

Best Evidence Summaries of Topics in Mental Healthcare

BEST in MH *clinical question-answering service*

Question

In adults with bipolar disorder, which group intervention is most effective in improving patient outcomes?

Clarification of question using *PICO* structure

Patients: Adults with bipolar disorder

Intervention: Group interventions

Comparator: Any other group interventions

Outcome: Patient outcomes

Plain language summary

There is limited evidence that adequately compares the effectiveness of different group therapies. Research suggests that group psychoeducation may be beneficial in reducing symptoms of bipolar disorder, when combined with medication. However, further trials are required to determine the most effective group intervention.

Clinical and research implications

Very limited data from two small randomised controlled trials, included in a larger systematic review, indicates that in group psychoeducation as an adjunct to pharmacotherapy may reduce the overall relapse rate, the manic relapse rate and the depressive relapse rate in people with bipolar compared to participation in an un-structured support group. A follow-up study using a small, non-randomised sample from one of these trials indicates that these effects are sustained over the longer term (5 years) and that participants in psychoeducational groups may also experience increased employment rates, job efficacy and autonomy.

Overall, more research is needed to confirm the initially positive findings about group psychoeducation and to adequately assess the effectiveness and comparative effectiveness of other group interventions for people with bipolar disorder.

What does the evidence say?

Number of included studies/reviews (number of participants)

We identified one systematic review¹ and one additional follow-up study of one of the randomised controlled trials (RCTs) included in the systematic review,² which were considered relevant to this evidence summary. The systematic review had a wide scope, which covered both pharmacological and psychological interventions for the prevention of relapse in people with bipolar disorder.¹ The review included 45 RCTs or quasi-RCTs, most of which were concerned with the evaluation of pharmacological interventions.¹ All of the group psychological interventions were assessed as adjuncts to pharmacological treatment. Two of the studies included in the systematic review, by Colom et al., compared a group psychoeducational intervention to an un-structured support group.¹ No other studies identified by the systematic review, compared effectiveness between different group interventions.¹ Three further studies, included in the systematic review, evaluated group interventions: one study compared integrated group therapy to treatment as usual, one study compared family therapy to individual psychoeducation, and one study compared family therapy to crisis management.¹ All studies included in the systematic review reported relapse rates.¹ The additional 5-year follow-up study included in this evidence summary followed up 20 of the 120 participants from one of the studies by Colom et al. that was included in the systematic review.² This study also reported relapse rates, as well as additional outcomes relating to social functioning.²

Main findings

The results of two studies (total n=170 participants), taken from a large systematic review of 45 studies, indicate that participation in group psychoeducation as an adjunct to pharmacotherapy can reduce the overall relapse rate, the manic relapse rate and the depressive relapse rate in people with bipolar compared to participation in an un-structured support group; summary odds ratios (ORs) 0.16 (95% CI: 0.07 to 0.40), 0.27 (95% CI: 0.14 to 0.53), and 0.24 (95% CI: 0.12 to 0.45), respectively.¹ A small follow-up study of 20/120 participants from one of these studies indicated that the effects on relapse rates are maintained at five years.² This study also reported that significantly more of the participants from the psychoeducation group were in work, and had good job effectiveness and good autonomy than those in the un-structured support group.² There was no further evidence to support the effectiveness of any other group intervention for people with

bipolar disorder, nor was there any evidence about the comparative effectiveness of different types of active group interventions.

Authors conclusions

Soares-Weiser (2007) – With respect to the studies included in the review, which assessed group psychological interventions, the authors concluded that there is some evidence that group psychoeducation and family therapy might be beneficial as adjuncts to pharmacological maintenance treatments.

Colom (2009) – The authors stated that, although their findings should be treated with caution, it appears that psychoeducation plus medication can benefit bipolar II subjects.

Reliability of conclusions/Strength of evidence

The evidence included in this summary was taken from two, generally good quality, but small RCTs that were included in a large, well conducted systematic review and from a follow-up study using a small, non-randomised sample from one of these RCTs. The main issue for this evidence summary is the very limited amount of data available.

What do guidelines say?

NICE guidelines for bipolar disorder (CG185, 2014) make the following recommendations regarding structure of psychological interventions in longer term, secondary care;

“Offer a structured psychological intervention (individual, group or family), which has been designed for bipolar disorder and has a published evidence-based manual describing how it should be delivered, to prevent relapse or for people who have some persisting symptoms between episodes of mania or bipolar depression.” (pp.9)

Date question received: 08/02/2016

Date searches conducted: 16/02/2016

Date answer completed: 25/04/2016

References

Systematic reviews

1. Soares-Weiser, K., Vergel, Y. B., Beynon, S., Dunn, G., Barbieri, M., Duffy, S., Geddes J., Gilbody, S., Paler, S. & Woolacott, N. (2007). A systematic review and economic model of the clinical effectiveness and cost-effectiveness of interventions for preventing relapse in people with bipolar disorder.

Randomised controlled trials

2. Colom, F., Vieta, E., Sánchez-Moreno, J., Goikolea, J. M., Popova, E., Bonnin, C. M., & Scott, J. (2009). Psychoeducation for bipolar II disorder: an exploratory, 5-year outcome subanalysis. *Journal of Affective Disorders*, 112(1), 30-35.

Guidelines

National Institute for Health and Clinical Excellence (2014) Bipolar Disorder: assessment and management. CG185. London: NICE.

<https://www.nice.org.uk/guidance/cg185/resources/bipolar-disorder-assessment-and-management-35109814379461>

Results

Systematic reviews

Author (year)	Search date	Inclusion criteria	Number of included studies	Summary of results	Risk of bias
Soares-Weiser et al. (2007)	September 2005	<p>Participants: People with bipolar I or bipolar II disorder, according to standard criteria (e.g. DSM-IV or ICD-10). Studies of people treated only in an acute manic or acute depressive phase were excluded.</p> <p>Intervention: Pharmacological (lithium salts, anticonvulsants, antipsychotics, antidepressants (tricyclics and/or SSRIs)) and/or psychosocial interventions (CBT, psychoeducation, family intervention, case management, integrated group therapy) for the prevention of relapse.</p> <p>Comparator: Any other included intervention</p> <p>Outcome: Overall relapse rate, manic relapse rate, depressive relapse rate, drop-out rate, adverse events and suicide or suicide attempts.</p> <p>Study design: Randomised or quasi-randomised controlled trials with at least three months follow-up.</p>	n=45 studies (studies comparing group interventions n=2 with a total of 170 participants)	<p>This systematic review aimed to assess the clinical effectiveness and cost-effectiveness of pharmacological and/or psychosocial interventions for the prevention of relapse in people with bipolar disorder.</p> <p>This evidence summary is concerned only with evidence which compares the effectiveness of different group interventions for people with bipolar.</p> <p>Only two of the included studies compared group interventions. Both studies were by Colom et al. and compared a group psychoeducational intervention (twenty-one 90 minute sessions, no further details described) to a non-structured group meeting (20 weekly meetings); in both studies the interventions were adjunctive to pharmacological treatment. One study included both bipolar I and bipolar II participants (n=120, 63% female) and the</p>	<p>The objective of the review was clearly stated and appropriately broad inclusion criteria were defined.</p> <p>A wide range of bibliographic databases were searched for relevant studies and this process was supplemented by searches of grey literature sources and hand searching of conference proceedings.</p> <p>Data extraction and</p>

				<p>other included only bipolar I patients (n=50, 62% female). No details of concomitant pharmacological treatments were reported.</p> <p>Summary estimates calculated from the two studies indicated that the group psychoeducational intervention was associated with statistically significant reductions in: the overall number of relapses, as reported by the study authors (OR 0.16 (95% CI: 0.07 to 0.40)); the number of manic relapses, as reported by the study authors (OR 0.27 (95% CI:0.14 to 0.53)); the number of depressive relapses, as reported by the study authors (OR 0.24 (95% CI: 0.12 to 0.45)); the number of relapse-related admissions to hospital (OR 0.42 (95% CI: 0.21 to 0.86). The length of follow-up was not reported.</p> <p>One study compared a group treatment (12 to 20 one hour sessions of integrated group therapy as an adjunct to pharmacotherapy, no further details given) to treatment as usual (TAU), which included pharmacotherapy and various individual and group therapies, which were</p>	<p>assessment of the methodological quality of included studies included measures to minimise error and bias. However duplicate screening of studies for inclusion was not complete (the authors state that this was done for “at least 30%” of article.</p> <p>Appropriate analysis methods were used.</p>
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				<p>available to all participants across both treatment groups. This study found no significant difference in overall relapse rates between the groups, and did not report separate data for manic and depressive relapses.</p> <p>Two studies assessed the effectiveness of family therapy as an adjunct to pharmacotherapy. One study compared family therapy to individual psychosocial therapy and the other compared family therapy to crisis management (unclear whether crisis management involved the family). Neither of the two studies found any significant between group differences in overall relapse rates, manic relapse rates, or depressive relapse rates.</p>	
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Randomised controlled trials

Author (year)	Inclusion criteria	Number of participants	Summary of results	Risk of bias
Colom	<i>Participants:</i> Patients with a diagnosis of	n = 20	This article reports a 5-year, post-RCT follow-up of a sample	This article

<p>et al. (2009)</p>	<p>bipolar II disorder according to DSM-IV, followed up after completion of an RCT. Intervention: Group psychoeducation plus standard pharmacological treatment Comparator: Unstructured support groups plus standard pharmacological treatment. Outcome: Manic (YMRS), hypomanic (HDRS-17) or depressive (YMRS) recurrence. Measures of social function.</p>	<p>(psychoeducation n=8, support group n=12).</p>	<p>of 20 patients with bipolar II who were taken from the larger of the two studies by Colom et al. included in the systematic review (described above).</p> <p>At baseline, there were no significant differences between the groups with respect to demographic characteristics, illness history, or pharmacological treatments received. The mean age of participants was 40 years and participants reported around 10 previous episodes over an average time of 15 years since diagnosis.</p> <p>In this sub-group, there were no statistically significant differences in relapse rates during the six month treatment phase of the RCT; 50% of participants in the un-structured support group arm met the criteria for relapse and 25% of participants in the group psychoeducation arm met the criteria for relapse. At the end of follow-up data were available for 7 participants from the psychoeducation group and 10 participants from the un-structured support group. At the end of the five year follow-up, participants in the psychoeducation group had experienced significantly fewer relapses (mean 4.14±7.15 vs. mean 10.6±4.92), significantly fewer manic relapses (mean 1.7±3.3 vs. mean 6.1±3.98) and significantly fewer depressive relapses (mean 2.43±4.31 vs. 4.5±2.01) than those in the un-structured support group. Participants in the psychoeducation group also spent significantly less time in any relapse state (mean 192.42±251.72 days) than those in the un-structured support</p>	<p>reports follow-up of 20 selected patients, after completion of an RCT; randomisation has therefore been broken.</p> <p>The nature of the intervention and follow-up study preclude blinding of participants and study personnel. It was not clear whether those assessing 5-year outcomes were blind to treatment</p>
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			<p>group (mean 859.9±438.38 days); a similar pattern was observed when time spent in manic and depressive relapses was considered separately. At the end of 5-year follow-up, significantly more of the participants in the psychoeducation group were in employment (5/8), had good job functioning (5/8) and had good autonomy (6/8), compared to 3/12, 3/12 and 4/12, respectively in the un-structured support group.</p>	<p>group.</p> <p>Results were reported for all specified outcomes and appropriate analytical methods were used.</p>
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Risk of bias

Systematic reviews

Author (year)	RISK OF BIAS				
	Inclusion criteria	Searches	Review process	Quality assessment	Synthesis
Soares-Weiser et al. (2007)					

Randomised controlled trials

Study	RISK OF BIAS					
	Random allocation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data	Selective Reporting
Colom et al. (2009)						

 Low risk

 High risk

 Unclear risk

Search details

Source	Search Strategy	Number of hits	Relevant evidence identified
<i>Guidelines</i>			
NICE	Bipolar disorder	21	
<i>Systematic Reviews</i>			
MEDLINE	<ol style="list-style-type: none"> 1 Psychotherapy, Group/ (12565) 2 (group adj2 therap\$.ab,ti. (15803) 3 (group adj2 intervention\$.ab,ti. (22031) 4 1 or 2 or 3 (46175) 5 Mood Disorders/ or Bipolar Disorder/ (44191) 6 (biploar\$ or bi-polar\$ or manic\$ or mania\$.ab,ti. (15954) 7 hypomani\$.ab,ti. (2293) 8 5 or 6 or 7 (49743) 9 4 and 8 (317) 10 (systematic\$ review\$ or meta-analytic\$ or metanalysis or metaanalysis or meta analysis or meta?synthesis or meta synthesis or meta?regression or meta regression).ab,ti. (129321) 11 ((synthes\$ adj3 (literature or evidence)) or integrative review or data synthesis or research synthesis or narrative synthesis or systematic study or systematic studies or systematic comparison\$ or systematic overview\$ or evidence based review or comprehensive review or critical review or quantitative review or 	35	

	<p>structured review or realist review or realist synthesis).ab,ti. (49788)</p> <p>12 exp Meta-Analysis/ (61543)</p> <p>13 meta-analysis.ab,ti,pt. (91081)</p> <p>14 10 or 11 or 12 or 13 (184045)</p> <p>15 (medline or pubmed or Cochrane or embase or cinahl or psyc?lit or psyc?info).ab. (113345)</p> <p>16 ((literature adj3 search\$) or (database\$ adj3 search\$) or (bibliographic adj3 search\$) or (electronic adj3 search\$) or (electronic adj3 database\$) or (computeri?ed adj3 search\$) or (internet adj3 search\$) or included studies or (inclusion adj3 studies) or inclusion criteria or selection criteria or predefined criteria or predetermined criteria).ab. (133783)</p> <p>17 ((assess\$ adj3 (quality or validity)) or (select\$ adj3 (study or studies)) or (data adj3 extract\$) or extracted data or (data adj2 abstracted) or (data adj3 abstraction) or published intervention\$ or ((study or studies) adj2 evaluat\$) or (intervention\$ adj2 evaluat\$) or confidence interval\$ or heterogeneity or pooled or pooling or odds ratio\$ or Jadad or coding).ab. (814362)</p> <p>18 15 or 16 or 17 (936414)</p> <p>19 review.pt. (2064794)</p> <p>20 18 and 19 (144577)</p> <p>21 18 and 19 (144577)</p> <p>22 (review\$ adj4 (papers or trials or studies or evidence or intervention\$ or evaluation\$)).ab,ti. (120826)</p> <p>23 14 or 18 or 20 or 21 (1014826)</p> <p>24 (letter or editorial or comment).pt. (1455023)</p> <p>25 23 not 24 (1007020)</p>		
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	<p>26 Animals/ (5766662)</p> <p>27 Humans/ (15660680)</p> <p>28 26 not 27 (4154861)</p> <p>29 25 not 28 (917746)</p> <p>30 9 and 29 (35)</p>		
EMBASE	<p>1 (group adj2 therap\$.ti,ab. (23553)</p> <p>2 (group adj2 intervention\$.ti,ab. (30729)</p> <p>3 group therapy/ (19004)</p> <p>4 1 or 2 or 3 (66654)</p> <p>5 *bipolar disorder/th [Therapy] (1707)</p> <p>6 *mood disorder/th [Therapy] (736)</p> <p>7 (bipolar\$ or bi-polar\$ or manic\$ or mania\$ or hypomani\$.ti,ab. (80856)</p> <p>8 5 or 6 or 7 (81755)</p> <p>9 4 and 8 (482)</p> <p>10 (systematic\$ review\$ or systematic\$ literature review\$ or meta-analytic\$ or meta?analysis or metanalysis or meta analysis or meta?synthesis or meta synthesis or meta?regression or meta regression).ab,ti. (169674)</p> <p>11 ((synthes\$ adj3 literature) or (synthes\$ adj3 evidence) or (synthes\$ adj2 qualitative) or integrative review or data synthesis or research synthesis or narrative synthesis or systematic study or systematic studies or systematic comparison\$ or systematic overview\$.ab,ti. (32037)</p> <p>12 ((systematic adj2 search\$) or systematic\$ literature research\$ or (review adj3 scientific literature) or (literature review adj2 side effect\$) or (literature review adj2 adverse effect\$) or (literature review adj2 adverse</p>	60	

	<p>event\$) or (evidence-based adj2 review) or (evidence-based adj2 review)).ab.ti. (19053)</p> <p>13 (comprehensive review or critical review or critical analysis or quantitative review or structured review or realist review or realist synthesis or (pooled adj2 analysis) or (pooled data adj6 (studies or trials)) or (medline and (inclusion adj3 criteria)) or (search adj (strateg\$ or term\$))).ab.ti. (77271)</p> <p>14 exp "systematic review"/ (101545)</p> <p>15 meta analysis/ (104164)</p> <p>16 (Medline or pubmed or Cochrane or embase or cinahl or psyc?lit or psyc?info or lilacs or (literature adj3 search\$) or (database\$ adj3 search\$) or (bibliographic adj3 search\$) or (electronic adj3 search\$) or (electronic adj3 database\$) or (computeri?ed adj3 search\$) or (internet adj3 search\$)).ab. (193458)</p> <p>17 ((inclusion adj3 studies) or inclusion criteria or selection criteria or predefined criteria or predetermined criteria or (assess\$ adj3 (quality or validity)) or (select\$ adj3 (study or studies)) or (data adj3 extract\$) or extracted data or (data adj2 abstracted)).ab. (234850)</p> <p>18 ((data adj3 abstraction) or published intervention\$ or ((study or studies) adj2 evaluat\$) or (intervention\$ adj2 evaluat\$) or confidence interval\$ or heterogeneity or pooled or pooling or odds ratio\$ or (Jadad or coding) or evidence-based).ab. (968943)</p> <p>19 10 or 11 or 12 or 13 or 14 or 15 (300086)</p> <p>20 16 or 17 or 18 (1254289)</p> <p>21 review.pt. (2128381)</p> <p>22 20 and 21 (152661)</p> <p>23 review.ti. (359123)</p> <p>24 20 and 23 (79964)</p>		
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	<p>25 (review\$ adj10 (papers or trials or trial data or studies or evidence or intervention\$ or evaluation\$ or outcome\$ or findings)).ab,ti. (353753)</p> <p>26 (retriev\$ adj10 (papers or trials or studies or evidence or intervention\$ or evaluation\$ or outcome\$ or findings)).ab,ti. (17614)</p> <p>27 19 or 22 or 24 or 25 or 26 (638800)</p> <p>28 (letter or editorial).pt. (1423975)</p> <p>29 27 not 28 (630531)</p> <p>30 exp animal/ (21123553)</p> <p>31 nonhuman/ (4685261)</p> <p>32 30 or 31 (22463965)</p> <p>33 human/ (16585198)</p> <p>34 32 not 33 (5878767)</p> <p>35 29 not 34 (602835)</p> <p>36 ("cochrane database of systematic reviews\$" or "the cochrane database of systematic reviews").jn. (12505)</p> <p>37 35 not 36 (591452)</p> <p>38 conference abstract.pt. (2145768)</p> <p>39 37 not 38 (515155)</p> <p>40 9 and 39 (60)</p>		
PsycINFO/CINAHL	<p>1 exp Group Psychotherapy/ (20705)</p> <p>2 exp Group Intervention/ (1396)</p>	19	

	<p>3 (group adj2 therap\$).ab,ti. (14485)</p> <p>4 (group adj2 intervention\$).ab,ti. (11227)</p> <p>5 1 or 2 or 3 or 4 (36972)</p> <p>6 *Bipolar Disorder/ (19345)</p> <p>7 (bipolar\$ or bi-polar\$ or manic\$ or mania\$ or hypomanic).ab,ti. (41718)</p> <p>8 (bipolar\$ or bi-polar\$ or manic\$ or mania\$ or hypomani\$).ab,ti. (42211)</p> <p>9 6 or 7 or 8 (42583)</p> <p>10 5 and 9 (310)</p> <p>11 (Cochrane\$ or review or overview or (review adj2 literature) or (synthes\$ adj3 (literature\$ or research or studies or data))).ti. (134815)</p> <p>12 (meta analysis or literature review or systematic review).md. (128660)</p> <p>13 (pooled analys\$ or ((data adj2 pool\$) and studies) or ((hand or manual\$ or database\$ or computer\$ or electronic\$) adj2 search\$) or ((electronic\$ or bibliographic\$) adj2 (database\$ or data base\$))).ab,ti. (9552)</p> <p>14 exp Meta Analysis/ (3781)</p> <p>15 11 or 12 or 13 or 14 (233322)</p> <p>16 (comment reply or editorial or letter or review book or review media).dt. (279749)</p> <p>17 (electronic collection or dissertation abstract or encyclopedia).pt. (450395)</p> <p>18 (rat or rats or mouse or mice or hamster or hamsters or animal or animals or dog or dogs or cat or cats or bovine or sheep).ab,sh,ti. (284297)</p> <p>19 16 or 17 or 18 (949015)</p> <p>20 15 not 19 (140797)</p>		
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	21 10 and 20 (19)		
<i>Primary Studies</i>			
MEDLINE	<p>1 Psychotherapy, Group/ (12565)</p> <p>2 (group adj2 therap\$.ab,ti. (15803)</p> <p>3 (group adj2 intervention\$.ab,ti. (22031)</p> <p>4 1 or 2 or 3 (46175)</p> <p>5 Mood Disorders/ or Bipolar Disorder/ (44191)</p> <p>6 (biploar\$ or bi-polar\$ or manic\$ or mania\$.ab,ti. (15954)</p> <p>7 hypomani\$.ab,ti. (2293)</p> <p>8 5 or 6 or 7 (49743)</p> <p>9 4 and 8 (317)</p> <p>10 "randomized controlled trial".pt. (406964)</p> <p>11 (random\$ or placebo\$ or single blind\$ or double blind\$ or triple blind\$.ti,ab. (889522)</p> <p>12 (retraction of publication or retracted publication).pt. (8520)</p> <p>13 10 or 11 or 12 (983010)</p> <p>14 (animals not humans).sh. (4154861)</p> <p>15 ((comment or editorial or meta-analysis or practice-guideline or review or letter or journal correspondence) not "randomized controlled trial").pt. (3531362)</p> <p>16 (random sampl\$ or random digit\$ or random effect\$ or random survey or random regression).ti,ab. not "randomized controlled trial".pt. (56432)</p> <p>17 13 not (14 or 15 or 16) (729430)</p>	107	

	18 9 and 17 (107)		
EMBASE	<p>1 (group adj2 therap\$.ti,ab. (23553)</p> <p>2 (group adj2 intervention\$.ti,ab. (30729)</p> <p>3 group therapy/ (19004)</p> <p>4 1 or 2 or 3 (66654)</p> <p>5 *bipolar disorder/th [Therapy] (1707)</p> <p>6 *mood disorder/th [Therapy] (736)</p> <p>7 (bipolar\$ or bi-polar\$ or manic\$ or mania\$ or hypomani\$.ti,ab. (80856)</p> <p>8 5 or 6 or 7 (81755)</p> <p>9 4 and 8 (482)</p> <p>10 (random\$ or placebo\$ or single blind\$ or double blind\$ or triple blind\$.ti,ab. (1166780)</p> <p>11 RETRACTED ARTICLE/ (7912)</p> <p>12 10 or 11 (1174495)</p> <p>13 (animal\$ not human\$.sh,hw. (3981623)</p> <p>14 (book or conference paper or editorial or letter or review).pt. not exp randomized controlled trial/ (4308067)</p> <p>15 (random sampl\$ or random digit\$ or random effect\$ or random survey or random regression).ti,ab. not exp randomized controlled trial/ (69329)</p> <p>16 12 not (13 or 14 or 15) (905365)</p> <p>17 9 and 16 (175)</p>	175	

PsycINFO/CINAHL	<p>1 exp Group Psychotherapy/ (20705)</p> <p>2 exp Group Intervention/ (1396)</p> <p>3 (group adj2 therap\$).ab,ti. (14485)</p> <p>4 (group adj2 intervention\$).ab,ti. (11227)</p> <p>5 1 or 2 or 3 or 4 (36972)</p> <p>6 *Bipolar Disorder/ (19345)</p> <p>7 (bipolar\$ or bi-polar\$ or manic\$ or mania\$ or hypomanic).ab,ti. (41718)</p> <p>8 (bipolar\$ or bi-polar\$ or manic\$ or mania\$ or hypomani\$).ab,ti. (42211)</p> <p>9 6 or 7 or 8 (42583)</p> <p>10 5 and 9 (310)</p> <p>11 (random\$ or placebo\$ or single blind\$ or double blind\$ or triple blind\$).ti,ab. (173018)</p> <p>12 (animals not humans).sh. (6268)</p> <p>13 exp Clinical Trials/ (9354)</p> <p>14 random*.mp. (151622)</p> <p>15 13 not 14 (4019)</p> <p>16 11 not (12 or 15) (172407)</p> <p>17 10 and 16 (80)</p>	80	
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