TECHNICAL COMMENTARY

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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 2000 that report results for people with a diagnosis of schizophrenia, schizoaffective disorder, schizophreniform disorder or first episode schizophrenia. Reviews were identified by searching the databases MEDLINE, EMBASE, CINAHL, Current Contents, PsycINFO and the Cochrane library. Hand searching reference lists of identified reviews was also conducted. When multiple copies of reviews were found, only the most recent version was included. Reviews with pooled data are prioritised 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[1]. 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 (RCTs) 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)[2]. 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 five systematic reviews that met inclusion criteria[3-7].

- Moderate to high quality evidence finds a medium-sized effect of less mammography screening in women with schizophrenia.
- Moderate quality evidence suggests people with a severe mental illness are prescribed medication for physical disorders less often than people without a severe mental disorder.
- Moderate to high quality evidence suggests a small effect of greater risk of

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rehospitalisation to a medical hospital after discharge.

- Moderate quality evidence suggests medical hospital inpatients with schizophrenia experience more adverse events than medical hospital inpatients without a psychiatric disorder. Common adverse events include; longer hospital stays, blood transfusion, post-operative infection, post-operative anaemia, post-operative sepsis, pulmonary insufficiency, respiratory failure, deep vein thrombosis, and mechanical interventions.
- 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

View review abstract online

Comparison	**Rates of medical hospital readmission in people with severe mental illness vs. people with no mental illness.**
Summary of evidence	**Moderate to high quality evidence (large sample, inconsistent, precise, direct) suggests a small effect of greater risk of medical hospital rehospitalisation in people with severe mental illness.**
Medical hospital readmission	
A small, significant effect of greater odds of readmission in people with a severe mental illness; 9 studies, N ~2,500,000, OR = 1.38, 95%CI 1.23 to 1.56, $p < 0.001$, $I^2 = 99\%$ 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.	
Consistency in results‡	Inconsistent
Precision in results§	Precise
Directness of results‖	Direct

Hwong A, Wang K, Bent S, Mangurian C

Breast Cancer Screening in Women With Schizophrenia: A Systematic Review and Meta-Analysis

Psychiatric services 2020; 71: 269-79.

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Comparison	**Rates of mammography screening in women with schizophrenia**

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	vs. women without schizophrenia.
Summary of evidence	**Moderate to high quality evidence (large sample, inconsistent, precise, direct) suggests a medium-sized effect of less mammography screening in women with schizophrenia.**
Medical hospital readmission	
A medium-sized effect showed women with schizophrenia were less likely to receive screening; 11 studies, N = 471,922, OR = 0.50, 95%CI 0.38 to 0.64, $p < 0.001$, $I^2 = 96\%$ There was no moderating effect of study quality.	
Consistency in results	Inconsistent
Precision in results	Precise
Directness of results	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

View review abstract online

Comparison	**Prescribing medication for physical disorders in people with schizophrenia vs. people without a mental illness.**
Summary of evidence	**Moderate quality evidence (unclear sample size for schizophrenia, inconsistent, precise, direct) suggests people with schizophrenia are prescribed medication for physical disorders less often than people without a mental illness.**
A small significant effect suggests less prescription of medicines for any physical disorder in people with schizophrenia; For schizophrenia alone (number of studies not reported): OR = 0.69, 95%CI 0.57 to 0.83, $p < 0.0001$ All severe mental disorders: 36 studies, N >1.5 million, OR = 0.74, 95%CI 0.63 to 0.86, $I^2 = 97.2\%$ *People with a severe mental illness received medications less frequently than expected for;* Angiotensin-converting enzyme inhibitors/angiotensin II receptor blockers: OR 0.89, 95%CI 0.81 to	

0.98, p = 0.02 Beta-blockers: OR 0.90, 95%CI 0.84 to 0.96, p = 0.001 Statins: OR 0.61, 95%CI 0.39 to 0.94, p = 0.02 Non-aspirin anticoagulants: OR 0.74, 95%CI 0.56 to 0.97, p = 0.02 No differences were reported for anticholesterol drugs in general (statins and non-statins combined), or for anticoagulants (aspirin and non-aspirin combined).	
Consistency in results	Inconsistent
Precision in results	Precise
Directness of results	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

Comparison	**Adverse events of inpatients with schizophrenia vs. inpatients without a mental illness.**
Summary of evidence	**Moderate quality evidence (large samples, unable to assess consistency or precision, direct) suggests inpatients with schizophrenia experience more adverse post-operative events than inpatients without a psychiatric disorder. Common adverse events included; longer hospital stay, blood transfusion, post-operative infection, post-operative anaemia, post-operative sepsis, pulmonary insufficiency, respiratory failure, deep vein thrombosis and mechanical intervention.**
1 US study (N = 326,499) found inpatients with schizophrenia had higher risk of blood transfusion despite not being anaemic, longer hospital stays, and higher rates of discharge to a short-term or long-term facility. 1 US study (N = 7,899,694) found inpatients with schizophrenia had a higher risk of a blood transfusion, acute post-operative infection, acute post-operative anaemia, acute myocardial infarction, induced mental illness, pulmonary insufficiency, intubation, intensive care admission, acute respiratory failure, and mechanical intervention. They had a lower risk of wound complications, post-operative shock, post-operative bleeding, acrenal failure, pneumonia, and deep	

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vein thrombosis. They also had longer hospital stays, a non-routine discharge, and were less likely to be discharged to home.

1 Taiwanese study (N = 3,796) found inpatients with schizophrenia had greater risk of intensive care admission, acute respiratory failure, mechanical intervention, admission into a lower-level district hospital than a medical centre or a public hospital than private hospital. They were less likely to be treated by a male doctor or by a pulmonary or critical care specialist.

1 Japanese study (N = 12,475) found inpatients with schizophrenia had more comorbidity, were more likely to have a higher stage of cancer, but were less likely to be admitted for cancer treatment, were more likely to receive open surgery treatment, had a higher 30-day in-hospital mortality and longer hospital stays. They were less likely to receive surgical or endoscopic treatment, or laparoscopic or endoscopic treatment.

1 US study (N = 37,362,038) found inpatients with schizophrenia were more likely to be non-White and male, to have a medical admission than a surgical admission, to be admitted as an emergency rather than a planned patient, more likely to be in receipt of Medicaid, more likely to live in an area with lower income, had higher prevalence of comorbidities, were more likely to die in hospital, had higher cost of care and a longer hospital stay, and were more likely to experience an adverse event. After adjusting for patient and hospital characteristics, they were also more likely to develop: decubitus ulcer, infection due to medical care, post-operative respiratory failure, post-operative sepsis, pulmonary embolism, or deep vein thrombosis. The risk of accidental puncture or laceration was lower in inpatients with schizophrenia.

1 Taiwanese study (N = 44,835) found fewer inpatients with schizophrenia received operations in a teaching hospital. There was a higher prevalence of long-term conditions, higher rates of post-operative complications (stroke, bleeding, pneumonia, renal failure, septicaemia), higher cost of care and a longer length of hospitalisation, higher likelihood of being admitted to intensive care and higher risk of post-operative mortality. The risk was highest in those with more severe symptoms of schizophrenia.

1 Japanese study (N = 5,423) found inpatients with schizophrenia had a higher risk of post-operative complications, higher cost of care and a longer length of hospital stay.

1 US study (N = 9,986,605) found inpatients with schizophrenia were less likely to be discharged home and more likely to be discharged to a facility, they had a longer length of hospital stay and a higher occurrence of adverse events, including more wound complications, acute post-haemorrhagic anaemia, acute renal failure, pulmonary congestion, deep vein thrombosis, and blood transfusion. They were also less likely to experience cardiac complications, pulmonary embolism, fat embolism, induced mental illness, pulmonary insufficiency, and intubation, and were less likely to die in hospital.

1 US study (N = 4,962,521) found inpatients with schizophrenia were more likely to be male and young, to have medical comorbidities (hypertensive disease, long-term pulmonary disease, diabetes), to be discharged to a rehabilitation facility, to have any adverse event, to have a longer hospital stay, to experience wound complications, acute renal failure, pulmonary embolism, induced mental illness, pulmonary insufficiency, deep vein thrombosis, and blood transfusion. They were less likely to have acute post-operative anaemia, general complications, cardiac complications, iatrogenic hypotension, pulmonary congestion, intubation, or mechanical ventilation, and had a

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lower rate of in-hospital death. 1 Taiwanese study (N = 97,413) found inpatients with schizophrenia were more likely to have a ruptured appendix. 1 Taiwanese study (N = 3,118) found inpatients with schizophrenia had a lower mean age at admission and lower income level, were more likely to have diabetes, hyperlipidaemia, and alcohol use disorders, and had a higher 30-day inpatient mortality rate. They were less likely to receive percutaneous transluminal coronary angioplasty or coronary artery bypass graft, or to be diagnosed in medical centres or teaching hospitals.	
Consistency in results	Unable to assess; no measure of consistency is reported.
Precision in results	Unable to assess; no measure of precision is reported.
Directness of results	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

Comparison	**General health advice for people with a severe mental illness vs. standard care.**
Summary of evidence	**Moderate quality evidence (mostly 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.**
One study reported greater uptake of ill-health prevention services in the advice group; 1 RCT, N = 363, MD = 36.90, 95%CI 33.10 to 40.70, $p < 0.05$ *One of two studies reported increased quality of life;* 1 RCT, N = 40, MD = 3.70, 95%CI 1.70 to 5.60, $p < 0.05$ 1 RCT, N = 54, MD = 0.00, 95%CI -0.67 to 0.67, $p > 0.05$ *No difference in death or attrition rates;* Death: 1 RCT, N = 407, RR = 1.30, 95%CI 0.30 to 6.00, $p > 0.05$ Attrition: 5 RCTs, N = 884, RR = 1.18, 95%CI 0.97 to 1.43, $p > 0.05$, $I^2 = 35\%$, $p = 0.19$	

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Consistency in results	Consistent for attrition; N/A for other outcomes (1 RCT).
Precision in results	Imprecise
Directness of results	Direct

Explanation of acronyms

CI = confidence interval, I^2 = the percentage of the variability in effect estimates that is due to heterogeneity rather than sampling error (chance), MD = mean difference, N = number of participants, OR = odds ratio, *p* = statistical probability of obtaining that result ($p < 0.05$ generally regarded as significant), 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[8].

† 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[8].

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[9]. lnOR stands for logarithmic OR where a lnOR of 0 shows no difference between groups. Hazard ratios measure the effect of an explanatory variable on the hazard or risk of an event.

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Correlation coefficients (eg, r) indicate the strength of association or relationship between variables. They can provide an indirect indication of prediction, but do not confirm causality due to possible and often unforseen 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;[8]

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

§ 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.[10]

‖ 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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References

1. Moher D, Liberati A, Tetzlaff J, Altman DG, PRISMAGroup (2009): Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *British Medical Journal* 151: 264-9.
2. GRADEWorkingGroup (2004): Grading quality of evidence and strength of recommendations. *British Medical Journal* 328: 1490.
3. Mitchell AJ, Lord O, Malone D (2012): Differences in the prescribing of medication for physical disorders in individuals with v. without mental illness: Meta-analysis. *British Journal of Psychiatry* 201: 435-43.
4. Tosh G, Clifton A, Bachner M (2011): General physical health advice for people with serious mental illness. *Cochrane Database of Systematic Reviews*: CD008567.
5. Germack HD, Caron A, Solomon R, Hanrahan NP (2018): Medical-surgical readmissions in patients with co-occurring serious mental illness: A systematic review and meta-analysis. *General hospital psychiatry* 55: 65-71.
6. Reeves E, Henshall C, Hutchinson M, Jackson D (2018): 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* 27: 46-60.
7. Hwong A, Wang K, Bent S, Mangurian C (2020): Breast Cancer Screening in Women With Schizophrenia: A Systematic Review and Meta-Analysis. *Psychiatric services* 71: 269-79.
8. CochraneCollaboration (2008): Cochrane Handbook for Systematic Reviews of Interventions. Accessed 24/06/2011.
9. Rosenthal JA (1996): Qualitative Descriptors of Strength of Association and Effect Size. *Journal of Social Service Research* 21: 37-59.
10. GRADEpro (2008): [Computer program]. Jan Brozek, Andrew Oxman, Holger Schünemann. *Version 32 for Windows*