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Network meta-analysis of psychosocial therapies used for the treatment of bipolar disorder in adults

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1. **Search strategy**

Table 1. Search strategy for electronic databases EBSCOhost, PsycINFO and Medline

2. #	Query	Limiters/Expanders	Last Run Via
S28	S25 AND S26	Limiters - English Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO
S27	S25 AND S26	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO
S26	TX trial	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO
S25	S19 AND S24	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO
S24	S20 OR S21 OR S22 OR S23	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO
S23	DE "Interpersonal Psychotherapy"	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO
S22	DE "Family Therapy"	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO
S21	DE "Cognitive Techniques" OR DE "Cognitive Restructuring" OR DE "Cognitive Therapy" OR DE "Self Instructional Training" OR DE "Cognitive Therapy"	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO
S20	DE "Psychotherapy" OR DE "Adlerian Psychotherapy" OR DE "Adolescent	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen -

	Psychotherapy" OR DE "Analytical Psychotherapy" OR DE "Autogenic Training" OR DE "Behavior Therapy" OR DE "Brief Psychotherapy" OR DE "Brief Relational Therapy" OR DE "Child Psychotherapy" OR DE "Client Centered Therapy" OR DE "Cognitive Behavior Therapy" OR DE "Conversion Therapy" OR DE "Eclectic Psychotherapy" OR DE "Emotion Focused Therapy" OR DE "Existential Therapy" OR DE "Experiential Psychotherapy" OR DE "Expressive Psychotherapy" OR DE "Eye Movement Desensitization Therapy" OR DE "Feminist Therapy" OR DE "Geriatric Psychotherapy" OR DE "Gestalt Therapy" OR DE "Group Psychotherapy" OR DE "Guided Imagery" OR DE "Humanistic Psychotherapy" OR DE "Hypnotherapy" OR DE "Individual Psychotherapy" OR DE "Insight Therapy" OR DE "Integrative Psychotherapy" OR DE "Interpersonal Psychotherapy" OR DE "Logotherapy" OR DE "Narrative Therapy" OR DE "Network Therapy" OR DE "Persuasion Therapy" OR DE "Primal Therapy" OR DE "Psychoanalysis" OR DE "Psychodrama" OR DE "Psychodynamic Psychotherapy" OR DE "Psychotherapeutic Counseling" OR DE "Rational Emotive Behavior Therapy" OR DE "Reality Therapy" OR DE "Relationship Therapy" OR DE "Solution Focused		Advanced Search Database - PsycINFO

	Therapy" OR DE "Supportive Psychotherapy" OR DE "Transactional Analysis" OR DE "Psychotherapy Training"		
S19	DE "Bipolar Disorder" OR DE "Cyclothymic Personality"	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO
S15	S10 AND S13	Limiters - English Language Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - MEDLINE;MEDLINE Complete
S14	S10 AND S13	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - MEDLINE;MEDLINE Complete
S13	S11 OR S12	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - MEDLINE;MEDLINE Complete
S12	TX randomi#ed controlled trial	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - MEDLINE;MEDLINE Complete
S11	(MH "Randomized Controlled Trial+") OR (MH "Controlled Clinical Trial")	Search modes - SmartText Searching	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - MEDLINE;MEDLINE Complete
S10	S1 AND S9	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen -

			Advanced Search Database - MEDLINE;MEDLINE Complete
S9	S2 OR S3 OR S4 OR S5 OR S6 OR S7 OR S8	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - MEDLINE;MEDLINE Complete
S8	TX interpersonal and social rhythm therapy	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - MEDLINE;MEDLINE Complete
S7	TX family focused therapy	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - MEDLINE;MEDLINE Complete
S6	family focused therapy	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - MEDLINE;MEDLINE Complete
S5	(MH "Family Therapy")	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - MEDLINE;MEDLINE Complete
S4	TX psychoeducation	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - MEDLINE;MEDLINE Complete
S3	(MH "Cognitive Therapy+")	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database -

			MEDLINE;MEDLINE Complete
S2	(MH "Psychotherapy+") OR (MH "Psychotherapy, Rational-Emotive") OR (MH "Psychotherapy, Brief") OR (MH "Psychotherapy, Psychodynamic") OR (MH "Psychotherapy, Multiple") OR (MH "Psychotherapy, Group+") OR (MH "Imagery (Psychotherapy)") OR (MH "Equine-Assisted Therapy")	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - MEDLINE;MEDLINE Complete
S1	(MH "Bipolar Disorder+")	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - MEDLINE;MEDLINE Complete

2. Included studies

Table 2. Details of included studies by intervention

Study & Country	n Consented/ Analysed	Entry criteria / population characteristics	Intervention characteristics	Comparator characteristics	Duration of follow-up
Cognitive Behavioural Therapy (CBT)					
Ball et al 2006 Australia	52/52	Lifetime DSM-IV diagnosis of BD I or II; able to be maintained on usual mood stabilising medication for duration of trial Included if euthymic, mildly depressed, or hypo-manic at initial assessment. Mean age: 42·0 Female: 57·7%	20 weekly 1 hour sessions over 5 months Cognitive Therapy (CT) modified for people with BD by the addition of emotive techniques. Sessions included: assessment, psychoeducation, identifying warning signs for relapse, establishing stable routines, identifying and modifying cognitions, identifying and modifying schemas	Treatment as usual (TAU) Participants received sessions as required by regular GP or Psychiatrist. Clinicians were provided with an educational package on BD with detailed instructions for managing mood	12 months
Cochran et al 1984 USA	28/28	Admission diagnosis of primary bipolar affective illness and prescribed prophylactic lithium treatment Mean age: 32·5 Female: 60·7%	4 weekly 1 hour individual sessions over 1·5 months Modified cognitive-behavioural intervention (adapted from Beck et al.1979) aimed at altering cognitions and behaviours that interfere with compliance	TAU Standard clinic care	6 months
Costa et al 2011 Brazil	41/39	DSM-IV criteria for BD I or II, and experienced at least one hypomanic, manic or depressive episode in the previous 12 months. Taking mood stabilizing medication for a minimum of one month before trial entry. Included if euthymic, mildly depressed, or mildly hypomanic at initial assessment Mean age: 40·5 Female: 67·6%	14 weekly 2 hour group sessions over 3·5 months Group CBT based on the treatment manual by Basco and Rush	TAU Participants attended sessions as prescribed by their respective psychiatrists, and did not attend any psychotherapy sessions	3.5 months

Gomes et al 2011 Brazil	50/50	DSM-IV diagnosis of BD I or II, euthymic state (YMRS <6 and HDRS <8), >5 years of schooling and currently using at least 1 mood stabiliser or atypical antipsychotic Mean age: 38·5 Female: 76%	18 weekly 1·5 hour group sessions over 4·5 months Cognitive behavioural group therapy with sessions divided into 4 domains, information and education about bipolar disorder, CBT to manage depression and manic episodes, problem solving techniques and assertiveness and techniques to improve relapse prevention	TAU Participants received pharmacotherapy and regular monitoring	24 months
Jones et al 2015 England	67/67	DSM-IV diagnosis of primary BD with onset in past 5 years, able to understand English. Excluded participants that were manic, hypomanic, depressed or in a mixed episode currently or in prior 4 weeks Mean age: 39·1 Female: 70.1%	18 weekly or fortnightly 0·75 - 1 hour individual sessions over 6 months Manual-based CBT including: introducing the recovery approach to bipolar, collecting historical information about mood and functioning, meaning and relevance of diagnosis, identification of recovery-informed therapy goals, initial formulation of relationships between mood experiences and progress toward recovery goals, identification and application of CBT techniques to facilitate positive coping, consideration of wider functioning issues in relation to recovery, development and completion of a recovery plan, sharing lessons from therapy with key stakeholders	TAU Routine medication (mood stabilisers, antipsychotics and antidepressants), with routine visits to clinician/support from community mental health team	15 months

Kirk 2014 UK	20/18	Experienced first or second treated episode of mania and or hypomania in the previous 12-months prior to study entry. Mean age: 37·5 Female: 14%	Individual Cognitive Interpersonal Therapy in Early Bipolar Disorder sessions for up to six months CBT emphasised assessment, engagement and formulation; normalizing and compassionate understanding; specific cognitive and behavioural strategies; self-management and social rhythm regulation; affect regulation, and staying well	TAU Normal psychiatric care	6 months
Lahera et al 2013 Spain	37/37	DSM-IV BD I or II or schizoaffective disorder, aged 18-65, receiving regular outpatient treatment for at least a year, being euthymic at intake Mean age:39·2 Female: 64·9%	24 weekly 1 hour group sessions over 6 months Social Cognition and Interaction Training (SCIT) - a manualised intervention originally designed for individuals with schizophrenia to improve emotion perception, attributional style and theory of mind abilities. SCIT comprises 3 phases: emotional training (definition of emotions, facial expression training, understanding of paranoid symptoms as an emotion), role-play social situations (distinguishing facts from guesses, jumping to conclusions, understanding bad events), and integration of learning	TAU Standard follow-up including clinical management and medication by a psychiatrist	6 months

Lam et al 2000 England	25/25	DSM-IV diagnosis of BD I, maintained on regular prophylactic medication, at least 2 episodes in the previous 2 years or 3 episodes in the previous 5 years, age 18-65. Participants were excluded if they had a diagnosis of schizoaffective Illness, currently in a rapid cycling or mixed affective episode, currently in an acute episode, currently having another form of psychotherapy, actively suicidal, or currently with a primary alcohol- or drug-addiction problem Mean age: 39 Female: 52%	20 weekly sessions over 6 months CT covering topics: education of the diathesis-stress model and how thoughts relate to behaviour, goal setting, CBT techniques (behavioural scheduling, including daily mood ratings, challenging abnormal/dysfunctional beliefs, addressing dysfunctional assumptions), medication compliance, self-management (importance of sleep, diet and routine, risks of sensation seeking and substance abuse), identifying early warning signs, consequences of mental health history (including stigma, guilt, grief)	TAU Routine appointments with outpatient and multidisciplinary health services	12 months
Lam et al 2003, 2005 England	103/103	BD I as per DSM-IV, prescribed prophylactic medication at an adequate dose as per the British National Formulary, aged 18-70, at least 2 episodes in the last 2 years or 3 episodes in the last 5 years, currently not fulfilling criteria for a bipolar episode, BDI <30 and MAS <9 Mean age:46·4 Female: 56·3%	18 weekly 1 hour individual sessions over 6 months CT based on a treatment manual and included diathesis-stress model emphasis for medications and psychological therapies, cognitive behavioural skills to monitor mood, prodromes to prevent full-blown episodes, importance of sleep and routine, attempts to deal with extreme striving attitudes	TAU Minimal psychiatric care defined as mood stabilizers at recommended levels with regular psychiatric follow up as outpatients	24 months

Meyer 2012 Germany	76/76	DSM-IV primary diagnosis of BD,18-65 years, willingness to continue current, or start medication Exclusion criteria was a primary diagnosis is a non-affective dis-order including schizo-affective disorder, current major affective episode (depressed, mixed or mania), substance-induced affective disorder, or affective disorder due to a general medical condition, current substance dependency requiring, serious cognitive deficits or currently in psychological treatment Mean age:43·9 Female: 50%	20 - 1 hour individual sessions over 9 months The first 12 sessions were weekly, then biweekly for the next 2 months, and the remainder were monthly. Individual CBT including information and motivation (symptoms, aetiology, medication), and mood monitoring (via a mood diary), understanding BD, addressing dysfunctional beliefs about BD and medication, a relapse module including identification and monitoring of early warning signs, functional behaviour analysis, CBT strategies for dealing with depression and mania (cognitive restructuring, activity schedule/daily routine, planning pleasurable activities), direct feedback on the mood diary (guided discovery, problem solving and reality testing) and training in communication skills and problem solving on the basis of the individuals' strengths and deficits	Psychoeducation Described as supportive therapy consisting of 20 manualised sessions (50-60 minutes duration) covering information provision, mood monitoring (via a mood diary) with a client-centered focus (whatever problems the client was facing at the time of the session was dealt with by providing emotional support and general advice). If no particular problem was presented, information about bipolar and medication was provided, without referring to written materials. In contrast to CBT, no effort was made to link the information to the patients' biography or experience. The mood diary was checked by the therapist who provided brief feedback, without using CBT related techniques	24 months

Perich et al 2013 Australia	95/95	DSM-IV diagnosis of BD I or II, maintained on mood stabilising medication for the duration of the study, at least 18 years of age, secondary school education, able to provide informed consent, fluent in written and spoken English, currently under the care of a GP or psychiatrist, at least one bipolar episode in the previous 12 months and lifetime incidence of at least 3 bipolar episodes Exclusion criteria were current DSM-IV major depressive, hypomanic or manic episode, lifetime diagnosis of schizophrenia or schizoaffective disorder ,current substance abuse disorder, organic brain syndrome, antisocial or borderline personality disorder, the presence of a concurrent significant medical condition impeding the ability to participate, currently receiving other psychological therapy Mean age: not reported Female: 65·3%	8 weekly 2·5 hour group sessions of mindfulness-based cognitive therapy (MBCT) over 2 months MBCT was an adaptation of the 8-week course developed by Segal et al. consisting of weekly mindfulness meditation practice and cognitive therapy regarding depression including psychoeducation. In this program, psychoeducation and relapse prevention information were adapted to include education about bipolar disorder, depression, hypo/mania, and anxiety	TAU Participants were sent weekly handouts comprising information about BD via email or mail (including causes of BD, available treatments, common symptoms)	12 months

Schmitz et al 2002 USA	53/46	English speaking adults between 18 and 55, dually diagnosed with BD and SUD, free of other axis I diagnoses requiring treatment without serious legal and medical problems and competent to give informed consent Exclusion criteria were a history of intolerance of divalproex or lithium, pregnancy, serious suicidal risk, and ongoing individual psychotherapy Mean age:34·6 Female: 52%	16 - 1 hour individual sessions over 3 months Sessions were twice a week for the first month then weekly thereafter and included medication monitoring and CBT adapted from the psychotherapy manual written by the authors for patients with unipolar depression and cocaine abuse	TAU Medication monitoring - consisted of four clinic visits at weeks 2, 4, 8 and 12. Visits were brief, approximately 20 minutes and were conducted by the study nurse practitioner. Individual sessions focused on discussion of medication compliance, side effects, drug use, and mood symptoms using the medication monitoring interview	3 months
Scott et al 2001 UK	42/42	Aged over 18 years with a lifetime diagnosis of BD I or II, and experienced one or more episodes of affective disorder in the last 2 years. Potential participants who were currently in an acute in-patient unit or who met criteria for mania were not immediately entered into the study but were accepted at the point of discharge or as soon as their mental state allowed them to give informed consent Mean age: 38·8 Female: 60%	25 – 45 minute individual CT sessions over 6 months CT included socialization into CT model and development of an individualized formulation and treatment goals, cognitive and behavioural approaches to symptom management and dysfunctional thoughts, dealing with cognitive and behavioural barriers to treatment adherence and modifying maladaptive beliefs, anti-relapse techniques and belief modification	TAU Wait list control	6 months

Scott et al 2006 UK	253/253	DSM-IV diagnosis of BD (recent episode or recurrent), aged 18+, history of 2+ episodes within past 12 months, in contact with mental health services in past 6 months Mean age:41·2 Female: 64·8%	The CBT approach used was based on Beck's model and was similar to the formulation-based approaches described for other severe mental disorders (Scott, 2002). The goals were to: facilitate acceptance of the disorder and need for treatment; help reduce day-to-day variability in mood and symptoms; recognise and manage psychosocial stressors and interpersonal problems; teach CBT strategies to cope with depression, cognitive and behavioural problems; identify and modify dysfunctional automatic thoughts, underlying maladaptive assumptions and beliefs; improve medication adherence and, if required, tackle substance misuse; teach early recognition of symptoms of recurrence and coping techniques for these symptoms	TAU Administered to all participants by their usual psychiatric team and included prescription of medications and contact with key mental health professionals with whatever frequency was considered appropriate	72 weeks

Weiss et al 2009 USA	61/61	DSM-IV criteria for BD disorder AND substance dependence (other than nicotine), substance use within 60 days prior to intake, currently on a mood stabilizer regimen for at least 2 weeks, able to attend group therapy sessions, aged ≥ 18 Exclusion criteria were current psychosis, current mania at intake, current danger to self or others, current need for medical detoxification, concurrent group treatment, or residential treatment restricting substance use Mean age:38·3 Female: 41%	12 weekly 1 hour group sessions of integrated group therapy over 3 months	Group Drug Counselling (GDC) Drug counselling designed to approximate the SUD treatment that patients receive in a SUD community treatment program delivered as 12 weekly 1 hour long sessions, each with a focus on a specific topic of SUD, with the goal of facilitating abstinence, encouraging mutual support and teaching new ways to cope with substance-related problems	6 months
Williams et al 2008 UK	17/14	In remission at intake and no manic episodes for the last 6 months with at least one prior episode of major depression accompanied by serious suicidal ideation, aged 18-65 years Mean age: Not reported Female: Not reported	Eight weekly two hour mindfulness-based CBT group sessions over two months. There was also a full-day of meditation practice following week 6 and participants completed homework expected to take at least 45 minutes per day 6 days per week	TAU Wait list control	2 months
Psychoeducation					

Cardoso et al 2015 Brazil	61/61	Diagnosis of BD by DSM (via SCID). Exclusions were suicide risk and psychoactive substance use Mean age: 24·1 Female: 68·9%	Six weekly one hour group sessions The psychoeducation protocol was an adaptation of Colom and Vieta's manual of psychoeducation for BD translated and adapted to Brazilian Portuguese and reduced to six sessions. The protocol covered symptoms of manic, hypomanic, and depressive episodes, how to detect their beginning, a structured action plan, and the importance of medication adherence	TAU Pharmacotherapy delivered in the psychiatry outpatient setting	12 months
Castle et al 2010 Australia	84/72	DSM-IV diagnosis of BD I or II, aged 18-65, able to speak English, under care of a GP and not in acute phase of mania or depression Mean age:42·1 Female: 76·2%	12 weekly 1·5 hour group sessions over three months plus three monthly booster sessions The programme developed for this study integrated effective coping strategies from existing psychosocial approaches, including monitoring mood and activities (M), assessing prodromes (A), preventing relapse (P) and setting Specific, Measurable, Achievable, Realistic, Time-framed (SMART) goals (S), known by the acronym MAPS	TAU + weekly telephone calls Calls were made during the initial 12-week intervention period to maintain engagement in the trial and to control for this aspect of facilitator contact time in the treatment condition	12 months
Colom et al 2003, 2009 Spain	120/120	DSM-IV criteria for BD I or II, aged 18-65, lifetime diagnosis by trained psychiatrist; euthymic for at least 6 months; sufficient data on prior course of illness of at least 24 months Mean age:34·1 Female: 60·8%	21 Weekly 1.5 hour group sessions over 5·25 months Sessions consisted of a 30-40 minute speech on the topic of the day with an exercise and discussion. They aimed at improving 4 main issues: illness awareness, treatment compliance, early detection of recurrence, lifestyle regularity	ACTIVE CONTROL (AC) 20 weekly group meetings of 8-12 patients with the same 2 psychologists who tried not to give any psychoeducational feedback	5 years

Dogan et al 2003 Turkey	26/26	Patients diagnosed with DSM-IV BD, who had been taking lithium for a long time Mean age:37·5 Female:34·6%	3 sessions of individual psychoeducation over 1·5 months The first two sessions were one week apart with the last one month later. Topics included education about BD, causative factors, clinical symptoms, goals of lithium therapy, its' side effects and important points to be aware of	TAU Waitlist control - control participants did not receive extra care, and commenced the intervention at the end of the final follow-up (3 months)	3 months
D'Souza et al 2010 Australia	58/45	Recently remitted (YMRS<10 and MADRS <8) recruited within 1 month of discharge from hospital for relapse of BD Diagnosis determined using MINI Mean age:40·1 Female: 51·7%	12 weekly 1·5 hour group sessions over 3 months Systematic Illness Management Skills Enhancement Program for bipolar disorder (SIMSEP-BD). Topics included education about BD, education about pharmacotherapy, psychotherapy including identifying stressors, coping strategies, identifying signals for relapse	TAU Community based case management model involving a trained mental health clinician review weekly with the patient for 45 minutes and a monthly medical review	18 months
Eker & Harkin 2012 Turkey	71/63	Met Bipolar Affective Disorder DSM-IV diagnosis criteria, accepted to participate in the study, able to learn the defined concepts in every learning activity, would stay calmly during the sessions and were in the remission period Mean age:34·6 Female: 45·7%	Six weekly 1·5 – 2 hour group sessions over 1·5 months Each session consisted of two parts that lasted 45–50 min each with a 10–15 minute break. The sessions covered the definitions, reasons and symptoms of BD, treatments and importance of adherence, medication effects and side effects, detecting and controlling prodromal symptoms, coping with stress, problem solving strategies and evaluation	TAU Participants were trained by the doctor about the medication in an outpatient setting for a maximum of 5–10 min	6 weeks

Javadpour et al 2013 Iran	108/86	Age 18–60 years inclusive, history of at least two episodes of relapse with two or three episodes in last five years, in euthymic state (the HDRS < 8 and Bech Rafaelsen Mania Rating Scale < 9) Mean age: Not reported Female: 40·7%	8 weekly 50 minute individual sessions over 2 months plus a booster session Sessions included psychoeducation about bipolar disorder, explanations about the relationship between thoughts, activities, physical feelings and mood, how to identify and monitor early warning symptoms and how to deal with them, anxiety control techniques (relaxation and breathing, self-instructions and cognitive distraction), sleep hygiene, how to plan engaging activities, how to detect irrational thoughts and use cognitive restructuring, problem solving, improvement of self-esteem, social skills (assertiveness, non-verbal communication, conversational skills	TAU Continued standard pharmacotherapy by psychiatrist of choice for 18 months	18 months

Lin et al In press Taiwan	68/68	Lifetime diagnosis of BD I by a board-certified psychiatrist in accordance with DSM-IV and clinical notes; symptom severity that did not interfere with the ability to participate in an estimated 2-hour group session; age of 18 years or older; ability to converse in Mandarin without an interpreter; current participation in psychiatric care; and the provision of written informed consent to participate in the study Mean age:40·1 Female: 47·4%	12 weekly 1·5 hour group sessions over 3 months The program integrated effective coping strategies from existing psychosocial approaches, including monitoring mood and activities (M), assessing prodromes (A), preventing relapse (P) and setting Specific, Measurable, Achievable, Realistic, Time-framed (SMART) goals (S), and is known by the acronym MAPS. A number of resources, including a participant workbook and information book were used throughout the program to reinforce and enhance skill development, promote self-efficacy, and develop effective relationships between the participants and their service providers	TAU Standard psychiatric care and standard pharmacological treatment without group-based psychosocial intervention. Weekly phone calls to the control group over the initial 12 weeks controlled for any extra contact time with researchers	12 months
Perry et al 1999 UK	69/69	Lifetime diagnosis of BD by a trained research assistant using a standardised psychiatric interview; two or more relapses, one in the previous 12 months. Exclusion criteria were an inability to read or write in English; drug or alcohol misuse or dependence and organic cerebral cause for bipolar disorder Mean age:43 Female:68%	12 individual sessions in two stages: training the patient to identify prodromal symptoms of manic or depressive relapse separately and producing and rehearsing an action plan once prodromes had been recognised by the patient	TAU Routine care delivered by psychiatrists and key workers consisting of drug treatment, monitoring of mood and adherence to treatment, support, education about bipolar disorder, and if necessary inpatient care	18 months

Sajatovic et al 2009 USA	164/164	BD I or II confirmed by the MINI Mean age:40·5 Female:69.8%	6 weekly group sessions delivered over 1·5 months with a booster session. The Life Goals Program was a manual-based structured group psychotherapy program for individuals with BD based on social learning and self-regulation theory, topics included illness education, management and problem solving. An optional phase II component was available that included monthly group sessions that involving goal setting and problem solving in an unstructured manner	TAU Delivered by the community mental health centre and typically included medication management, psychosocial therapy and counselling, as well as access to social services or case management	12 months
Simon et al 2005 USA	441/441	DSM-IV diagnosis of BD I or II, regardless of mood state (included depression, mania and mixed) or severity of symptoms. 40% met criteria for current mood episode, 20% were in remission Mean age:44·2 Female: 68·3%	53 one hour group sessions over 24 months. The first five sessions were held weekly and then twice a month for the remaining 24 months. The group psychoeducational program was adapted from Bauer and McBride's Life Goals Program. Phase 1 (weekly sessions) included structured education regarding the nature of bipolar illness, triggers and early symptoms of mood episodes, and self-management strategies for triggers and early symptoms. Phase 2 (twice monthly) used a structured problem solving format to focus on accomplishment of specific life goals. Participants created and updated personalized self-management plans describing triggers, warning signs, and coping strategies	TAU Participants continued existing treatment and could receive any and all services normally available either inside or outside of their health plan	24 months

Smith et al 2011 UK	50/37	Age 18-65, diagnosis of BD I, II or NOS based on DSM-IV and currently in clinical remission (not depressed, manic or in a mixed episode) in the preceding three months PLUS MADRS <=10 and a YMRS <=8 Mean age:42·7 Female: 64%	Nine fortnightly individual sessions over four months Initial face to face meeting then eight modules delivered online covering accurate diagnosis, causes, role of medications, role of lifestyle changes, relapse prevention and early intervention, psychological approaches, gender specific considerations, advice for family and carers	TAU Usual care delivered in a collaborative model between GPs and local multidisciplinary community mental health teams	6 months
CBT & Psychoeducation					
Gonzalez Isasi 2010, 2014 Spain	40/40	DSM-IV diagnosis of BD I or II treated with pharmacotherapy for at least 2 years, refractory disorder defined as history of severe or unfavourable progression of the disease despite pharmacological treatment, suicide attempts, persistent affective symptoms (BDI score > 7, YMRS score > 6) or severe difficulties in socio-occupational functioning (inadaption scale > 14), euthymic or with subsyndromal symptoms at study intake, not receiving other psychotherapy, aged 18-65 Mean age:41·3 Female: 47.5%	20 weekly 1·5 hour group sessions over 5 months The program consisted of an initial psychoeducation session about BD, followed by an explanation of the relationship between thoughts, activities, physical feelings and mood, and about identifying and monitoring early warning symptoms in order to deal with them. Subsequently, they were trained in the use of anxiety-control techniques (relaxation and breathing, self-instructions and cognitive distraction), sleep hygiene habits and planning gratifying activities. Later on, they were trained in detecting distorted thoughts and using the process of cognitive restructuring. Finally, for the purpose of consolidating the treatment and in an attempt to prevent relapse, participants were trained in problem solving and improvement of self-esteem.	TAU Participants received individualized psychoactive drugs and regularly visited their psychiatrist	5 years

Lauder et al 2015 Australia	156/156	Persons aged18–65 years with a diagnosis of BD I or II, confirmed using DSM-IV-criteria via telephone clinical interview. Participants needed access to an internet-enabled computer. Mean age:39·9 Female: 73%	5 fortnightly online sessions with a booster MoodSwings Plus comprises Moodswings which is on online delivery system for the MAPS program that covers monitoring mood and activities, assessing prodromes, preventing relapse and setting Specific, Measurable, Achievable, Realistic,Time-framed (SMART)goals with the addition of CBT-based interactive elements including tools to support mood and medication monitoring, development of a life chart, cognitive strategies such as thought monitoring use of simple motivational interviewing techniques, self-reflection, problem solving, identification of personal triggers and a preventing relapse plan	Psychoeducation The online Moodswings core modules	12 months

Van Dijk et al 2013 Canada	26/24	Over 18 referred to the Brief Therapy Clinic at Southlake Regional Health Centre with a diagnosis of BD Mean age:43·2 Female: 75%	12 weekly 1·5 hour group sessions over 3 months The intervention was the bipolar disorder group (BDG), a dialectical behaviour therapy skills-based psychoeducational group with emphasis on mindfulness practice. BDG focused on providing education about BD including symptoms types and causes of BD; one full session was a presentation by a psychiatrist on medications used to treat BD and one full session on the importance of self-care. The other sessions focused on distress tolerance skills, emotion regulation skills. Mindfulness was taught and emphasized throughout the 12 weeks. Participants were instructed to continue usual maintenance medication.	TAU Waitlist Control	3 months
Zaretsky et al 2008 Canada	79/46	Between 18 and 65, diagnosis of BD I or II not currently in full episode (mania, hypomania, depressive, mixed), taking standard mood stabilizer regimen in the last month. At least a grade 8 education, fluency in English and ability to provide informed consent. Mean age:40·7 Female: NR	20 weekly individual sessions over 5 months Participants received 6 sessions of individual psychoeducation followed by 14 weekly individual CBT sessions	Psychoeducation Participants received 6 sessions of individual psychoeducation	12 months
Psychoeducation and personalized Real-time Intervention for stabilizing mood (PRISM)					

Depp et al 2015 USA	104/82	Outpatients diagnosed with BD I or II, aged 18+, currently prescribed medications for BD, free of any visual or manual dexterity disabilities that would preclude use of a touch screen device. Exclusions were meeting criteria for substance use disorder in the prior 3 months, psychiatrically hospitalized in the prior month, or scored in the severe range for either depressive symptoms or manic symptoms Mean age: 47·5 Female: 58·5%	Psychoeducation included 4 individual face to face sessions with the therapist, covering general education about bipolar disorder; identifying symptoms of depression or mania and responding to early warning signs; developing implementation intentions keyed to level of symptom severity. Participants were then provided an internet-enabled smart phone to deliver the remainder of the intervention. PRISM is a web-based program that delivers personalized questionnaires capable of delivering pre-programmed interactive, algorithm-based responses based on symptoms or early warning signs reported. The program schedules and initiates interactive content vis SMS that automatically opened web browsers that contained surveys with likert style responses. The aim of the program is for patients to coach themselves for how to respond in critical moments.	Psychoeducation + pen and paper mood management. Control group participants received the same 4 sessions of psychoeducation as the intervention participants and then received 10 weeks of pen and paper mood monitoring and were provided with mood charts to complete once a day	3 months
Family Focused Therapy (FFT)					

Miklowitz et al 2000, 2003 USA	101/101	Acute state DSM-III BD I, manic, mixed or depressed episode in previous 3 months, aged 18-60, no neurologic disorder or developmental disability, no DSM-III drug or alcohol disorders in the previous 6 months, living with, or in close contact with relatives, willingness to commit to pharmacotherapy Mean age:35·6 Female: 63.4%	21 one hour family/marital sessions over nine months (weekly for three months; biweekly for three months; monthly for three months) FFT consisted of seven or more sessions in which patients and relatives became acquainted with the symptoms, nature, causes, and treatment of BD. Participants identified prodromal signs of illness and developed a relapse prevention plan. The second module (seven to 10 sessions) had patients and relatives learning communication skills for dealing with intrafamilial stress using a role-playing/behavior-rehearsal format. The third module (four to five sessions) involved participants learning a framework for defining problems, generating and implementing solutions to those problems	TAU This group received what was called Crisis management (CM). Over the 9-month treatment interval, project clinicians offered CM patients emergency counselling sessions as needed, typically when suicidal crises or severe family conflicts erupted. At a minimum, clinicians telephoned each CM patient monthly to monitor his or her status. CM patients and their relatives were also given two home-based sessions of family education covering the same topical areas as FFT, but in abridged form. These sessions were conducted within the first 2 months after entry into the study by the same trained therapists who delivered FFT in the experimental condition. In both FFT and CM, family members and patients were encouraged to contact the clinician if the patient appeared to be relapsing, at which point the clinician arranged appropriate medical services	24 months

Miller et al 2004 USA	92/92	DSM-III current BD I mood episode (mania, major depression or mixed), no DSM-III alcohol or drug dependence within 12 months of enrolment, 18-65 years, living with, or in regular contact with a relative or significant other, English speaking Mean age:39·3 Female: 56·5%	a.Family therapy sessions varied depending on the needs of each family and ranged from six to ten sessions of 50 minutes. They consisted of a therapist with a masters degree in social work and extensive clinical experience meeting together with a study patient and his or her family members. The therapist provided Problem Centered Systems Therapy of the Family, a short-term, problem-focused, semi-structured family intervention that includes a manual. This therapy is based upon the principles of the McMaster Model of the Family Functioning, where the most clinically relevant dimensions of family functioning are problem solving, communication, roles, affective responsiveness, affective involvement, and behaviour control. b.The multifamily psychoeducational group therapy consisted of two psychotherapists (one with a doctoral degree in clinical psychology, the other with a masters degree in social work; and both with extensive clinical experience) leading a group, which included four to six patients and their respective family members above the age of 12. This semi-structured intervention was implemented according to a manual that was developed for the study. The group therapy provided information about the nature and effects of BD, and taught members different coping strategies for common problems and the various phases of this chronic illness. The group leaders encouraged patients and family members to share their perspectives	TAU Pharmacotherapy was provided and monitored by a psychiatrist including managing adverse side effects, adjusting medication regimen, support, encouragement and advice when necessary.	28 months

Rea et al 2003 USA	53/53	DSM-III diagnosis of BD - manic type, aged 18-45, able to give informed consent, currently taking mood-regulating medication, and one close family member to participate with the patient Mean age:25·6 Female: 56·6%	21 one hour sessions over nine months FFT was modelled after the original structure of Falloon, Boyd, and McGill behavioural family management for patients with schizophrenia but substantially modified by Miklowitz. The sessions were delivered by two therapists and included three primary components: psychoeducation about BD, communication enhancement training, and problem-solving skills training. Allocation of time to each component was dependent on the individual family's needs and preparation, given their prior knowledge of BD, current family difficulties, and the patient's clinical status.	Individual psychoeducation and CBT Participants with BD met with a therapist for 30 minute sessions, titrated over 9 months (12 weekly, 6 biweekly, 3 monthly). The treatment was supportive, problem-focused, and educational. The goals were to educate the patient about the illness, monitor and increase the patient's awareness of symptoms, conduct crisis intervention, and reduce ongoing life stress.	24 months
Carer focussed interventions					
Bordbar et al 2009 Iran	60/57	Diagnosis of BD I based on DSM-IV confirmed by a psychiatrist, disease onset < 5 years, no neurological disorder or developmental disability, lived in Mashhad with at least two other adults Mean age:29·9 Female:21.7%	One group session two hours long Available adult family members received an additional two hour psycho-educational session before patients' discharge from hospital. The session covered the symptoms, nature, type and length of treatment especially medications and their possible side effects as well as aggravating factors of BD	TAU Family members of the control group did not receive psycho-educational sessions and the patients had their usual treatment condition including prophylactic pharmacotherapy	12 months

Madigan et al 2012 Ireland	47/31	Living in the community, age over 18, with an IQ over 80 and fluent in English Mean age:42 Female: 65%	Five group sessions weekly over 5 weeks (1·25 months) Intervention a: Multifamily group psychoeducation comprising two hour manualised sessions delivered over the 5-week period based on the framework developed by Mueuser and adapted for BD by Miklowitz's guidelines for carers. Joint facilitation included a psychiatric nurse and a psychiatric social worker Intervention b: Solution Focussed Group Psychotherapy (SFGP) comprising five sessions each lasting the 5-week period and delivered by two psychiatric nurses	TAU Consisted of care from a multidisciplinary team in their local service without any additional intervention	24 months

Perlick et al 2010 USA	46/40	Caregivers of patients aged >18, diagnosed with DSM-IV BD I or II. Caregivers were required to be a spouse or parent, have more frequent contact with the patient than any other caregiver, helps to support the patient financially, is the contact person by treatment staff in case of emergency and is involved in the patients' treatment. Caregivers also had to demonstrate current physical and mental health problems defined as scoring positive for at least one health risk behaviour on the Health Risk Behaviour Scale and either scoring >10 on the CES-D or >4 on the Social Behaviour Assessment Schedule Mean age: 34·7 Female:62.5%	12 to 15 weekly sessions of 45 minutes each over 4·7 months Family Focused Treatment Health Promoting Intervention (FFT-HPI), a manualised psychoeducational intervention for family members of patients with bipolar disorder which aims to provide the caregiver with enhanced skills for managing the relative's illness, defining self-care goals, and resolving barriers to patient care and self-care through education, examination of core beliefs that maintain dysfunctional interaction patterns, and problem solving. The intervention comprises 2 phases: Phase 1 - Psychoeducation and Goal setting, Phase II - Behavioural analysis of barriers to patient illness management and self-care	Active Control Eight to 12 session DVD/vidoetape delivered health education intervention, which involved a didactic approach to inform family members about health problems and concerns that are relevant to caregivers. Information was delivered via professionally produced DVDs on topics ranging from depression to heart disease and chronic pain	5 months
Reinares et al 2008 Spain	113/113	DSM-IV BD I or II, aged 18-60, euthymic for at least three months [scoring lower than 9 on HDRS and lower than 7 on the YMRS], and on standard pharmacological treatment for BD. The patients had to be living with a relative or partner for at least one year prior to entering the study and to be in daily contact with him or her Mean age:33 Female:28%	12 weekly 1.5 hour sessions over 3 months Psychoeducational group intervention for up to two relatives of the person with BD	TAU Relatives did not receive any specific intervention. The person with BD received standard psychiatric care consisting of out-patient follow up and medications following the treatment algorithms of the clinic	12 months

Van Gent et al 1991 Netherlands	26/26	DSM-III criteria for BD, and a current partner Mean age: 44 intervention group 55 control group Female: Not reported	Five structured group education session with an emphasis on information regarding the disease and medication as well as practical advice on associating with the patient and dealing with one's own daily functioning	TAU There was no intervention for the control group and they were only asked to complete assessments	12 months

3. Risk of bias in included studies

Figure 1. Risk of bias summary: review authors' judgements about each risk of bias item for each included study

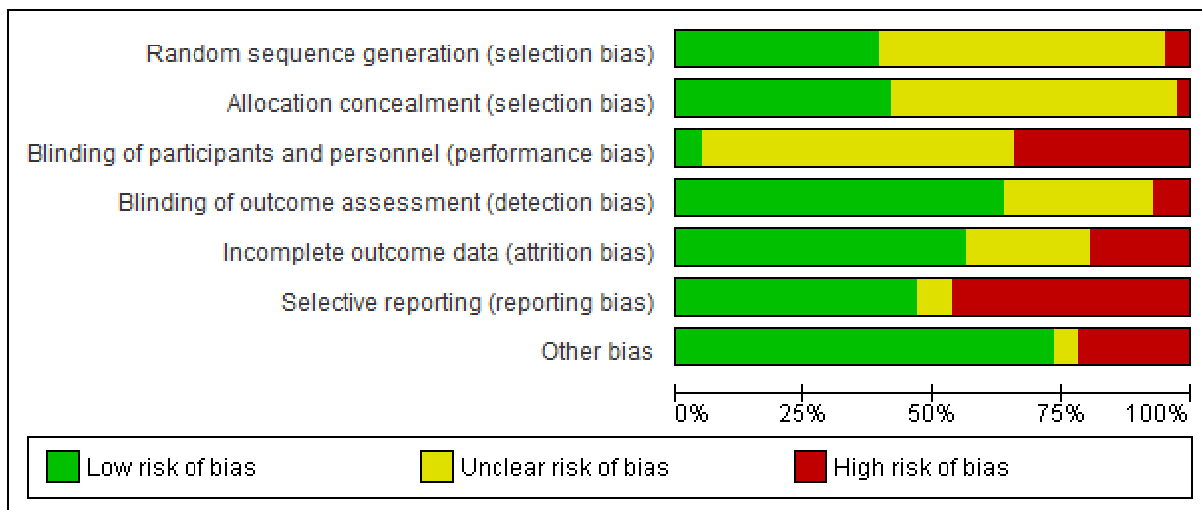


Figure 2. Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies

4. **Network diagrams**

Each circle or node in a network diagram represents an intervention including the comparators from the trials included and the lines represent direct comparisons made in the included trials. The size of each node is proportional to the number of study arms with the intervention and the width of the line corresponds to the number of studies that compared the two interventions.

Figure 3: Network of comparisons for the primary outcome of manic or depressive relapse

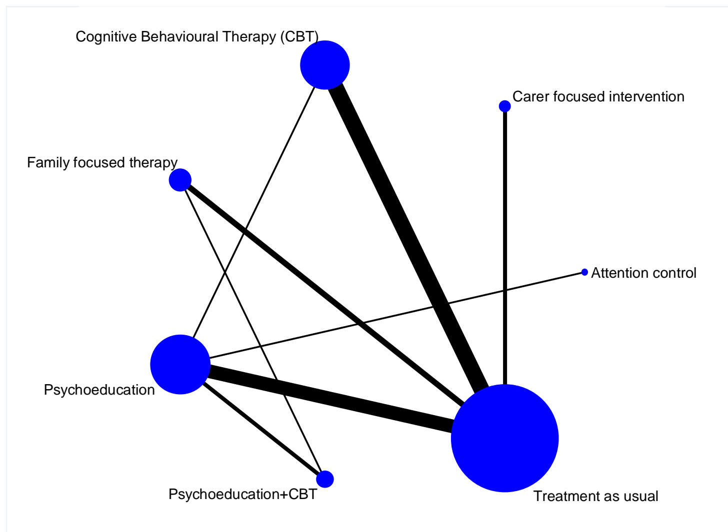


Figure 4: Network of comparisons for the secondary outcome of depression symptom scale scores

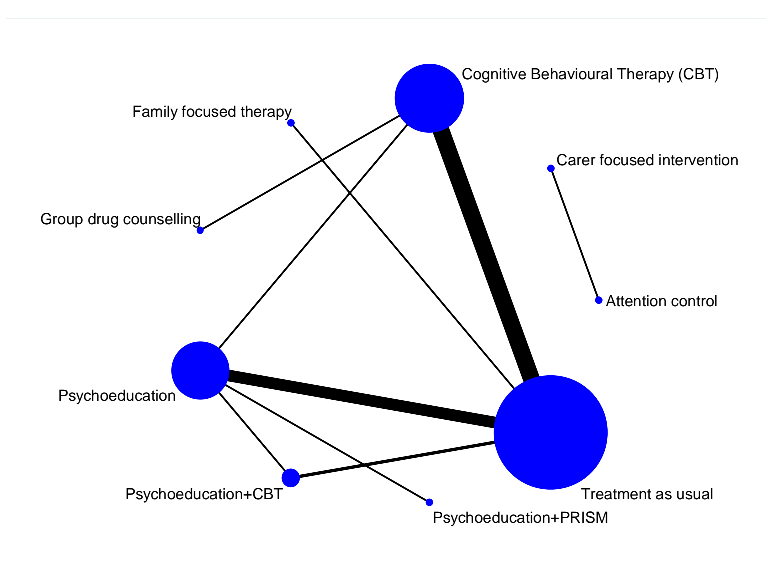


Figure 5: Network of comparisons for the secondary outcome of mania symptom scale scores

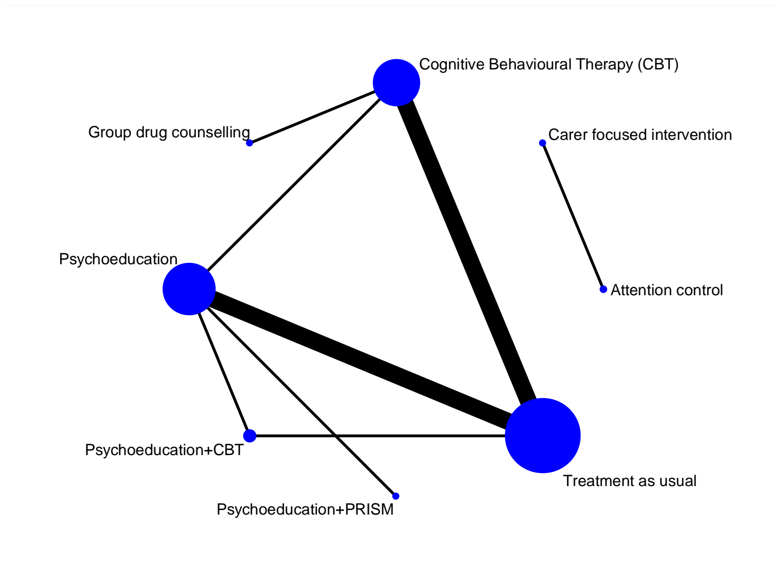


Figure 6: Network of comparisons for the secondary outcome of medication adherence

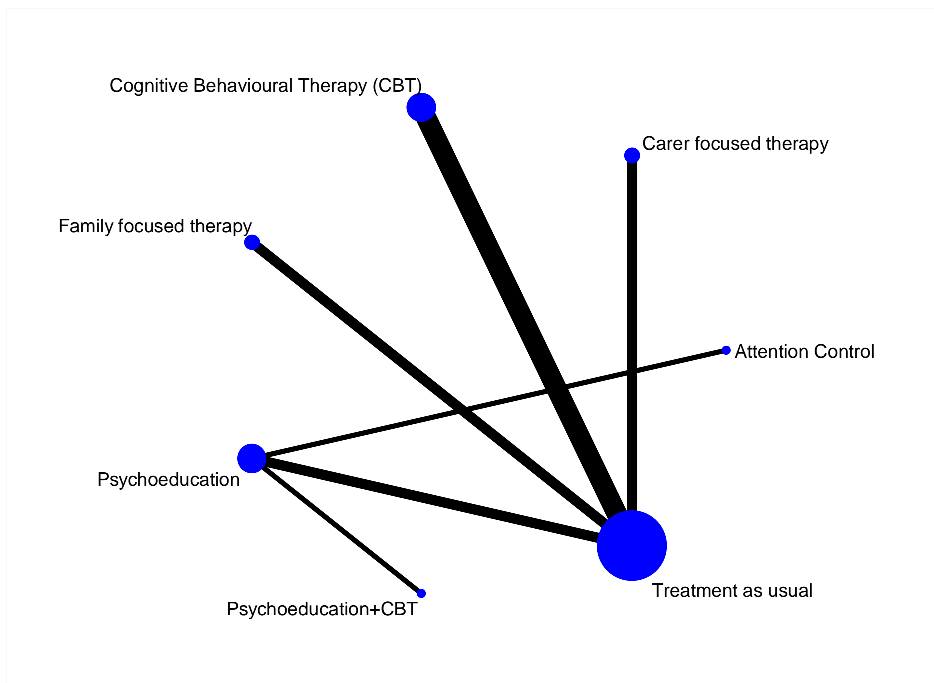
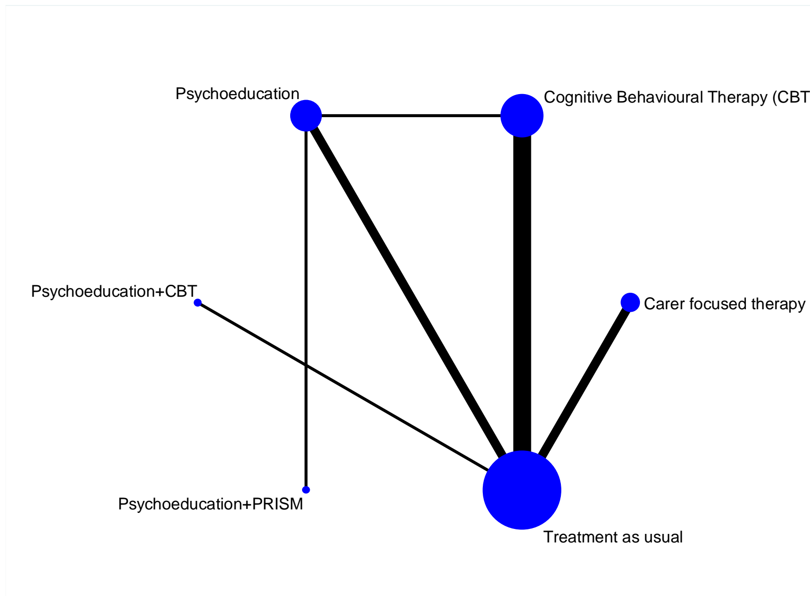


Figure 7: Network of comparisons for the secondary outcome of global assessment of functioning (GAF)



5. Network meta-analyses using alternate models

Figure 8. Forest plot for the outcome of relapse to depression or mania using the quality effects model

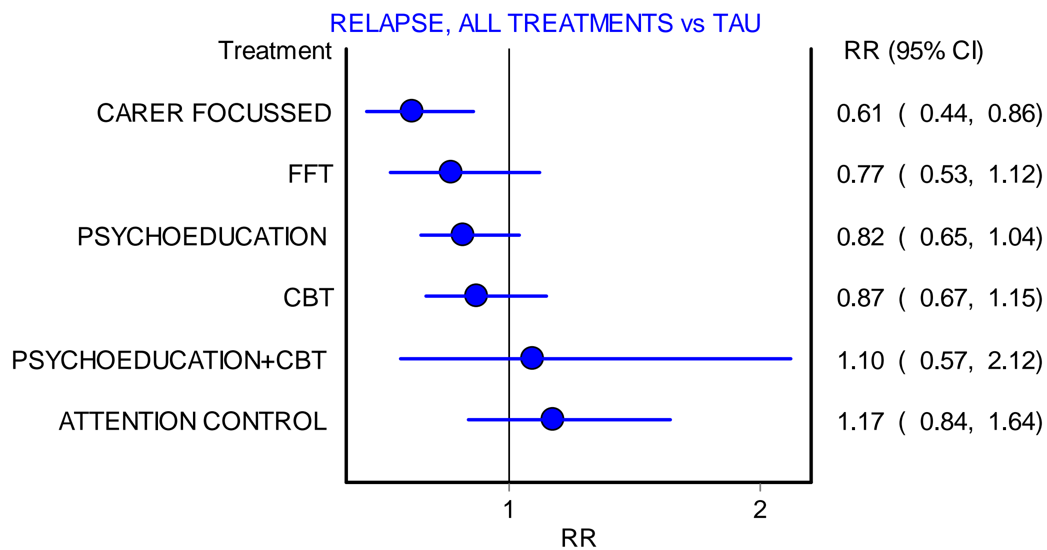


Figure 9. Forest plot for the outcome of relapse to depression or mania using the random effects model

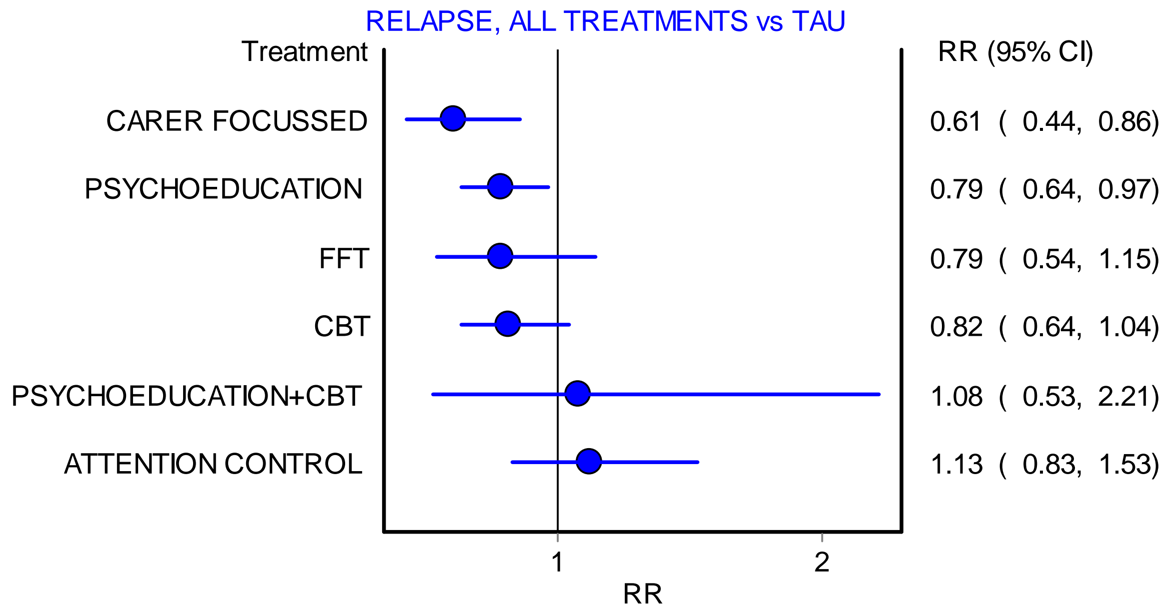


Figure 10. Forest plot for the outcome of depression symptom scores using the quality effects model

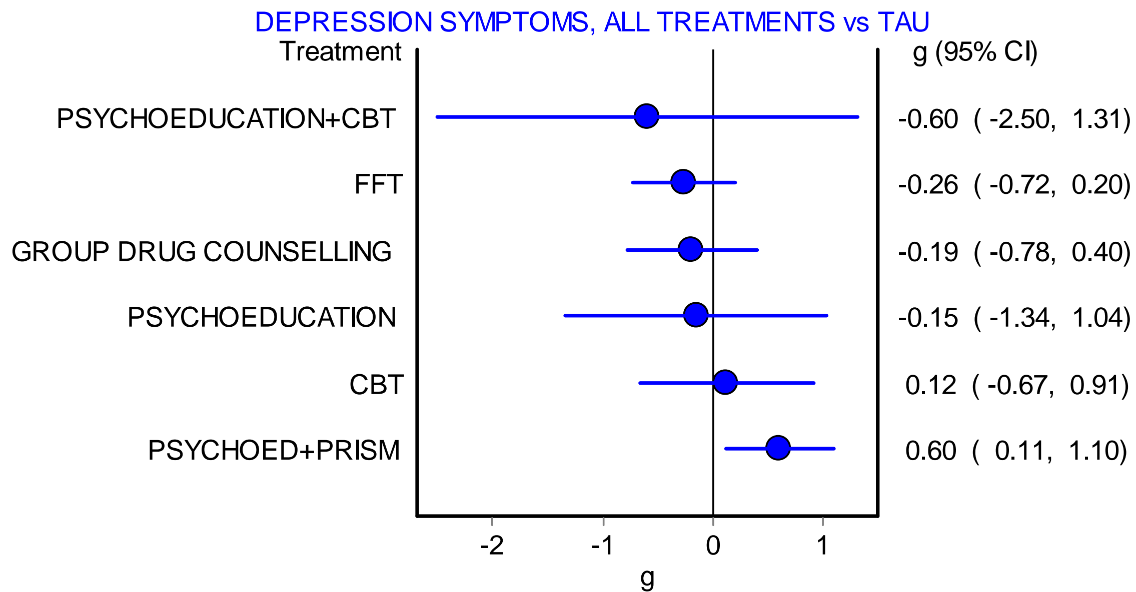


Figure 11. Forest plot for the outcome of depression symptom scores using the random effects model

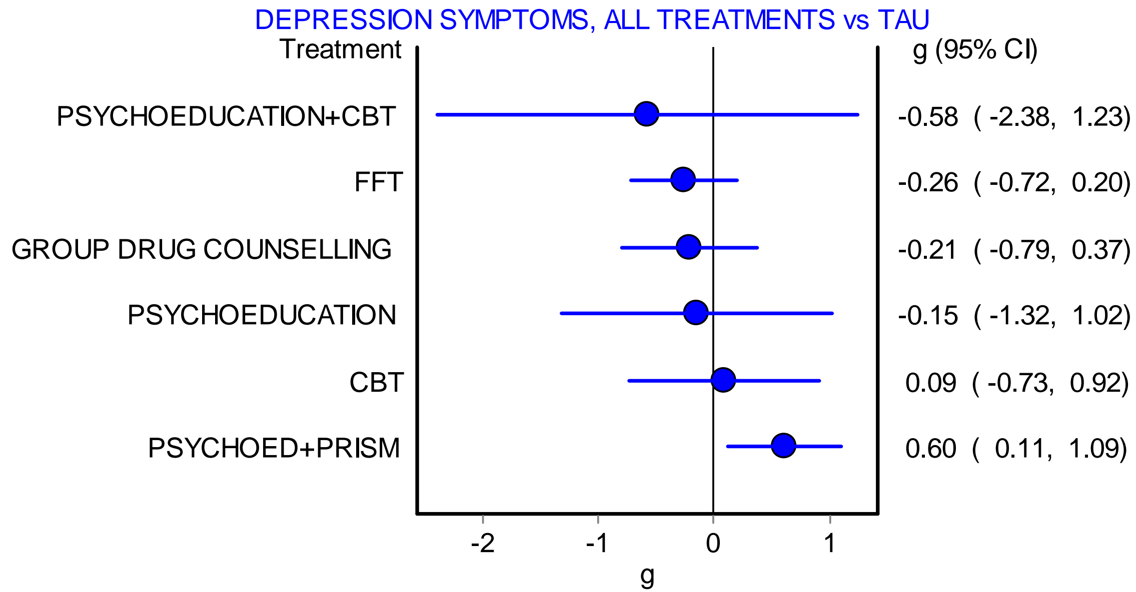


Figure 12: Forest plot for the outcome of mania symptom scores using the quality effects model

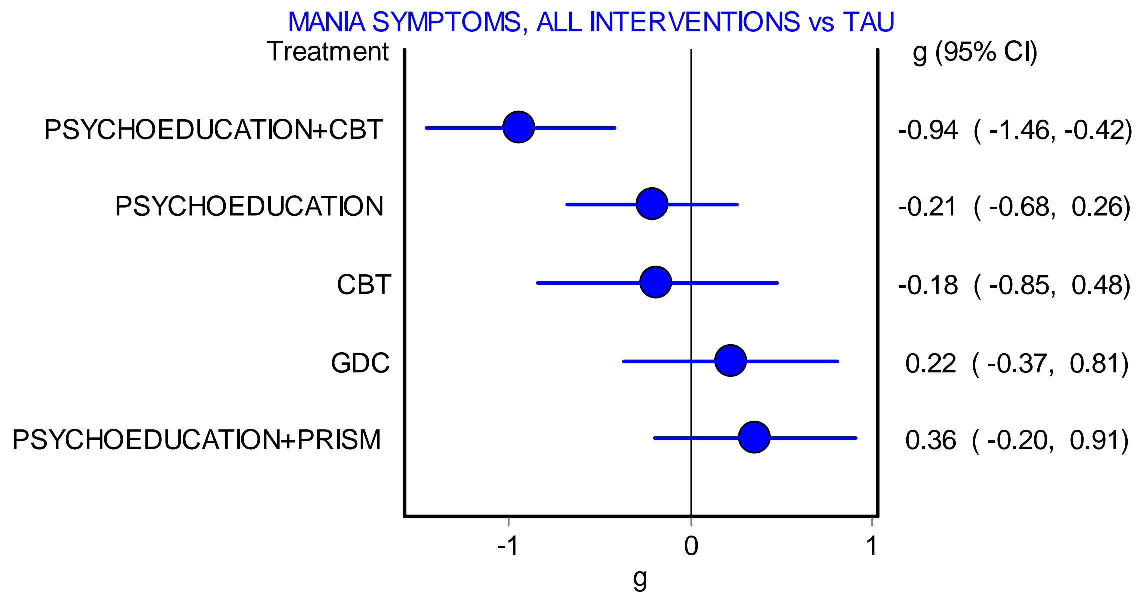


Figure 13: Forest plot for the outcome of mania symptom scores using the random effects model

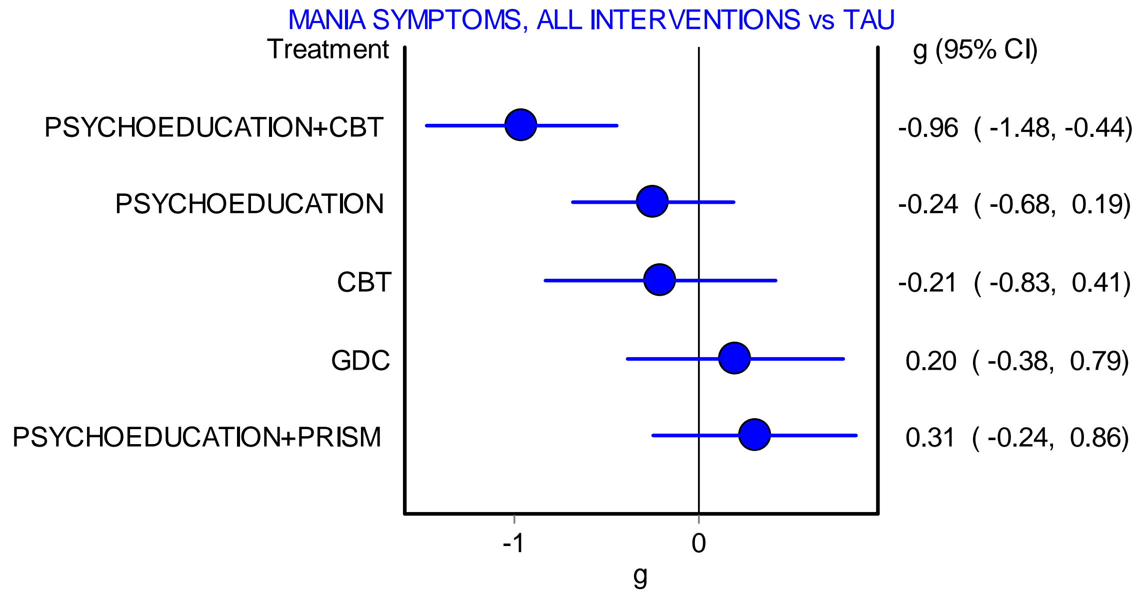


Figure 14: Forest plot for the outcome of medication adherence using the quality effects model

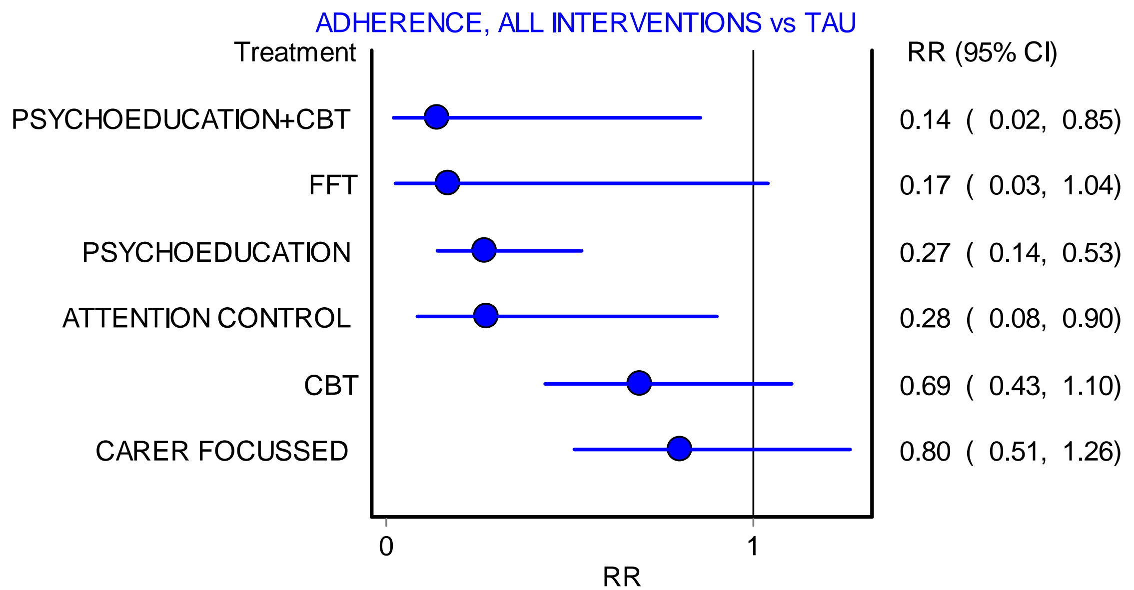


Figure 15: Forest plot for the outcome of medication adherence using the random effects model

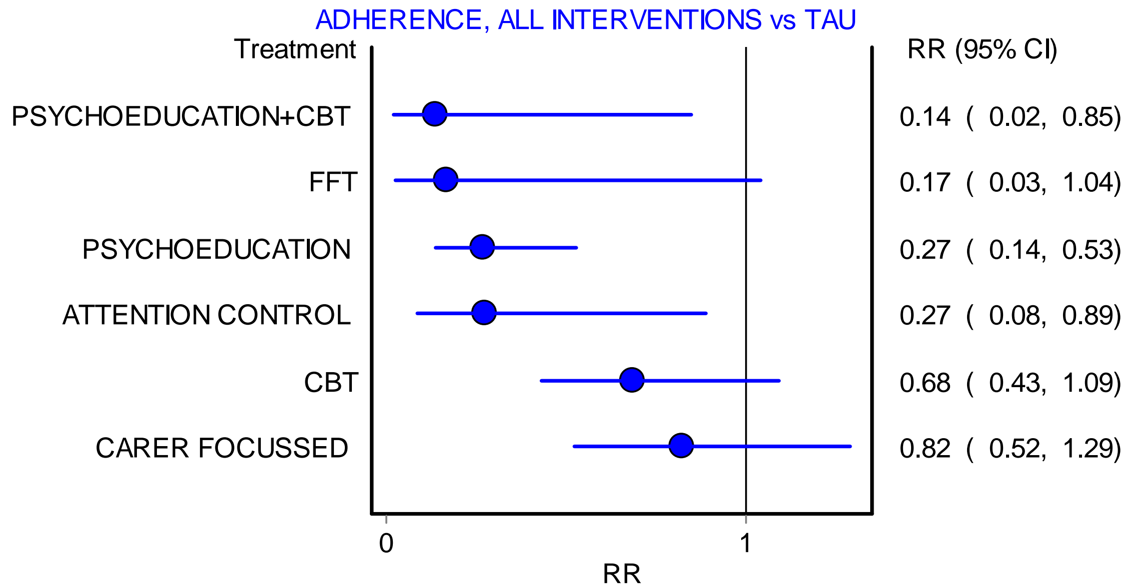


Figure 16: Forest plot for the outcome of GAF using the quality effects model

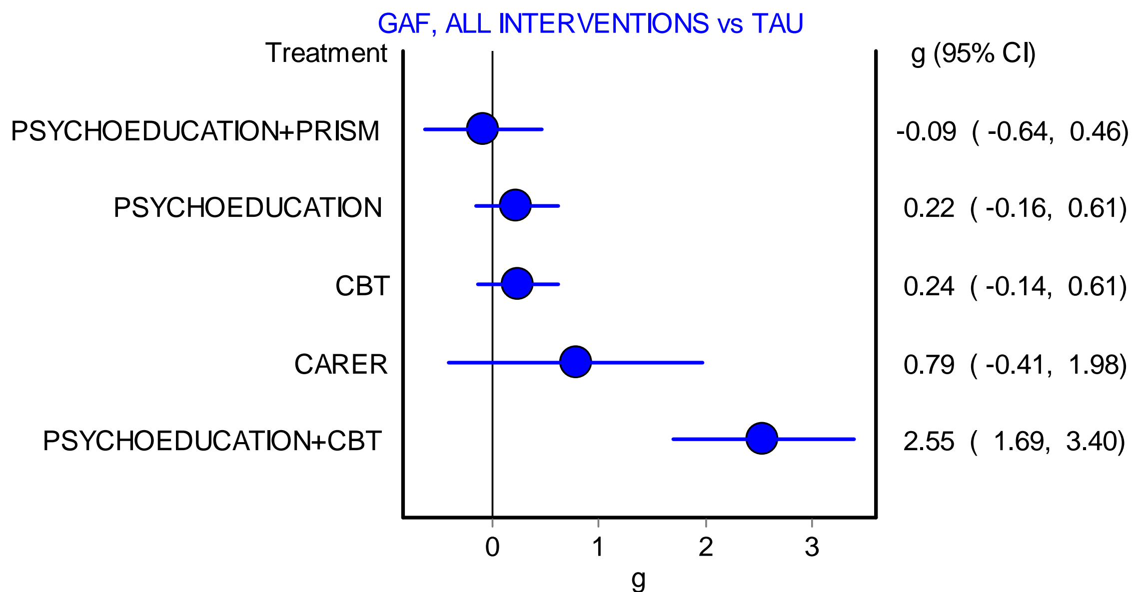
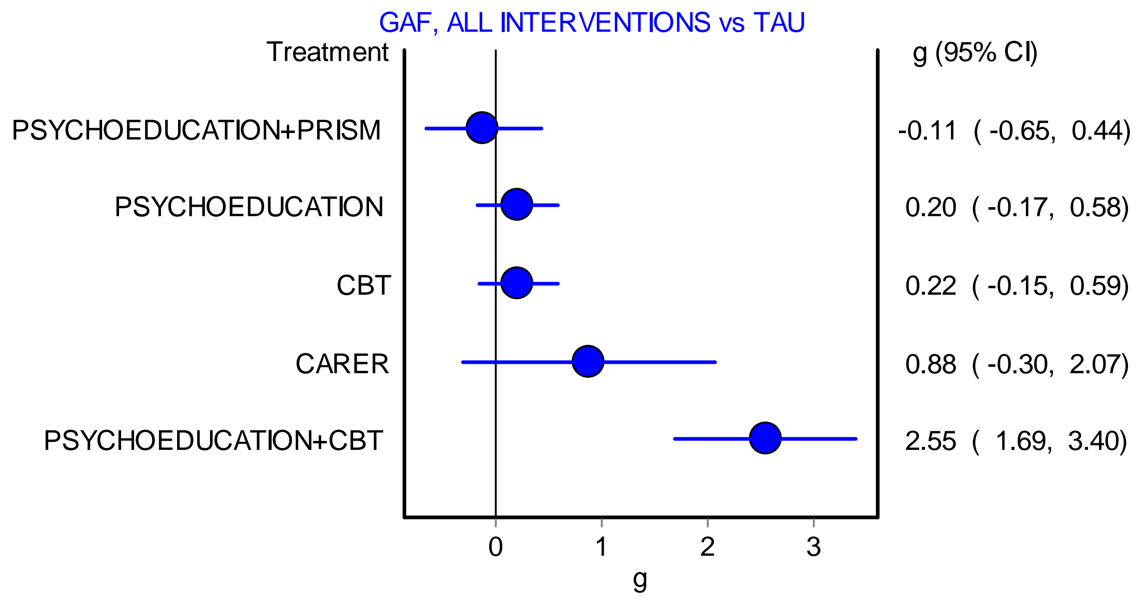


Figure 17: Forest plot for the outcome of GAF using the random effects model



6. Results of meta-regressions

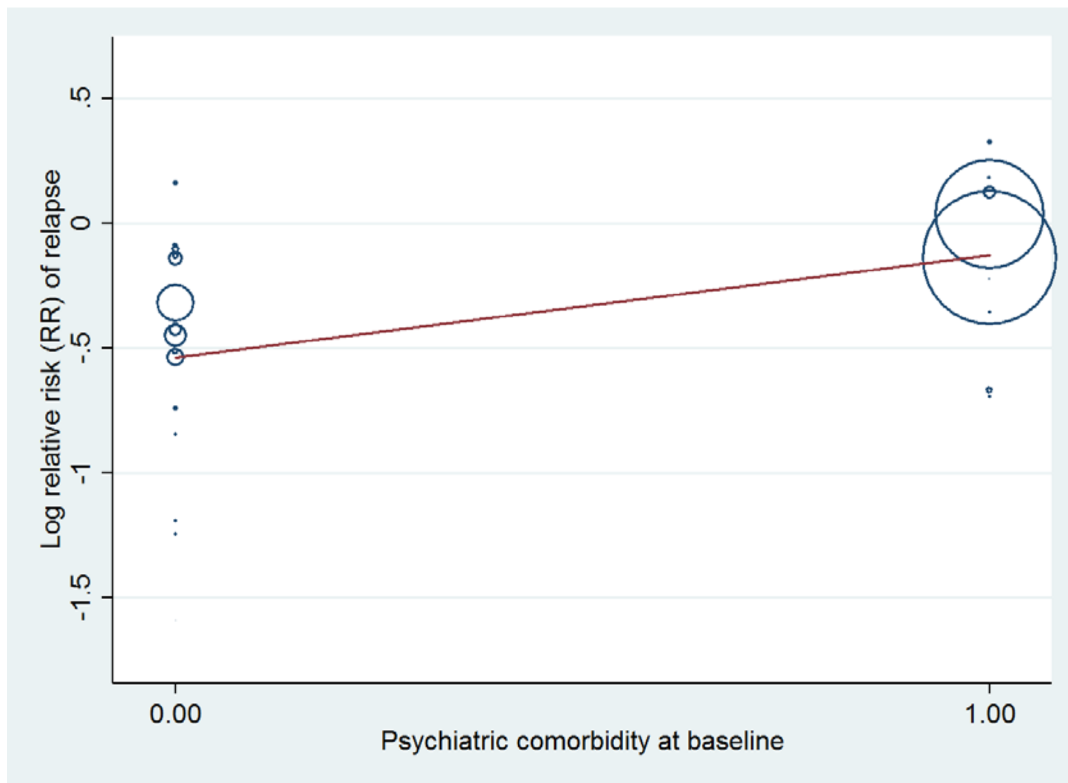


Figure 18. Bubble plot of natural log relative risk (RR) of relapse at the primary endpoint in 25 trials, according to presence of any psychiatric comorbidity in each study sample at baseline (where 0 = no comorbid disorders in sample and 1 = presence of comorbid disorders in sample). Larger natural log RR values represent increased risk of relapse. The area of the circle is inversely proportional to the variance of the log relative risk estimate.

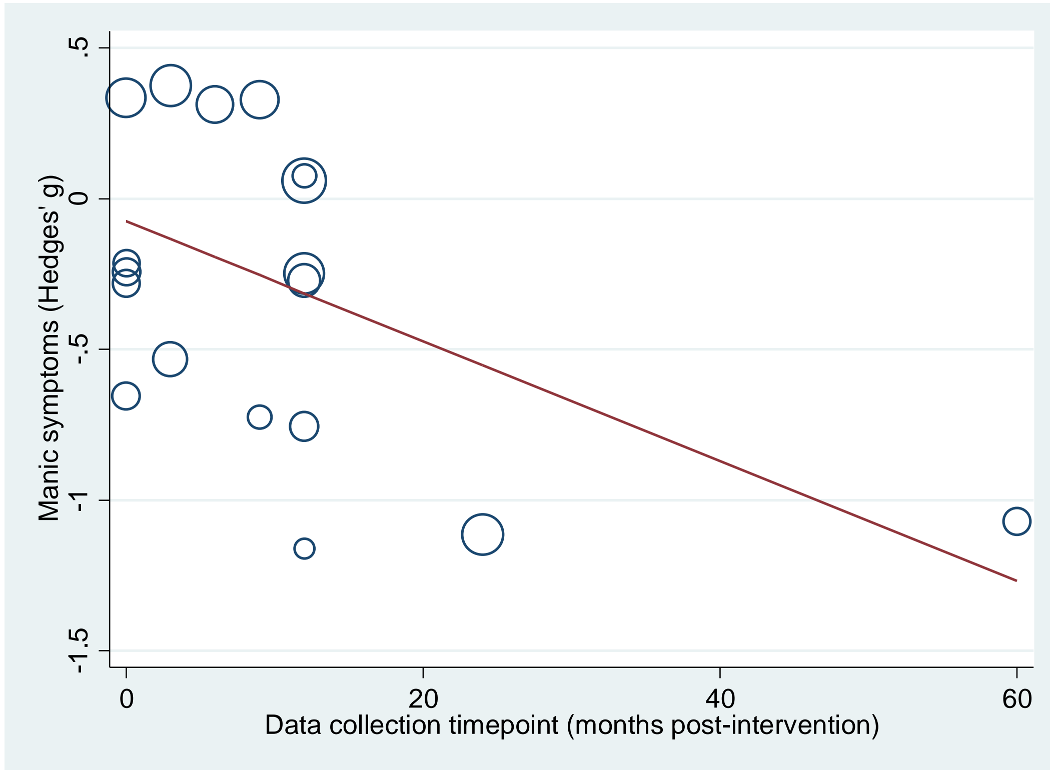


Figure 19. Bubble plot of standardised mean differences (Hedges' g) in manic symptoms at the primary endpoint in 18 trials according to the timing of the final data collection time point (months post-intervention). Smaller hedges' g values indicate greater reductions in manic symptoms. The area of the circle is inversely proportional to the variance of the standardised mean difference estimate.

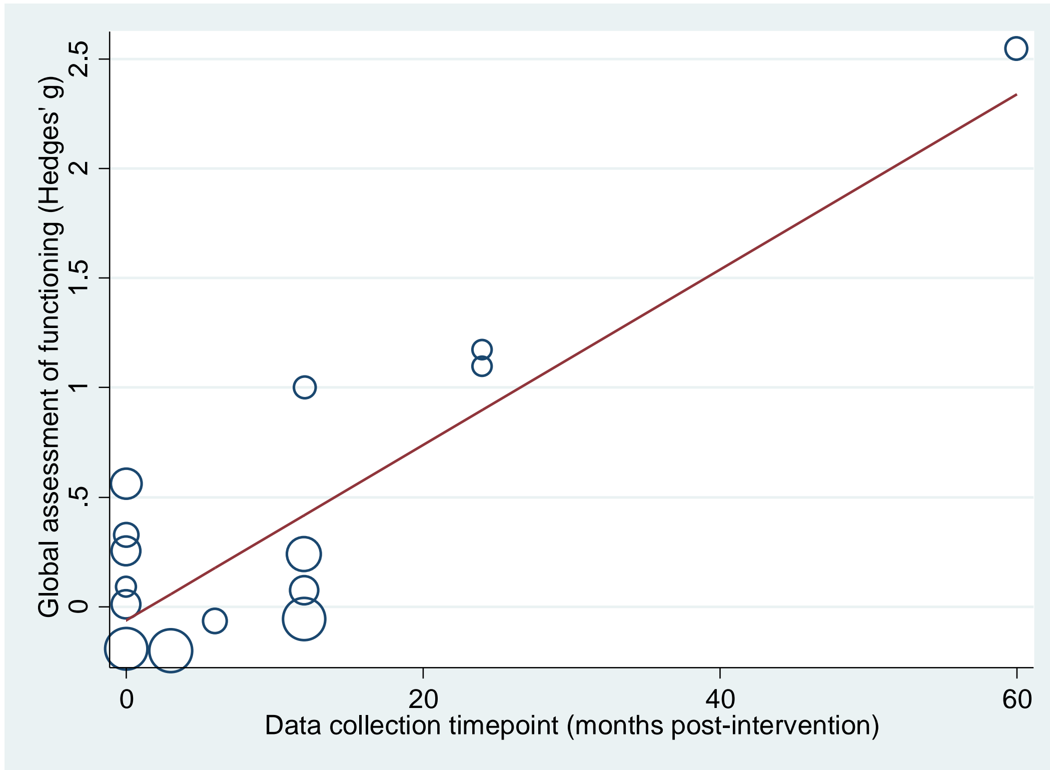


Figure 20. Bubble plot of standardised mean differences (Hedges' g) in global assessment of functioning measures at the primary endpoint in 15 trials according to the timing of the final data collection time point (months post-intervention). Larger hedges’ g values indicate greater improvements in global functioning. The area of the circle is inversely proportional to the variance of the standardised mean difference estimate.

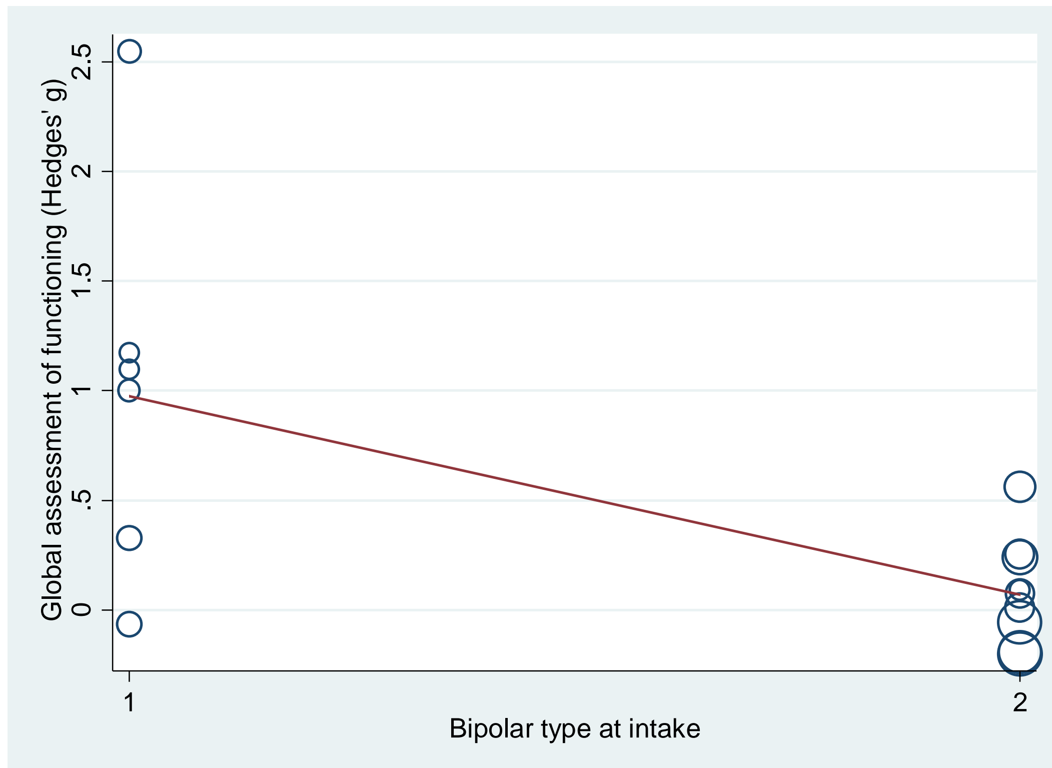


Figure 21. Bubble plot of standardised mean differences (Hedges' g) in global assessment of functioning measures at the primary endpoint in 15 trials according to the type of bipolar at intake to the trial (where 1 = participants with bipolar I only and 2 = participants with either bipolar types I or II). Larger hedges’ g values indicate greater improvements in global functioning. The area of the circle is inversely proportional to the variance of the standardised mean difference estimate.