

## Physical health monitoring

### Introduction

People with severe mental disorders such as bipolar disorder may be at increased risk for physical conditions. Many treatments, such as antipsychotics, can be associated with adverse side effects; furthermore, some people with severe mental disorders may be hesitant to seek advice from a medical professional. A program of well organised and regular physical health monitoring could be beneficial for these patients.

### Method

We have included only systematic reviews (systematic literature search, detailed methodology with inclusion/exclusion criteria) published in full text, in English, from the year 2010 that report results for people with a diagnosis of bipolar or related disorders. Reviews were identified by searching the databases MEDLINE, EMBASE, and PsycINFO. Hand searching reference lists of identified reviews was also conducted. When multiple copies of review topics were found, only the most recent or comprehensive review was included. Reviews with pooled data are given priority for inclusion.

Review reporting assessment was guided by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist that describes a preferred way to present a meta-analysis<sup>1</sup>. Reviews with less than 50% of items checked have been excluded from the library. The PRISMA flow diagram is a suggested way of providing information about studies included and excluded with reasons for exclusion. Where no flow diagram has been presented by individual reviews, but identified studies have been described in the text, reviews have been checked for this item. Note that early reviews may have been guided by less stringent reporting checklists than the PRISMA, and that some reviews may have been limited by journal guidelines.

Evidence was graded using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) Working Group approach where high quality evidence such as that gained from randomised controlled trials (RCT) may be downgraded to moderate or low if review and study quality is limited, if there is inconsistency in results, indirect comparisons, imprecise or sparse data and high probability of reporting bias. It may also be downgraded if risks associated with the intervention or other matter under review are high. Conversely, low quality evidence such as that gained from observational studies may be upgraded if effect sizes are large or if there is a dose dependent response. We have also taken into account sample size and whether results are consistent, precise and direct with low associated risks (see end of table for an explanation of these terms)<sup>2</sup>. The resulting table represents an objective summary of the available evidence, although the conclusions are solely the opinion of staff of NeuRA (Neuroscience Research Australia).

### Results

We found four systematic reviews that met our inclusion criteria<sup>3-6</sup>.

- Moderate to high quality evidence suggests a small effect of greater risk of medical hospital rehospitalisation in people with bipolar disorder or other severe mental illnesses after discharge from medical hospitals.
- Moderate to high quality evidence suggests people with a severe mental illness are prescribed medication for physical disorders less often than people without a mental illness.
- Moderate to low quality evidence suggests people with bipolar disorder were younger at acute myocardial infarction (64.2 years vs. 66.8 years), less likely to receive percutaneous transluminal coronary angioplasty or coronary artery bypass graft,

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and less likely to be diagnosed in medical centres or teaching hospitals than people without a mental illness.

- Moderate quality evidence suggests greater uptake of prevention services by people with a severe mental illness after being given general health advice.

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*Germack HD, Caron A, Solomon R, Hanrahan NP*

**Medical-surgical readmissions in patients with co-occurring serious mental illness: A systematic review and meta-analysis**

General Hospital Psychiatry 2018; 55: 65-71

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<b>Comparison</b>	<b>Rates of medical hospital readmission in people with bipolar disorder or another severe mental illness vs. people with no mental illness.</b>
<b>Summary of evidence</b>	<b>Moderate to high quality evidence (large sample, inconsistent, precise, direct) suggests a small effect of greater risk of medical hospital rehospitalisation in people with bipolar disorder or other severe mental illness.</b>
<b>Medical hospital readmission</b>	
<p><i>A small, significant effect of greater odds of readmission in people with a severe mental illness;</i>            9 studies, N ~2,500,000, OR = 1.38, 95%CI 1.23 to 1.56, <math>p &lt; 0.001</math>, <math>I^2 = 99\%</math>            Subgroup analyses of studies of psychiatric outpatients, inpatients, those with a substance use disorder, and surgical or non-surgical patients all showed small effect sizes.            There were no moderating effects of sex, race or age.            There was no evidence of publication bias.</p>	
<b>Consistency in results<sup>†</sup></b>	Inconsistent
<b>Precision in results<sup>§</sup></b>	Precise
<b>Directness of results<sup>  </sup></b>	Direct

*Mitchell AJ, Lord L, Malone D*

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

The British Journal of Psychiatry 2012; 201: 435-443

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<b>Comparison</b>	<b>Prescribing medication for physical disorders in people with a</b>
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	<b>severe mental disorder (including bipolar disorder) vs. people without a mental disorder.</b>
<b>Summary of evidence</b>	<b>Moderate to high quality evidence (large sample, inconsistent, precise, direct) suggests people with a severe mental illness are prescribed medication for physical disorders less often than people without a severe mental disorder.</b>
<p><i>A small significant effect suggests less prescription of medicines for any physical disorder in people with a severe mental disorder;</i></p> <p>All severe mental disorders: 36 studies, N &gt; 1.5 million, OR = 0.74, 95%CI 0.63 to 0.86, I<sup>2</sup> = 97.2%  <i>People with a severe mental illness received medications less frequently than expected for;</i></p> <p>Angiotensin-converting enzyme inhibitors/angiotensin II receptor blockers: OR = 0.89, 95%CI 0.81 to 0.98, <i>p</i> = 0.02</p> <p>Beta-blockers: OR = 0.90, 95%CI 0.84 to 0.96, <i>p</i> = 0.001</p> <p>Statins: OR = 0.61, 95%CI 0.39 to 0.94, <i>p</i> = 0.02</p> <p>Non-aspirin anticoagulants: OR = 0.74, 95%CI 0.56 to 0.97, <i>p</i> = 0.02</p> <p>No differences were reported for anticholesterol drugs in general (statins and non-statins combined), or for anticoagulants (aspirin and non-aspirin combined).</p>	
<b>Consistency in results</b>	Inconsistent
<b>Precision in results</b>	Precise
<b>Directness of results</b>	Direct

Reeves E, Henshall C, Hutchinson M, Jackson D

### **Safety of service users with severe mental illness receiving inpatient care on medical and surgical wards: A systematic review**

International Journal of Mental Health Nursing 2018; 27: 46-60

[View review abstract online](#)

<b>Comparison</b>	<b>Characteristics of inpatients with bipolar disorder vs. inpatients without a mental illness.</b>
<b>Summary of evidence</b>	<b>Moderate to low quality evidence (large sample, unable to assess precision, direct) suggests people with bipolar disorder were younger at acute myocardial infarction (64.2 years vs. 66.8 years), less likely to receive percutaneous transluminal coronary angioplasty or coronary artery bypass graft, and less</b>

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	<b>likely to be diagnosed in medical centers or teaching hospitals than people without a mental illness.</b>
	One study (N = 2,770) found people with bipolar disorder were younger at acute myocardial infarction (64.2 years vs. 66.8 years), less likely to receive percutaneous transluminal coronary angioplasty or coronary artery bypass graft, and less likely to be diagnosed in medical centres or teaching hospitals than people without a mental illness.
<b>Consistency in results</b>	N/A; 1 study
<b>Precision in results</b>	Unable to assess; no measure of precision is reported.
<b>Directness of results</b>	Direct

*Tosh G, Clifton A, Mala S, Bachner M*

### General physical health advice for people with serious mental illness

Cochrane Database of Systematic Reviews 2011; Issue 2. Art. No.: CD008567. DOI: 10.1002/14651858.CD008567.pub2.

[View review abstract online](#)

<b>Comparison</b>	<b>General health advice for people with a severe mental illness, (including bipolar disorder) vs. standard care.</b>
<b>Summary of evidence</b>	<b>Moderate quality evidence (medium to large samples, imprecise, consistent where applicable, direct) suggests greater uptake of prevention services by people with a severe mental illness after being given general health advice.</b>
	<p><i>One study reported greater uptake of ill-health prevention services in the advice group;</i></p> <p>1 RCT, N = 363, MD = 36.90, 95%CI 33.10 to 40.70, <math>p &lt; 0.05</math></p> <p><i>One of two studies reported increased quality of life;</i></p> <p>1 RCT, N = 40, MD = 3.70, 95%CI 1.70 to 5.60, <math>p &lt; 0.05</math></p> <p>1 RCT, N = 54, MD = 0.00, 95%CI -0.67 to 0.67, <math>p &gt; 0.05</math></p> <p><i>No difference in death or attrition rates;</i></p> <p>Death: 1 RCT, N = 407, RR = 1.30, 95%CI 0.30 to 6.00, <math>p &gt; 0.05</math></p> <p>Attrition: 5 RCTs, N = 884, RR = 1.18, 95%CI 0.97 to 1.43, <math>p &gt; 0.05</math>, <math>I^2 = 35%</math>, <math>p = 0.19</math></p>
<b>Consistency in results</b>	Consistent for attrition; N/A for other outcomes (1 RCT).
<b>Precision in results</b>	Imprecise

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<b>Directness of results</b>	Direct
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## Explanation of acronyms

CI = confidence interval,  $I^2$  = measure of heterogeneity across study results, MD = mean difference, N = number of participants, N/A = not applicable, OR = odds ratio,  $p$  = probability of finding a significant effect, RCT = randomised controlled trial, RR = risk ratio, vs. = versus

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### Explanation of technical terms

\* Bias has the potential to affect reviews of both RCT and observational studies. Forms of bias include; reporting bias – selective reporting of results; publication bias - trials that are not formally published tend to show less effect than published trials, further if there are statistically significant differences between groups in a trial, these trial results tend to get published before those of trials without significant differences; language bias – only including English language reports; funding bias - source of funding for the primary research with selective reporting of results within primary studies; outcome variable selection bias; database bias - including reports from some databases and not others; citation bias - preferential citation of authors. Trials can also be subject to bias when evaluators are not blind to treatment condition and selection bias of participants if trial samples are small<sup>7</sup>.

† Different effect measures are reported by different reviews.

Prevalence refers to how many existing cases there are at a particular point in time. Incidence refers to how many new cases there are per population in a specified time period. Incidence is usually reported as the number of new cases per 100,000 people per year. Alternatively some studies present the number of new cases that have accumulated over several years against a person-years denominator. This denominator is the sum of individual units of time that the persons in the population are at risk of becoming a case. It takes into account the size of the underlying population sample and its age structure over the duration of observation.

Reliability and validity refers to how accurate the instrument is. Sensitivity is the proportion of actual positives that are correctly identified

(100% sensitivity = correct identification of all actual positives) and specificity is the proportion of negatives that are correctly identified (100% specificity = not identifying anyone as positive if they are truly not).

Weighted mean difference scores refer to mean differences between treatment and comparison groups after treatment (or occasionally pre to post treatment) and in a randomised trial there is an assumption that both groups are comparable on this measure prior to treatment. Standardised mean differences are divided by the pooled standard deviation (or the standard deviation of one group when groups are homogenous) that allows results from different scales to be combined and compared. Each study's mean difference is then given a weighting depending on the size of the sample and the variability in the data. Less than 0.4 represents a small effect, around 0.5 a medium effect, and over 0.8 represents a large effect<sup>7</sup>.

Odds ratio (OR) or relative risk (RR) refers to the probability of a reduction ( $< 1$ ) or an increase ( $> 1$ ) in a particular outcome in a treatment group, or a group exposed to a risk factor, relative to the comparison group. For example, a RR of 0.75 translates to a reduction in risk of an outcome of 25% relative to those not receiving the treatment or not exposed to the risk factor. Conversely, a RR of 1.25 translates to an increased risk of 25% relative to those not receiving treatment or not having been exposed to a risk factor. A RR or OR of 1.00 means there is no difference between groups. A medium effect is considered if  $RR > 2$  or  $< 0.5$  and a large effect if  $RR > 5$  or  $< 0.2$ <sup>8</sup>. InOR stands for logarithmic OR where a InOR of 0 shows no difference between groups. Hazard ratios measure the effect of an explanatory variable on the hazard or risk of an event.

Correlation coefficients (eg,  $r$ ) indicate the strength of association or relationship between variables. They can provide an

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indirect indication of prediction, but do not confirm causality due to possible and often unforeseen confounding variables. An  $r$  of 0.10 represents a weak association, 0.25 a medium association and 0.40 and over represents a strong association. Unstandardised ( $b$ ) regression coefficients indicate the average change in the dependent variable associated with a 1 unit change in the independent variable, statistically controlling for the other independent variables. Standardised regression coefficients represent the change being in units of standard deviations to allow comparison across different scales.

‡ Inconsistency refers to differing estimates of effect across studies (i.e. heterogeneity or variability in results) that is not explained by subgroup analyses and therefore reduces confidence in the effect estimate.  $I^2$  is the percentage of the variability in effect estimates that is due to heterogeneity rather than sampling error (chance) - 0% to 40%: heterogeneity might not be important, 30% to 60%: may represent moderate heterogeneity, 50% to 90%: may represent considerable heterogeneity and over this is considerable heterogeneity.  $I^2$  can be calculated from  $Q$  (chi-square) for the test of heterogeneity with the following formula<sup>7</sup>;

$$I^2 = \left( \frac{Q - df}{Q} \right) \times 100\%$$

§ Imprecision refers to wide confidence intervals indicating a lack of confidence in the effect estimate. Based on GRADE recommendations, a result for continuous data (standardised mean differences, not

weighted mean differences) is considered imprecise if the upper or lower confidence limit crosses an effect size of 0.5 in either direction, and for binary and correlation data, an effect size of 0.25. GRADE also recommends downgrading the evidence when sample size is smaller than 300 (for binary data) and 400 (for continuous data), although for some topics, these criteria should be relaxed<sup>9</sup>.

|| Indirectness of comparison occurs when a comparison of intervention A versus B is not available but A was compared with C and B was compared with C that allows indirect comparisons of the magnitude of effect of A versus B. Indirectness of population, comparator and/or outcome can also occur when the available evidence regarding a particular population, intervention, comparator, or outcome is not available and is therefore inferred from available evidence. These inferred treatment effect sizes are of lower quality than those gained from head-to-head comparisons of A and B.



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