TECHNICAL COMMENTARY

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Family intervention

Introduction

Family intervention involves the introduction of a patient's immediate family into a psychosocial treatment setting. Its goals involve preventing relapse, improving the family's relationships and understanding of the disorder as well as improving their own mental health, should that be compromised. Family interventions have a focus on psychoeducation which provides information on the disorder, medication, and treatment adherence. They can also employ cognitive and behavioural strategies to improve problem solving, communication skills, and coping, and to reduce high expressed emotion in the family unit.

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 a diagnosis of bipolar or related disorders. Due to the high volume of systematic reviews we have now limited inclusion to systematic meta-analyses. Where no systematic meta-analysis exists for a topic, systematic reviews without meta-analysis are included for that topic. Reviews were identified by searching the databases MEDLINE, EMBASE, and PsycINFO. Hand searching reference lists of identified review topics was also conducted. When multiple copies of review topics were found, the most recent and/or comprehensive review was included.

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 reporting less than 50% of items 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, there is a dose dependent response or if results are reasonably 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 two systematic reviews that met our inclusion criteria[3, 4].

- Moderate quality evidence suggests with family psychoeducation is associated with a medium-sized reduced risk of mania relapse for up to one year post-treatment compared to treatment as usual.
- Moderate to low quality evidence suggests carer focused therapy may reduce relapses in patients, with no significant benefits of Family Focused Therapy for relapse, depressive symptoms, treatment adherence, or general functioning.

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Chatterton ML, Stockings E, Berk M, Barendregt JJ, Carter R, Mihalopoulos C

Psychosocial therapies for the adjunctive treatment of bipolar disorder in adults: network meta-analysis

British Journal of Psychiatry 2017; 210: 333-41

View review abstract online

Comparison	**Family interventions for people with bipolar disorder and/or their families or carers vs. treatment as usual.** **This meta-analysis uses direct and indirect comparisons from 41 trials (N = 3,119).**
Summary of evidence	**Moderate to low quality evidence (large sample, unable to assess consistency, imprecise, direct and indirect) suggests only carer focused therapy may reduce relapses in patients, with no benefits of Family Focused Therapy for relapse, depressive symptoms, treatment adherence or general functioning.**
Relapse	
No significant differences between groups (Family Focused Therapy vs. treatment as usual); RR = 0.79, 95%CI 0.54 to 1.15, $p > 0.05$ *Carer focused therapy resulted in fewer relapses in patients;* RR = 0.61, 95%CI 0.44 to 0.86, $p < 0.05$	
Depressive symptoms	
No significant differences between groups (Family Focused Therapy vs. treatment as usual); g = -0.26, 95%CI -0.72 to 0.20, $p > 0.05$	
Treatment adherence	
No significant differences between groups (Family Focused Therapy vs. treatment as usual); RR = 0.17, 95%CI 0.03 to 1.04, $p > 0.05$ *Carer focused therapy yielded similar results;* RR = 0.86, 95%CI 0.5 to 1.36, $p > 0.05$	
General functioning	

No significant differences between groups (carer focused therapy); g = 0.62, 95%CI -0.63 to 1.87, p > 0.05	
Consistency in results	Unable to assess; no measure of consistency is reported.
Precision in results	Imprecise.
Directness of results	Indirect for relapse (patient and carers; mixed control conditions).

Oud M, Mayo-Wilson E, Braidwood R, Schulte P, Jones SH, Morriss R, Kupka R, Cuijpers P, Kendall T

Psychological interventions for adults with bipolar disorder: systematic review and meta-analysis

British Journal of Psychiatry 2016; 208: 213-22

View review abstract online

Comparison 1	**Family psychoeducation for 14 weeks vs. treatment as usual.**
Summary of evidence	**Moderate quality evidence (medium-sized sample, consistent, imprecise, direct) suggests a medium-sized reduced risk of mania but not depression relapse by 1 year post-treatment with family psychoeducation compared to treatment as usual.** **Low quality evidence (small sample sizes, imprecise) is unable to determine any benefit of family psychoeducation over treatment as usual for symptoms, hospital admissions or treatment response.**
Relapse	
A significant, medium-sized reduced risk of any or mania relapse with family psychoeducation at follow-up; Follow-up 52-65 weeks, any relapse: 3 RCTs, N = 228, RR = 0.52, 95%CI 0.32 to 0.84, p < 0.05, I^2 = 23%, p = 0.27 Follow-up 65 weeks, mania relapse: 1 RCT, N = 113, RR = 0.35, 95%CI 0.15 to 0.85, p < 0.05 Follow-up 65 weeks, depression relapse: 1 RCT, N = 113, RR = 0.73, 95%CI 0.44 to 1.21, p > 0.05	
Hospital admissions	
A significant, large reduced risk of hospitalisation with family psychoeducation at follow-up; Follow-up 60 weeks: 1 RCT, N = 57, RR = 0.05, 95%CI 0.00 to 0.83, p < 0.05	

Treatment response	
No significant differences between groups; Follow-up 52-65 weeks: 1 RCT, N = 59, RR = 0.67, 95%CI 0.34 to 1.32, $p > 0.05$	
Depressive symptoms	
A significant, medium-sized effect of improved depressive symptoms with family psychoeducation post-treatment, but not at follow-up; Post-treatment: 1 RCT, N = 43, SMD = -0.73, 95%CI -1.35 to -0.10, $p < 0.05$ Follow-up 60 weeks: 1 RCT, N = 53, SMD = -0.15, 95%CI -0.69 to 0.39, $p > 0.05$	
Mania symptoms	
A significant, medium-sized effect of improved depressive symptoms with family psychoeducation post-treatment and at follow-up; Post-treatment: 1 RCT, N = 43, SMD = -0.66, 95%CI -1.28 to -0.04, $p < 0.05$ Follow-up 60 weeks: 1 RCT, N = 53, SMD = -0.78, 95%CI -1.34 to -0.22, $p < 0.05$	
Comparison 2	**Family Focused Therapy for 39 weeks vs. active controls.**
Summary of evidence	**Low quality evidence (small sample sizes, unable to assess consistency or precision) is unable to determine any benefit of Family Focused Therapy over active controls.**
Relapse	
No significant differences between groups; Post-treatment: 1 RCT, N = 53, RR = 0.89, 95%CI 0.52 to 1.54, $p > 0.05$ Follow-up 52 weeks, any relapse: 1 RCT, N = 101, RR = 0.67, 95%CI 0.34 to 1.30, $p < 0.05$	
Hospital admissions	
No significant differences between groups post-treatment, a large effect at follow-up of reduced hospital admissions with Family Focused Therapy; Post-treatment: 1 RCT, N = 53, RR = 0.71, 95%CI 0.33 to 1.52, $p > 0.05$ Follow-up 104 weeks: 1 RCT, N = 38, RR = 0.24, 95%CI 0.08 to 0.74, $p < 0.05$	
Treatment response	
No significant differences between groups; Follow-up 121 weeks: 1 RCT, N = 62, RR = 1.15, 95%CI 0.68 to 1.94, $p > 0.05$	

Family intervention

Depressive symptoms	
No significant differences between groups; Post-treatment: 1 RCT, N = 79, SMD = -0.40, 95%CI -0.80 to 0.00, $p > 0.05$ Follow-up 52 weeks: 1 RCT, N = 79, SMD = -0.10, 95%CI -0.56 to 0.36, $p > 0.05$	
Mania symptoms	
No significant differences between groups; Post-treatment: 1 RCT, N = 79, SMD = 0.00, 95%CI -0.40 to 0.40, $p > 0.05$ Follow-up 52 weeks: 1 RCT, N = 79, SMD = -0.30, 95%CI -0.68 to 0.08, $p > 0.05$	
Consistency in results	Consistent where applicable (comparison 1, any relapse).
Precision in results	Imprecise.
Directness of results	Direct

Explanation of acronyms

CI = Confidence Interval, *d* = Cohen's *d* and *g* = Hedges' *g* = standardised mean differences, I^2 = the percentage of the variability in effect estimates that is due to heterogeneity rather than sampling error (chance), *p* = statistical probability of obtaining that result ($p < 0.05$ generally regarded as significant), RCT = randomised controlled trial, RR = risk ratio, SMD = standardised mean difference, 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[5].

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† Different effect measures are reported by different reviews.

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) 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[5].

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[6]. 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.

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).

Correlation coefficients (eg, r) indicate the strength of association or relationship

between variables. They are an 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 dependent 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 substantial heterogeneity and 75% to 100%: considerable heterogeneity. I^2 can be calculated from Q (chi-square) for the test of heterogeneity with the following formula[5];

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

§ 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[7].

‖ 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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