorder	1 (REF)	1 (REF)	1 (REF)	1 (REF)	1 (REF)	1 (REF)	1 (REF)
Schizophrenia and other non-affective psychoses	4.6 (4.2-5.0)	4.3 (3.4-5.3)	1.9 (1.5-2.5)	3.4 (2.4-4.9)	3.0 (2.1-4.1)	16.1 (12.9-20.3)	6.2 (4.5-8.6)
Affective disorder	2.8 (2.7-3.1)	2.2 (1.9-2.7)	1.5 (1.2-1.7)	3.0 (2.4-3.8)	1.4 (1.1-2.0)	17.2 (14.6-20.2)	4.9 (3.8-6.2)
Anxiety disorder	2.8 (2.5-3.0)	2.7 (2.1-3.5)	1.5 (1.2-2.0)	2.3 (1.6-3.4)	2.3 (1.7-3.2)	8.3 (6.5-10.6)	4.5 (3.4-6.1)
Other mental disorder (including substance abuse disorder) Adjusted for age	4.8 (4.6-5.0)	3.7 (3.3-4.2)	1.9 (1.6-2.1)	3.9 (3.3-4.6)	5.5 (4.8-6.3)	12.6 (10.8-14.8)	11.8 (10.3-13.6)

Table 3. Associations of mental disorder and substance abuse in relation to mortality (incidence rate ratios* with 95% confidence intervals)

Mental disorder group	N	All-cause mortality	Ischemic heart disease	Cancer (all types)	Avoidable mortality: Medical Care Indicators	Avoidable mortality: National Health Policy Indicators	Suicide	Death from external causes (suicide excluded)
Females								
No mental disorder	3 039 954	1 (REF)	1 (REF)	1 (REF)	1 (REF)	1 (REF)	1 (REF)	1 (REF)
Schizophrenia and other non-affective psychoses with substance abuse disorder	502	10.8 (7.1-16.6)	5.7 (0.8-40.4)	5.2 (2.2-12.6)	-	21.5 (8.9-51.8)	44.6 (14.3-138.8)	43.1 (13.8-134.1)
Schizophrenia and other non-affective psychoses without substance abuse disorder	10 663	3.6 (3.2-4.0)	4.1 (3.0-5.6)	1.8 (1.5-2.3)	3.5 (2.5-5.0)	1.7 (1.0-2.7)	24.2 (17.4-33.6)	5.5 (3.1-9.8)
Affective disorder with substance abuse disorder	1 919	6.4 (4.9-8.3)	3.5 (1.1-10.9)	2.7 (1.5-4.8)	3.4 (1.1-10.6)	6.5 (3.1-13.6)	61.1 (37.1-100.6)	24.1 (11.4-50.8)
Affective disorder without substance abuse disorder	35 326	2.3 (2.1-2.5)	2.1 (1.6-2.7)	1.2 (1.1-1.4)	2.2 (1.7-2.8)	1.8 (1.3-2.3)	20.3 (16.3-25.2)	5.4 (3.9-7.5)
Anxiety disorder with substance abuse disorder	1 551	7.3 (5.4-9.8)	10.9 (4.9-24.3)	2.0 (0.9-4.4)	1.7 (0.2-12.2)	6.8 (2.8-16.4)	63.1 (36.3-109.7)	22.9 (9.5-55.4)
Anxiety disorder without substance abuse disorder	31 139	2.4 (2.2-2.7)	2.6 (1.9-3.5)	1.7 (1.4-2.0)	2.2 (1.6-3.0)	2.2 (1.6-3.0)	13.8 (10.5-18.2)	4.5 (3.0-6.9)
Other mental disorder <u>with</u> substance abuse disorder	387	17.0 (10.4-27.7)	-	-	11.3 (1.6-80.4)	-	171.6 (85.1-346.0)	21.6 (3.0-153.5)
Other mental disorder without substance abuse disorder	10 773	2.6 (2.3-3.0)	2.9 (2.0-4.1)	1.4 (1.1-1.8)	2.6 (1.8-3.8)	0.9 (0.4-1.8)	10.0 (5.9-17.0)	1.8 (0.7-4.9)
Substance abuse disorder without a psychiatric diagnosis	9 240	7.9 (7.1-8.7)	8.4 (6.2-11.4)	2.4 (1.9-3.1)	5.3 (3.6-7.8)	13.4 (10.7-16.7)	39.8 (29.8-53.2)	28.1 (20.5-38.5)
Males								
No mental disorder	3 061 939	1 (REF)	1 (REF)	1 (REF)	1 (REF)	1 (REF)	1 (REF)	1 (REF)
Schizophrenia and other non-affective psychoses with substance abuse disorder	1 088	12.5 (9.8-15.9)	4.9 (1.9-13.2)	3.8 (1.7-8.4)	5.3 (1.3-21.1)	11 (5.2-23.1)	41.3 (25.6-66.7)	22.3 (12.3-40.3)
Schizophrenia and other non-affective psychoses <u>without</u> substance abuse disorder	10 905	4.2 (3.8-4.6)	4.3 (3.4-5.3)	1.8 (1.4-2.4)	3.4 (2.3-4.9)	2.5 (1.7-3.6)	13.9 (10.7-17.9)	4.9 (3.4-7.1)
Affective disorder with substance abuse disorder	2 237	6.7 (5.6-8.1)	5.4 (3.4-8.6)	1.6 (0.9-3.0)	5.8 (3.0-11.2)	5.3 (2.9-9.5)	43.7 (31.8-60.2)	11.3 (6.5-19.4)
Affective disorder without substance abuse disorder	21 525	2.6 (2.4-2.8)	2 .0 (1.6-2.4)	1.5 (1.2-1.7)	2.8 (2.2-3.6)	1.1 (0.8-1.6)	14.5 (12.1-17.4)	4.3 (3.3-5.6)
Anxiety disorder with substance abuse disorder	1 900	9.7 (7.9-11.8)	7.7 (4.5-13.2)	2.5 (1.2-4.9)	2.5 (0.6-10.2)	8.9 (4.9-16.1)	27.7 (17.8-43.1)	24.8 (16.3-37.8)
Anxiety disorder without substance abuse disorder	19 309	2.2 (2.0-2.5)	2.4 (1.8-3.1)	1.5 (1.2-1.9)	2.3 (1.6-3.4)	1.8 (1.2-2.6)	6.5 (4.9-8.6)	2.7 (1.8-4.0)
Other mental disorder with substance abuse disorder	380	9.8 (6.7-14.4)	21.0 (11.3-39.0)	2.3 (0.6-9.1)	8.7 (2.2-35.0)	-	47.6 (22.6-100.1)	10.6 (2.7-42.5)
Other mental disorder without substance abuse disorder	9 298	2.5 (2.2-2.8)	1.7 (1.3-2.2)	1.4 (1.1-1.8)	3.5 (2.7-4.7)	1.2 (0.7-2.0)	5.4 (3.5-8.4)	2.3 (1.4-3.9)
Substance abuse disorder without a psychiatric diagnosis	24 304	6.1 (5.8-6.4)	4.8 (4.2-5.5)	2.1 (1.8-2.4)	4.0 (3.3-5.0)	7.7 (6.7-8.8)	14.8 (12.5-17.6)	16.1 (14.0-18.6)
* Adjusted for age								

^{*} Adjusted for age

Table 4. Relative risk of mortality in psychiatric	pai	tients with substa	ince abuse dis	soraer (IRR With S	15% confidence inte	rvais)
	N	All-cause mortality	Ischemic heart	Cancer (all	Avoidable mortality:	Avoidal
			disease	types)	Medical Care Indicators	He

	N	All-cause mortality	Ischemic heart disease	Cancer (all types)	Avoidable mortality: Medical Care Indicators	Avoidable mortality: National Health Policy Indicators	Suicide	Death from external causes (suicide excluded)
<u>Females</u>								
No substance abuse disorder	3 127 855	1 (REF)	1 (REF)	1 (REF)	1 (REF)	1 (REF)	1 (REF)	1 (REF)
Substance abuse disorder, alcohol	8 185	7.7 (6.9-8.5)	4.1 (0.6-29.3)	2.3 (1.8-3.0)	4.8 (3.2-7.2)	13.8 (11.1-17.2)	29.5 (22.1-39.4)	22.6 (16.0-32.0)
Substance abuse disorder, drug abuse	4 589	6.6 (5.5-8.0)	4.7 (2.3-9.4)	2.7 (1.8-4.1)	3.9 (1.9-8.2)	6.1 (3.5-10.8)	36.9 (25.8-52.8)	22.9 (13.9-37.6)
Substance abuse disorder, both alcohol and drug abuse	825	11.2 (8.0-15.7)	8.7 (6.4-11.8)	2.6 (1.0-6.9)	3.7 (0.5-26.5)	7.8 (2.5-24.1)	54.4 (28.1-105.1)	65.8 (32.7-132.4)
Males								
No substance abuse disorder	3 122 976	1 (REF)	1 (REF)	1 (REF)	1 (REF)	1 (REF)	1 (REF)	1 (REF)
Substance abuse disorder, alcohol	20 429	5.5 (5.3-5.9)	4.8 (4.2-5.5)	2.0(1.7-2.4)	3.8 (3.1-4.7)	7.5 (6.6-8.7)	12.5 (10.4-14.9)	12.8 (10.8-15.0)
Substance abuse disorder, drug abuse	7 753	9.4 (8.4-10.6)	5.8 (3.9-8.7)	2.7 (1.7-4.1)	4.9 (2.6-9.1)	4.1 (2.4-7.0)	22.4 (17.7-28.4)	22.5 (18.0-28.3)
Substance abuse disorder, both alcohol and drug abuse * Adjusted for age	1 727	14.5 (12.2-17.2)	6.8 (3.7-12.7)	2.5 (1.2-5.2)	8.7 (3.9-19.4)	16.0 (10.0-25.4)	35.2 (24.2-51.2)	29.3 (19.6-43.9)

^{*} Adjusted for age

Table 5. Age-standardised percentage (with 95% confidence intervals) as measures of health care quality indicators for individuals aged 40-79, 2006

Mental disorder group

N Avoidable inpatient medical care (95% CI)

Wyocardial infarction - 28-day case fatality (15% CI)

Wyocardial infarction - 28-day case fatality (15% CI)

Wyocardial infarction - 28-day case fatality (15% CI)

		% (95% CI)	% (95% CI)	% (95% CI)
<u>Females</u>				
No mental disorder	1 961 968	1.1 (1.1-1.1)	26.5 (25.7-27.3)	56.1 (55.7-56.4)
Schizophrenia and other non-affective psychoses	8 413	2.9 (2.6-3.3)	53.5 (42.0-65.0)	40.9 (36.8-45.1)
Affective disorder	22 833	2.4 (2.2-2.6)	34.8 (26.5-43.2)	51.9 (49.0-54.8)
Anxiety disorder	17 078	3.0 (2.7-3.3)	36.1 (28.8-43.4)	54.9 (50.9-58.8)
Other mental disorder (including substance abuse disorder)	11 171	4.1 (3.7-4.5)	45.0 (35.8-54.3)	49.0 (44.8-53.1)
<u>Males</u>				
No mental disorder	1 931 860	1.6 (1.5-1.6)	28.1 (27.5-28.6)	56.2 (55.9-56.5)
Schizophrenia and other non-affective psychoses	7 864	3.8 (3.3-4.4)	51.4 (40.4-62.3)	41.9 (37.2-46.5)
Affective disorder	15 502	3.4 (3.1-3.7)	39.2 (32.6-45.7)	53.8 (50.8-56.8)
Anxiety disorder	11 126	4.4 (3.9-4.9)	32.5 (23.1-42.0)	56.4 (51.9-60.8)
Other mental disorder (including substance abuse disorder)	22 762	5.4 (5.1-5.7)	43.9 (38.6-49.1)	44.2 (41.7-46.7)

No 1	Recommendation (a) Indicate the study's design with a commonly used term in the title or the abstract
	Page 1
	(b) Provide in the abstract an informative and balanced summary of what was done
	and what was found
	Page 3
2	Explain the scientific background and rationale for the investigation being reported
	Page 4
3	State specific objectives, including any prespecified hypotheses
	Page 5
4	Present key elements of study design early in the paper
	Page 6
5	Describe the setting, locations, and relevant dates, including periods of recruitment,
	exposure, follow-up, and data collection
	Page 6
6	(a) Give the eligibility criteria, and the sources and methods of selection of
	participants. Describe methods of follow-up
	Page 6
	(b) For matched studies, give matching criteria and number of exposed and
	unexposed
	N/A
7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect
	modifiers. Give diagnostic criteria, if applicable
	Page 6 - 8
8*	For each variable of interest, give sources of data and details of methods of
	assessment (measurement). Describe comparability of assessment methods if there is
	more than one group
	Page 6 - 8
9	Describe any efforts to address potential sources of bias
	N/A
10	Explain how the study size was arrived at
	Page 6
11	Explain how quantitative variables were handled in the analyses. If applicable,
	describe which groupings were chosen and why
	N/A
12	(a) Describe all statistical methods, including those used to control for confounding
	Page 8 - 9
	(b) Describe any methods used to examine subgroups and interactions
	N/A
	(c) Explain how missing data were addressed
	N/A
	(d) If applicable, explain how loss to follow-up was addressed
	N/A
	3 4 5 6 7 8* 9 10 11

		(e) Describe any sensitivity analyses
Results		
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed
		Page 10 and page 20
		(b) Give reasons for non-participation at each stage N/A
		(c) Consider use of a flow diagram
		N/A
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and
		information on exposures and potential confounders
		Page 20
		(b) Indicate number of participants with missing data for each variable of interest
		N/A
		(c) Summarise follow-up time (eg, average and total amount)
		Page 20
Outcome data	15*	Report numbers of outcome events or summary measures over time
		Page 10 and page 20
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and
		their precision (eg, 95% confidence interval). Make clear which confounders were
		adjusted for and why they were included
		Page 10-11 and page 21-23
		(b) Report category boundaries when continuous variables were categorized
		N/A
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a
		meaningful time period N/A
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and
Other analyses	17	sensitivity analyses
		Page 11 and page 24
Discussion		0 10
Key results	18	Summarise key results with reference to study objectives
,		Page 2 and page 12 – 16
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or
		imprecision. Discuss both direction and magnitude of any potential bias
		Page 2 and page 12
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations,
		multiplicity of analyses, results from similar studies, and other relevant evidence
		Page 12 – 16
Generalisability	21	Discuss the generalisability (external validity) of the study results
		Page 15
Other information		
Funding	22	Give the source of funding and the role of the funders for the present study and, if
		applicable, for the original study on which the present article is based
		Page 16

^{*}Give information separately for exposed and unexposed groups.