Revascularisation and mortality rates following acute coronary syndromes in people with severe mental illness: comparative meta-analysis

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Background
High levels of comorbid physical illness and excess mortality rates have been previously documented in people with severe mental illness, but outcomes following myocardial infarction and other acute coronary syndromes are less clear.

Aims
To examine inequalities in the provision of invasive coronary procedures (revascularisation, angiography, angioplasty and bypass grafting) and subsequent mortality in people with mental illness and in those with schizophrenia, compared with those without mental ill health.

Method
Systematic search and random effects meta-analysis were used according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines. Studies of mental health and cardiovascular procedures following cardiac events were eligible but we required a minimum of three independent studies to warrant pooling by procedure type. We searched Medline/PubMed and EMBASE abstract databases and ScienceDirect, Ingenta Select, SpringerLink and Online Wiley Library full text databases.

Results
We identified 22 analyses of possible inequalities in coronary procedures in those with defined mental disorder, of which 10 also reported results in schizophrenia or related psychosis. All studies following acute coronary syndrome originated in the USA. The total sample size was 825754 individuals. Those with mental disorders received 0.86 (relative risk, RR: 95% CI 0.80–0.92, P < 0.0001) of comparable procedures with significantly lower receipt of coronary artery bypass graft (CABG, RR = 0.85, 95% CI 0.72–1.00), cardiac catheterisation (RR = 0.85, 95% CI 0.76–0.95) and percutaneous transluminal coronary angioplasty or percutaneous coronary intervention (PTCA/PCI; RR = 0.87, 95% CI 0.72–1.05). People with a diagnosis of schizophrenia received only 0.53 (95% CI 0.44–0.64, P < 0.0001) of the usual procedure rate with significantly lower receipt of CABG (RR = 0.69, 95% CI 0.55–0.85) and PTCA/PCI (RR = 0.50, 95% CI 0.34–0.75). We identified 6 related studies examining mortality following cardiac events: for those with mental illness there was a 1.11 relative risk of mortality up to 1 year (95% CI 1.00–1.24, P = 0.05) but there was insufficient evidence to examine mortality rates in schizophrenia alone.

Conclusions
Following cardiac events, individuals with mental illness experience a 14% lower rate of invasive coronary interventions (47% in the case of schizophrenia) and they have an 11% increased mortality rate. Further work is required to explore whether these factors are causally linked and whether improvements in medical care might improve survival in those with mental ill health.

Declaration of interest
None.

Coronary heart disease is the leading cause of death worldwide.1,2 Acute coronary syndrome refers to acute myocardial ischaemia caused by atherosclerotic coronary disease and includes myocardial infarction and unstable angina. Patients with ST elevation myocardial infarction are recommended for immediate reperfusion therapy using thrombolytic agents or percutaneous coronary intervention (PCI).3,4 From 1980 to 1990 there was a 34% decline in coronary heart disease mortality in the USA.5 Over the same period there was a substantial growth in the number of cardiovascular procedures performed, particularly PCI. Improvements in the quality of care are thought to be a major factor underlying declining mortality.5 Yet despite these improvements evidence of sociodemographic inequalities in procedural rates has been accumulating.6–11 Inequalities have also been documented with regard to the medical care of those with known mental health diagnoses. Medical care includes medical treatment and processes of care such as investigations and monitoring. Mitchell et al evaluated 27 studies that examined receipt of medical care in those with and without mental illness (including 11 studies of severe mental illness or schizophrenia and 10 of dual diagnosis or substance use disorder).12 The majority of studies demonstrated significant inequalities in receipt of quality of care including 7 of 10 studies that examined the quality of cardiovascular care. Lord et al recently reviewed 25 studies that examined preventive care in individuals with or without psychiatric illness; for individuals with schizophrenia, 8 of 9 analyses suggested inferior receipt of preventive care in several areas including blood pressure monitoring, vaccinations, mammography and cholesterol monitoring.13 From these narrative reviews it is clear that the magnitude of the deficits in quality of care varies considerably depending on the setting and method of data collection.

There is substantial concern about the cardiovascular health of those with known mental health diagnoses, especially severe mental illness and schizophrenia.14,15 National guidelines from several countries are agreed that the medical care of patients with mental disorders is of paramount importance.16–19 However, serious concerns have been raised about the quality of medical care offered to patients with severe mental illness. People with schizophrenia have higher rates of several important conditions including the metabolic syndrome.20,21 Most studies,15,22–28 but not all,29,30 suggest that incidence of cardiovascular disease is higher in people with schizophrenia. Such individuals often have higher than expected rates of contributing background risk factors including smoking,31 obesity,32 dyslipidaemia,33 lack of exercise,34 and possibly essential hypertension.35 A meta-analysis suggested a relative risk of 1.87 (95% CI 1.68–2.09) for diabetes in schizophrenia, but with no significant elevation of hypertension.
or cholesterol. Of these factors, smoking and obesity may be most critical to future cardiovascular health. An estimated 42% of patients with schizophrenia have a body mass index above 27 kg/m² compared with 27% among the general US population; three-quarters are regular cigarette smokers compared with a quarter of the general population. It is therefore not surprising that people with schizophrenia have higher than expected non-suicide-related mortality; in fact, mortality from comorbid physical illness outnumbers the excess mortality from suicide. A systematic review of 37 studies found that those with schizophrenia have a 2.6 times greater rate of mortality compared with the general population, including 1.8 times the mortality rate from cardiovascular disease.

Given these numerous concerns regarding cardiovascular health in severe mental illness and in particular in schizophrenia, we aimed to examine and quantify, first, the receipt of medical procedures following acute coronary syndrome, and second, the mortality rate following acute coronary syndrome using meta-analysis of published data. We were interested in comparative studies that examined the adequacy of appropriate procedures and subsequent mortality for people with cardiac disorders stratified into those with and without severe mental illness/schizophrenia.

**Method**

**Search**

We used the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, a checklist of 27 items that ensure the quality of systematic review or meta-analysis. Inclusion criteria were studies of patients with acute coronary syndromes (with data on rates of subsequent invasive coronary procedures or mortality) which reported data for those with defined mental illness as well as those without mental ill health. We only included those with severe mental illness provided there was a subgroup with schizophrenia. We excluded non-comparative studies, and also those concerning depression or anxiety only. We searched Medline/PubMed and EMBASE abstract databases from inception to 20 July 2010. In these databases the keywords/MeSH terms (‘ACS or REVASCULARISATION or REVASCULARIZATION or PROCEDURES or GRAFT or ANGIOPLASTY or PERCUTANEOUS or CATHETERIZATION or CARDIA* or HEART’) and (‘PSYCHI* or MENTAL or PSYCHOSIS or PSYCHOTIC or SCHIZOPHR* or SEVERE MENTAL ILLNESS or SMI’) were used. In addition, four full text collections were searched: ScienceDirect, Ingenta Connect, SpringerLink and Wiley Online Library. In these online databases the same search terms were used as a full text search and as a citation search. The abstract databases Web of Knowledge and Scopus were searched, using the above terms as a text word search, and using key papers in a reverse citation search. Finally, a number of journals were hand-searched and several experts contacted. We excluded studies where the event rate was measured in the general population rather than in those with cardiovascular disease. Where 30-day and 365-day mortality rates were cited, we examined only 365-day rates. Data were extracted using a standard form (available from the authors on request) by A.J.M. and checked by D.L.

**Meta-analysis**

We used summary meta-analysis, pooling hazard ratios where reported. All hazard ratios were entered adjusted rather than unadjusted (where reported and except where indicated). Odds ratios were converted into relative risks (hazard ratios) using the reported control event rate. Confidence intervals were obtained from all studies or calculated from the data provided. Heterogeneity was reduced by stratifying using type of mental illness and procedure type; despite this, heterogeneity (defined by I²) remained high and so random effects meta-analysis was preferred. We required a minimum of three independent studies to justify pooling by procedure type. Any potential sources of bias were reported. Publication bias was assessed using the Begg–Mazumdar statistic.

The initial PubMed search generated 372 hits. Of these, only 16 discussed cardiac procedures and 58 discussed mortality (online data supplement). Searches in the four full-text collections generated 1572 hits (Fig. 1). Using these strategies we identified 241 references of interest but only 74 were primary data studies. After excluding studies with no relevant outcome, no comparison group or other methodological issues, we identified 9 papers relating to cardiac procedures following acute coronary syndrome and 6 papers relating to mortality following acute coronary syndrome.

**Results**

**Studies examining procedure rate after acute coronary syndrome**

Our search identified 9 publications relating to cardiac procedures following acute coronary syndrome and contained in these reports were 22 analyses using broadly defined mental disorder or severe mental illness and 10 using an adequate definition of schizophrenia or related psychosis (online Table DS1). There was no evidence of publication bias using the Begg–Mazumdar statistic (Fig. DS1). The total sample size was 825754 (mean 91750, s.d. = 120158). Druss et al examined cardiovascular care following an acute myocardial infarction. After adjusting for demographic, clinical, hospital and regional factors, those with mental disorders were only 41% (for schizophrenia) to 78% (for substance use) as likely to undergo cardiac catheterisation as those without mental disorder. In a further study, Druss et al found patients hospitalised for myocardial infarction with mental health diagnoses were less likely to have reperfusion conducted. Young & Foster identified people with mental illness who had experienced a myocardial infarction: this group had significantly lower levels of all three revascularisation procedures – cardiac catheterisation, percutaneous transluminal coronary angioplasty (PTCA) and coronary artery bypass graft (CABG) – compared with those without mental illness, with the lowest rates seen in those over 64 years old. Petersen et al examined the records of 4340 male veterans discharged after a clinically confirmed myocardial infarction: those with mental illness were less likely to have undergone in-patient diagnostic angiography (age-adjusted RR = 0.90, 95% CI 0.83–0.98) but there was no difference in CABG. Kisely et al carried out a population-based record-linkage analysis of related data from 1995 through 2001 compared with the general public for each outcome (n = 215889): in psychiatric in-patients the adjusted rate ratios for cardiac catheterisation, PTCA and CABG were 0.41, 0.22 and 0.34 respectively. However, Plomondon et al found no difference in cardiac procedure rates after acute coronary syndromes presenting to Veterans Health Administration (VHA) hospitals. Similarly, Jones & Carney found no difference in the rates of revascularisation. Patients admitted with heart disease in Denmark between 1994 and 2007: people with admissions for severe mental disorder had higher mortality rates from heart disease following cardiac procedures but received lower rates of cardiac revascularisation. Abrams et al examined the rate of PCI or CABG within 30 days of...
They examined mixed mental disorders, defined by ICD–9 codes, in 21,745 patients admitted following acute myocardial infarction. They reported results in two related samples: patients with psychiatric comorbidity had lower receipt of coronary revascularisation (hazard ratio, HR = 0.92, 95% CI 0.85–0.99) in the out-patient sample but equal rates (HR = 1.00, 95% CI 0.91–1.1) in the in-patient sample.52

Quantitative differences in procedure rates

For those with mental illness or severe mental illness there was significant heterogeneity (I² = 98.1%). The meta-analytic random effects size was 0.86 (95% CI 0.80–0.92, P < 0.0001), suggesting that those with any mental illness received a 14% lower rate of cardiac procedures (Fig. 2). Looking at each procedure individually, there was significantly lower receipt of CABG (RR = 0.85, 95% CI 0.72–1.00), cardiac catheterisation (RR = 0.85, 95% CI 0.76–0.95) and PTCA/PCI (RR = 0.87, 95% CI 0.72–1.05). For those with schizophrenia there was moderate heterogeneity (I² = 77.6%). The meta-analytic relative risk was 0.53 (95% CI 0.44–0.64, P < 0.0001), suggesting that those with schizophrenia received about half the comparable rate of cardiac procedures (Fig. 3). Looking at each procedure individually, there was significantly lower receipt of CABG (RR = 0.69, 95% CI 0.55–0.85) and PTCA/PCI (RR = 0.50, 95% CI 0.34–0.75).

Studies examining mortality after acute coronary syndrome

We identified ten studies relating to mortality following cardiac events but two reported mortality as the general population rate, one had a significant methodological issue and one had insufficient data for analysis. The total sample size from six valid studies was 596,368 (mean 99,394, s.d. = 132,344). In Druss et al’s 2000 study, patients with mental disorders had a small but statistically significantly lower risk of mortality at baseline, and in unadjusted analysis 12.8% of those with schizophrenia died within 30 days compared with 10.8% in the comparator population; however, this was not significant after adjustments.44 Yet in their replication study, Druss et al found that mental disorder of all types was associated with a 19% increase in mortality at 1 year.45 Importantly, when the five quality indicators were added to the model the association was no longer significant, suggesting that elevated mortality is related to poor quality of care. Petersen et al examined the records of 4,340 male veterans discharged after a clinically confirmed myocardial infarction and found a trend towards higher rate of death at 1 year in those with mental illness; the risk of death within 1 year was 1.25 (95% CI 1.00–1.53).47 Plomondon et al studied 14,194 patients (including 18% with severe mental illness) with acute coronary syndromes presenting to VHA hospitals between October 2003 and September 2005.49 One-year mortality was lower for patients with severe mental illness (15.8% v. 19.1%, P < 0.001). However, in multivariable analysis there was no significant difference in mortality (HR = 0.91, 95% CI 0.81–1.02) between patients with and without severe mental illness.49

Four additional studies were noteworthy but could not be entered into the meta-analysis. Young & Foster found that in the older cohort (>65 years old) with mental illness there was a 21% lower risk-adjusted likelihood of death (P < 0.001) compared...
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with those without mental illness. In the younger cohort those with schizophrenia and substance misuse had higher in-patient mortality rates (both P<0.001). Unfortunately, data were inadequately reported for extraction. Kisely et al examined mortality and revascularisation in a general population sample. They conducted a population-based record-linkage analysis of related data from 1995 through 2001 compared with the general population for each outcome (n = 215889): the age-standardised mortality rate ratio for psychiatric patients was 1.31 (95% CI 1.25–1.36). In the study from Lawrence et al, ischaemic heart disease was the major cause of excess mortality in psychiatric patients. The standardised mortality rate from ischaemic heart disease in mental health users was almost twice that in the overall population (1.91 in total ischaemic heart disease, 1.74 in acute myocardial infarction). However, in the latter two studies the risk was measured at the population level, not specifically in those with acute coronary syndrome. Recently, Blecker et al examined mortality in 341 individuals with heart failure and severe mental

Fig. 2 Meta-analytic summary for receipt of cardiac procedures in patients with mental illness v. those with no mental illness. CABG, coronary artery bypass graft; CC, cardiac catheterisation; IP, in-patient; OP, out-patient; PTCA, percutaneous transluminal coronary angioplasty; PCI, percutaneous coronary intervention.

Fig. 3 Meta-analytic summary for receipt of cardiac procedures in patients with schizophrenia v. those with no mental illness. CABG, coronary artery bypass graft; CC, cardiac catheterisation; PTCA, percutaneous transluminal coronary angioplasty.
illness compared with 1460 with heart failure and no severe mental illness.53 Mortality was 29.9% in the severe mental illness group compared with 31.7% in those without severe mental illness. However, we excluded this study from the meta-analysis because it was not clear whether the follow-up period was identical in the two groups.

Quantitative differences in mortality following acute coronary syndrome

For those with severe mental illness there was significant heterogeneity (I² = 91.6%), therefore random effects meta-analysis was preferred. The pooled relative risk for mortality was 1.15 (95% CI 1.02–1.29). Excluding the studies by Kisely et al and Lawrence et al which did not focus on acute coronary syndrome, the pooled relative risk for mortality was 1.11 (95% CI 1.00–1.24; P = 0.05), suggesting an 11% increase in mortality rates (Fig. 4).

**Discussion**

It is already known that people with depression have higher than expected mortality after myocardial infarction.54,55 We also know that background cardiovascular mortality in those with schizophrenia or severe mental illness is at least double the expected rate.27,29,39,56–60 Here, we extend these findings to a population with established acute coronary syndrome, largely myocardial infarction. Pooled results suggest an 11% increase in comparator mortality rates in those with severe mental illness. This is lower than previously documented in depression but nevertheless statistically significant. We also extend previous narrative reviews that highlighted inferior quality of medical care.12,16 From 22 analyses of coronary interventions following serious cardiac events, we found that those with defined mental disorder received 86% of comparable procedures with significantly lower receipt of CABG, cardiac catheterisation and PTCA/PCI. From 10 analyses, people with a diagnosis of schizophrenia or related psychosis received only 0.53 of the usual procedure rate, with significantly lower receipt of CABG and PTCA/PCI. One possible explanation is that physicians do not offer procedures to those with mental illness because they believe that such individuals are likely to have poorer uptake of care. However, findings regarding uptake of medical care are conflicting.62 Another possibility is that the needs of those with mental illness are crowded out by the focus on mental concerns or possibly other medical factors, which may lead physicians to think that procedures are not a priority in this group. There is also a question whether people with severe mental illness follow through with advice they are given. These questions can only be answered by good-quality studies examining physician responses to unmet medical needs in those with mental ill health as well as follow-up of patient behaviour.

**Possible mechanisms underlying elevated mortality rates**

In the general population prolonged QTc interval and low heart rate variability have been associated with increased cardiovascular mortality and sudden death, particularly in people with prior cardiovascular disease and diabetes.61,62 Schizophrenia appears to be associated with similar QT abnormalities, possibly even in the absence of antipsychotic medication, and it is possible that these factors are influential following acute coronary syndrome.63–65 It is also well known that metabolic syndrome and diabetes increase the risk of mortality,66,67 and these conditions are often more common in those with severe mental illness. There is also a higher rate of sudden cardiac death in those taking antipsychotics,68 that said, sudden cardiac death accounts for only a small proportion of excess mortality in schizophrenia.69 Unfortunately none of the studies cited here examined use of psychotropic drugs. A second mechanism might be the influence of severe mental illness on the effectiveness of cardiac treatment, for example through low engagement in rehabilitation. Preliminary evidence suggests similar uptake but lower completion of physical exercise programmes in those with known mental ill health.70 Confounding factors such as alcohol and drug use and medical comorbidities may also be influential. Most concerning is whether deficits in quality of care influence high mortality in this population. Li et al analysed New York’s publicly released Cardiac Surgery Report of surgeons’ risk-adjusted mortality rates.71 After adjustments, patients with both substance use and psychiatric disorders were more likely to receive care from surgeons in the high-mortality group (OR = 1.76, P = 0.024). Druss et al found that the excess mortality following myocardial infarction was negated when five quality measures were added to the model, suggesting that poor quality of care may be an important explanatory variable.45 More recently, Copeland et al analysed whether patients’ reduced primary care use over time was a significant predictor of mortality over a 4-year period among VHA patients; those with schizophrenia were likely to have low primary care use decreasing with time, and this was linked with inferior survival.72 Despite the large sample size we acknowledge several limitations in this meta-analysis. Our results may not be representative of all healthcare systems as all studies following acute coronary syndrome originated in the USA. It is not clear that inequalities would exist in other healthcare systems where there are fewer barriers to care for those who are most socially disadvantaged. One limitation is that the definition of severe mental illness varied in some studies, and although most used ICD–8 or ICD–9 coding the definition employed by one group was not entirely clear.44 A second limitation is that all studies were retrospective and none distinguished current from historical mental ill health and thus it is uncertain if risk applies to those with prior as well as current diagnoses. A third limitation in relation to mortality was that the studies by Lawrence et al and Kisely et al reported risk in population samples not specifically following acute coronary syndrome and were therefore excluded from the analysis.41,68 Additionally, Druss et al and Young & Foster did not report 1-year mortality rates,44,46 adding to the heterogeneity in mortality analysis. Finally, there was poor data
quality regarding hospitalisation and patient–provider factors underlying poor outcomes.

Improving inequalities in cardiac care

The disparities in cardiac care noted here are consistent with the wider literature documenting disparities in treatment of other medical domains including diabetes, general medicine and cancer care. Individuals with schizophrenia and severe mental illness receive as little as half of the monitoring offered to people without mental ill health. For example, in the Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) study, patients with schizophrenia had limited access to or received suboptimal medical care. In a retrospective analysis of 1998–2003 Medicaid claims, fewer than 20% of people starting treatment with antipsychotic medication received baseline glucose testing and fewer than 10% received baseline lipid testing. Unfortunately, professional responsibility for comorbid medical disorders is often unclear. Poor mental health status is linked with poor general practitioner accessibility and perceived barriers to medical treatment. Hence medical comorbidity often is overlooked in those with severe mental illness, with up to half of all chronic conditions remaining unrecognised. Yet there is great interest in effective interventions that might reduce cardiovascular mortality in schizophrenia as well as in mental illness in general. Several groups have developed screening and monitoring guidelines. However, implementation of these has been inconsistent. In the general population lifestyle interventions can significantly influence mortality. In diabetes glycaemic control has similar benefits. The magnitude of the effect of intensive glycaemic control in diabetes is of the same order as the excess risk documented here. Interventions specifically targeting weight control and eating habits in people with chronic mental illness have shown some promising results. However, it is uncertain if benefits are maintained and whether there is any measurable effect on mortality. Ultimately it has been suggested that a reorganisation of mental health services would help redefine responsibility for physical health. There is some support for a collaborative model of care, co-locating psychiatric and primary care. Yet to improve cardiac care in severe mental illness, interventions must be effective at the secondary-care level for hospital specialists with limited interest in mental illness.

In conclusion, following cardiac events individuals with mental illness appear to receive about 14% less frequent therapeutic cardiac procedures (47%) in the case of schizophrenia), and they have about an 11% increased mortality rate. Further work is required to explore whether these factors are causally linked and whether improvements in medical care might improve survival in those with mental ill health.

References


## Table DS1 Summary of comparative studies reporting on receipt of cardiac procedures

<table>
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<tr>
<th>Author, country</th>
<th>Cardiac procedure examined</th>
<th>Mental illness definition</th>
<th>Sample and possible biases</th>
<th>Setting</th>
<th>Result</th>
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<tbody>
<tr>
<td>Abrams 2009 USA</td>
<td>Rate of cardiac procedure (PCI or CABG) within 30 days of admission (using ICD–9–CM codes)</td>
<td>ICD–9 diagnosis from out-patient contacts in 12 months before admission or on admission, includes depressive disorders, PTSD, bipolar disorders and psychotic disorders</td>
<td>21,745 patients with acute myocardial infarction admitted to VHA hospitals Possible selection bias in VA sampling</td>
<td>Hospitalised patients (includes previous out-patient contact)</td>
<td>Patients with psychiatric comorbidity had lower receipt of coronary revascularisation (HR = 0.92, 99% CI 0.85–0.99) in out-patient sample but equal rates (HR = 1.00, 95% CI 0.91–1.1) in in-patient sample</td>
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<td>Druss 2001 USA</td>
<td>Cardiac care treatment: reperfusion therapy</td>
<td>ICD–9 definition, any mental disorder (n = 4664), schizophrenia (n = 161), affective disorder (n = 271), substance use disorder (n = 882)</td>
<td>88,241 Medicare patients hospitalised for a clinically confirmed myocardial infarction (data from Medicare) Controlled for eligibility for procedure, demographics, cardiac risk factors, left ventricular function, admission and hospital characteristics and regional factors</td>
<td>Hospitalised patients</td>
<td>Compared with those without a psychiatric disorder, patients with schizophrenia were less likely to have reperfusion</td>
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<tr>
<td>Petersen 2003 USA</td>
<td>Cardiac care treatment: thrombolytic therapy</td>
<td>ICD–9-defined patients who had an admission to an in-patient psychiatric or substance misuse unit in the year prior to cardiac admission including event; ICD–9–CM codes schizophrenia (295.xx), other psychoses (297.xx–299.xx), bipolar (296.xx, 296.xx), major depression (296.2–296.39), PTSD (309.81) or substance use diagnosis (alcohol 303.xx or 303.00, drug 292.01–292.99, 304.xx or 305.2–305.99)</td>
<td>4340 veterans discharged after a clinically confirmed myocardial infarction; 859 (19.8%) had mental illness, identified if patient had been admitted to a psychiatric hospital, received a mental health diagnosis or been seen in a psychiatric or drug/alcohol clinic, all in the year before (therefore mental illness may not have been current or ongoing and thus more likely to be minor). Controlled for age, comorbidity and hospital characteristics. Possible selection bias in VA sampling</td>
<td>Secondary care</td>
<td>Those with mental illness less likely to undergo in-patient diagnostic angiography (age-adjusted RR = 0.9, 95% CI 0.83–0.98). No difference in RR of CABG or receipt of medications</td>
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<tr>
<td>Jones 2005 USA</td>
<td>Cardiac care treatment: likelihood of PTCA or CABG</td>
<td>ICD–9 and DSM–IV. Patients were classified as having a mental health disorder if ICD–9 codes (290–319, 607.84, 608.89, 625.00, 625.80, 780.09, 780.52, 780.54, 780.59, 787.60) for mental health diagnoses were identified in the claims data before or within the 30-day period</td>
<td>3368 adults hospitalised for a myocardial infarction, 40% (n = 1342) diagnosed as having a mental disorder. Included those who received their first diagnosis of mental disorder within the first 30 days of myocardial infarction. Mental disorder identified from insurance claims between 1996 and 2001 and associated ICD–9 codes Adjusted for demographic and clinical characteristics (age, gender, number of days hospitalised, residence, hospital transfer, cardiovascular risk factors and other medical comorbidity)</td>
<td>Hospitalised patients</td>
<td>No significant difference in rates of revascularisation was demonstrated</td>
</tr>
<tr>
<td>Druss 2000 USA</td>
<td>Cardiac care treatment: likelihood of CC, PTCA or CABG</td>
<td>ICD–9 defined; included mental disorder (n = 5365), schizophrenia (n = 188), affective disorder (n = 315), substance use (n = 1138), other (n = 3724), no mental disorder (n = 108,288)</td>
<td>National cohort of 113,653 patients &gt;64 years old, hospitalised for a confirmed myocardial infarction; 3366 had a diagnosis of mental illness (data from Medicare) Controlled for demographic, clinical, hospital and regional variables</td>
<td>Hospitalised patients</td>
<td>Patients with any comorbid mental illness less likely to undergo PTCA (11.8% v. 16.8%, P &lt; 0.0001) and CABG (8.2% v. 12.6%, P &lt; 0.001). Those with mental illness were 41% (for schizophrenia) to 78% (for substance use) less likely to undergo CC compared with those without mental illness (P &lt; 0.001 for all)</td>
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<td>Plomondon 2007 USA</td>
<td>Rate of cardiac procedures including coronary angiogram and coronary revascularisation</td>
<td>ICD–9 defined; 18.4% (n = 2623) of the study population had a diagnosis of serious mental illness. Of the patients with SMI, 65.5% (n = 1718) had a diagnosis of anxiety disorder, 47.1% (n = 1235) had a diagnosis of mood disorder, 15.5% (n = 406) had a diagnosis of schizophrenia and 11.7% (n = 307) had a diagnosis of personality disorder (not mutually exclusive categories)</td>
<td>14,194 patients (including 18% with mental illness) and 406 with schizophrenia with acute coronary syndrome, including unstable angina and acute myocardial infarction in VHA Possible selection bias in VA sampling</td>
<td>Hospitalised patients</td>
<td>There was no significant difference in cardiac procedure use, including coronary angiogram (38.7% v. 40.3%, P = 0.14) or coronary revascularisation (31.0% v. 32.3%, P = 0.19) and discharge medications between those with and without SMI.</td>
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(continued)
### Table DS1  Summary of comparative studies reporting on receipt of cardiac procedures (continued)

<table>
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<tr>
<th>Author, country</th>
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<td>Acute coronary syndrome (continued)</td>
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<td>Laursen 2009</td>
<td>Rate of invasive cardiac procedures (coronary artery bypass graft and/or percutaneous transluminal coronary angioplasty) and mortality</td>
<td>Hospital admission for severe mental disorder: bipolar disorder Eighth Revision [ICD-8] code 296.19 or 296.39; ICD-10 code F30 or F31; schizoaffective disorder (ICD-8 code 297.9; ICD-10 code F25); and schizophrenia (ICD-8 code 295 excluding 295.79; ICD-10 code F20).</td>
<td>605,669 patients admitted with heart disease in Denmark between 1994 and 2007. People with admissions for severe mental disorder had higher mortality rates from heart disease following cardiac procedures but received lower rates of cardiac revascularization.</td>
<td>Hospitalised patients</td>
<td>The proportion undergoing invasive procedures was reduced among patients with severe mental disorder as compared with the nonpsychiatric general population (4% v. 8% at one year and 7% v. 12% at 5 years) in those under 70 years and (2% v. 4% at one year and 3% v. 6.5% at 5 years) in those 70 years or older.</td>
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<td>Young 2000</td>
<td>Mental illness (general), schizophrenia, affective disorder, substance misuse, other v. no mental disorder, stratified into &gt; 65 and ≤ 65 age groups. Definitions as in Druss et al.</td>
<td>HCA-Sachs database: 354,195 patients included with a principal diagnosis of acute myocardial infarction (143,421, 40.5% &lt;65 years old). Using definitions similar to Druss et al. identified 25,237 (7.1%) with mental illness. Possible bias in that none of the data adjusted for admission characteristics or left ventricular function.</td>
<td>Hospitalised patients</td>
<td>Those with mental illness significantly less likely to undergo CC, PTCA or CABG. Those with schizophrenia had disparities that were greater in older patients. In those aged 65 years or older, rates of CC as were follows: (all statistically significant): schizophrenia RR = 0.32, affective disorders RR = 0.8, substance use RR = 0.9. In this age group the odds of PTCA for a patient with schizophrenia was 32%, the rate in those without mental illness.</td>
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<td>Lawrence 2003</td>
<td>Cardiac care treatment: revascularisation procedures, removal of coronary artery obstruction, CABG</td>
<td>ICD–9 diagnosis: (a) ICD–9 codes 290, 293–296: dementia, organic psychotic conditions, schizophrenia and affective psychosis (b) ICD–9 codes 291–292, 297–305, 313–315: alcohol and drug psychoses, paranoid states, other non-organic psychoses, neurotic disorders, personality disorders, sexual deviations, alcohol and orders, drug dependence, childhood disorders (c) ICD–9 codes 306–312, 317–319: miscellaneous disorders not elsewhere classified</td>
<td>Western Australia linked database used to identify 210,129 users of mental health services and diagnosis (ICD–9). A hierarchical model used, so most severe diagnosis carried forward and coded as the main diagnosis. (Note: psychiatric diagnosis examined included dementia) Possible bias in that unable to adjust for demographic and clinical characteristics.</td>
<td>Secondary care</td>
<td>Revascularisation rates lowest for those with dementia followed by those with schizophrenia, substance disorder, other psychosis and affective psychosis (rate ratios 0.14, 0.31, 0.60, 0.66, 0.77 respectively) but significant only for men. The only significant difference in revascularisation in women was in those with schizophrenia, with a rate ratio of 0.34 (95% CI 0.18–0.64).</td>
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<tr>
<td>Kisely 2007</td>
<td>Cardiac care treatment: rate of receiving revascularisation procedures</td>
<td>ICD–9 diagnoses coded 290 through 319. We also included non-specific mental disorders outside the formal disorders covered by chapter 5 of ICD–9, such as injury of undetermined intention or psychosocial factors that influence health status. We grouped disorders into dementia and other organic conditions (290–294), psychoses (schizophrenia or non-affective psychoses: 295, 297, 299), alcohol or drug disorders (303–305), mood disorders (affective psychoses or depression: 296, 298, 300.4, 311), neuroses (300 except 300.4), personality disorders (301), adjustment reactions (308, 309), and other mental disorders (all remaining chapter 5 and all non-chapter 5 ICD–9 diagnoses of non-specific mental disorders)</td>
<td>15,889 individuals from Nova Scotia’s mental health service. Comprised 13,626 specialised or revascularisation procedures (1,885 in psychiatric patients). Results were adjusted for age, gender, socioeconomic status and comorbid illness</td>
<td>Hospitalised patients</td>
<td>In psychiatric in-patients the adjusted rate ratios for CC, PTCA and CABG were 0.41, 0.22 and 0.34 respectively, in spite of psychiatric in-patients’ increased risk of death.</td>
</tr>
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</table>

CABG, coronary artery bypass graft; CC, cardiac catheterisation; HCA, Healthcare Investment Analysis; HR, hazard ratio; PO, percutaneous coronary intervention; PTCA, percutaneous transluminal coronary angioplasty; PTSD, post-traumatic stress disorder; RR, relative risk; SMI, severe mental illness; VA, Veterans Affairs; VHA, Veterans Health Administration.
### Table DS2: Summary of studies linking mortality and quality of care in severe mental illness

<table>
<thead>
<tr>
<th>Author/country</th>
<th>Measure of mortality</th>
<th>Mental illness definition</th>
<th>Sample and possible biases</th>
<th>Setting</th>
<th>Effect on mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Included studies</td>
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<tr>
<td>Abrams 2009&lt;sup&gt;92&lt;/sup&gt; USA</td>
<td>Mortality after ACS at 30 days and 365 days</td>
<td>ICD-9 diagnosis from out-patient contacts in 12 months before admission or on admission. Includes depressive disorders, PTSD, bipolar disorders and psychotic disorders</td>
<td>21 745 patients with acute myocardial infarction admitted to VHA hospitals, adjusted for severity, age and comorbidity. Possible selection bias in VA sampling</td>
<td>Hospitalised patients (includes previous out-patient contact)</td>
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<tr>
<td>Druss 2000&lt;sup&gt;94&lt;/sup&gt; USA</td>
<td>Mortality after MI at 30 days</td>
<td>ICD-9 defined; includes mental disorder (n = 5365), schizophrenia (n = 188), affective disorder (n = 315), substance use (n = 1136), other (n = 3724), no mental disorder (n = 108288)</td>
<td>Data from Medicare acute care non-governmental hospitals in national sample of 113653 receiving cardiac care post MI aged &gt;64 years. Controlled for demographic, clinical, hospital, and regional variables. Possible selection bias in older sample</td>
<td>Hospitalised patients</td>
<td></td>
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<tr>
<td>Young 2000&lt;sup&gt;96&lt;/sup&gt; USA</td>
<td>Mortality after MI during hospitalisation</td>
<td>Mixed mental illness, schizophrenia, affective disorder, substance misuse, other, v. no mental disorder stratified into &gt;65 and &lt;65 age groups. Definitions as Druss et al</td>
<td>Hospitalised patients</td>
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<td></td>
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<tr>
<td>Druss 2001&lt;sup&gt;95&lt;/sup&gt; USA</td>
<td>Mortality after MI at 1 year</td>
<td>ICD-9 definition; any mental disorder (n = 4664), schizophrenia (n = 61), affective disorder (n = 271), substance use disorder (n = 882)</td>
<td>88241 Medicare patients hospitalised for a clinically confirmed MI (data from Medicare). Controlled for eligibility for procedure, demographics, cardiac risk factors, left ventricular function, admission and hospital characteristics and regional factors. Possible bias in that none of the data adjusted for admission characteristics or left ventricular function</td>
<td>Hospitalised patients</td>
<td></td>
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<tr>
<td>Petersen 2003&lt;sup&gt;97&lt;/sup&gt; USA</td>
<td>Age-adjusted mortality at 30 days and 1 year after MI</td>
<td>ICD-9 defined disorders or problems in patients who had an admission to an in-patient psychiatric or substance misuse unit in the year prior to cardiac admission event. ICD-9-CM codes schizophrenia (295.xx), other psychoses (297.xx-299.xx), bipolar (296.0x, 296.1x, 296.40-296.89), major depression (293.2-293.39), PTSD (307.8) or substance use diagnosis alcohol (303.xx or 303.0x), drug 292.01-292.99 or 304.xx or 315.2-315.99</td>
<td>4340 veterans discharged after a clinically confirmed MI; 859 (19.8%) had mental illness (identified if had been admitted to a psychiatric hospital, received a mental health diagnosis or been seen in a psychiatric or drug/alcohol clinic; all in the year before; mental illness might not be current or ongoing and therefore more likely to be minor). Controlled for age, comorbidity and hospital characteristics</td>
<td>Secondary care</td>
<td>Trend towards higher rate of death at 1 year in those with mental illness</td>
</tr>
<tr>
<td>Plomondon 2007&lt;sup&gt;99&lt;/sup&gt; USA</td>
<td>Mortality after ACS at 1 year</td>
<td>ICD-9 defined; 18.4% (n = 2623) of the study population had a diagnosis of SMI. Of the patients with SMI, 65.9% (n = 1718) had a diagnosis of anxiety disorder, 47.1% (n = 1239) had a diagnosis of mood disorder, 15.9% (n = 466) had a diagnosis of schizophrenia and 11.7% (n = 307) had a diagnosis of personality disorder (not mutually exclusive categories)</td>
<td>14 194 patients, including 18% with mental illness and 406 with schizophrenia and acute coronary syndromes. Possible selection bias in VA sampling</td>
<td>Secondary care</td>
<td>1-year mortality was lower for patients with SMI (15.8% v. 19.1%, P&lt;0.001). However, in multivariable analysis there was no significant difference in mortality (HR = 0.91, 95% CI 0.81–1.02) between patients with and without SMI. For schizophrenia this ratio was 0.83 (95% CI 0.60–1.13).</td>
</tr>
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</table>
### Table DS2: Summary of studies linking mortality and quality of care in severe mental illness (continued)

<table>
<thead>
<tr>
<th>Author/country</th>
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<th>Mental illness definition</th>
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<tr>
<td><strong>Included studies (continued)</strong></td>
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<tr>
<td><strong>Laursen 2009</strong>&lt;sup&gt;51&lt;/sup&gt;</td>
<td>Rate of invasive cardiac procedures (coronary artery bypass graft and KFNA-KFNF or percutaneous transluminal coronary angioplasty) and mortality</td>
<td>Hospital admission for severe mental disorder: bipolar disorder Eighth Revision [ICD-8 code 296.19 or 296.39], ICD-10 code F30 or F31, schizoaffective disorder (ICD-8 code 295.79 or 295.9, ICD-10 code F25), and schizophrenia (ICD-8 code 295 excluding 295.79), ICD-10 code F20.</td>
<td>605,649 patients admitted with heart disease in Denmark between 1994 and 2007 of whom 580,065 were followed-up, 43,090 died during 5-year follow-up.</td>
<td>Hospitalised patients</td>
<td>There was a higher rate of mortality RR of 2.90 (95% CI 2.71–3.10) for those with SMI 21% v. 17% died during 5-year follow-up. 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).</td>
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<td><strong>Excluded studies</strong></td>
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<td><strong>Kisely 2007</strong>&lt;sup&gt;48&lt;/sup&gt;</td>
<td>Mortality rate ratio over 1 year</td>
<td>ICD–9 diagnosis codes 410–414, stroke (431–438) and other circulatory diseases (390–459).</td>
<td>215,889 individuals identified from Nova Scotia’s Mental Health Outpatient Information System, comprising 13,626 specialised or revascularisation procedures (1,885 in psychiatric patients) Results were adjusted for age, gender, socioeconomic status and comorbid illness</td>
<td>Secondary care</td>
<td>The age-standardised mortality rate ratio (over 1 year) for psychiatric patients was 1.31 (95% CI 1.25–1.36). Patients seen by a psychiatric specialist had more than double the risk of death (mortality rate ratio 2.42, 95% CI 1.9–2.9) compared with those seen only in primary care.</td>
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<td><strong>Blecker 2010</strong>&lt;sup&gt;53&lt;/sup&gt;</td>
<td>Mortality after heart failure to fixed date in 2004</td>
<td>Definition of SMI if patient had a diagnosis of schizophrenia or a diagnosis of bipolar disorder, major depression or other mental disorder diagnosis and specialty mental healthcare use</td>
<td>Of 1801 individuals identified with heart failure, 341 had comorbid SMI. Mortality adjustment for age, gender, race, geographic location and comorbidities</td>
<td>Medicaid participants in Maryland with ICD–9–CM codes for heart failure (412.1, 404.1, 404.3, 428)</td>
<td>SMI was not associated with differences in quality measures, including left ventricular assessment. Individuals with and without SMI had comparable mortality rates of 14.0 and 13.9 per 100 person-years respectively, with no difference in relative hazard of death.</td>
</tr>
<tr>
<td><strong>Lawrence 2003</strong>&lt;sup&gt;41&lt;/sup&gt;</td>
<td>Standardised mortality rates due to IHD or MI</td>
<td>ICD–9 diagnosis: (a) ICD–9 codes 290, 293–296: dementia, organic psychiatric conditions, schizophrenia and affective psychosis (b) ICD–9 codes 291–292, 297–305, 313–315: alcohol and drug psychoses, paranoid states, other non-organic psychoses, neurotic disorders, personality disorders, sexual deviations, alcohol and order, drug dependence, childhood disorders (c) ICD–9 codes 306–312, 317–319: miscellaneous disorders not elsewhere classified</td>
<td>Western Australia linked database used to identify 210,129 mental health service users and their diagnoses ICD–9 (00), hierarchical model used so severe diagnosis carried forward and coded as the main diagnosis. Psychiatric diagnoses examined included dementia Possible bias in that authors unable to adjust for demographic and clinical characteristics</td>
<td>Secondary care</td>
<td>SMRs due to IHD in mental health users almost twice that in overall population SMR 1.91 for total IHD, 1.74 for acute MI. Majority of deaths ascribed to MI (69%). Significant increase in mortality rates seen in female patients with a psychiatric diagnosis, compared with a reduction over time in the general population. Men with schizophrenia were only 60% as likely to be admitted for IHD compared with men in the general population, despite being 1.8 times as likely to die from IHD.</td>
</tr>
</tbody>
</table>

ACS, acute coronary syndrome; HCIA, Healthcare Investment Analysis; HR, hazard ratio; IHD, ischaemic heart disease; MI, myocardial infarction; OR, odds ratio; PTSD, post-traumatic stress disorder; SMI, serious mental illness; SMR, standardised mortality ratio; VA, Veterans Affairs; VHA, Veterans Health Administration.
Alex J. Mitchell and David Lawrence

Revascularisation and mortality rates following acute coronary syndromes in people with severe mental illness: comparative meta-analysis

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