Differences in the prescribing of medication for physical disorders in individuals with v. without mental illness: meta-analysis

Alex J. Mitchell, Oliver Lord and Darren Malone

Background
There is some concern that patients with mental illness may be in receipt of inferior medical care, including prescribed medication for medical conditions.

Aims
We aimed to quantify possible differences in the prescription of medication for medical conditions in those with v. without mental illness.

Method
Systematic review and random effects meta-analysis with a minimum of three independent studies to warrant pooling by drug class.

Results
We found 61 comparative analyses (from 23 publications) relating to the prescription of 12 classes of medication for cardiovascular health, diabetes, cancer, arthritis, osteoporosis and HIV in a total sample of 1,931,509 people. In those with severe mental illness the adjusted odds ratio (OR) for an equitable prescription was 0.74 (95% CI 0.63–0.86), with lower than expected prescriptions for angiotensin-converting enzyme inhibitors or angiotensin II receptor blockers (ACE/ARBs), beta-blockers and statins. People with affective disorder had an odds ratio of 0.75 (95% CI 0.55–1.02) but this was not significant. Individuals with a history of other (miscellaneous) mental illness had an odds ratio of 0.95 (95% CI 0.92–0.98) of comparable medication with lower receipt of ACE/ARBs but not highly active antiretroviral therapy (HAART) medication. Results were significant in both adjusted and unadjusted analyses.

Conclusions
Individuals with severe mental illness (including schizophrenia) appear to be prescribed significantly lower quantities of several common medications for medical disorders, largely for cardiovascular indications, although further work is required to clarify to what extent this is because of prescriber intent.

Declaration of interest
None.

Search and appraisal
A review strategy and extraction sheet was agreed according to the PRISMA standard. We decided to focus on non-organic reviewed studies that examined preventive care in individuals with v. without psychiatric illness. For those individuals with schizophrenia, eight of nine analyses showed inferior preventive care in several areas including in relation to osteoporosis screening, blood pressure monitoring, vaccinations, mammography and cholesterol monitoring. Although many of these chronic conditions may be unavoidable given our current state of knowledge, many deaths in those with mental illness appear to be avoidable. Unfortunately, medical disorders are often overlooked by mental health specialists in psychiatric settings and by physicians in primary care and medical settings. As a result up to half of all chronic conditions may go unrecognized in severe mental illness. In addition, many people with mental ill health who have an unmet need for medical care also have other risk factors for poor treatment such as low income, social isolation, homelessness, substance misuse and lack of healthcare insurance.

Method

National guidelines from several countries are agreed that the medical care of patients with mental disorders is of paramount importance. Yet, serious concerns have been raised about the quality of medical (and screening) services offered to patients with severe mental illness. Individuals with schizophrenia receive as little as half of the monitoring offered to people without schizophrenia in some studies. Further, there is evidence that people with severe mental illness receive suboptimal treatment for established medical conditions. These disparities in treatment exist in some of the most critical areas of patient care such as general medicine, cardiovascular and cancer care. This is particularly concerning given that people with schizophrenia appear to have higher rates of post-operative complications, higher post-operative mortality and higher than expected non-suicide-related mortality. Indeed, the physical health of individuals with severe mental illness is poorer than the general population. Looking at comorbidity in more detail shows that individuals with schizophrenia have higher rates of hypothyroidism, dermatitis, eczema, obesity, epilepsy, viral hepatitis, diabetes (type 2), essential hypertension, chronic obstructive pulmonary disease and fluid/electrolyte disorders. Patients with bipolar I disorder also have higher rates of arthritis, hypertension, gastritis, angina and stomach ulcer. The presence of these medical comorbidities adversely affects not just quality of life but also recovery from the underlying psychiatric disorder, length of hospital admissions and paradoxically the likelihood of being offered psychotropic medication.

Patients with severe mental illness are also at risk of receiving less than adequate preventive services such as medical screening procedures. Medical screening is important not just for the reduction in future morbidity but also low receipt of preventive care is associated with lower quality of life. Lord et al recently performed a population-based cohort study with 1,931,509 people to explore mortality and causes of death among people with severe mental illness. They found that mortality related to physical causes was higher in the group with severe mental illness, particularly due to cardiovascular disease and other causes. The findings of this study suggest that preventive care and screening services should be improved for people with severe mental illness.

Discussion

Given these numerous concerns regarding quality of medical care, elevated mortality and low receipt of preventive services for people with a psychiatric disorder, we undertook a data synthesis of comparative studies that have examined the adequacy of medication prescribing for existing physical disorders in individuals with and without severe mental illness. To the best of our knowledge this is the first meta-analysis using prescribing data in mental ill health groups.
psychiatric disorders, thus excluding studies pertaining to delirium or dementia.\textsuperscript{31} We searched Medline/PubMed and Embase abstract databases from inception to November 2010. The initial search strategy is listed in the online supplement. We included any study (observational/interventional) that had measured the prescription or receipt of medication for medical conditions in patients with and without defined mental illness. Four full-text collections were searched: Science Direct, Ingenta Select, Springer-Verlag’s LINK and Blackwell-Wiley. In these online databases the same search terms were used but as a full-text search and as a citation search. The abstract databases Web of Knowledge and Scopus were searched, using the terms in the online supplement as a text-word search, and using key papers in a reverse citation search. Finally, a number of journals were hand-searched (British Journal of Psychiatry, Schizophrenia Research, Schizophrenia Bulletin, Psychological Medicine, Acta Psychiatria Scandinavica, American Journal of Psychiatry, Archives of General Psychiatry, Canadian Journal of Psychiatry, Journal of Psychiatric Research, Psychiatric Services, The Psychiatrist (previously known as Psychiatric Bulletin); all from 2000) and several experts contacted. Using this strategy we identified 84 primary data publications and of these 61 reported aspects of quality of medical care other than prescribed medication. Several were excluded due to lack of extractable data despite attempts to find data from the original authors.\textsuperscript{32} Data were extracted by two authors (O.L. and A.J.M.) and independently checked by a third (D.F.) (see online supplement). Appraisal of individual studies was performed and the Newcastle-Ottawa evaluation scale for observational studies was used.\textsuperscript{33} In addition, we performed a PRISMA evaluation of our meta-analysis using a standard checklist of 27 items that ensure the quality of a systematic review or meta-analysis.\textsuperscript{34} The Newcastle-Ottawa evaluation scale is a specific set of nine items used to evaluate individual studies. All medication listed in each publication was fully extracted to avoid meta-analytic bias resulting in 61 drug-level analyses.

**Meta-analysis**

From the available data, we entered or calculated odds ratios (OR) and \( r \) values. We extracted data on the rate of prescribed medication is those with \( v \) without mental illness. Relative risks (hazard ratios) were converted into odds ratios with reference to the reported control event rate, an adaption of a method described elsewhere.\textsuperscript{35} We then used a summary meta-analysis, pooling odds ratios. We attempted to account for potential confounders but these were variably handled by primary studies. We therefore extracted and stratified results into adjusted and unadjusted analysis and specified types of adjustment. Confidence intervals were obtained from all studies or calculated from the data provided. Between-study heterogeneity was assessed using the \( I^2 \) statistic.\textsuperscript{36} Heterogeneity was reduced by stratifying by either type of mental illness or drug class or type of medical condition. Where heterogeneity (defined by > 80% \( I^2 \)) was high, random-effects meta-analysis was preferred otherwise fixed-effects meta-analysis. Potential study bias was examined using Kendall’s tau and Egger bias statistics,\textsuperscript{37} but no evidence of publication bias was detected (see online supplement). In order to offer a qualitative interpretation of quantitative data we defined the following grades of treatment adequacy \( a \) priori with reference to the comparator population rates: < 80% ‘inadequate’; \( \geq 80 \% < 90 \% \) ‘suboptimal’; \( \geq 90 \% < 95 \% \) ‘inequitable’; and \( \geq 95 \% \) ‘adequate’.

**Results**

Our search identified 61 drug-level analyses regarding prescribing adequacy in 23 publications\textsuperscript{38–60} involving 1931 509 patients (study-level results shown in online Table DS1; overview of search results shown in Fig. 1). Subgroups included 13 analyses (36 drug-level comparisons) in patients with severe mental illness, 8 analyses (13 comparisons) in patients with affective disorder and 7 analyses (12 comparisons) for other miscellaneous mental illness groups. We used British National Formulary (BNF) codes to classify medications (www.bnf.org). In total, there were 12 classes of medication in the analysis: angiotensin-converting enzyme inhibitors or angiotensin II receptor blockers (ACE inhibitors/ARBs, BNF 2.5.5.1 and 2.5.5.5.2), nitroglycerine (BNF 2.6.1), anti-inflammatory medication for arthritis (BNF 4.7.1), anti-platelet drugs (BNF 2.9), anticoagulants (BNF 2.8), beta-blockers (BNF 2.4), cytotoxic chemotherapy (BNF 8.1), insulin (BNF 6.1.1), highly active antiretroviral therapy (HAART, BNF 5.3.1), lipid-regulating drugs (includes statin and non-statin, BNF 2.12) and medication for osteoporosis (largely hormone replacement therapy (HRT), BNF 6.4.1.1). Thus, most were for cardiovascular health indications. We evaluated the quality of studies using the Newcastle-Ottawa criteria (online Table DS2). Using these nine domains we rated 2 studies as having a low overall quality, 12 as having moderate overall quality and 9 with high overall quality but all were considered sufficient for analysis.

**Severe mental illness (including schizophrenia)**

There were 36 analyses of drug prescribing from a combined pool of over 1.5 million individuals (Fig. 2). The pooled odds ratio for equitable prescribing was 0.74 (95% CI 0.63–0.86) favouring non-mental ill health. \( I^2 \) was 97.2 suggesting high heterogeneity. Lower than expected receipt of medication was in evidence for ACE/ARBs (OR = 0.89, 95% CI 0.81–0.98, \( P = 0.02 \)), beta-blockers (OR = 0.90, 95% CI 0.84–0.96, \( P = 0.001 \)) and statins (OR = 0.61, 95% CI 0.59–0.94, \( P = 0.02 \)) but not for anticholesterol drugs in general (statins and non-statin combined), or for anticoagulants (aspirin and non-aspirin combined). However, for non-aspirin anticoagulants alone (clopidogrel and ticlopidine) there was a significantly lower rate (OR = 0.74, 95% CI 0.56–0.97, \( P = 0.02 \)). Results were similar when stratified by schizophrenia alone. For schizophrenia alone the pooled odds ratio across all medication was 0.69 (95% CI 0.57–0.83, \( P < 0.0001 \)).

**Affective disorder**

Across 13 analyses involving 232 882 individuals the \( I^2 \) was 94.6%. The combined meta-analysis showed a trend towards low receipt with a pooled odds ratio of 0.75 (95% CI 0.53–1.02, \( P = 0.07 \)), which was significant in fixed-effect but not random-effects analysis (Fig. 3). Lower receipt of medication was evident for beta-blockers (OR = 0.76, 95% CI 0.45–1.29) and lipid-regulating drugs (OR = 0.92, 95% CI 0.64–1.32), but neither were statistically significant. There was inadequate data to examine other classes of medication.

**Other mental illness**

Across 12 analyses (involving 19 637 individuals with mental illness from a sample of 188 627) the \( I^2 \) was 64.5%, suggesting low heterogeneity and permitting fixed-effects analysis. The
Mental illness and medication for comorbid physical disorders

Combined pooled odds ratio was 0.95 (95% CI 0.92–0.98, Fig. 4). Lower receipt of medication was evident for ACE or ARBs (OR = 0.92, 95% CI 0.85–0.99) but not HAART medication (OR = 0.98, 95% CI 0.75–1.28). There was inadequate data to examine other classes of medication.

A summary of results is shown in Table 1.

**Discussion**

**Main findings**

We found 61 comparative analyses relating to the prescription of 12 classes of medication including lipid-regulating agents (includes statins), beta-blockers, antipatelet and anticoagulant drugs, ACE/ARBs, insulin, cytotoxic chemotherapy, anti-inflammatories, HRT for osteoporosis and HAART for HIV. Patients with severe mental illness had an odds ratio of 0.74 (95% CI 0.63–0.86) for a comparable medication prescription. The differences were found largely in drugs for cardiovascular indications. For example, patients with severe mental illness received lower than expected prescriptions for ACE/ARBs, beta-blockers and statins. Combining all types of mental illness and all classes of drug suggested that patients with any type of mental illness had an odds ratio of 0.78 (95% CI 0.73–0.84, P = 0.0001) of comparable medication (data not shown). Given a typical control event rate (i.e. receipt of medication in the comparison group) of 70%, the actual rate of undertreatment can be estimated at 8% (95% CI 5–12) in those with other mental illness, 10% in those with severe mental illness and 12% in schizophrenia, a disparity that could be classified as 'inequitable' or 'suboptimal' receipt of medication according to our *a priori* definition.

**Limitations**

Several limitations should be acknowledged. First, we had no *a priori* protocol for this study but attempted to follow the review strategy suggested in the PRISMA standard. Heterogeneity was found in 5 out of 11 main analyses (Table 1) and this had the effect of rendering the odds ratios observed for affective disorders non-significant. We used the Newcastle-Ottawa scale, which is only one of several possible methods.61 In two studies involving HAART there was no adjustment made for demographic, illness or prescribing variables51,60 (see Table DS1) and therefore these data should be interpreted with caution. Without adjustment it is possible that the group with mental illness had more severe physical illness than the comparison group – although this should of course favour higher rates of prescribing, not lower rates. One study reported hazard ratios with no control event rate,36 therefore we estimated the control event rate using data from related publications from the same group (pending confirmation from the authors). Another limitation is that the definition of mental illness, particularly severe mental illness varied...
considerably between studies, with seven studies defining mental illness using routine clinical interviews and one using prescription of haloperidol as a marker of mental ill health. The remaining studies used ICD-9 coding. A further important limitation is that most studies specified only that the mental health diagnosis was present in the year preceding the prescription of medication and therefore concurrent mental illness, symptoms of mental illness and severity of mental illness cannot be adequately reported. We also note that although the majority of disparities were manifest in drugs prescribed for cardiovascular conditions, the sample size was modest for most other medical conditions. We also note that in all but 1 of the 23 studies the setting was a country where health insurance is operating (largely USA), as opposed to socialised healthcare. Further studies should examine potential prescribing inequalities in countries with nationalised healthcare. Finally, and perhaps most importantly, all but two studies (see overleaf) measured prescribing from electronic databases based on naturalistic observational data and thus no information was available on patient v. prescriber influences on low receipt of necessary medication.
Possible explanations for suboptimal prescribing

It is already widely known that people with mental ill health have problems with psychotropic medication adherence.\textsuperscript{62,63} This also applies to adherence to physical health medications.\textsuperscript{64–66} However, the studies reviewed here measure medication prescribing according to notations in medication databases (with the exception of Bishop et al who used notations in medical notes\textsuperscript{39} and Suvisaari et al who used patient-reported medication at interview\textsuperscript{26}). Thus, uptake of medication and adherence to medication was not measured. We suggest therefore that the amount of medication actually taken as directed was probably less than that recorded here, and actual disparities in medication consumption may be more severe than disparities in prescribing.

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{fig3}
\caption{Prescribing differences for affective disorder v. no mental illness: summary meta-analysis plot (random effects).}
\end{figure}

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{fig4}
\caption{Prescribing differences for other mental illness\textsuperscript{a} v. no mental illness: summary meta-analysis plot (fixed effects).}
\end{figure}
Table 1. Overview of meta-analytic results.

<table>
<thead>
<tr>
<th>Condition</th>
<th>OR (95% CI)</th>
<th>Z</th>
<th>p</th>
<th>I² (%)</th>
<th>OR (95% CI)</th>
<th>Z</th>
<th>p</th>
<th>I² (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All classes</td>
<td>0.74 (0.63–0.86)</td>
<td>–0.83</td>
<td>0.80</td>
<td></td>
<td>97.2 (96.7–97.6)</td>
<td>0.25</td>
<td>0.79</td>
<td></td>
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<tr>
<td>ACEs or ARBs</td>
<td>0.89 (0.80–0.98)</td>
<td>–3.21</td>
<td>0.001</td>
<td>90.9 (89.6–92.2)</td>
<td>0.53</td>
<td>0.59</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anticoagulant (including aspirin)</td>
<td>0.99 (0.96–1.03)</td>
<td>0.67</td>
<td>0.50</td>
<td></td>
<td>3.2 (0–57.8)</td>
<td></td>
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<tr>
<td>Beta-blockers</td>
<td>0.90 (0.84–0.96)</td>
<td>–1.75</td>
<td>0.08</td>
<td>90.1 (88.3–91.9)</td>
<td>0.57</td>
<td>0.54</td>
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<tr>
<td>ACEs, angiotensin-converting enzyme inhibitors, ARBs, angiotensin II receptor blockers, HMG-CoA reductase inhibitors, statins, highly active antiretroviral therapy (HAART) medication</td>
<td>0.93 (0.88–0.99)</td>
<td>–0.40</td>
<td>0.68</td>
<td></td>
<td>92.8 (92.0–93.6)</td>
<td>0.15</td>
<td>0.88</td>
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</table>

ACEs, angiotensin-converting enzyme inhibitors; ARBs, angiotensin II receptor blockers; HAART, highly active antiretroviral therapy.

Analysis:
- Test that odds ratio differs from 1;
- I²: inconsistency;
- 80% equals low;
- 90% equals high.

Other mental illness includes any type of mental ill health other than pure affective disorder, severe mental illness or schizophrenia.

Fixed-effects odds ratio.

Significant for statins alone.

Previous work has shown that mental health professionals often miss physical conditions in their patients, and undertake physical examinations in less than 50% of their patients. Mental health professionals often do not feel confident in prescribing physical health medication. In the majority of cases physical health medication is prescribed by physicians in primary care, internal medicine and related medical specialties. We already know that mental health status and prescription of antipsychotics reduces likelihood of medical monitoring (such as glycated haemoglobin (HBA1c) testing). Primary care physicians often consider such patients to be ‘difficult to manage’, although many primary care physicians are willing to help with physical healthcare. Where primary care physicians lack expertise in mental health they are less likely to offer general care to those with mental illness. Similarly when people with mental illness attend emergency departments they are less likely to be offered hospital care than other people. In general practice, cardiovascular risk factors are often recorded in the medical records for adults with long-term mental illness, but primary care physicians appear reluctant to intervene. Clinician factors such as willingness to investigate, ability and enthusiasm to treat and willingness to offer follow-up are important predictors of quality of care. Because of medical and psychiatric comorbidity, seemingly unrelated conditions compete for clinicians’ attention. Against this, studies suggest that the adequacy of medical care may not be adversely influenced by the number of comorbid medical disorders.

Indeed, some have found that comorbidity favours superior care by virtue of higher than average healthcare visits. Indirect evidence suggests that clinicians’ attitudes towards patients directly influence health outcomes. In one study in primary care, poor mental health status was linked with poorer general practitioner attitude and less time spent with the general practitioner. In a study of 59 patients seen in a US community mental health centre, 14% reported that they used the medical emergency department for their routine medical care needs and 45% said that their mental health provider did not ask them about medical issues.

Three mitigating factors might explain low physician prescribing of physical health medication namely cautious prescribing, deferred prescribing and low patient acceptance of suggested medication. Regarding intentionally cautious prescribing, physicians’ prescription of cardiovascular medication may be cautious in light of possible links with suicide. Most plausibly this could apply to cholesterol-lowering agents, beta-blockers and angiotensin-receptor antagonists. Less likely but theoretically possible, physicians might be cautious about using aspirin together with selective serotonin reuptake inhibitors due to gastrointestinal bleeding, and ACE inhibitors and beta-blockers in people with mental illness who smoke. A second possibility is that treatment in some circumstances is deferred rather than omitted, although evidence suggests that in the context of mental illness most deferred treatment is not received at a later date. A third hypothesis underlying inadequate prescriptions is low uptake of care on account of patient preference. It is not yet clear.
if this is the primary explanation.91–93 For example, Salsberry and colleagues (2005) found that compared with the general population, those with severe mental illness had more emergency department visits and visited a doctor more frequently, but despite this high healthcare utilisation had very low rates of cervical smears and mammograms.94 People with mental ill health perceive barriers to accessing primary physical healthcare,84,92–97 Patients often cite lack of availability of medical advice and poor quality of medical advice as influential.84,99 Observational evidence shows many have difficulty getting timely access to appropriate primary healthcare.7,9,96,101 For example, data from the 1999 Large Health Survey of Veterans found that veterans with schizophrenia, bipolar disorder or a drug use disorder were less likely to have had any primary care visit than those without these diagnoses, even after controlling for medical comorbidity.101

**Intervention to improve therapeutic care**

Assuming these disparities in prescribing are robust, what can be done to improve quality of medical care? Druss & von Esenwein (2006)102 reviewed six randomised trials designed to improve medical care in psychiatric conditions. These studies demonstrated a substantial positive impact on linkage to and quality of medical care albeit with a diverse range of interventions. One study showed that a simple intervention could improve readiness to begin HAART.103 Ismail et al and Winkley et al pooled 46 trials regarding the effect of psychological treatment on glycaemic control but showed only very modest effects in pooled 46 trials regarding the effect of psychological treatment.84,98,99 Observational evidence shows HAART; in treated patients there was no significant difference.57 Two studies examined the effect of antidepressant treatment on controlling for medical comorbidity.101

From a research perspective, a detailed examination of patient and provider influences on received medication is urgently needed. Clinically, we suggest that treatment of comorbid physical conditions is prioritised in patients with mental health concerns and closely monitored.113 Clinicians caring for patients with physical and mental illness should take particular care to ensure optimal treatment is maintained in both areas. At an organisation level, monitoring systems are needed to ensure that the medical care of people with mental ill health is not overlooked.

**Acknowledgements**

We thank David Ferguson for helping with the extraction of quality appraisal of primary studies.

**References**

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Callre´ us T, Agerskov Andersen U, Hallas J, Andersen M. Cardiovascular drugs
Sorensen HT, Mellemkjaer L, Olsen JH. Risk of suicide in users of beta-
Muldoon MF, Manuck SB, Mendelsohn AB, Kaplan JR, Belle SH. Cholesterol
Reith DM, Edmonds L. Assessing the role of drugs in suicidal ideation and
Min LC, Wenger NS, Fung C, Chang JT, Ganz DA, Higashi T, et al. The impact of
Bobes J, Alegrı´a AA, Saiz-Gonzalez MD, Barber I, Pe´ rez JL, Saiz-Ruiz J. Change
Oud MJT, Schuling J, Slooff CJ, Groenier KH, Dekker JH, Meyboom-de Jong B.
Banta JE, Morrato EH, Lee SW, Haviland MG. Retrospective analysis of
Levinson Miller C, Druss BG, Dombrowski EA, Rosenheck RA. Barriers to
Al-Mandhari AS, Hassan AA, Haran D. Association between perceived health
Piette JD, Kerr EA. The impact of comorbid chronic conditions on diabetes
92 Dickerson FB, McNary SW, Brown CH, Kreyenbuhl J, Goldberg BW, Dixon LB. Somatic healthcare utilization among adults with severe mental illness who are receiving community psychiatric services. Med Care 2003; 41: 560–70.
Online supplement

Search one (MEDLINE/Embase)

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Search two (Web of Knowledge)

Title = (Mental OR schizophrenia OR depress* OR bipolar OR affective OR psychosis OR psychotic OR psychiatric OR psycholo* OR antipsychotic*) AND Topic = (RR OR HR OR Relative risk OR hazard ratio OR odds OR ORs) AND Topic = (prescribed OR prescription OR medication OR receipt*) AND (angiotensin converting enzyme OR ACE OR angiotensin receptor blocker OR ARB OR statin OR cholesterol OR beta-block* OR beta-blocker OR HAART OR Clopidogrel OR warfarin OR osteopor* OR Nitroglycerine OR chemothera*)

Result = 100
Table DS1  Summary of comparative studies reporting receipt of medication

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<th>Sample</th>
<th>Setting</th>
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<td>Desai et al (2002)</td>
<td>Cardiac care</td>
<td>Psychotic illness</td>
<td>National sample of 5886 veterans discharged from VA hospitals with a principal diagnosis of acute MI up to 6 months before the index study date. Overall, 27.4% had a diagnosed mental illness. Aged under 65 years. Controlled for age, gender, ethnicity, level of VA service connectedness and distance from veteran’s home to nearest VA medical facility, chronic medical conditions and use of medical services in the past year (number of primary care visits, number of specialty medical visits, and number of medical in-patient days). and hospital size.</td>
<td>Community patients</td>
<td>In fully adjusted analyses, use of beta-blockers was 5% less likely among patients with a substance use disorder compared with those with no such disorder. Aspirin: 181/188 v. 523/5423 RR = 0.94, 95% CI 0.45–2.37. Beta-blocker: 170/188 v. 5070/5423 (RR = 0.70, 95% CI 0.43–1.2)</td>
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<tr>
<td>Hippsley-Cox et al (2007)</td>
<td>Cardiac care</td>
<td>Severe mental illness and affective disorder defined by: schizophrenia from EMIS medical records system (primary carerecord)</td>
<td>127-932 patients with CHD of whom 701 had a diagnosis of schizophrenia or bipolar disorder. The results were adjusted for age, gender, deprivation, diabetes, stroke and smoking status, and allowed for clustering by practice.</td>
<td>Primary care</td>
<td>Although there were no differences in several parameters, patients with schizophrenia were 15% less likely to have a recent record of cholesterol level (95% CI 8–20%) and 7% less likely to have a recent prescription for a statin (95% CI 7–20%) but no difference in RR of CABG or receipt of medications.</td>
</tr>
<tr>
<td>Petersen et al (2003)</td>
<td>Cardiac care</td>
<td>Severe mental illness defined by: ICD-9 defined patients who had an admission to an in-patient psychiatric or substance misuse unit in the year prior to cardiac admission</td>
<td>4340 veterans discharged after a clinically confirmed MI. 89% (19.8%) had mental illness (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). Therefore mental illness may 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>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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(continued)
<table>
<thead>
<tr>
<th>Study description</th>
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<td><strong>Result</strong></td>
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<tr>
<td><strong>ACE inhibitor</strong></td>
<td>adj OR = 0.96 (95% CI 0.80–1.14)</td>
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<tr>
<td><strong>Beta blockers</strong></td>
<td>adj OR = 0.41 (95% CI 0.15–1.1)</td>
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<tr>
<td><strong>Nitroglycerine</strong></td>
<td>adj OR = 1.1 (95% CI 0.39–2.6)</td>
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<tr>
<td><strong>ASA or anticoagulant</strong></td>
<td>adj OR = 0.85 (95% CI 0.33–2.1)</td>
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<tr>
<td><strong>ACE inhibitor unadj</strong></td>
<td>OR = 1.1 (95% CI 0.30–3.7)</td>
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<tr>
<td><strong>Beta blockers</strong></td>
<td>unadj OR = 0.41 (95% CI 0.15–1.1)</td>
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<tr>
<td><strong>Nitroglycerine</strong></td>
<td>unadj OR = 1.1 (95% CI 0.39–2.6)</td>
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<td><strong>ASA or anticoagulant</strong></td>
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<td><strong>ACE inhibitor unadj</strong></td>
<td>OR = 1.1 (95% CI 0.30–3.7)</td>
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(continued)
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<tr>
<th>Author</th>
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<th>Sample</th>
<th>Setting</th>
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<tr>
<td><strong>Study description</strong></td>
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<td><strong>Statistical summary</strong></td>
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<tr>
<td><strong>Affective disorder</strong></td>
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</tbody>
</table>

- USA
- Specific medical indication: Cardiac care
- Mental illness types: Affective disorder defined as: depression according to an ICD-9 diagnosis of depression, filled more than 1 prescription for an antidepressant drug, and had no diagnoses or treatments for asthma/COPD, gastrointestinal disorders, or osteoarthritis during the calendar year.
- Sample: 51,517 patients, >64 years of age, enrolled in a state prescription benefits programme with a diagnosis of hypertension.
- Setting: Community
- Result: Antihypertensive use lower in those with depression OR = 0.50 (95% CI 0.45–0.55)

**Kisely et al (2009)**
- Canada
- Specific medical indication: Cardiac care (IHD) Stroke
- Mental illness types: Psychotic illness defined as: schizophrenia and non-affective psychoses (ICD-9 codes 295, 297, 298) including schizoaffective disorders
- Sample: 65,039 with IHD (n = 49,248) or stroke (n = 15,791)
- Setting: Mixed settings
- Result: Those with psychosis were less likely to receive guideline consistent treatment and had higher 1-year mortality and had lower levels of beta-blockers and statins.

**Blecker et al (2010)**
- USA (Medicaid)
- Specific medical indication: Cardiac care for heart failure
- Mental illness types: Severe mental illness defined as: a diagnosis of schizophrenia or if they had a diagnosis of bipolar disorder, major depression or other mental disorder diagnosis and specialty mental health
- Sample: 1,801 patients with ICD-9 heart failure of whom 341 had comorbid severe mental illness.
- Setting: Mixed settings
- Result: Severe mental illness was not associated with differences utilisation of ACE or ARB (adj RR = 1.04, 95% CI 0.92–1.17), or beta-blocker use (adj RR = 1.13, 95% CI 0.99–1.29). During the study period, 52.2% of individuals in the cohort filled a prescription for an ACE inhibitor or ARB and 48.5% filled a beta-blocker prescription.
<table>
<thead>
<tr>
<th>Author</th>
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<th>Severe mental illness/schizophrenia</th>
<th>Affective disorder</th>
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<tr>
<td>Kreyenbuhl et al (2006)</td>
<td>Diabetes</td>
<td>Psychotic illness and affective disorder from 6 public and private outpatient mental health clinics in urban and suburban communities in Maryland, USA</td>
<td>Cross-sectional study using medical charts. 201 with serious mental illness and 99 without serious mental illness</td>
<td>Mixed settings</td>
<td>Less than a quarter of patients with diabetes and with schizophrenia and mood disorders were prescribed lipid-lowering statins and angiotensin-blocking medications compared with approximately half of patients with diabetes without severe mental illness</td>
<td>ACE: adj OR = 0.23 (95% CI 0.12–0.44)</td>
<td>ACE: adj OR = 0.46 (95% CI 0.18–1.19)</td>
<td>Statin: adj OR = 0.29 (95% CI 0.11–0.77)</td>
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<td>Weiss et al (2006)</td>
<td>Diabetes</td>
<td>Psychotic illness defined by: schizophrenia on the ICD-9 code (295, 297 or 298)</td>
<td>214 patients with schizophrenia or a schizophrenia-related syndrome v. 3,594 with diabetes but no severe mental illness</td>
<td>Mixed settings</td>
<td>Patients with elevated blood glucose (HbA1c greater than 7%) were taking a hypoglycaemic medication (92% of comparison patients and 95% of patients with schizophrenia). However, patients with schizophrenia were slightly more likely than comparison patients to specifically receive insulin therapy (47% compared with 38%; adj OR = 1.44, P = 0.08). In addition, although the patients with hyperlipedema in the two groups were equally likely to receive some form of lipid-lowering therapy, those with schizophrenia were significantly more likely to receive one of the older, non-statin agents (14% compared with 7%, adj OR = 1.85, P &lt; 0.05).</td>
<td>ACE: adj OR = 0.83 (95% CI 0.61–1.14)</td>
<td>Aspirin: adj OR = 0.89 (95% CI 0.64–1.28)</td>
<td>Beta-blocker: adj OR = 0.94 (95% CI 0.54–1.71)</td>
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<tr>
<td>Bogart et al (2006)</td>
<td>HIV/AIDS</td>
<td>Severe mental illness defined as: schizophrenia, schizoaffective disorder, bipolar disorder or depression with psychotic illness</td>
<td>154 patients with serious mental illness infected with HIV. Data from 762 HIV-only patients from a separate Western US probability sample were used for comparison</td>
<td>Secondary care</td>
<td>HAART use did not differ significantly between patients with both serious mental illness and HIV, and patients with HIV only after adjustment (all P &gt; 0.05)</td>
<td>HAART: adj OR = 0.755 (95% CI 0.445–1.94)</td>
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<tr>
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<td>Statistical summary</td>
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<tr>
<td>Chander et al (2009)</td>
<td>2004 data from HIV Research Network (19 sites) n = 10284; 22% with mental illness; 19% drug use and 22% both mental illness and drug use.</td>
<td>in multivariate analysis, co-occurring mental illness/drug use was associated with the lowest odds of HAART receipt (adj OR = 0.63, 95% CI 0.55–0.72), followed by those with drug use only (0.75, 95% CI 0.63–0.87)</td>
<td>Mental illness/drug use: adj OR = 0.63 (95% CI 0.55–0.72) Drug use: adj OR = 0.75 (95% CI 0.63–0.87) Mental illness: adj OR = 0.93 (95% CI 0.81–1.07)</td>
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<tr>
<td>Himelhoch et al (2004)</td>
<td>549 patients from Johns Hopkins University HIV clinic including 18% with psychiatric disorder.</td>
<td>Using Kaplan–Meier estimates of time to HAART adj HR of receiving HAART was 1.37 (1.01–1.87)</td>
<td>HAART: adj OR = 2.28 (95% CI 1.24–3.23)</td>
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<tr>
<td>Himelhoch et al (2007)</td>
<td>Data from minimum data-set of the HIV Research Network. 5119 HIV-infected patients in primary care. 504 had severe mental illness, 1298 injection drug misuse and 267 both severe mental illness and drug misuse.</td>
<td>After adjustment for age, gender, ethnicity, CD4 count and site, those with severe mental illness and drug problems (dual diagnosis) had a 0.32 odds of receiving HAART; those with severe mental illness alone 0.85. Those with severe mental illness and/or drug misuse were significantly more likely to have in-patient admission</td>
<td>HAART: adj OR = 0.85 (95% CI 0.71–1.23)</td>
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<tr>
<td>Mijch et al (2006)</td>
<td>Retrospective cohort of 2981 individuals with HIV matched to Victorian Psychiatric Case Register of whom 525 have mental illness.</td>
<td>30.9% of those with mental ill health received HAART compared with 25.9% with no disorder. Those with mental health diagnosis received a greater number of antiretrovirals</td>
<td>HAART: OR = 1.28 (95% CI 1.04–1.57)</td>
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<td>Setting</td>
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<td>HAART: adj HR = 0.4 (95% CI 0.2–0.9) for untreated depression</td>
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<td>Tegger et al (2008)</td>
<td>HIV/AIDS</td>
<td>Affective disorder defined as:</td>
<td>1774 patients in the University of Washington (MV) HIV re: initiation</td>
<td>Secondary</td>
<td>After adjustments, patients with depression and/or anxiety were significantly less likely to initiate HAART compared with patients without a mental illness (RR = 0.4, P = 0.02). Patients with mental illness or substance use disorders receive HAART at lower CD4+ cell counts and higher HIV-1 RNA levels than patients without these disorders.</td>
<td>HAART: adj HR = 0.4 (95% CI 0.2–0.9) for untreated depression</td>
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<td>depression and/or anxiety only</td>
<td>of HAART within 9 months of becoming eligible for HAART</td>
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<tr>
<td>Yun et al (2005)</td>
<td>HIV/AIDS</td>
<td>Affective disorder defined as:</td>
<td>1713 HIV-infected patients seen in an urban healthcare setting (1997–2001) from chart review and administrative and pharmacy files</td>
<td>Primary</td>
<td>52% received HAART. Antiretroviral adherence was lower among patients with depression not on antidepressant treatment (v. those on antidepressant treatment; P = 0.012). Adherence to antiretroviral treatment was higher among patients adherent to antidepressant treatment (v. those non-adherent to antidepressant treatment; P = 0.0014).</td>
<td>HAART: unadj OR = 1.43 (95% CI 1.18–1.74)</td>
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<td>diagnosis of depression (57% depressed)</td>
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<td>care</td>
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<tr>
<td>Redelmeier et al (1998)</td>
<td>Medical care for arthritis, osteoporosis, lipids and HRT</td>
<td>Psychotic illness defined by:</td>
<td>1344 145 patients &gt;64 years and part of Ontario drug benefit programme. Those with psychotic illness identified by prescriptions for haloperidol (17’336). Adjusted for age and gender</td>
<td>Community</td>
<td>Those with psychotic illness less likely to receive medical treatment for arthritis OR = 0.59 (95% CI 0.57–0.62), 30 669 identified as having diabetes (by insulin prescriptions); less likely to receive HRT P &lt; 0.001. 56 779 identified as having emphysema (by ipratropium prescriptions); less likely to receive lipid-lowering drugs (P &lt; 0.001).</td>
<td>Arthritis medications: OR = 0.59 (95% CI 0.57–0.62)</td>
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<td></td>
<td>prescription of haloperidol among residents of Ontario, Canada for psychotic illness</td>
<td></td>
<td>patients</td>
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<tr>
<td>Bishop et al (2004)</td>
<td>Osteoporosis</td>
<td>Psychotic illness defined by:</td>
<td>46 patients with schizophrenia and osteoporosis</td>
<td>VA Medical</td>
<td>Patients with schizophrenia were less likely to receive osteoporosis care including medication (especially HRT)</td>
<td>Osteoporosis drugs: unadj OR = 0.38 (95% CI 0.15–0.97)</td>
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<td>schizophrenia by routine clinical examination</td>
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<td>Centres</td>
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(continued)
### Table DS1 Summary of comparative studies reporting receipt of medication (continued)

<table>
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<tr>
<th>Author</th>
<th>Specific medical indication</th>
<th>Mental illness types</th>
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<th>Other mental illness</th>
<th>Severe mental illness/ schizophrenia</th>
<th>Affective disorder</th>
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</thead>
<tbody>
<tr>
<td>Baxter et al (2009)</td>
<td>Asthma</td>
<td>Mental illness, affective disorder and psychotic illness defined by ICD-9 definitions of substance misuse, depression, anxiety disorder, bipolar disorder, schizophrenia and psychotic disorders</td>
<td>Medicaid claims from 5 states comprising 19,064 individuals with asthma, of whom about 50% had mental illness diagnoses</td>
<td>Primary care</td>
<td>HEDIS defined prescription was lower in those with substance misuse or schizophrenia in 2 out of 5 states but higher for affective disorders in 1 state e.g. asthma OR = 0.69 (95% CI = 0.51–0.93) for schizophrenia in 1 state</td>
<td>Any mental illness pooled adj OR = 0.98 (99% CI 0.93–1.04)</td>
<td>Schizophrenia: pooled adj OR = 0.77 (95% CI 0.66–0.90)</td>
<td>Affective disorder: pooled adj OR = 1.16 (95% CI 1.07–1.26)</td>
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<tr>
<td>Goodwin et al (2004)</td>
<td>Cancer</td>
<td>Affective disorder defined by: a priori diagnosis of depression for each participant was based (ICD-9 codes 296.2, 296.3, 296.5, 296.6, 296.7, 298.0, 301.10, 301.12, 301.13, 309.0, 309.1, 311)</td>
<td>Cancer database and medicare database. Identified 24.6% women aged 67 years and older, with a diagnosis of breast cancer. Of them 7.5% (1841) had received a diagnosis of depression in the 2 years prior to recruitment</td>
<td>Secondary care</td>
<td>Women with depression associated with a 19% increase in the odds of receiving less than definitive therapy (P &lt; 0.0001). 42% more likely to die in the 3-year follow-up period (after controlling for other factors that might affect survival) (RR = 1.42, 95% CI 1.13–1.79). This difference remained significant after restricting the analysis to women who did receive definitive treatment, implying this difference in survival cannot be explained by differences in treatment. Healthcare utilisation (number of doctor visits in past 2 years) was examined</td>
<td>Chemotherapy: unadj OR = 0.65 (0.429–1)</td>
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VA, Veterans Affairs; MI, myocardial infarction; RR, relative risk; adj, adjusted; unadj, unadjusted; ACE, angiotensin-converting enzyme inhibitor; CHD, coronary heart disease; CABG, coronary artery bypass graft; LVEF, left ventricular ejection fraction; ONAP, other non-affective psychotic disorder; ASA, acetyl salicylic acid; COPD, chronic obstructive pulmonary disease; IHD, ischaemic heart disease; ARB, angiotensin receptor blocker; HAART, highly active antiretroviral therapy; PTSD, post-traumatic stress disorder; HR, hazard ratio; HRT, hormone replacement therapy; HEDIS, Health Effectiveness Data and Information Set. 
a. Other mental illness includes any type of mental illness other than pure affective disorder, severe mental illness or schizophrenia 
b. Odds ratio estimated assuming control event rate of 52%. 

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**Notes:**
- Any mental illness pooled adj OR = 0.98 (99% CI 0.93–1.04)
- Schizophrenia: pooled adj OR = 0.77 (95% CI 0.66–0.90)
- Affective disorder: pooled adj OR = 1.16 (95% CI 1.07–1.26)
- Depression alone: adj OR = 1.19 (95% CI 1.08–1.31)
- Bipolar disorder: adj OR = 1.07 (95% CI 0.91–1.27)
<table>
<thead>
<tr>
<th>Author</th>
<th>Cases independently validated</th>
<th>Cases are representative of population</th>
<th>Community controls</th>
<th>Controls have no history of mental illness</th>
<th>Study controls for age?</th>
<th>Study controls for additional factor(s)?</th>
<th>Ascertainment of exposure by masked interview or record?</th>
<th>Same method of ascertainment used for cases and controls?</th>
<th>Non-response rate the same for cases and controls?</th>
<th>Overall quality</th>
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<tr>
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VA, Veterans Affairs; IDU, Injection drug use; PCP, Pneumocystis jiroveci pneumonia; COPD, chronic obstructive pulmonary disease; LVEF, left ventricular ejection fraction.
Differences in the prescribing of medication for physical disorders in individuals with v. without mental illness: meta-analysis
Alex J. Mitchell, Oliver Lord and Darren Malone
Access the most recent version at DOI: 10.1192/bjp.bp.111.094532

Supplementary Material
Supplementary material can be found at: http://bjp.rcpsych.org/content/suppl/2012/11/08/201.6.435.DC1

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