Cochrane Library

Cochrane Database of Systematic Reviews

Family interventions for bipolar disorder (Review)

Justo L, Soares BGDO, Calil H

Justo L, Soares BGDO, Calil H.
Family interventions for bipolar disorder.
Cochrane Database of Systematic Reviews 2007, Issue 4. Art. No.: CD005167.
DOI: 10.1002/14651858.CD005167.pub2.

www.cochranelibrary.com

WILEY

TABLE OF CONTENTS

[Intervention Review]

Family interventions for bipolar disorder

Luis Justo[1], Bernardo Garcia de Oliveira Soares[2], Helena Calil[3]

[1]Departmento de Psicobiologia, Universidade Federal de Sao Paulo, Sao Paulo, Brazil. [2]Universidade Federal de São Paulo, São Paulo, Brazil. [3]Departamento de Psicobiolgia, Universidade Federal de Sao Paulo, Sao Paulo, Brazil

Contact address: Luis Justo, Departmento de Psicobiologia, Universidade Federal de Sao Paulo, Rua Napoleao de Barros 925, Vila Clementino, Sao Paulo, CEP 04024002, Brazil. luisjusto1@ig.com.br.

Editorial group: Cochrane Common Mental Disorders Group.
Publication status and date: Edited (no change to conclusions), published in Issue 1, 2010.

Citation: Justo L, Soares BGDO, Calil H. Family interventions for bipolar disorder. *Cochrane Database of Systematic Reviews* 2007, Issue 4. Art. No.: CD005167. DOI: 10.1002/14651858.CD005167.pub2.

ABSTRACT

Background

Pharmacological treatments are the principal intervention for bipolar disorder. Alone, however, they are not sufficient to control symptoms and maintain psychosocial functioning. Adjunctive psychosocial interventions may help to improve the patient's condition and the course of the illness. Family interventions are deserving of special attention, since they may help to relieve the burden of care borne by relatives and caregivers, which in turn may facilitate the task of supporting the patient.

Objectives

The objective of this review was to investigate the effectiveness of family interventions in the treatment of bipolar disorder compared with no intervention and other forms of intervention.

Search methods

We searched the electronic databases CCDANRCT-Studies and CCDANCTR-References on 1/8/2007, CENTRAL (2006-3), MEDLINE (2006), EMBASE (2006) and LILACS (2006), and searched the reference lists of included studies. We also made personal contact with authors.

Selection criteria

We included randomised controlled trials (RCTs) and quasi-randomised trials. Participants were people with bipolar disorder and their relatives or caregivers; family psychosocial interventions of any type were considered; primary outcomes were changes in the status of symptoms and relapse rates.

Data collection and analysis

Data were independently extracted by two review authors. Quality assessment of included studies was carried out. The findings were presented descriptively. Where there were sufficient studies, dichotomous data were combined using relative risk, and continuous data were combined using weighted mean difference, with their 95% CIs.

Main results

Seven RCTs were included in the review, involving a total of 393 participants. All of the included studies assessed psychoeducational methods, and one study also assessed a type of systems psychotherapy. In all trials, participants continued to receive pharmacotherapy treatment. Due to the diversity of interventions, outcome measures and endpoints used across studies, it was not possible to perform meta-analyses for primary outcomes. Five studies compared a variety of family interventions, involving carers, families or spouses, against no intervention, with individual findings indicating no significant added effect for family interventions. Three studies compared one type or modality of family intervention against another family intervention, with inconsistent findings.

Authors' conclusions

To date there is only a small and heterogeneous body of evidence on the effectiveness of family oriented approaches for bipolar disorder, and it is not yet possible to draw any definite conclusions to support their use as an adjunctive treatment for bipolar disorder. Further well designed RCTs should be a research priority.

PLAIN LANGUAGE SUMMARY

Family interventions for bipolar disorder

Drug treatments are the primary treatment for bipolar disorder. Alone, however, they are not sufficient to manage the disorder. Studies on psychosocial interventions for mental disorders such as schizophrenia and anxiety show that they are effective treatments. Reports in the literature suggest that they may be useful for people with bipolar disorder as well. The role of the family is important in the care of people with bipolar disorder, with effective family functioning helping to maintain a person's psychological balance. This systematic review investigated the effectiveness of any psychosocial family intervention for people with bipolar disorder and/or their families and carers. Seven randomised controlled trials (393 participants) were included in the review, all of which evaluated psychoeducational interventions. Five studies compared family interventions against no treatment, and three studies compared one type or delivery of family intervention against another family intervention. Differences in the interventions, outcome measures and end points used in the trials did not allow us to perform a meta-analysis. Whilst results from individual studies did not suggest a significant effect for family interventions when added to drug therapy, the studies provide insufficient evidence to draw conclusions which can be generalised to everyday practice. Further research using appropriate randomised controlled trial methodology and evaluating family interventions other than psychoeducation is called for in this under-researched and important topic.

BACKGROUND

Bipolar disorder is a group of illnesses characterised by the presence of symptoms of pathologic variations of mood. According to DSM-IV-TR, people suffering from bipolar disorder type I have at least one episode of mania, commonly presenting with more than one episode, with or without depressive episodes. In bipolar disorder type II there is at least one episode of depression and one or more episodes of hypomania (never one episode of mania) associated. People may also exhibit mood symptoms that do not meet the criteria for bipolar disorder I or II, leading to a diagnosis of bipolar disorder not otherwise specified. Cyclothymic disorder may be diagnosed in people who do not meet the criteria for manic, mixed, or major depressive episode but exhibit periods of depressive symptoms and periods of hypomaniac symptoms for at least two years (adults) and no symptom-free period longer than two months. Although bipolar disorder is usually described as a periodic disease, mood liability may occur between episodes and become an important cause of impairment in general abilities with potential harmful changes in the lives of affected people (Gitlin 1995; Kalbag 1999; Judd 2005). Consequently it is associated with significant morbidity, psychosocial and laborative maladjustment and high suicide risk (Judd 2005).

The lifetime prevalence of bipolar disorder I ranges from 0.4% to 1.6% and the lifetime prevalence of bipolar disorder II is 0.5%, in the adult population (APA 2002). Different ethnic groups do not show differences in these rates (APA 2002). Bipolar I disorder affects the same proportion of men and women, but bipolar II disorder is more common in women (APA 2002). The first episode in men is more likely to be manic, but for both genders the first episode is more frequently a depressive one (APA 2002). Divorce rates are two or three times higher among people with bipolar disorder than the general population, and occupational status is twice as likely to deteriorate (APA 2002). It is estimated that 25% to 50% of all people suffering from bipolar disorder will attempt suicide in their lives (Jamison 2000).

Bipolar and unipolar mood disorders may be distinct entities (Goodwin 1990), although this concept lacks consensus. Currently the diagnosis is mostly made according to ICD-10 and DSM-IV-TR. The concept of bipolar disorder has now been broadened and so this illness is identified more often (Akiskal 2006). Aetiology seems to be strongly associated to genetic and biologic factors, but the involvement of psychosocial factors is increasingly gaining attention (Alloy 2005).

The prognosis for bipolar disorder, in spite of continual pharmacological maintenance treatment, is not always favourable. There is evidence suggesting that the course is less benign than previously thought. One study demonstrated a 73% relapse risk over a period of five years post recovery of an episode, and that morbidity appeared to be a more sensitive correlate of psychosocial functioning than the number of relapses (Gitlin 1995). Psychosocial impairments may persist even when mood symptoms are controlled by medications (Zaretsky 2003). Treatment consists predominantly of pharmacological agents such as mood stabilisers, antidepressants and antipsychotics when necessary, sometimes benzodiazepines and more rarely electroconvulsive therapy. Compliance is often a significant problem.

Pharmacological treatments are the fundamental tool in managing the illness, however they are not sufficient to control all the problems associated with the course of the disorder and its consequences in a person's life condition (Hilty 1999). It is especially difficult to achieve satisfactory prevention of relapse through the use of medication alone (Gelemberg 1989; Gitlin 1995). In addition, the sophistication and complexity of questions linked to human psychological functioning and social performance demand more specific interventions in order to address subtle aspects of the ill person. It is also important to remember that subsyndromal symptoms persisting after the acute episode may be very difficult to manage, even with appropriate pharmacological treatment, and may cause non-compliance, thus impairing restoration of former capacities and wellness (Coryell 1993). Additionally, it seems to be important with life events and correlated stress in order to prevent the negative impact they may have on the illness, specially regarding depressive symptoms and episodes (Johnson 2005; Johnson 2006). There is evidence that stressful events inside family milieu are connected to symptoms of bipolar disorder and expressed emotion is an important predictor of symptoms severity (Miklowitz 2005; Kim 2007). Bipolar disorder may represent a significative psychologic burden for family members and other caregivers (Perlick 1999). Family psychosocial interventions appear to be useful for people with other mental illnesses like schizophrenic disorders (Falloon 1984; Tomaras 2000).

Psychosocial interventions have been used for bipolar disorder since the pre-pharmacological treatment era. In the early days they mostly appeared not to be useful therapies for people with this disorder, probably due to the lack of concomitant medication. However, the course of bipolar disorder has changed, through use of suitable biological treatments, and several forms of psychotherapies and psychoeducational methods are now applied as adjunctive care, with more evident success (Huxley 2000; Gonzales-Pinto 2004; Jones 2004). Different types of individual, group, and family psychosocial interventions are now applied, using a non-specific or a specially tailored design for bipolar disorder (Jones 2004). Cognitive-behavioural therapy, interpersonal therapy, interpersonal and social rhythm therapy, psychoanalytically-based psychotherapy, family therapies (based on different theoretical orientations including cognitive-behavioural, psychoanalytical and systemic theories) (Mikolwitz 1990 ; Huxley 2000 ; Reinares 2002 ; Fristad 2003 ; Jones 2004), and several types of group therapies are examples of psychotherapies that can be used to treat bipolar patients. Psychoeducational methods may also use different formats according to individuals, groups of patients or family settings.

There is general consensus that bipolar disorder affects relationships in patients' families, and that family relationships also affect the course of bipolar disorder (Reinares 2002). Family interventions seem to be useful in controlling the illness (Reinares 2002; Kim 2004). Under the name of family therapy one can find very different kinds of interventions with diverse concepts in foundation. They can operate as direct psychoeducational methods with the explicit objective of instructing patients and relatives or carers about vicissitudes of the illness, or they can be behavioural therapy models with more or less educational purposes, often with communication enhancement and problem-solving training. Alternatively, they can signify efforts for modifications in the functioning of the whole family group, treating them as a system where none is isolated and none is the

single owner of the illness, as in the case of systemic family therapy models.

The aim of this review was to obtain and summarise all relevant trials that evaluate the effectiveness of all possible different forms of family interventions, according to their differing theoretical basis, for bipolar disorder. Family interventions were understood here to be any type of psychosocial interventions for family members of people with biploar, with or without the participation of the individual with bipolar disorder. It also included therapies with groups of families.

OBJECTIVES

1) To investigate the effectiveness (improvement of symptoms or reduction of relapse rates) of family interventions for bipolar disorder as compared to:
a) no intervention
b) other family psychosocial interventions

METHODS

Criteria for considering studies for this review

Types of studies

All relevant randomised controlled trials (RCTs) evaluating family psychosocial interventions for bipolar disorder. Specific relevant outcome data from quasi-randomised studies were included. Cluster randomised trials were also considered.

Types of participants

People with a diagnosis of bipolar disorder based on DSM-III, DSM-III-R, DSM-IV, DSM-IV-TR, IDC 9 or ICD 10 criteria and their relatives or caregivers. There were no restrictions regarding gender, age, ethnical group, nationality, stage of the disease (remitted or in acute phase), presence of co-morbidity, and use of concomitant medication (as long as these were balanced by design).

Types of interventions

We included any family psychosocial interventions used for treating bipolar disorder in acute phase, or as preventive intervention in stable participants. Family psychosocial interventions could include any type of psychological therapy or psychoeducational methods for the treatment of bipolar patients and their families or caregivers (couples or group of relatives of a bipolar patient, or group of families of different bipolar patients, with or without the attendance of the bipolar patient),drawing from diverse theoretical foundations.

The term psychoeducation means to teach patients, family and caregivers about the illness and possible coping strategies. Psychological therapies are more difficult to define due to the diversity of theoretical approaches, but generally speaking, mean methods oriented to address psychological problems using a therapeutic relationship. The types of family psychosocial interventions could be: family psychoeducation methods, cognitive-behavioural family therapy, cognitive family therapy, behavioural family therapy, interpersonal family therapy, psychodynamic family therapy, systemic family therapy, a mixed modality between this types (e.g. an intervention mixing psychoeducational and cognitive-behavioural techniques). Couples therapy and therapies with groups of families were also included. Family interventions could be administered by psychiatrists, psychologists or other health care professionals.

The meaning of 'family' in this review was an extended one that encompassed people who were closely related to the patient, living in the same home or not, a biological relative or a significant and closely connected person for the patient, including close caregivers. Spouses were considered family.

As specified in the Background section, family interventions were categorised according to three different theoretical orientations, as follows:
1) Cognitive Behavioural Family Therapy (CBFT) (to include cognitive-behavioural family therapy, cognitive family therapy, behavioural family therapy and family psychoeducation methods)
2) Psychodynamic therapy (including psychoanalytic psychotherapy, object relations)
3) Systemic therapy (including structural and post-Milan)

Main comparisons:
1) Family interventions (stratified by category) versus no intervention
2) Family intervention versus other family psychosocial intervention
Where further studies become available in future updates of the review, the following additional comparisons are planned:
3) CBFT versus psychodynamic therapy
4) CBFT versus systemic therapy
5) Systemic therapy versus psychodynamic therapy

Types of outcome measures

Primary outcome
Effectiveness of interventions measured by:
1) Changes in the status of the illness, as measured by standard scales, such as Young Mania Rating Scale-YMRS, Montgomery Affective Disorders Rating Scale-MADRS, Hamilton Rating Scale for Depression-HRSD, Schedule for Affective Disorders and Schizophrenia-SADS, Brief Psychiatric Rating Scale-BPRS, Bech-Raphaelson Manic Scale, or any other validated scale; for studies where subjects are in the acute phase of disease or have subsyndromic symptoms in maintenance phase;
2) Relapse rates, for studies where participants are stable (not in an acute phase of disease).

Secondary outcomes:
1) Hospitalisation
2) Length of remission
3) Suicide attempts
4) Treatment compliance (attendance at psychosocial treatment appointments)
5) Dropout rates at endpoint
a) Number of participants who dropped out because of lack of efficacy
b) Number of participants who dropped out because of symptoms worsening
6) Employment related events (Work Adjustment Scale, and any other validated scale or objective event like as loss of job, interruption or return to work)
7) Social and family functioning (UCLA-Social Attainment Survey, Family Assessment Device-FAD, Global Functioning Scale-GFS, or any other validated scale)

8) Quality of life (SF-36, World Health Organisation Quality of Life Scale - WHOQOL, or any other validated scale)
9) Anxiety levels (post-hoc outcome)

Outcomes would be grouped for analysis according to the duration of active treatment and follow up: less than 6 months, 6 to 12 months, 12 to 24 months. For the current version of the review, this was not performed due to limited number of studies and heterogeneity of data.

Search methods for identification of studies

1)Electronic search
The CCDAN registers were searched using the following search strategies:

CCDANCTR-Studies - searched on 1/8/2007
Diagnosis = "Bipolar Disorder" or "Bipolar I Disorder" or "Bipolar II Disorder" or "Depression, Bipolar" or "Depression, Psychotic" or "Major Affective Disorders" or "Manic Disorder" or Mania or "Mood Disorders" or "Bipolar Not Otherwise Specified" or "Psychotic Disorders" or Psychoses or "Treatment resistant"
and
Intervention = Family or Marital or Spous* or Couples*

CCDANCTR-References - searched on 1/8/2007
Free-text = "Bipolar III Disorder" or "Unipolar Mania" or "Rapid Cycling Disorder" or "Affective Disorders" or "Affective Psychosis, Bipolar" or "Bipolar Disorder " or "Bipolar Disorder" or "Bipolar I Disorder" or "Bipolar II Disorder" or "Cyclothymic Disorder " or "Depressive Psychosis" or "Excited Psychosis" or "Hypomania" or "Mania" or "Manic-Depressive" or "Manic Disorder" or "Manic Episode" or "Melancholia" or "Mixed Depression" or "Mood Disorders" or "Bipolar Affective Disorder " or "Bipolar Not Otherwise Specified " or "Dysphoric Mania" or "Manic Episode" or "Manic Symptoms" or "Schizoaffective Disorder" or "Psychoses" or "Psychotic Disorders" or "Puerpal Psychosis " or "Reactive Depressive Psychosis"
and
Free-text = family* or marital or couple* or spous*

The following databases were searched to identify randomised or quasi-randomised controlled trials: The Cochrane Central Register of Controlled Trials (CENTRAL) (2006-3), MEDLINE (1966-2006) EMBASE (1980-2006), and LILACS (1982-2006). The "optimal" MEDLINE, EMBASE and LILACS sensitive search strategies for identification of controlled clinical trials (Castro 1997; Dickersin 1994) were combined with the following phrases:

#1 affective disorders OR mood disorder OR bipolar disorder OR bipolar psychosis OR manic disorder OR mania OR manic psychosis OR manic depression OR hypomanic OR hypomania OR mixed mania OR mixed states OR mixed episodes OR affective symptoms OR bipolar depression OR cyclothymic disorder OR cyclothymia

#2 family therapy OR family intervention OR family treatment OR family process therapy OR family management OR psychoanalytical family therapy OR psychodynamic family therapy OR supportive family therapy OR cognitive behavioral family therapy OR systemic family therapy OR continuation family treatment OR maintenance family treatment OR prophylactic family treatment OR interpersonal family therapy OR cognitive family therapy OR couples therapy OR marital therapy OR spouses treatment

2) Handsearches
Bibliography of the identified studies were checked.

3) Personal Communication
Attempts to contact the authors of included studies were made when any clarification was needed, and to find out about ongoing and unpublished studies.

Data collection and analysis

Selection of trials
LPJ and BGOS screened the abstracts of all publications obtained by the search strategy (a track record was kept). The articles potentially suitable for the review were obtained in full to assess their relevance, based on broad inclusion criteria (all potential RCTs in family interventions).

Quality assessment
The quality of each trial was based on the criteria of quality specified by Shultz 1995, which measure the following range of factors:
1) Minimisation of selection bias: a) was the randomisation procedure adequate? b) was the allocation concealment adequate?
2) Minimisation of attrition bias: a) were the withdrawals and dropouts completely described? b) was analysis by intention to treat?
3) Minimisation of detection bias: a) were outcome assessors blind to the intervention?
Based on these criteria, studies were classified according to the criteria described in the Cochrane Handbook (Higgins 2005)
A-Low risk of bias (all quality criteria met)
B-Moderate risk of bias (quality criteria partially met)
C-High risk of bias (one or more criteria not met)
Trials were assessed independently by two review authors (LPJ, BGOS). In cases of disagreement the third review author (HMC) would be contacted.

Data extraction
Data were extracted independently by two review authors (LPJ, BGOS) using a standard data extraction form (Higgins 2005). This included data on: methods (generation of the allocation sequence, concealment of allocation, sample size estimation, length of follow-up), participant characteristics (diagnostic procedures, age, gender, ethnic origin, criteria used to classify recurrence, number of patients randomised, reasons for withdrawal from the trial), interventions, and outcomes (specified previously, any other assessed outcomes, other events, length of follow-up, reporting of outcomes quality).

Data analysis
Review Manager software developed by the Cochrane Collaboration was used to organise and process the results. Interventions were only grouped if clinically compatible, otherwise the findings were presented descriptively.

For dichotomous data, relative risks (RR) with 95% confidence intervals (CI) were estimated based on the fixed effects model, or on the random effects model when heterogeneity is present. An intention-to-treat analysis would be used in which the reviewers would assume that people who dropped out had a negative outcome, except in case there are death outcomes. For all statistically significant results, number needed to treat to benefit

(NNTB) or number needed to harm (NNTH) were calculated with 95% confidence intervals (CI).

Continuous outcomes were analysed if the mean and standard deviation of endpoint measures were presented in the original articles. For the meta-analysis of continuous outcomes, mean differences (MD) between groups were estimated. The weighted mean difference (WMD) would be used if the data were obtained from the same measurement scales, and the standardised mean difference (SMD) would be used if the measurement scales differed. Data on continuous outcomes are frequently skewed, the mean not being the centre of distribution. To avoid this potential pitfall, the following standards were applied to all data before inclusion: a) standard deviations and means would be obtained from authors, and b) for data with finite limits, such as endpoint scale data, the standard deviation (SD), when multiplied by two, was less than mean. Otherwise the mean is unlikely to be an appropriate measure of the centre of the distribution (Altman 1996). Only non-skewed data would be used in meta-analyses.

In order to describe the percentage of the variability in effect that occurs due to heterogeneity rather than to chance, it was planned to perform an I-squared calculation (values greater than 50% to be considered substantial heterogeneity).Heterogeneity would also be assessed by the chi-square test, and was assumed to be present when the significance level was lower than 0.10 ($p<0.10$). When significant heterogeneity was present, and a sufficient number of studies were available for comparisons, an attempt would be made to explain the differences, through use of subgroup analyses according to clinical characteristics of the included studies, or through the use of sensitivity analyses according to methodological differences in study design or degree of control over bias (e.g. allocation concealment).

Subgroup analyses
The following subgroup analyses were planned:
1) Family interventions directed at spouse and patient (couples therapy) versus family interventions for relatives and patient
2) Individual family versus group family interventions
3) Family interventions conducted with the individual versus family interventions conducted with the family
4) Family interventions with family members only versus family interventions with family members and patients
5) Family psycho-educative methods versus other family intervention (CBT, psychodynamic, systemic) methods
6) Structural therapy versus post-Milan therapy

Sensitivity analyses
Randomised versus quasi-randomised trials

Publication bias
To assess potential publication bias, trial data (trial effect versus trial size) would be used to produce a funnel graph.

Where it was not possible to pool data from studies due to heterogeneity of interventions and outcomes, and a small number of studies for inclusion, the findings were presented descriptively under the appropriate comparison headings.

RESULTS

Description of studies

Results of the search

Electronic searches from all databases generated 1892 references, most of which were excluded because they did not cover the subject of our study, based on scrutiny of the title alone or after reading the abstract. From the search, 20 studies were considered potentially relevant, and articles were obtained and scrutinised. Nine studies did not meet the inclusion criteria, and are described in the Characteristics of excluded studies table. Two studies are ongoing (Miklowitz 2004, Miklowitz 2006a). Two studies are awaiting assessment to see if they are dual publications of included studies (Keitner 1996b, Miller 2000). The remaining seven studies were included in the review. These are described below and in the Characteristics of included studies table.

Excluded Studies
Five studies were excluded because they were not randomised or quasi-randomised controlled trials. Two studies did not examine the effectiveness of family interventions on bipolar disorder as a primary or secondary outcome. Two studies were secondary reports from a trial already included in the review.

Studies awaiting assessment
There are two studies awaiting assessment (Keitner 1996b, Miller 2000)..

Included Studies
Participants
The total number of participants in included trials was 393, of whom 84 participants (Reinares 2004 and van Gent 1991), were spouses or caregivers (generally relatives). All participants were adults, with ages ranging from 18 to 62 years. Further information on characteristics of the participants is presented in the Characteristics of included studies table.

Interventions
Experimental family interventions were largely psychoeducational treatments for patients with their families, or for the families without participation of the patient. One intervention, Problem Centered Systems Therapy for the Family, was not specifically psychoeducational (Ryan 2003). Patients in experimental and control groups received concurrent pharmacological treatment.

1) Family Focused Therapy (FFT): Two studies (Miklowitz 1996, Goldstein 1996) used FFT as the experimental treatment. FFT was adapted for bipolar patients (Miklowitz 1997) from a previous psychosocial intervention model created for schizophrenic patients (Falloon 1984), and is a type of education for patients and their families. FFT consists of three components: psychoeducation about bipolar disorder, communication enhancement training and problem-solving skills training. FFT was administered in 21 one-hour session (12 weekly, 6 biweekly and 3 monthly) in 3 consecutive modules: psychoeducation (7 sessions), communication enhancement training (7-10 sessions) and problem-solving skills (4-5 sessions), administered in the 9 month period following an episode of bipolar illness. One of the studies (Goldstein 1996) compared FFT with an individual intervention, named individually focused patient treatment, in which the goals were to educate the patient about the illness, conduct crisis interventions and reduce ongoing life stress. The other (Miklowitz 1996) used a less intensive psychoeducational family intervention called crisis management (CM) as the control condition, with two 1-hour home-based sessions of family psychoeducation within the first 2 months after study entry and crisis intervention sessions

as needed during the remaining 9-month treatment period. Both studies were performed with outpatients.

2) Problem Centered Systems Therapy of the Family: This is a short-term, problem-focused, semi-structured family intervention that is manualised and is based upon the McMaster Model of family functioning (Epstein 1990). The therapy focus is directed to clinically relevant dimensions of family functioning as problem solving, communication, roles, affective responsiveness, affective involvement and behaviour control. This therapy relies on a core set of therapeutic principles tailored to the individual family's problems. The specific problems of the family are determined by the therapist and the family together. The therapy is performed through a progressive series of stages: assessment, contracting, treatment and termination. The number of sessions varies depending on the needs of the family ranging from 6 to 10 fifty-minute sessions. This intervention was studied in Ryan 2003 in a comparison with two other groups of treatment that were multifamily psychoeducation and pharmacotherapy alone. Inpatients, partial hospital patients and outpatients were included.

3) Multifamily Psychoeducational Group Therapy: This is a manual based semi-structured intervention developed for the study conducted by Ryan 2003, which included 4 to 6 patients and their family members above the age of 12 years. The sessions provided information about the bipolar disorder and taught members different coping strategies for common problems. The psychotherapists encouraged patients and family members to share their perspectives on family interactions. It was conducted in weekly 90-minutes 6 sessions, each of them focusing on a specific topic. Inpatients, partial hospital patients and outpatients were included.

4) Couple Psychoeducational Intervention: This is a manual-based psychoeducational intervention for patients and their partners, administered by social workers trained in family therapy. Couples in the experimental group received 25 (10 weekly and 15 bimonthly) sessions. In Clarkin 1998, this intervention was compared to standard medication for patients only. Inpatients and outpatients were included.

5) The psychoeducational family intervention studied in Reinares 2004 consisted of 12 ninety-minute group sessions for patients' caregivers, and took place in a hospital setting. Relatives of 10 mood stabilised patients were included in each group and the patients themselves did to attend the group sessions. Oral information about the illness and guidelines on its management were provided. Encouraging discussion between participants was facilitated. After each session the participants received a written summary about the topic of the day. The same psychologist conducted all the groups. In the control group patients received pharmacological treatment using the same algorithms of the Barcelona Bipolar Disorders Program that were administered to patients in the experimental group, but the patients' relatives did not receive psychoeducational intervention. Similarly, in the study by van Gent 1991, only patients' partners received a psychoeducational intervention. The partners attended five sessions in which information about the illness, pharmacological treatment and practical advice was provided, and written material was given to participants. Partners' experiences were solicited and discussed in the sessions. The group sessions were conducted by a psychiatrist and a social worker.

6) Inpatient family intervention: this type of intervention was used in Clarkin 1990. It was designed for inpatients and their families to be performed during the period that the patient was hospitalised through at least six 45 min to one hour family intervention sessions. It was a manual based psychoeducational method, whose goals were acceptance and understanding by the patient and family of the reality of the illness, identification of precipitating stresses for present episode and future, within and outside of the family, elucidation of family interactions, planning strategies for managing stresses and acceptance of the need for continued treatment after discharge.

Outcomes

Primary

1) Patients' affective symptoms: measured by standard rating scales as Hamilton Depression Rating Scale, Young Mania Rating Scale, Schedule for Affective Disorders and Schizophrenia-Change version, Brief Psychiatric Rating Scale, Bech-Rafaelsen Mania Scale.

2) Recovery (numbers of patients that have recovered in the comparison groups): using symptom rating scales and transforming them into dichotomous measures (yes/no).

Secondary

1) Hospitalisations or rehospitalisations.

2) Adherence to pharmacologic treatment measured through self-report scales provided by patients and their family, or by laboratory tests.

3) Dropouts (after randomisation): dropout data were reported in all studies.

46) Relationship within the family: measured through Family Environment Scale.

Settings

Two of the included studies were performed in Europe, one in Spain (Reinares 2004) and another in Netherlands (van Gent 1991). The remaining five included studies were conducted in USA.

Risk of bias in included studies

Allocation

All studies included in this review were described as randomised by their authors, nevertheless only three studies (Reinares 2004, Miklowitz 1996, Clarkin 1998) provided some specific information regarding randomisation processes. Only one study mentioned allocation concealment (Miklowitz 1996), with randomisation sequence concealed until assignments had been made. Regarding allocation concealment, the study by Miklowitz 1996 was classified as A ,and all the others were classified as B, for the reason that only the first study described concealment, and the others did not give sufficient information.

Blindness to Evaluation of Outcomes

Four of the included studies reported blindness for outcome measurements (Reinares 2004, Miklowitz 1996, Goldstein 1996, Clarkin 1990). One of these studies (Miklowitz 1996) provided secondary blinded evaluators to analyse information through video-tapes of interviews, and the authors compared the primary and secondary outcome rates because they considered it very difficult to keep the patients' psychosocial group assignments blind. The other studies (Reinares 2004, Goldstein 1996, Clarkin 1990) simply utilised evaluators blinded to the type of patients' psychosocial treatment group.

Intention-To-Treat Analysis and Loss to Follow Up
Intention-to-treat analysis was performed in two studies (Ryan 2003, Goldstein 1996), in that all participants randomised were included in final analyses. One study (Miklowitz 1996) did not include patients who terminated prematurely in the final statistical analysis, but provided data for them. Another trial (Reinares 2004) mentioned the loss of two participants who failed to complete endpoint assessments, but the authors did not clarify whether or not their data were included in final analyses. In another study (van Gent 1991) five of the 19 participants randomised to the experimental group and eight of the 20 participants randomised to the control group were not allowed to be enrolled in the study by the patients (their partners) and they were considered dropouts. One study reported missing data, and there is a mention of an intention-to-treat analysis procedure related to composite outcomes, but not for individual measures (Clarkin 1990). With just one exception (Clarkin 1998), all reported studies included explanations on reasons for dropouts.

Effects of interventions

Comparison 1. Family intervention versus no intervention (see Graphs 01 - 05)
We found five studies comparing any type of psychosocial family intervention (partners, caregivers or other members of family) (Ryan 2003, Reinares 2004, Clarkin 1998, van Gent 1991, Clarkin 1990) to no intervention. Clinical improvement outcomes (van Gent 1991, Clarkin 1990) and recovery (Ryan 2003) were reported, but were not combinable because they were measured in different ways. Secondary outcomes measured in individual studies included hospitalisation, medication compliance, relationships in the family environment and anxiety. Dropout outcome data were extracted from all five studies. Clarkin 1998 contributed dropout data only.

Graphs 01.01 to 01.09 present outcomes from all five studies. Graphs 02 to 05 present outcomes from four of the five studies individually (Clarkin 1990, Reinares 2004, Ryan 2003, van Gent 1991).

Primary outcome
1) Recovery: There was no significant difference in recovery rates between groups at 28 months' post-treatment for all patients (62 participants, RR 0.87, 95% CI 0.52 to 1.47) or for manic patients only (45 participants, RR 0.82, 95% CI 0.43 to 1.55) (Ryan 2003).

2) Clinical improvement: In the study by Clarkin 1990, there was no significant difference in clinical improvement rates between groups at post-treatment (26 participants, RR 0.49, 0.10 to 2.45) or at 6 months follow-up (RR 0.73, 95% CI 0.05 to 10.49). Similarly, in the study by van Gent 1991, there was no significant difference in SCL-90 total symptoms between groups at 12 months' post treatment (39 participants (RR, 0.03, 95% CI -0.59 to 0.66).

3) Relapse: No studies provided data on relapse rates.

Secondary outcomes
1) Hospitalisation: No patients were rehospitalised during the study by van Gent 1991.

2) Medication compliance: There were no significant differences between the family intervention and no intervention groups for medication compliance (van Gent 1991)

3) Relationships in the family environment: There were no significant differences between the family intervention and no intervention groups for relationships in the family environment (expressiveness, cohesion and conflict) (Reinares 2004).

4) Dropout: A meta-analysis of dropout rates (5 studies, 214 participants) did not show any significant difference between the family interventions group and the no intervention group (RR 0.70 95%CI 0.43-1.14) (Clarkin 1990, Clarkin 1998, Ryan 2003, van Gent 1991, Reinares 2004).

5) Anxiety (post-hoc outcome): Patients in the family intervention group had increased levels of anxiety when compared to the no intervention group (WMD 0.69; 95% CI 0.05-1.34) (van Gent 1991).

Comparison 2. Family intervention versus other family psychosocial intervention (See Graphs 06 - 07)
One study compared a systems therapy family intervention called Problem Centered Systems Therapy of the Family to a multifamily group psychoeducation intervention (Ryan 2003).

Primary outcome
1) Recovery: There was no significant difference in recovery rates between the two intervention groups for all patients (63 participants, RR 1.72, 95% CI 0.91 to 3.25), or for manic patients only.

Secondary outcomes
There was no significant difference between the multifamily psychoeducative intervention and Problem Centered Systems Therapy of the family for medication compliance or dropout rates.

Subgroup analyses

1. Family intervention versus individual intervention - subgroup analysis 3 (see Graphs 08)
One study compared a family psychosocial intervention to an individual psychosocial intervention (Goldstein 1996). Both interventions were based on similar principles. The main difference was the administration to participants alone or with their family.

Primary outcome
Relapse: There were no significant differences between the family and individual psychosocial intervention at post-treatment (12 months) (53 participants, RR 0.89, 95% CI 0.52 to 1.54).

Secondary outcomes
There were no significant differences between family and individual interventions for rehospitalisation, medication compliance and dropout rates.

2. Psychoeducative methods versus other family psychosocial intervention - subgroup analysis 5
One study compared Family Focused Therapy (FFT) with a more simple psychoeducative intervention called Crisis Management (CM), which was also administered to the family, but in a less intensive and complex way (Miklowitz 1996).

Primary outcome
Relapse: For relapse prevention, FFT was significantly superior to CM in preventing relapse (101 participants, RR 0.59, 95% CI 0.39-0.88; NNT=3.1; CI 1.9-8.3)

Secondary outcomes

There was no significant difference between CM and FFT for medication compliance or dropout rates.

Other data

1) Survival analysis

Data from survival analysis cannot be re-analysed in Review Manager. Two studies presented primary outcomes using survival analysis. Miklowitz 1996 demonstrated superiority of the Family Focused Therapy group over the Crisis Management group for time to relapse (Wilcoxon x2 = 8.71, p = 0.03) and Ryan 2003 reported no significant statistical difference between the three groups for time to recovery (log rank x2 = 1.21, df = 2, p = 0.55).

2) ANOVA

Miklowitz 1996 reported results of a repeated-measure mixed-model ANOVA regarding effect of time on total affective symptoms scores (measured by SADS-C). There was a statistically significant treatment group versus time interaction (F7,549=2.81, p=0.007) for symptom severity stabilised at lower level, which means that the FFT group presented significantly lower symptomatology scores from 6 months of treatment.

Data available for analysis

Further information about results can be found in the Characteristics of Included Studies table. Some outcomes were not suitable for meta-analysis due to lack of complete information, such as standard deviations for means. Other outcome data could not be re-analysed in this review because of the way they were measured or presented, for example, outcomes measured through survival analysis (although it is perhaps worth mentioning that the outcomes and measures are absolutely valid). We attempted to obtain additional information through making contact with the authors of studies, but it has not yet been possible to obtain this information.

DISCUSSION

In the process of conducting this review we found a number of studies examining the usefulness of different types of psychosocial interventions as an adjunctive treatment for bipolar disorders, many of which reported on a modality of family psychosocial intervention. However, the majority of the papers retrieved from the literature were not randomised or quasi-randomised controlled trials, therefore, only seven trials have so far been included in the review. Participants in all included studies were adults. All seven trials examined family psychoeducational methods, with only one trial assessing another specific type of psychotherapy, problem centered systems therapy of the family, in addition to psychoeducation (Ryan 2003).

The seven studies included in the review presented characteristics of the samples at baseline, described diagnostic procedures, and set out inclusion/exclusion criteria. Moreover, they used relevant outcomes, and provided detailed descriptions of interventions. However, outcomes were diverse and data were often presented in a way that prevented their inclusion for the purposes of meta-analysis, as in the case of those trials that used survival analysis (Ryan 2003; Miklowitz 1996; Goldstein 1996). A further problem was the lack of essential information, as in one study that did not present standard deviations for means of continuous data (Clarkin 1998). In that particular study, we were unsuccessful in obtaining further information from the authors (Clarkin 1998). Some outcomes were not directly clinical, for instance, focusing on the illness outcome itself. Other outcomes were not directly linked to any modification in the manifestations or evolution of the disease, such as the patients' and their family members' knowledge of the disease, and therefore we did not include all their findings in analyses (Reinares 2004; van Gent 1991).

Findings from individual studies appear inconclusive in demonstrating an effect for family interventions when compared with no family intervention. For studies comparing one family intervention against another type of family intervention, the Miklowitz 1996 study, a psychoeducational trial carefully conducted over a two year period, presented significant findings on relapse rates, from which the NNT shows that out of every three patients treated with family focused therapy, one less patient would relapse over time in comparison with patients undergoing crisis management intervention. For secondary outcomes, a result with clinical and statistical significance came from van Gent 1991, where participants attending for marital psychoeducation had a higher mean score in the anxiety scale than the control group (WMD 0.69; 95%CI 0.05-1.34). This could be considered a side-effect, which might be accounted for by the discomfort induced by the knowledge of the dificult aspects of the disorder, such as chronicity, and the fact that patients can relapse even with adequate medication. This increase in the levels of anxiety might be attributed to chance, and is also acknowledged as a post-hoc finding. Further studies may elucidate this issue.

Results of our review are limited due to the small number of randomised controlled trials on this subject. Additionally, the heterogeneity of studies, specially because they assessed different outcomes, and the lack of trials for each type of comparison performed, were major limitations. Although a non-randomised controlled study might produce useful information in this research field, we wished to follow the standards and criteria of the Cochrane Collaboration, in which the randomisation is a fundamental procedure in a health treatment study. In any case, we agree with the idea according to which the randomisation is really an important step in the trial process in order to minimise selection bias.

In general, there is increased acceptance of the need for adjuvant psychosocial interventions (psychotherapies and psychoeducational methods) added to standard medications in the treatment of bipolar disorder. It is suggested that the addition of psychosocial interventions may reduce symptoms, enhance social functioning, reduce hospitalisations and relapse rates and increase adherence to the treatment of bipolar disorder (Vieta 2005 b; Gutierrez 2004). Results of a systematic review on psychosocial interventions in bipolar disorder (Vieta 2005 a) found evidence of benefits of these interventions in combination with pharmacologic treatment. Furthermore, the same review considers the possibility that different types of psychosocial intevention have a distinct impact on the treatment of different types of bipolar patients. A related observation in another article suggests that mood fluctuations may have multiple distinct aspects in different patients, which might require different psychosocial intervention models in order for the health professional to manage the complexity of the illness (Jones 2005). In other words, bipolar disorder might present in different ways within the same phase or in the same patient, and possibly family intervention treatment could

be more effective if these variations of clinical presentation were assessed at the point at which the intervention is initiated.

Family members or caregivers may play a very important role in detecting subtle mood fluctuations of the patient, and could act therapeutically if properly prepared. It is possible that improving the environment, in which family functioning plays a major role, may be one kind of help for patients. On the other hand, stressful conditions in the family context, such as excessive hostility or overinvolvement (also denominated "expressed emotion"), could result in increased risk for patients (Miklowitz 1998). Among psychosocial interventions, family interventions may be as promising as other psychosocial interventions in improving therapeutic outcomes, and perhaps even more so, because they involve the patient's immediate world. Some important authors working in this field recommend the implementation of family interventions for the treatment of bipolar disorders (Miklowitz 2006a). Nevertheless, given that studies with adequate methods to produce good quality evidence appear to be the exception rather than the rule in the literature, it will be necessary to gather more data yielded by good quality randomised controlled trials about effectiveness of family psychosocial interventions to provide a sound scientific basis for the use of these interventions. The fact that there are researchers working with samples of bipolar patient in child and adolescent populations is important (Fristad 2002), as these young people can present with different symptoms, behaviours and responses to psychosocial interventions, and in addition, may be more dependent on their family and its functioning.

The majority of interventions included in this review used psychoeducational methods, and the heterogeneity of interventions and outcomes, together with the small number of trials for inclusion, means that the evidence is not yet compelling. In the case of psychotherapies, the paucity of data is especially significant. Randomised controlled trials involving more specific family psychotherapies such as those based on cognitive behavioural, systemic family therapy and psychodynamic principles are needed. It is important to stress that although few significant results favouring psychosocial interventions were found in this review, it is not appropriate to conclude that family psychosocial interventions added to pharmacological treatment for bipolar disorders are not useful. Family interventions might be an important means of increasing the effectiveness of treatment for biolar patients, and of helping relatives and clinicians in the task of better dealing with the illness and its consequences. What is clear with this review is that it is difficult to make a precise evaluation of family psychosocial interventions' effectiveness, mainly due to the small and heterogeneous number randomised controlled trials and some of their methodological limitations. It is highly desirable that professionals working in this field concern themselves with carrying out further well designed studies.

AUTHORS' CONCLUSIONS

Implications for practice

Whilst the addition of family psychotherapy or psychoeducation interventions to medications in the treatment of bipolar patients might be considered good practice, it is important to be aware that there is insufficient evidence in the literature to allow clear conclusions to be drawn on their effectiveness. Therefore, it is not possible to recommend without restriction that clinicians or health policy makers should use family interventions in the treatment of bipolar disorder or to recommend one family intervention as more effective than another. It is also important to bear in mind the cost/benefit ratio in this type of intervention, not only regarding the economic aspects, but also patients' and their families' affective investment and expectations.

Implications for research

We suggest that researchers should carry out further randomised controlled trials to answer more clearly the questions about efficacy and effectiveness of family psychosocial interventions in the treatment of bipolar disorder. Use of rigorous methods of randomisation, larger sample sizes, standard outome assessments, measurement of adverse effects/acceptability and precise reporting of findings are called for, to produce reliable and applicable information on this important and under-researched topic.

ACKNOWLEDGEMENTS

We woudl like to thank staff of the Brazilian Cochrane Centre and AFIP (Associação Fundação de Incentivo à Psicofarmacologia) of São Paulo, Brazil. We would also like to acknowledge the contribution of Dr Vivien Hunot on the final draft of this review.

REFERENCES

References to studies included in this review

Clarkin 1990 *{published data only}*

* Clarkin JF, Glick ID, Haas GI, Spencer JH, Lewis AB, Peyser J, et al. A randomized clinical trial of inpatient family intervention V. Results for affective disorders. *Journal of Affective Disorders* 1990;**18**:17-28.

Glick ID, Clarkin JF, Haas GL, Spencer JH Jr. Clinical significance of inpatient family intervention: Conclusions from a clinical trial. *Hospital and Community Psychiatry* 1993;**44**(9):869-73.

Glick ID, Clarkin JF, Haas GL, Spencer JH Jr, Chen CL. A randomized clinical trial of inpatient family intervention: VI. Mediating variables and outcome. *Family Process* 1991;**30**:85-99.

Clarkin 1998 *{published data only}*

* Clarkin JF, Carpenter D, Hull J, Wilner P, Glick I. Effects of psychoeducational intervention for married patients with bipolar disorders. *Psychiatric Services* 1998;**49**:531-3.

Goldstein 1996 *{published data only}*

Goldstein MJ, Rea M, Miklowitz DJ. Family factors related to the course and outcome of bipolar disorder. In: Mundt C, Goldstein MJ, Hahlweg K, Fiedler P editor(s). Interpersonal Factors in the Origin and Course of Affective Disorders. London: Gaskell Books., 1996:193-203.

* Rea MM, Tompson MC, Miklowitz DJ, Goldstein JM, Hwang S, Mintz J. Family-focused treatment versus indivividual treatment for bipolar disorder: Results of a randomized clinical trial. *Journal of Consulting and Clinical Psychology* 2003;**71**(3):482-92.

Tompson MC, Rea MM, Goldstein MJ, Miklowitz DJ, Weisman AG. Difficulty in implementing a family intervention for bipolar disorder: the predictive role of patient and family attributes. *Family Process* 2000;**39**(1):105-20.

Weisman A, Tompson MC, Okazaki S, Gregory J, Goldstein MJ, Rea M, et al. Clinicians' fidelity to a manual-based family treatment as a predictor of the one-year course of bipolar disorder. *Family Process* 2002;**41**(1):2002.

Weisman AG, Okazaki S, Gregory J, Goldstien MJ, Tompson MC, Rea M, et al. Evaluating therapist competency and adherence to behavioral family management with bipolar patients. *Family Process* 1998;**37**(1):107-21.

Miklowitz 1996 *{published data only}*

Goldstein TR, Miklowitz DJ, Richards JA. Expressed emotion attitudes and individual psychopathology among the relatives of bipolar patients. *Family Process* 2002;**41**(4):645-57.

Kim EY, Miklowitz DJ. Expressed emotion as a predictor of outcome among bipolar patients undergoing family therapy. *Journal of Affective Disorders* 2004;**82**(3):343-52.

* Miklowitz DJ, George EL, Richards JA, Simoneau TL, Suddath RL. A randomized study of family-focused psychoeducation and pharmacotherapy in the outpatient management of bipolar disorder. *Archives of General Psychiatry* 2003;**60**(9):904-12.

Miklowitz DJ, Richards JA, George EL, Frank E, Suddath RL, Powell KB, et al. Integrated family and individual therapy for bipolar disorder: results of a treatment development study. *Journal of Clinical Psychiatry* 2003;**64**(2):182-91.

Miklowitz DJ, Simoneau TL, George EL, Richards JA, Kalbag A, Sachs-Ericsson N, et al. Family-focused treatment of bipolar disorder: 1-year effects of a psychoeducational program in conjunction with pharmacotherapy. *Biological Psychiatry* 2000;**48**(6):582-92.

Miklowitz DJ, Simoneau TL, Sachs-Ericsson N, Warner R, Suddath R. Family risk indicators in the course of bipolar affective disorder. In: Mundt C, Goldstein MJ, Hahlweg K, Fiedler P editor(s). Interpersonal Factors in the Origin and Course of Affective Disorders. London: Gaskell Books, 1996:204-17.

Simoneau TL, Miklowitz DJ, Richards JA, Saleem R, George EL. Bipolar disorder and family communication: effects of a psychoeducational treatment program. *Journal of Abnormal Psychology* 1999;**108**(4):588-97.

Reinares 2004 *{published data only}*

* Reinares M, Vieta E, Colom F, Martinez-Arán A, Torrent C, Comes M, et al. Impact of a psychoeducational family intervention on caregivers of stabilized bipolar patients. *Psychotherapy and Psychosomatics* 2004;**73**(5):312-9.

Reinares M, Vieta V, Colom F, Martinez-Aran A, Comes M, Goikolea JM, et al. Psychoeducational family intervention on caregivers of bipolar patients. 156th Annual Meeting of the American Psychiatric Association, May 17-22, San Francisco CA. 2003:NR119.

Ryan 2003 *{published data only}*

Gaudiano BA, Miller IW. Anxiety disorder comorbidity in Bipolar I Disorder: Relationship to depression severity and treatment outcome. *Depression and Anxiety* 2005;**21**(2):71-7.

Keitner G, Solomon D, Ryan C, Kelley J, Miller I. Recovery from acute mood episodes of bipolar 1 disorder. 34th International Meeting of the Society for Psychotherapy Research; 2003 June 25 - 29; Weimar. 2003:146-7.

* Miller IW, Solomon AD, Ryan CE, Keitner GI. Does adjunctive family therapy enhances recovery from bipolar I mood episodes?. *Journal of Affective Disorders* 2004;**82**(3):431-6.

Miller IW, Uebelacker LA, Keitner GI, Ryan CE, Solomon DA. Longitudinal course of bipolar I disorder. *Comprehensive Psychiatry* 2004.;**45**(6):431-40.

Ryan CE, Keitner GI, Solomon DA, Kelley JE, Miller IW. Factors related to a good, poor, or fluctuating course of bipolar disorder. 156th Annual Meeting of the American Psychiatric Association, May 17-22, San Francisco CA. 2003:NR458.

Ryan CE, Keitner GI, Solomon DI. Factors related to a good, poor, or fluctuating course of bipolar disorder. 156th Annual

Meeting of the American Psychiatric Association, May 17-22, San Francisco CA. 2003:P. 138.

Solomon DA, Keitner GI, Ryan CE, Kelley JE, Miller IW. Recurrence of bipolar I mood episodes and hospitilization: Pharmacotherapy plus family psychotherapy versus pharmacotherapy alone as prophylaxis. 45th Annual NCDEU (New Clinical Drug Evaluation Unit) Meeting; 2005 June 6 - 9; Boca Raton, FL. 2005:261.

Uebelacker LA, Beevers CG, Battle CL, Strong D, Keitner GI, Ryan CE, et al. Family functioning in bipolar I disorder. *Journal of Family Psychology* 2006;**20**(4):701-4.

van Gent 1991 *{published data only}*

van Gent EM, Zwart FM. Psychoeducation of partners of bipolar-manic patients. *Journal of Affective Disorders* 1991;**21**(1):15-8.

References to studies excluded from this review

Anderson 1986 *{published data only}*

* Anderson CM, Griffin S, Rossi A, Pagonis I, Holder DP, Treiber R. A comparative study of the impact of education vs. process groups for families of patients with affective disorders. *Family Process* 1986;**25**:185-205.

Catanzaro 1973 *{published data only}*

Catanzaro RJ, Pisani VD. Familization therapy: An alternative to traditional mental health care. *Deseases of the Nervous System* 1973;**34**(5):212-8.

Davenport 1977 *{published data only}*

Davenport YB, Ebert MH, Adland ML, Goodwin FK. Couples group therapy as an adjunct to lithium maintenance of the manic patient. *American Journal of Orthopsychiatry* 1977;**47**(3):495-502.

Fitzgerald 1972 *{published data only}*

Fitzgerald RG. Mania as a message. *American Journal of Psychotherapy* 1972;**26**(4):547-54.

Fristad 2002 *{published data only}*

Fristad MA. Psychoeducational treatment for school-aged children with bipolar disorder. *Development and Psychopathology* 2006;**18**(4):1289-306.

Fristad MA, Goldberg-Arnold JS, Gavazzi SM. Multi-family psychoeducation groups in the treatment of children with mood disorders. *Journal of Marital and Family Therapy* 2003;**29**(4):491-504.

* Fristad MA, Goldberg-Arnold JS, Gavazzi SM. Multifamily psychoeducation groups (MFPG) for families of children with bipolar disorder. *Bipolar Disorders* 2002;**4**:254-62.

Honig 1995 *{published data only}*

* Honig A, Hofman A, Hilwig M, Noorthorn E, Ponds R. Psychoeducation and expressed emotion in bipolar disorder: preliminary findings. *Psychiatry Research* 1995;**56**:299-301.

Kim 2004 *{published data only}*

Kim EY, Miklowitz D. Expressed emotion as a predictor of outcome among bipolar patients undergoing family therapy. *Journal of Affective Disorders* 2004;**82**:343-52.

Miklowitz 2000 *{published data only}*

Miklowitz JD, Simoneau TL, George EL, Richards JA, Kalbag A, Sachs-Ericsson N, et al. Family-focused treatment of bipolar disorder: 1-year effects of psychoeducational program in conjunction with pharmachotherapy. *Biological Psychiatry* 2000;**48**:582-92.

Simoneau 1999 *{published data only}*

Simoneau LT, Miklowitz JD, Richards JA, Saleen R, George EL. Bipolar disorder and family communication: Effects of a psychoeducational treatment program. *Journal of Abnormal Psychology* 1999;**108**(4):588-97.

References to studies awaiting assessment

Keitner 1996b *{published data only}*

Keitner G, Miller IW, Ryan CE. Adjunctive family treatment of bipolar disorder. Xth World Congress of Psychiatry, Madrid, Spain. 1996.

Miller 2000 *{published data only}*

Miller IW, Keitner GI, Ryan ER, Solomon DA. Family treatment of bipolar disorder. *Acta Neuropsychiatrica* 2000;**12**(3):164.

References to ongoing studies

Miklowitz 2004 *{published data only}*

Miklowitz DJ, George EL, Axelson DA, Kim EY, Birmaher B, Schneck C, et al. Family-focused treatment for adolescents with bipolar disorder. *Journal of Affective Disorders* 2004;**82 Suppl**:113-28.

Miklowitz 2006a *{published data only}*

Miklowitz DJ, Kowatch RA, Axelson DA. Family-focused treatment for bipolar adolescents. www.controlled-trials.com.

Additional references

Akiskal 2006

Akiskal HS, Vasquez GH. Widening the borders of the bipolar disorder: validation of the concept of bipolar spectrum. *Vertex* 2006;**17**(69):340-6.

Alloy 2005

Alloy LB, Abramson LY, Urosevic S, Walshow PD, Nusslock R, Neeren AM. The psychosocial context of bipolar disorder: Enviromental, cognitive and developmental risk factors. *Clinical Psychology Review* 2005;**25**:1043-75.

Altman 1996

Altman DG, Bland JM. Detecting Skewness From Summary Information. *BMJ* 1996;**313**:1200.

APA 2002

American Psychiatric Association. Practice Guideline for Treatment of Patients of Bipolar Disorder (Revision). *American Journal of Psychiatry* 2002;**159 Suppl 4**:1-150.

Castro 1997

Castro AA, Clarke OA, Atallah AN. Optimal search strategy for clinical trials in the Latin American and Caribbean Health Science Literature Database (LILACS). *Sao Paulo Medical Journal* 1997;**115**(5):1423-26.

Coryell 1993

Coryell W, Scheftner W, Keller M, Endicott J, Maser J, Klerman GL. The enduring psychosocial consequences of mania and depression. *American Journal of Psychiatry* 1993;**15**:720-7.

Dickersin 1994

Dickersin K, Scherer R, Lefebvre C. Identifying relevant studies for systematic reviews. *BMJ* 1994;**309**:1286-9.

Epstein 1990

Epstein NB, Bishop DS, Keitner GI, Miller IW. A systems therapy. Problem-centered systems therapy of the family.. In: Wells RA, Giannetti VJ editor(s). Handbook of Brief Psychotherapies. New York, NY: Plenum, 1990:405-36.

Falloon 1984

Falloon IR, Boyd JL, McGill CW. Family Care of Schizophrenia: A Problem-Solving Approach to the Treatment of Mental Illness. New York, NY: Guilford Press, 1984.

Fristad 2003

Fristad MA, Gavazzi SM, Mackinaw-Koons B. Family psychoeducation: An adjunctive intervention for children with bipolar disorder. *Biological Psychiatry* 2003;**53**:1000-8.

Gelemberg 1989

Gelemberg AJ, Kane JN, Keller MB, Lavori P, Rosembaum JF, Cole K, et al. Comparison of standard and serum levels of lithium for maintenance treatment of bipolar disorders. *New England Journal of Medicine* 1989;**321**:1489-93.

Gitlin 1995

Gitlin MJ, Swendsen J, Heller T, Hammen C. Relapse and Impairment in Bipolar Disorder. *American Journal of Psychiatry* 1995;**152**(11):1635-40.

Gonzales-Pinto 2004

Gonzales-Pinto A, Gonzales C, Enjuto S, Corres BF, Lopez P, Palomo J, et al. Psychoeducation and cognitive-behavioral therapy in bipolar disorder: an update. *Acta Psychiatrica Scandinavica* 2004;**109**:83-90.

Goodwin 1990

Goodwin FK, Jamison KR. Manic-Depressive Illness. New York, NY: Oxford University Press, 1990.

Gutierrez 2004

Gutierrez M J, Scott J. Psychological treatment for bipolar disorders. *European Archives of Psychiatry and Clinical Neuroscience* 2004;**254**:92-8.

Higgins 2005

Higgins JPT, Green S, editors. Cochrane Handbook for Systematic Reviews of Interventions 4.2.5 [updated May 2005]. In: The Cochrane Library. Vol. **Issue 3**, Chichester, UK: John Wiley & Sons Ltd, 2005.

Hilty 1999

Hilty DM, Brady KT, Hales RE. A review of bipolar disorder among adults. *Psychiatric Services* 1999;**50**:201-13.

Huxley 2000

Huxley NA, Parikh SV, Baldessarini RJ. Effectiveness of Psychosocial treatments in Bipolar Disorder: State of the Evidence. *Harvard Review of Psychiatry* 2000;**8**:126-40.

Jamison 2000

Jamison KR. Suicide and bipolar disorder. *Journal of Clinical Psychiatry* 2000;**61**(9):47-51.

Johnson 2005

Johnsosn SL. Life events in bipolar disorder: towards more specific models. *Clinical Psychology Review* 2005;**25**(8):1008-27.

Johnson 2006

Johnson SL, McMurrich S. Life events and juvenile bipolar disorder: conceptual issues and early findings. *Development and Psychopathology* 2006;**18**(4):1169-79.

Jones 2004

Jones S. Psychotherapy of bipolar disorder: a review. *Journal of Affective Disorders* 2004;**80**:101-14.

Jones 2005

Jones SH, Sellwood W, McGovern J. Psychological therapies for bipolar disorder: the role of model-driven approaches to therapy integration. *Bipolar Disorders* 2005;**7**(1):22-32.

Judd 2005

Judd LL, Akiskal HS, Schetler PJ, Endicott J, Leon AC, Solomon DA, et al. Psychosocial disability in the course of bipolar I and II disorders. A prospective, comparative, longitudinal study. *Archives of General Psychiatry* 2005;**62**:1322-30.

Kalbag 1999

Kalbag AS, Miklowitz DJ, Richards JA. A method for classifying the course of illness of bipolar I disorder. *Behavior Therapy* 1999;**30**:355-72.

Kim 2007

Kim EY, Miklowitz DJ, Biuchians A, Mullen K. Life stress and the course of early-onset bipolar disorder. *Journal of Affective Disorders* 2007;**99**:37-44.

Miklowitz 1997

Miklowitz DJ, Goldstein MJ. Bipolar Disorder: A Family-Focused Treatment Approach. New York, NY: Guilford Press, 1997.

Miklowitz 1998

Miklowitz DJ. Psychosocial approaches to the course and treatment of bipolar disorder. *CNS Spectrums* 1998;**3**:48-52.

Miklowitz 2005

Miklowitz DJ, Wisniewski SR, Miyahara S, Otto MW, Sachs GS. Perceived criticism from family members as a predictor of the one-year course of bipolar disorder. *Psychiatry Research* 2005;**136**:101-11.

Miklowitz 2006

Miklowitz DJ. A review of evidence-based psychosocial interventions for bipolar disorders. *Journal of Clinical Psychiatry* 2006;**67 Suppl 11**:28-33.

Mikolwitz 1990

Miklowitz DJ, Goldstein MJ. Behavioral family treatment for patients with bipolar disorder. *Behavior Modification* 1990;**14**:457-89.

Perlick 1999

Perlick D, Clarckin JF, Sirey J, Raue P, Greenfield S, Struening E, et al. Burden experienced by care-givers of persons with bipolar affective disorder. *British Journal of Psychiatry* 1999;**175**:56-62.

Reinares 2002

Reinares M, Colom F, Martinez-Aran A, Benabarre A, Vieta E. Therapeutic Interventions Focused on the Family of Bipolar Patients. *Psychotherapy and Psychosomatics* 2002;**71**:2-10.

Shultz 1995

Shultz KF, Hayes RJ, Altman DG. Empirical evidence of bias: Dimensions of methodological quality associated with estimates of treatment effects in controlled trials. *JAMA* 1995;**273**:408-12.

Tomaras 2000

Tomaras V, Mavreas V, Economou M, Ioanovich E, Karydi V, Stefanis C. The effect of family intervention on chronic schizophrenics under individual psychosocial treatment: a 3-year study. *Social Psychiatry and Psychiatric Epidemiology* 2000;**35**(11):487-93.

Vieta 2005 a

Vieta E, Pacchiarotti I, Scott J, Sanches-Moreno J, Di Marzo S, Colom F. Evidence-based research on the efficacy of psychologic interventions in bipolar disorders: a critical review. *Current Psychiatry Reports* 2005;**7**(6):449-55.

Vieta 2005 b

Vieta E. Improving treatment adherence in bipolar disorder through psychoeducation. *Journal of Clinical Psychiatry* 2005;**66 Suppl 1**:24-29.

Zaretsky 2003

Zaretsky A. Targeted Psychosocial Interventions for Bipolar Disorder. *Bipolar Disorders* 2003;**5 Suppl 2**:80-7.

* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Clarkin 1990

Methods	Allocation: randomisation without specification of methods. Duration: hospitalisation period (mean=36 days) plus18 month follow up. Blinded assessments: reported Analysis: Analysis of variance and analysis of covariance, correlation coeficients, chi-square and t-tests. ITT not used. No of centres: 1 Country: USA
Participants	Diagnosis: current bipolar disorder mood episode - mania (DSM-III) N: 26 (experimental group n=15; control group n=11) Mean (sd) age: 32.3 (15.4) Gender: 14 (%) female Race: 17 white Setting: Payne Whitney Clinic, New York, USA. History: 10 of them had had no previous episodes, 8 had had 1 or 2 previous episodes and 4 had had 3 or more previous episodes.
Interventions	1 - Standard multimodal hospital treatment (fixed drug regimen - lithium 600-2100mg/day, tricyclic antidepressants 100-400mg/day, monoamine oxidase inhibitors 45-90mg/day of phenelzine, antipsychotics in doses equivalent to 100-800mg/day of chlorpromazine). 2 - Standard multimodal hospital treatment plus the psychosocial family intervention for patient with his family Inpatient Family Intervention (at least 6 45 minutes to 1 hour- manualized psychoeducational plus systemic-dynamic interventions sessions, conducted by 2 therapists.
Outcomes	USED:

Clarkin 1990 *(Continued)*

	1 - Dropouts at discharging 2 - Improvement clinically significant at discharge, 6 months. NOT USED: 2 - Improvement clinicaly significant at 18 months. 3 - Family functioning measures
Notes	26 patients were randomised but 5 withdrew and were not included in analysis

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Clarkin 1998

Methods	Allocation: randomised, according to an algorithm that took into account prior admissions, prehospital treatment compliance and level of functioning; no information about allocation concealment. Blindness assessments: not reported. Duration: 11 months. Analysis: t-tests and likelihood ratios; no ITT analysis. No of centres: not mentioned Country: USA
Participants	Diagnosis: bipolar disorder utilizing the SADS . N: 42 (19 patients and their partners designated for esperimental group and 23 patients for control group). Age: ranging between 21 - 65 years (patients' average age was 47.7 years). Gender: distribution of patients was almost the same. Setting: not mentioned. History: Married or living with other of the opposite sex for at least 6 months (average of 17 years); no mention of illness duration or number of episodes.
Interventions	1 - Structured Marital Psychoeducational Intervention: 25 sessions for the couple plus standard medication treatment for the bipolar patient (mood stabilizers, antidepressants and antipsychotics). 2 - Standard medication (bipolar patient), no marital psychoeducation.
Outcomes	USED: 1 - Dropouts at month 11 NOT USED: 2 - Patients' symptoms (SADS-C and BPRS) - means without sd 3 - Overall functioning (SAS and GAS) - means without sd 4 - Adherence to medication treatment (Scale developed by the authors) - means without sd
Notes	Forty six patients have fullfiled inclusion criteria and signed informed consent, but 4 of them dropped out before randomisation. So we have considered only 42 participants.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Goldstein 1996

Methods	Allocation: randomisation without specification of methods. Blinded assessments: reported. Duration: 2 years. Analysis: survival analysis, t-test, ITT. No of Centres: not mentioned. Country: USA.
Participants	Diagnosis: bipolar manic patients,diagnosis following DSM-III-R criteria - SCID and confirmed by Present State Examination. N: 53 (n = 25 in the individual treatment and n = 28 in the family-focused treatment). Age: range 18-46 years; mean = 24.6, SD = 5.8 for the individual treatment and mean = 26.5 SD = 6.86 for the family-focused treatment. Gender: 40% of male and 60% of female in the individual treatment; 46% of male and 54% of female in the family-focused treatment. Race: Caucasian 60% (n=32), African American 23% (n=12), Asian American 9% (n=5) and others 9% (n=4). Setting: treatment on outpatients basis and no more information about setting. History: ages of onset: mean = 21.2 SD = 3.68 and mean = 23.5 SD = 4.51, for family and individual treatments respectively. Education level: mean = 14.2 years SD = 2.2, equaly distributed in both groups. . Sixty percent had had multiple episodes of mania and 40% had had 1 episode of mania.
Interventions	1 - Medication: all patients, in both groups received individual medication management sessions for the first 1 year (with a staf research psychiatrist); after this period they were referred to treatment providers in the community. Pharmacotherapy was individually tailored to the patients' clinical state and included mood-regulating medications as tithium, carbamazepine and divalproex sodium, and at times antipsychotics, anticholinergics, antidepressants, and anxiolytic agents. Contacts with psychiatrist were as intensive as the contacts with psychosocial intervention team; N = 53. 2 - Family-Focused Therapy: 21 sessions, 1 hour each, weekly for the first 3 months, every other week for the second 3 months and monthly thereafter; during the first 9 months of the study; n = 28. 3 - Individually Focused Patient Treatment: 21 sessions, 30-min each, with the same distribution in time of the family-focused treatment; n = 25.
Outcomes	USED: 1 - Relapse (period of treatment - first 1 year): symptoms (BPRS plus SADS-C), relapse defined as 6 or 7 on the BPRS/SADS-C core symptoms of depression, mania or psychosis and at least 2 ancillary symptoms, nonrelapse defined as 5 or below on all relevant BPRS/SADS-C core symptoms during the 3-month interval. 2- Rehospitalization (period of treatment - first 1 year). 3- Medication compliance (end of study - 2 years - using a 7-point Likert scale and blood serum levels) was the last. Evaluation each 3 months. 4- Dropouts (end of study - 2 years).
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Miklowitz 1996

Methods	Allocation: randomisation procedure using random number table. Randomisation sequence was concealed until assignments had been made. Duration: 9 months for therapy and 2 years of total follow up. Blinded assessments: reported. Analysis: Survival analysis using Kaplan-Meier product-limit formula

Miklowitz 1996 *(Continued)*

	and Cox proportional hazards models when incorporating covariates; mixed analysis of variance; ITT for survival analysis. No of centres: not clear. Country: USA
Participants	Diagnosis: bipolar disorder (post-episode phases) DSM-III-R (SCID-P). A posteriori confirmation by DSM-IV showed that two patients of the sample were bipolar II while the others (99) were bipolar I. N: 101 (experimental group n=31; control group n=70). Age: 18-62 years (mean 35.6 sd 10.2). Gender: 64 women and 37 men. Setting: Family interventions performed at patients' homes. Race: not informed. History: mania, depression or mixed episode within the past 3 months, living with or in regular contact with a caregiving family member, willingness to take medication, english speaking. Excluded disability or neurologic disorder, alcohol or substance abuse disorder within the previous 6 months.
Interventions	1 - Family-Focused Therapy: 21 sessions (psychoeducation, communication enhancement training, problem-solving skills training; 12 weekly, 6 biweekly, 3 monthly - one-hour). 2 - Crisis Management: 2 one-hour home based sessionsof family psychoeducation (within 2 months after entry) and more crisis intervention sessions during the rest of 9 months if necessary. All patients in both groups were receiving pharmacologic treatment (mood-stabilizers and/or antipsychotics, antidepressants).
Outcomes	USED: 1 - Relapse at the end of treatment (24 months) - symptoms: SADS-C (ranging from 1 (absent) to 7 (very extreme). 2 - Medication compliance during follow up: all available compliance data and laboratory results were assembled into a dosier and assigned a 3-point adherence rating - 1 is fully nonadherent, 2 is partially nonadherent and 3 is fully adherent. 3 - Dropouts NOT USED: 4 - Rehospitalization 5 - Time to relapse - survival analysis
Notes	We have considered as relapsed the patients that have have been computed as dropouts during the study duration.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Low risk	A - Adequate

Reinares 2004

Methods	Allocation: randomisation in a 2:1 formula, without mention about concealment procedures. Blinded assessments: reported. Duration: 6 months Analysis: chi-squared test, Students' t test, Mann-Whitney U test, mixed analysis of variance. No of centres: 1 Country: Spain
Participants	Diagnosis: bipolar I and II disorder by SCID-DSM-IV, stabilized for at least 3 months (the participants of psychosocial intervention were the relatives and not the patients). N: 45 (30 in experimental group and 15 in control group). Age: Means (SD), for bipolar patients in experimental group 34.9(11.56) and in control group 35.9(7.52); for caregivers in experimental group 50.20(10.37) and in contrl group 45.07(16.25).

Reinares 2004 *(Continued)*

	Gender: for bipolar patients in experimental group 12 women and 18 men and for control group 10 women and 5 men; for caregivers in experimental group 25 women and 5 men and for control group 9 women and 6 men. Race: not mentioned. Setting: hospital History: Age of onset in means (SD) for experimental group 24.23((7.87) and for control group 23.00(7.17). Manic episodes 2.00(2.78) and 2.60(2.56) respectively. Hypomanic episodes 2.24(3.81) and 2.71(3.15) respectively. Depressive episodes 4.69(4.51) and 5.64(2.95) respectively. Mixed episodes 0.67(1.12) and 1.47(2.36) respectively. N of hospitalizations 1.67(1.32) and 2.36(1.78) respectively.
Interventions	1- Psychoeducational Family Intervention: 12 psychoeducational 90-min weekly group sessions taking place at hospital. In each group there were a maximum of 10 patients' relatives. The psychoeducation was structured. All patients (experimental and control) received standard pharmacologic treatment . 2 - The relatives of control group received no psychoeducational intervention. The psychoeducational intervention was administered only for caregivers without the presence of patients.
Outcomes	USED: 1 - Relationships in the family invironment - Cohesion, Expressiveness, Conflict - (Family Environment Scale). 2 - Dropouts of caregivers. NOT USED: 3 - Caregivers' knowledge of bipolar disorder (Bipolar Disorder Knowledge Questionnaire). 4 - Caregivers' burden (Social Behavior Assessment Schedule).
Notes	Only the relationships in the family invironment was included in this review because it seems to us to be the one with direct clinical relevance.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Ryan 2003

Methods	Allocation: randomisation without specification of methods. Blinded assessments: reported only for pharmacologic outcomes. Duration: 28 months Analysis: survival analysis for time to recovery, cumulative probability of recovery estimated with Kaplan-Meir product limit. N of centres: 1 Country: USA
Participants	Diagnosis: current bipolar I disorder mood episode, using the Structured Clinical Instrument for DSM-III-R-Patient Version, current episode. N = 92 (29 in 1-pharmacotherapy alone; 33 in 2-family therapy plus pharmacotherapy; 30 in 3-multi-family psychoeducational group therapy plus pharmacotherapy). Age: 18-65; means (SD) 39(13), 40(10), 39(12), for each group of comparison respectively. Gender: for each group (female + male): (19 + 10); (15 + 18); (18 + 12), respectively. Race: not informed. Setting: tratment on outpatient basis; no more informations about setting. History: Age of onset in mean of years (SD) - with major depression in group 1: 20(8), group 2 25(10) and group 3 19(10); with mania in group 1 27(10), in group 2 29(10) and group 3 29(11). Lifetime number of episodes of major depression in means (SD): group 1 6(9), in group 2 5(5) and in group 3 10(12). Lifetime number of episodes of mania in means (SD): in group 1 4(3), in group 2 5(6) and in group3 6(5). Lifetime number of hospitalizations in means (SD): in group 1 5(5), in group 2 4(3) and in group 3 4(4). Education years, means (SD): 12.3 (2); 13 (3); 14 (2) respectively for group 1, 2 and 3.

Ryan 2003 *(Continued)*

Interventions	1 - Pharmacotherapy alone: mood stabilizers and other medications based on type, intensity and duration of symptoms. 2 - Problem Centered Systems Therapy of the Family (semi-structured with manual) - 6 to 10 sessions (50 minutes), plus pharmacotherapy. 3 - Multifamily Psychoeducational Group Therapy (semi-structured with manual) - 6 weekly topic sessions (90 minutes), plus pharmacotherapy.
Outcomes	USED: 1 - Recovery for all patients after 28 months, using the Modified Hamilton Rating Scale for Depression and Bech-Rafaelsen Mania Scale. Recovery definied as two consecutive months with scores < 7 in Hamilton and < 6 in Bech-Rafaelsen. 2 - Recovery for the subjects with mania after 28 mths: assessed in the same way described above. 3 - Dropouts (patients that did not stay in the study for at least 6 months). NOT USED: 4 - Time to recovery (median time) for all patients. 5 - Time to recovery (median time) for subjects with mania.
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

van Gent 1991

Methods	Allocation: randomisation without methods specification. Blinded assessments: not reported. Duration: 12 months. Analysis: Analysis of Variance for repeated measuresand Wilcoxon test. N of centres: 1 Country: Netherlands
Participants	Diagnosis: bipolar patients through DSM-III-R criteria, by two independent psychiatrists. N: 39 (19 in experimental group and 20 in control group). Age: Experimental group (partners) - mean 42 (sd 12); control - 56 (sd 8). Experimental group (patients) - 44 (sd 11); control - 55 (sd 8). Gender: distribuition not mentioned. Race: not mentioned. Settingnot mentioned. History: onset of illness in means (SD) of age for experimental group 26(10) and control 36(10). Duration of illness 18(10) years and 18(11) years respectively. Number of hospitalizations 4.4(4.5) and 4.4(2.8) respectively.
Interventions	1 - Psychoeducation: Experimental group: requested to fill questionaires and take part in 5 sessions of structured psychoeducational intervention regarding the information about desease and medication plus practical advice. 2 - Control group: only requested to fill questionaires. All patients were in pharmacological treatment with lithium.
Outcomes	USED: 1 - Patients' total symptoms (SCL-90-total), before/after intervention. 2 - Patients' anxiety (subscale SCL-90-Anxiety and Trait Anxiety Inventory), before/after intervention. 3 - Medication compliance (compliant or not - non compliance defined as a difference of more than 0.3mmol/l in serum lithium levels without changing the medication). 4 - Rehospitalizations. 5 - Dropouts NOT USED: 6 - Partners' knowledge of the illness.

van Gent 1991 *(Continued)*

	7 - Partners' social strategies.	
Notes		
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Allocation concealment?	Unclear risk	B - Unclear

BPRS: Brief Psychiatry Rating Scale
DSM-III: Diagnostic and Statistical Manual of Mental Disorders - Third Edition
DSM-III-R: Diagnostic and Statistical Manual of Mental Disorders - Third Edition Revised
DSM-IV: Diagnostic and Statistical Manual of Mental Disorders - Fourth Edition
N: total number of participants in the study
n: number of participants in a group of comparison
SADS-C: Schedule for Affective Disorders and Schizophrenia - Change Version
SCID: Structured Clinical Interview (DSM)
SCID-P: Structured Clinical Interview- Patient Version
SCL: Symptom Checklist
SD: Standard Deviation
IMPORTANT: The distinction between bipolar I and II disorders became clear and formal after DSM-IV, so in some of included studies this difference in diagnosis is not mentioned. In the Miller 2004 the authors did not mention a confirmation diagnostic procedure after the application of DSM-III-R criteria, but they have considered the sample as composed of bipolar I patients. In another context it should be clarified, but we did not consider indispensable the distinction between bipolar I and II disorders, for the objectives of this review.

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Anderson 1986	The outcomes assessed were not clinical outcomes directly related to bipolar disorder ie they did not examine the impact of interventions on the disorder itself.
Catanzaro 1973	The study was not a RCT. It was a theoretical explanation of a type of family therapy.
Davenport 1977	The study was not a RCT.
Fitzgerald 1972	The study was not a RCT.
Fristad 2002	The outcomes considered in this study were not of direct clinical relevance. No data were presented on the possible impact of the intervention on the disorder.
Honig 1995	The study was not a RCT.
Kim 2004	This was not an primary RCT. Data were collected from two others studies, one of them included in the present review (Miklowitz 2003).
Miklowitz 2000	This paper reports on one year follow-up data from the study by Miklowitz 2003, which is included in this review.
Simoneau 1999	This presents some results from the study reported by Miklowitz 2003, which is included in this review.

DATA AND ANALYSES

Comparison 1. Family interventions versus No intervention

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 No recovery at end of study	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
1.1 all patients (28 months)	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
1.2 patients with mania (28 months)	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
2 No significant clinical improvement	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
2.1 at post-treatment	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
2.2 at 6 month follow-up	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
4 Patients' total symptoms post-treatment (SCL-90)	1		Std. Mean Difference (IV, Fixed, 95% CI)	Totals not selected
5 Positive relationship within the family (high score=more positive)	1		Std. Mean Difference (IV, Fixed, 95% CI)	Totals not selected
5.1 cohesion	1		Std. Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
5.2 expressiveness	1		Std. Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
6 Negative relationship within the family (low score=more positive)	1		Std. Mean Difference (IV, Fixed, 95% CI)	Totals not selected
6.1 conflict	1		Std. Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
7 Medication compliance	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
7.1 at end of study (12 months)	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
8 Patients anxiety post-treatment (Trait Anxiety Inventory)	1		Std. Mean Difference (IV, Fixed, 95% CI)	Totals not selected
9 Patients' anxiety post-treatment (subscale SCL-90)	1		Std. Mean Difference (IV, Fixed, 95% CI)	Totals not selected
10 Dropouts at end of study	5	214	Risk Ratio (M-H, Fixed, 95% CI)	0.70 [0.43, 1.14]
10.1 at 6 months	1	45	Risk Ratio (M-H, Fixed, 95% CI)	0.5 [0.03, 7.45]
10.2 at 11 months	1	42	Risk Ratio (M-H, Fixed, 95% CI)	0.15 [0.02, 1.10]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
10.3 at 12 months	1	39	Risk Ratio (M-H, Fixed, 95% CI)	0.66 [0.26, 1.66]
10.4 at 18 months	1	26	Risk Ratio (M-H, Fixed, 95% CI)	1.1 [0.22, 5.51]
10.5 at 28 months	1	62	Risk Ratio (M-H, Fixed, 95% CI)	1.05 [0.54, 2.07]

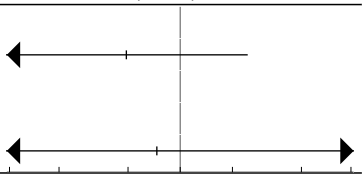
Analysis 1.1. Comparison 1 Family interventions versus No intervention, Outcome 1 No recovery at end of study.

Study or subgroup	No intervention n/N	Family intervention n/N	Risk Ratio M-H, Fixed, 95% CI	Risk Ratio M-H, Fixed, 95% CI
1.1.1 all patients (28 months)				
Ryan 2003	13/29	17/33		0.87[0.52,1.47]
1.1.2 patients with mania (28 months)				
Ryan 2003	9/22	12/24		0.82[0.43,1.55]

Favours fam interven — Favours no interven

Analysis 1.2. Comparison 1 Family interventions versus No intervention, Outcome 2 No significant clinical improvement.

Study or subgroup	Family intervention n/N	No intervention n/N	Risk Ratio M-H, Fixed, 95% CI	Risk Ratio M-H, Fixed, 95% CI
1.2.1 at post-treatment				
Clarkin 1990	2/15	3/11		0.49[0.1,2.45]
1.2.2 at 6 month follow-up				
Clarkin 1990	1/15	1/11		0.73[0.05,10.49]



Favours fam interven — Favours No interven

Analysis 1.4. Comparison 1 Family interventions versus No intervention, Outcome 4 Patients' total symptoms post-treatment (SCL-90).

Study or subgroup	Family intervention N	Mean(SD)	No intervention N	Mean(SD)	Std. Mean Difference Fixed, 95% CI	Std. Mean Difference Fixed, 95% CI
van Gent 1991	19	121.4 (31.7)	20	120.4 (24.1)		0.03[-0.59,0.66]

Favours fam interven — Favours no interven

Analysis 1.5. Comparison 1 Family interventions versus No intervention, Outcome 5 Positive relationship within the family (high score=more positive).

Study or subgroup	No intervention N	No intervention Mean(SD)	Family intervention N	Family intervention Mean(SD)	Std. Mean Difference Fixed, 95% CI	Std. Mean Difference Fixed, 95% CI
1.5.1 cohesion						
Reinares 2004	15	7 (2)	30	6.8 (2.1)		0.1[-0.52,0.72]
1.5.2 expressiveness						
Reinares 2004	15	5.7 (1.5)	30	5.8 (2.1)		-0.03[-0.65,0.59]

Analysis 1.6. Comparison 1 Family interventions versus No intervention, Outcome 6 Negative relationship within the family (low score=more positive).

Study or subgroup	Family intervention N	Family intervention Mean(SD)	No intervention N	No intervention Mean(SD)	Std. Mean Difference Fixed, 95% CI	Std. Mean Difference Fixed, 95% CI
1.6.1 conflict						
Reinares 2004	30	2.4 (1.5)	15	2.9 (1.6)		-0.33[-0.95,0.29]

Analysis 1.7. Comparison 1 Family interventions versus No intervention, Outcome 7 Medication compliance.

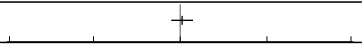
Study or subgroup	No intervention n/N	Family intervention n/N	Risk Ratio M-H, Fixed, 95% CI	Risk Ratio M-H, Fixed, 95% CI
1.7.1 at end of study (12 months)				
van Gent 1991	10/12	11/14		1.06[0.73,1.54]

Analysis 1.8. Comparison 1 Family interventions versus No intervention, Outcome 8 Patients anxiety post-treatment (Trait Anxiety Inventory).

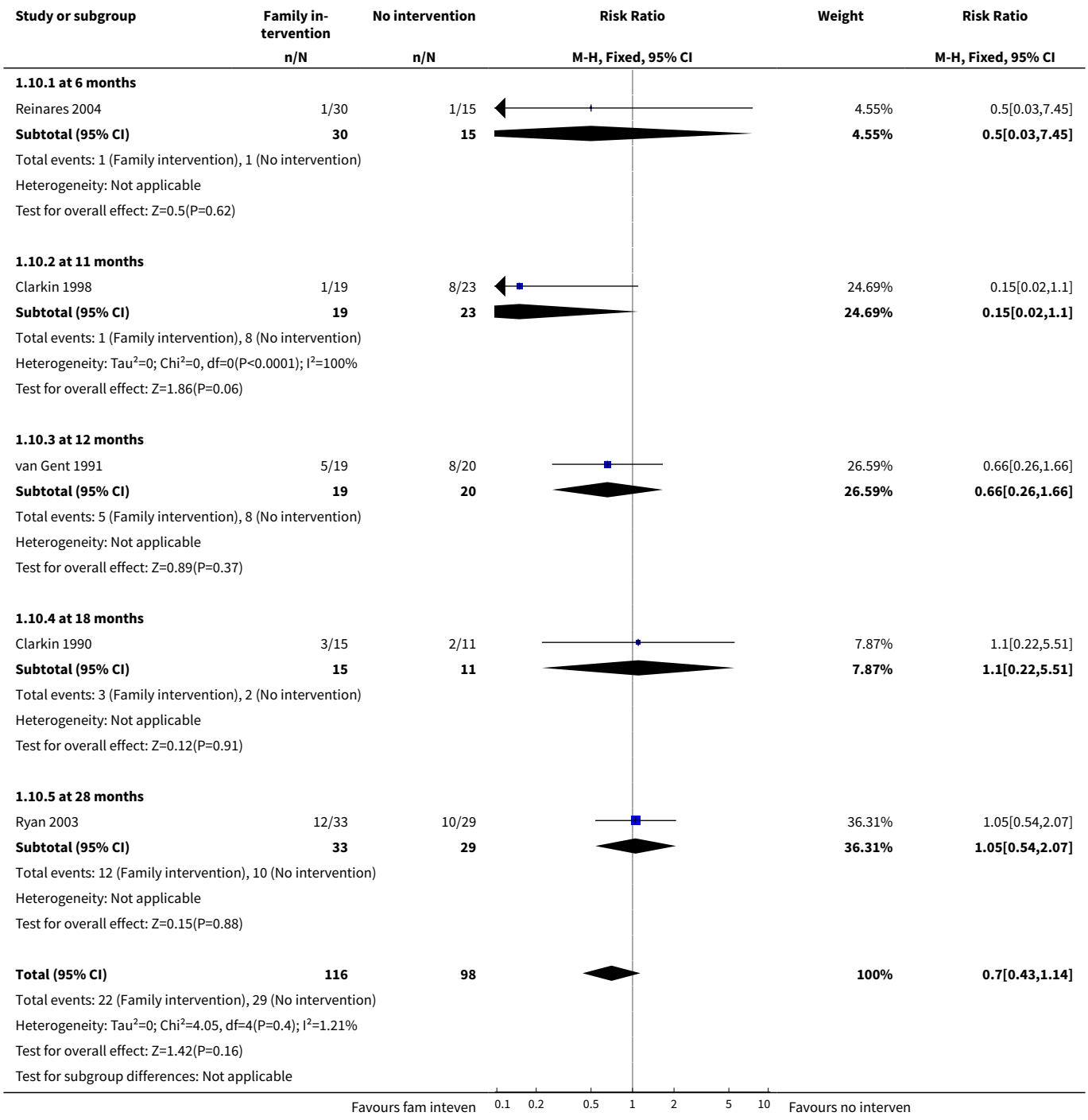
Study or subgroup	Family intervention N	Family intervention Mean(SD)	No intervention N	No intervention Mean(SD)	Std. Mean Difference Fixed, 95% CI	Std. Mean Difference Fixed, 95% CI
van Gent 1991	19	43.4 (13.5)	20	35.1 (9.7)		0.69[0.05,1.34]

Analysis 1.9. Comparison 1 Family interventions versus No intervention, Outcome 9 Patients' anxiety post-treatment (subscale SCL-90).

Study or subgroup	Family intervention N	Family intervention Mean(SD)	No intervention N	No intervention Mean(SD)	Std. Mean Difference Fixed, 95% CI	Std. Mean Difference Fixed, 95% CI
van Gent 1991	19	13.5 (5)	20	13 (4)		0.11[-0.52,0.74]



Analysis 1.10. Comparison 1 Family interventions versus No intervention, Outcome 10 Dropouts at end of study.

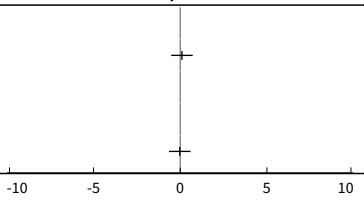


Comparison 2. Psychoeducation for caregivers versus No intervention

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Positive relationship within the family (high score=more positive)	1		Std. Mean Difference (IV, Fixed, 95% CI)	Totals not selected
1.1 cohesion	1		Std. Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
1.2 expressiveness	1		Std. Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
2 Negative relationship within the family (low score=more positive)	1		Std. Mean Difference (IV, Fixed, 95% CI)	Totals not selected
2.1 conflict	1		Std. Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]

Analysis 2.1. Comparison 2 Psychoeducation for caregivers versus No intervention, Outcome 1 Positive relationship within the family (high score=more positive).

Study or subgroup	No Psychoeducation N	No Psychoeducation Mean(SD)	Psychoeducation N	Psychoeducation Mean(SD)	Std. Mean Difference Fixed, 95% CI	Std. Mean Difference Fixed, 95% CI
2.1.1 cohesion						
Reinares 2004	15	7 (2)	30	6.8 (2.1)		0.1[-0.52,0.72]
2.1.2 expressiveness						
Reinares 2004	15	5.7 (1.5)	30	5.8 (2.1)		-0.03[-0.65,0.59]



Analysis 2.2. Comparison 2 Psychoeducation for caregivers versus No intervention, Outcome 2 Negative relationship within the family (low score=more positive).

Study or subgroup	Psychoeducation N	Psychoeducation Mean(SD)	No Psychoeducation N	No Psychoeducation Mean(SD)	Std. Mean Difference Fixed, 95% CI	Std. Mean Difference Fixed, 95% CI
2.2.1 conflict						
Reinares 2004	30	2.4 (1.5)	15	2.9 (1.6)		-0.33[-0.95,0.29]

Comparison 3. Marital psychoeducation for partners versus No intervention

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Patients' total symptoms post-treatment (SCL-90)	1		Std. Mean Difference (IV, Fixed, 95% CI)	Totals not selected

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
2 No medication compliance	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
2.2 at end of study (12 months)	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
3 Patients anxiety post-treatment (Trait Anxiety Inventory)	1		Std. Mean Difference (IV, Fixed, 95% CI)	Totals not selected
4 Patients' anxiety post-treatment (subscale SCL-90)	1		Std. Mean Difference (IV, Fixed, 95% CI)	Totals not selected
5 Dropouts	1	39	Odds Ratio (M-H, Fixed, 95% CI)	0.54 [0.14, 2.08]

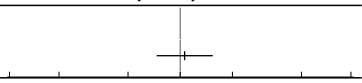
Analysis 3.1. Comparison 3 Marital psychoeducation for partners versus No intervention, Outcome 1 Patients' total symptoms post-treatment (SCL-90).

Study or subgroup	Marital Psychoeduc N	Marital Psychoeduc Mean(SD)	No Psychoeduc N	No Psychoeduc Mean(SD)	Std. Mean Difference Fixed, 95% CI	Std. Mean Difference Fixed, 95% CI
van Gent 1991	19	121.4 (31.7)	20	120.4 (24.1)		0.03[-0.59,0.66]

Favours Marital Psyc — Favours No Psychoed

Analysis 3.2. Comparison 3 Marital psychoeducation for partners versus No intervention, Outcome 2 No medication compliance.

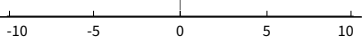
Study or subgroup	No Marital Psychoedu n/N	Marital Psychoeducat n/N	Risk Ratio M-H, Fixed, 95% CI	Risk Ratio M-H, Fixed, 95% CI
3.2.2 at end of study (12 months)				
van Gent 1991	10/12	11/14		1.06[0.73,1.54]



Favours Marital Psyc — Favours No Marital P

Analysis 3.3. Comparison 3 Marital psychoeducation for partners versus No intervention, Outcome 3 Patients anxiety post-treatment (Trait Anxiety Inventory).

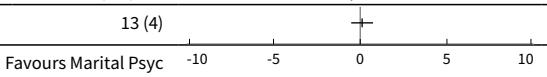
Study or subgroup	Marital Psychoeduc N	Marital Psychoeduc Mean(SD)	No Psychoeducation N	No Psychoeducation Mean(SD)	Std. Mean Difference Fixed, 95% CI	Std. Mean Difference Fixed, 95% CI
van Gent 1991	19	43.4 (13.5)	20	35.1 (9.7)		0.69[0.05,1.34]



Favours Marital Psyc — Favours No Psychoed

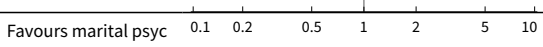
Analysis 3.4. Comparison 3 Marital psychoeducation for partners versus No intervention, Outcome 4 Patients' anxiety post-treatment (subscale SCL-90).

Study or subgroup	Marital Psychoeduc N	Marital Psychoeduc Mean(SD)	No Psychoeducation N	No Psychoeducation Mean(SD)	Std. Mean Difference Fixed, 95% CI	Std. Mean Difference Fixed, 95% CI
van Gent 1991	19	13.5 (5)	20	13 (4)		0.11[-0.52,0.74]



Analysis 3.5. Comparison 3 Marital psychoeducation for partners versus No intervention, Outcome 5 Dropouts.

Study or subgroup	Multifamily psychoed n/N	No intervention n/N	Odds Ratio M-H, Fixed, 95% CI	Weight	Odds Ratio M-H, Fixed, 95% CI
van Gent 1991	5/19	8/20		100%	0.54[0.14,2.08]
Total (95% CI)	**19**	**20**		**100%**	**0.54[0.14,2.08]**
Total events: 5 (Multifamily psychoed), 8 (No intervention)					
Heterogeneity: Not applicable					
Test for overall effect: Z=0.9(P=0.37)					

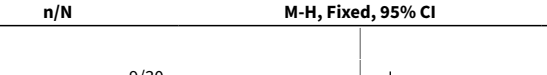


Comparison 4. Multifamily psychoeducation group intervention versus No intervention

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 No recovery for all patients	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
1.1 at the end of study (28 months)	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
2 No recovery for patients with mania	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
2.1 at the end of study (28 months)	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
3 Dropouts	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
3.1 at month 6	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]

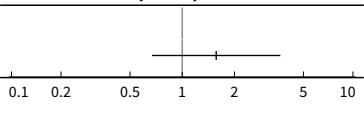
Analysis 4.1. Comparison 4 Multifamily psychoeducation group intervention versus No intervention, Outcome 1 No recovery for all patients.

Study or subgroup	No Multifamily Psych n/N	Multifamily Psych n/N	Risk Ratio M-H, Fixed, 95% CI	Risk Ratio M-H, Fixed, 95% CI
4.1.1 at the end of study (28 months)				
Ryan 2003	13/29	9/30		1.49[0.76,2.95]



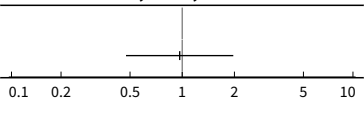
Analysis 4.2. Comparison 4 Multifamily psychoeducation group intervention versus No intervention, Outcome 2 No recovery for patients with mania.

Study or subgroup	No Multifamily Psych n/N	Multifamily Psych n/N	Risk Ratio M-H, Fixed, 95% CI	Risk Ratio M-H, Fixed, 95% CI
4.2.1 at the end of study (28 months)				
Ryan 2003	9/22	6/23		1.57[0.67,3.68]



Analysis 4.3. Comparison 4 Multifamily psychoeducation group intervention versus No intervention, Outcome 3 Dropouts.

Study or subgroup	Multifamily Psychoed n/N	No Multifamily Psych n/N	Risk Ratio M-H, Fixed, 95% CI	Risk Ratio M-H, Fixed, 95% CI
4.3.1 at month 6				
Ryan 2003	10/30	10/29		0.97[0.47,1.97]

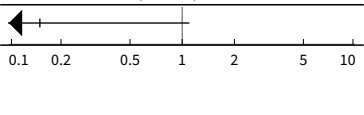


Comparison 5. Couples psychoeducation for patient + partner versus No intervention

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Dropouts	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected

Analysis 5.1. Comparison 5 Couples psychoeducation for patient + partner versus No intervention, Outcome 1 Dropouts.

Study or subgroup	Couples psychoeducat n/N	No couples psychoedu n/N	Risk Ratio M-H, Fixed, 95% CI	Risk Ratio M-H, Fixed, 95% CI
Clarkin 1998	1/19	8/23		0.15[0.02,1.1]



Comparison 6. Problem centered systems therapy for the family versus Multifamily psychoeducational group therapy

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 No recovery at end of study (28 months)	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
1.1 all patients	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]

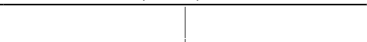
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1.2 patients with mania	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
2 Dropouts	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
2.1 at 6 months	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]

Analysis 6.1. Comparison 6 Problem centered systems therapy for the family versus Multifamily psychoeducational group therapy, Outcome 1 No recovery at end of study (28 months).

Study or subgroup	Favours systems ther n/N	Favours multi-family n/N	Risk Ratio M-H, Fixed, 95% CI	Risk Ratio M-H, Fixed, 95% CI
6.1.1 all patients				
Ryan 2003	17/33	9/30		1.72[0.91,3.25]
6.1.2 patients with mania				
Ryan 2003	6/23	12/24		0.52[0.24,1.16]

Analysis 6.2. Comparison 6 Problem centered systems therapy for the family versus Multifamily psychoeducational group therapy, Outcome 2 Dropouts.

Study or subgroup	Favours systems ther n/N	Favours multifamily n/N	Risk Ratio M-H, Fixed, 95% CI	Risk Ratio M-H, Fixed, 95% CI
6.2.1 at 6 months				
Ryan 2003	12/33	10/33		1.2[0.6,2.38]



Comparison 7. Family intervention versus Individual intervention (subgroup analysis)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Relapse rates	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
1.1 at the end of treatment (12 months)	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
2 Rehospitalisation	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
2.1 at the end of treatment (12 months)	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
3 Medication compliance (high score is better)	1		Std. Mean Difference (IV, Fixed, 95% CI)	Totals not selected

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
3.1 at the end of study (24 months)	1		Std. Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
4 Dropouts	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
4.1 at the end of study (24 months)	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]

Analysis 7.1. Comparison 7 Family intervention versus Individual intervention (subgroup analysis), Outcome 1 Relapse rates.

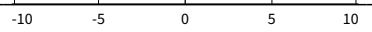
Study or subgroup	Family intervention n/N	Individ intervention n/N	Risk Ratio M-H, Fixed, 95% CI	Risk Ratio M-H, Fixed, 95% CI
7.1.1 at the end of treatment (12 months)				
Goldstein 1996	13/28	13/25		0.89[0.52,1.54]

Analysis 7.2. Comparison 7 Family intervention versus Individual intervention (subgroup analysis), Outcome 2 Rehospitalisation.

Study or subgroup	Family intervention n/N	Individ intervention n/N	Risk Ratio M-H, Fixed, 95% CI	Risk Ratio M-H, Fixed, 95% CI
7.2.1 at the end of treatment (12 months)				
Goldstein 1996	8/28	10/25		0.71[0.33,1.52]

Analysis 7.3. Comparison 7 Family intervention versus Individual intervention (subgroup analysis), Outcome 3 Medication compliance (high score is better).

Study or subgroup	Individ intervention N	Individ intervention Mean(SD)	Family intervention N	Family intervention Mean(SD)	Std. Mean Difference Fixed, 95% CI	Std. Mean Difference Fixed, 95% CI
7.3.1 at the end of study (24 months)						
Goldstein 1996	13	4.1 (2.7)	16	3.9 (2.7)		0.08[-0.65,0.82]



Analysis 7.4. Comparison 7 Family intervention versus Individual intervention (subgroup analysis), Outcome 4 Dropouts.

Study or subgroup	Family T n/N	Individual T n/N	Risk Ratio M-H, Fixed, 95% CI	Risk Ratio M-H, Fixed, 95% CI
7.4.1 at the end of study (24 months)				

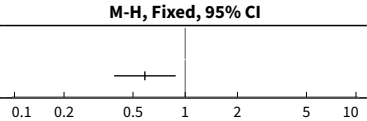
Study or subgroup	Family T n/N	Individual T n/N	Risk Ratio M-H, Fixed, 95% CI	Risk Ratio M-H, Fixed, 95% CI
Goldstein 1996	12/28	12/25		0.89[0.49,1.61]

Comparison 8. Crisis management versus Family focused therapy (subgroup analysis)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Relapse	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
1.1 at the end of study (24 months)	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
2 Medication compliance (high is better)	1		Std. Mean Difference (IV, Fixed, 95% CI)	Totals not selected
2.1 during the follow up	1		Std. Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
3 Dropouts	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
3.1 before 6 months	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
3.2 at end of study (24 months)	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]

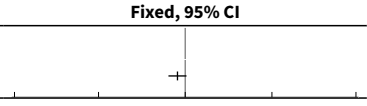
Analysis 8.1. Comparison 8 Crisis management versus Family focused therapy (subgroup analysis), Outcome 1 Relapse.

Study or subgroup	Family-Focused Thera n/N	Crisis Management n/N	Risk Ratio M-H, Fixed, 95% CI	Risk Ratio M-H, Fixed, 95% CI
8.1.1 at the end of study (24 months)				
Miklowitz 1996	14/31	54/70		0.59[0.39,0.88]



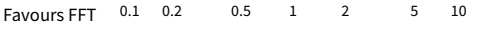
Analysis 8.2. Comparison 8 Crisis management versus Family focused therapy (subgroup analysis), Outcome 2 Medication compliance (high is better).

Study or subgroup	Crisis Management N	Crisis Management Mean(SD)	Family Focused Thera N	Family Focused Thera Mean(SD)	Std. Mean Difference Fixed, 95% CI	Std. Mean Difference Fixed, 95% CI
8.2.1 during the follow up						
Miklowitz 1996	43	2.6 (0.5)	22	2.8 (0.4)		-0.45[-0.97,0.07]



Analysis 8.3. Comparison 8 Crisis management versus Family focused therapy (subgroup analysis), Outcome 3 Dropouts.

Study or subgroup	Family-Focused Thera n/N	Crisis Management n/N	Risk Ratio M-H, Fixed, 95% CI	Risk Ratio M-H, Fixed, 95% CI
8.3.1 before 6 months				
Miklowitz 1996	3/31	16/70		0.42[0.13,1.35]
8.3.2 at end of study (24 months)				
Miklowitz 1996	9/31	27/70		0.75[0.4,1.41]



WHAT'S NEW

Date	Event	Description
1 November 2008	Amended	Converted to new review format.

HISTORY

Protocol first published: Issue 1, 2005
Review first published: Issue 4, 2007

Date	Event	Description
1 August 2007	New citation required and conclusions have changed	Substantive amendment

CONTRIBUTIONS OF AUTHORS

LPJ - protocol writing; seach, selection, and analysis of data; completion of report

BGOS - protocol writing; seach, selection, and analysis of data; completion of report

HMC - protocol writing, expertise overview, completion of report

DECLARATIONS OF INTEREST

None known.

SOURCES OF SUPPORT

Internal sources

- Brazilian Cochrane Centre, Brazil.

External sources

- No sources of support supplied

INDEX TERMS

Medical Subject Headings (MeSH)

*Family Therapy; Bipolar Disorder [*therapy]; Family Relations; Randomized Controlled Trials as Topic; Treatment Outcome

MeSH check words

Humans