TECHNICAL COMMENTARY

Impact on families

Introduction

A diagnosis of bipolar disorder can have considerable impact not only on the affected individual, but also on the people closest to them. Sometimes families experience different types of burden, particularly during acute phases of the illness. Burden is considered in terms of objective effects, such as illness severity or financial strain, but also in terms of subjective effects, such as the emotional impact of the illness on family members.

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 separately for people with 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 and/or comprehensive review was included. Reviews with pooled data have been 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[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 three systematic reviews that met our inclusion criteria[3-5].

- Moderate to low quality evidence suggests increased caregiver knowledge and reduced short-term burden with psychoeducation.

- Moderate to low quality evidence suggests caregiver burden is apparent, both during depressive and manic episodes. Patient behaviours of most concern to caregivers included; impulsive spending, over activity and lack of sleep, over talkativeness, lack of insight, and odd, aggressive or unpredictable behaviours.

- Moderate to low quality evidence suggests up to half of caregivers report depression symptoms and up to one third report contact with mental health services for their own symptoms.

Baruch E, Pistrang N, Barker C

Psychological interventions for caregivers of people with bipolar disorder: A systematic review and meta-analysis

Journal of Affective Disorders 2018; 236: 187-98

View review abstract online

Comparison	Psychoeducation about the nature of bipolar disorder, triggers and warning signs, treatment, management, and the impact on and role of caregivers vs. treatment as usual or wait-list.
Summary of evidence	Moderate to low quality evidence (small to medium-sized samples, inconsistent, imprecise, direct) suggests increased caregiver knowledge and reduced burden (short-term only) with psychoeducation.

Caregiver knowledge
A significant, large effect of increased caregiver knowledge post-treatment and at follow-up;
Post treatment: 4 studies, N = 183, g = 2.60, 95%CI 1.39 to 3.82, $p < 0.0001$, I^2 = 88%, $p < 0.001$
Follow-up: 3 studies, N = 127, g = 2.41, 95%CI 0.85 to 3.98, $p = 0.003$, I^2 = 89%, $p < 0.001$

Caregiver burden
A significant, large effect of reduced caregiver burden post-treatment but not at follow-up;
6 RCTs, N = 379, g = -0.80, 95%CI -1.32 to -0.27, $p = 0.003$, I^2 = 81%, $p < 0.0001$
3 RCTs, N = 137, g = -1.22, 95%CI -3.19 to 0.75, $p = 0.22$, I^2 = 95%, $p < 0.00001$

Caregiver psychological symptoms
There were no significant effects on psychological symptoms;
Post treatment: 3 studies, N = 155, g = -1.76, 95%CI -4.21 to 0.70, $p = 0.16$, I^2 = 97%, $p < 0.001$
Follow-up: 2 studies, N = 101, g = -2.44, 95%CI -5.91 to 1.03, $p = 0.003$, I^2 = 97%, $p < 0.001$

Consistency in results[‡]	Inconsistent
Precision in results[§]	Imprecise
Directness of results[‖]	Direct

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Beentjes TA, Goossens PJ, Poslawsky IE

Caregiver burden in bipolar hypomania and mania: a systematic review

Perspectives in Psychiatric Care 2012; 48: 187-97

View review abstract online

Comparison	Overview of burden in people caring for someone with bipolar mania.
Summary of evidence	**Moderate to low quality evidence (small to medium-sized samples, unable to assess consistency or precision, direct) suggests caregiver burden is apparent during both depressive and manic episodes. The behaviour of concern most consistently reported included; impulsive spending, over activity/lack of sleep, over talkativeness, lack of insight, and odd, aggressive or unpredictable behaviour.**

Caregiver burden

2 studies, N = 480 and N = 266, found depressive episodes were more burdensome than mood elevation. 1 study, N = 58, found no differences in caregiver coping styles between index episodes of mania or depression.

1 study, N = 86, found the most frequent distressing behaviour that causes severe and moderate distress was hyperactivity.

1 study, N = 41, found 46% of caregivers reported both depression and anxiety equally distressing, 30% rated mania as most distressing, and 19% rated depression as most distressing. 49% took significant responsibility for the patient's finances during episodes of illness, and 46% saw this as a significant stress. 90% believed the manic behaviour was caused by the illness; 5% believed the patient could control it. 44% had experienced violence or were frightened violence was going to occur when the patient was unwell. Distressing manic behaviours included odd behaviour, impulsive spending, over activity, over talkativeness, and suspiciousness.

1 study, N = 48, found manic behaviour that is burdensome includes; inability to handle money, lack of insight, unstable mood, over activity, delusions, unpredictable behaviour, up all night, extreme distress, irritability, non-compliance, blaming others, talking to self, poor hygiene and grooming, aggressiveness, strange appearance or behaviour. There were significant differences in reported burden and the professionals' burden appraisal.

1 study, N = 32, found 75% of the caregivers were burdened by manic symptoms and 75% because of switches between depression and mania. The burden from switches between depression and mania were correlated with caregiver's suspension of social contacts and lack of understanding patient's behaviour and hopelessness of the caregiver.

1 study, N = 37, found the most problematic manic behaviour involved verbal aggression (100%), unwise spending (100%), offensive behaviour (93%), unpredictability (89%), attention seeking

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(89%), and increased sociability (63%). Partners were more dissatisfied with their marriage during mania than during depressive episodes.

1 study, N = 19, found perceived burden to mania was extreme in 33% of spouses, high in 44%, moderate in 17%, low in 6%, none in 0%. Perceived burden to depression was extreme in 11%, high in 61%, moderate in 28%, low in 0%, none in 0%. Burdensome hypomanic and manic behaviours included decreased need for sleep (42%), over talkativeness (42%), violence (32%), poor judgment (32%), anger (32%), and recurrences of the illness (32%).

1 study, N = 100, reported partner frustration, thoughts of killing oneself or the patient, problems with children being unable to concentrate due to problems created by the patient, inability to control patient's money spending.

1 study, N = 12, found caregivers feared the patient may cause mayhem. There was dissatisfaction with what mental health services could provide.

1 study, N = 15, found there was negative interaction with the patient during delusions and manic behaviour, and an urgent feeling of need to protect the patient from harm.

1 study, N = 50 found caregiver difficulty empathising with the patient during grandiosity in mania or hypomania and terror during paranoid delusions.

1 study, N = 8, found partner concerns included personality changes, loss of reality, and fear. Partners developed a watchful attitude to changes in behaviour and signs of illness in their partner.

Consistency in results	Unable to assess; no measure of consistency is reported
Precision in results	Unable to assess; no CIs reported
Directness of results	Direct

Steele A, Maruyama N, Galynker I

Psychiatric symptoms in caregivers of patients with bipolar disorder: a review

Journal of Affective Disorders 2010; 121: 10-21

View review abstract online

Comparison	**Psychiatric symptoms in people caring for a person with bipolar disorder.**
Summary of evidence	**Moderate to low quality evidence (large sample, unable to assess consistency or precision, direct) suggests up to half of caregivers reported depression symptoms and up to one third reported contact with mental health services for their own symptoms.**

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Caregiver psychiatric symptoms	
21 studies, N = 63,382 Up to 46% of caregivers reported depression and up to 32.4% reported mental health service use.	
Consistency in results	Unable to assess; no measure of consistency is reported
Precision in results	Unable to assess; no CIs reported
Directness of results	Direct

Explanation of acronyms

CI = Confidence Interval, g = Hedge's standardised mean difference, I^2 = magnitude of heterogeneity between study results, N = number of participants, p = statistical probability of obtaining that result ($p < 0.05$ generally regarded as significant), 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 which 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.[6]

† 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 which are correctly identified (100% sensitivity = correct identification of all actual positives) and specificity is the proportion of negatives which 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 randomized trial there is an assumption that both groups are comparable on this measure prior to treatment. Standardized mean differences are divided by the pooled standard deviation (or the standard deviation of one group when groups are homogenous) which 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.[6]

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[7]. 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. Unstandardized (*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) which is not explained by subgroup analyses and therefore reduces confidence in the effect estimate. I² 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. I² can be calculated from Q (chi-square) for the test of heterogeneity with the following formula;[6]

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

§ 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.[8]

‖ 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 which 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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