

## PRIORITY BRIEFING

The purpose of this briefing paper is to aid Stakeholders in prioritising topics to be taken further by PenCLAHRC as the basis for a specific evaluation or implementation research project. This paper was compiled in 2-3 days.

### **How can we best meet the needs of individuals with Bipolar Disorder who are referred to Improving Access to Psychological Therapies (IAPT) services?**

#### **Question ID: 8**

**Question type:** Implementation

**Question:** How can we best meet the needs of individuals with bipolar disorder who are referred to Improving Access to Psychological Therapies (IAPT) services?

**Current problem:** The IAPT programme does not specifically seek to treat bipolar depression. However, given that bipolar and unipolar depression have similar presentations, and that several studies suggest that at least one fifth of individuals who present with depression will meet criteria for bipolar disorder on closer assessment, it seems likely that a substantial minority of individuals referred to IAPT because of depressive symptoms will be those with bipolar depression. This will have implications for treatment in the IAPT setting, as some aspects of management for bipolar depression differ from that of unipolar depression. The effectiveness of the interventions for unipolar depression has not been assessed in individuals with bipolar disorder in the IAPT setting. At the same time, psychological therapies for bipolar depression are not currently available within IAPT services.

At present, we do not know:

1. The proportion of individuals referred to IAPT who would meet lifetime diagnostic criteria for bipolar disorder.
2. Whether treatment for depression provided by IAPT offers similar benefits to individuals with bipolar depression as it does to individuals with unipolar depression.
3. Whether we can provide more effective interventions for individuals with bipolar disorder within the constraints of the IAPT framework.

**Service and setting:** IAPT is a nationwide initiative, piloted in 2006 and rolled out incrementally nation-wide since 2007, aimed at increasing population access to psychological services within primary care. In this programme, relatively brief, evidence-based psychological therapies are delivered to individuals with mild to moderate depression or anxiety. These are delivered by IAPT therapists in various primary care settings. The majority of referrals are from general practitioners, but may be from other sources, including self-referral. Therapists are purpose-trained and deliver therapies at two levels of intensity. Low intensity therapies, such as guided self-help and brief behavioural activation therapy, are designed to incur relatively low therapist burden in terms of time commitment,

and training and costs per therapist are relatively low. Low intensity therapies are provided by a new category of therapists called 'Psychological Wellbeing Practitioners'. High intensity therapies, primarily cognitive behavioural therapy, incur a relatively high burden in terms of therapist time and training cost.

**Population:** Those individuals referred to IAPT services who are likely to meet lifetime diagnostic criteria for bipolar type I or bipolar type II disorder.

**Proposed solution:**

Stage 1. Determine the proportion of individuals assessed by IAPT services who suffer from bipolar disorder, by adding a stem screening question and follow-up questions (such as by using the 'Structured Clinical Interview for DSM (Diagnostic and Statistical Manual of Mental Disorders) disorders' (SCID) framework, or by using other validated questionnaires) to the standard IAPT assessment interview.

Stage 2. Determine whether outcomes for individuals with bipolar disorder who enter IAPT services are comparable with outcomes for individuals with unipolar depression.

Stage 3. Dependent upon the findings of the previous two stages, investigate whether therapy tailored to address bipolar depression may result in superior outcomes to standard therapy for depression as delivered within IAPT services.

**Outcome:**

During Stage 1. The proportion of individuals assessed by IAPT who screen positive for a likely diagnosis of bipolar type I or bipolar type II disorder.

During Stage 2. The level of change in depressive symptoms in individuals with and without a positive screen for bipolar disorder (and receiving therapy for depression) pre to post intervention (main outcome), as well as the change in other variables routinely collected (e.g. anxiety symptom levels, work and social adjustment, and employment status), and in variables pertaining to the client's care pathway (i.e. number of individuals offered high/low intensity intervention, attendance rates, and completion rates).

During Stage 3: As in stage 2, but now individuals with bipolar disorder receiving a tailored version of psychological therapy for bipolar disorder would be compared with individuals with bipolar disorder receiving standard treatment within IAPT.

\*Please note that the details included in the box are from the original submission and have been edited where necessary for clarity and precision

**Bipolar disorder** is a mood disorder characterised by repeated periods of variable levels of both depressed mood and elated mood, interspersed with periods of more or less full recovery. It is often divided into two types; type I (mania - elated activity and mood - with or without depression) and type II (hypomania – a less severe type of mania - with depression). The diagnosis is made independently from the presence or absence of psychotic episodes. Bipolar disorder can be associated with significant

impairment of personal and social functioning. The peak age of onset is in late adolescence or early adult life, with a further small increase in incidence in mid to late life. Bipolar disorder can be managed via medication and/or psychological therapies depending on severity.

### **The Health Problem:**

The NICE guideline on the management of bipolar disorder (2006) reports that the lifetime prevalence of bipolar disorder is approximately 1%. The evidence suggests that the mean age of onset is between 18 and 30 years, that bipolar type I has a roughly equal gender distribution, that type II probably has a female dominance and that the prevalence of bipolar disorder is higher among ethnic minority groups and in those with learning difficulties.

The social burden imposed by bipolar disorder is considerable; it is reported that amongst individuals with bipolar disorder the suicide rate has been conservatively estimated at nine times that of the general UK population. The same NICE guideline also suggests that bipolar disorder is associated with a considerable economic burden, estimated in 2002 at £2 billion annually in the UK.

Most individuals with bipolar disorder reside in the community and are therefore under the care of a general practitioner. Whilst individuals with bipolar disorder may also be treated within secondary or tertiary care, in between episodes, care is provided within primary care. In addition, many individuals with bipolar disorder seen within primary care may not have been diagnosed with the condition. Currently, IAPT services do not select out individuals with bipolar disorder, nor do they ask referrers to do so. Therefore it is likely that of those individuals referred to IAPT with current depression, a significant proportion would meet criteria for bipolar disorder.

As for information on the South West, data from the South West SHA collected between Sept 2008 and the end of March 2011 reveal that there are a total of 613,546 people diagnosed with depression / anxiety disorders (in a population of just over 5 million).

With regards to the impact or performance of IAPT throughout the UK (between October 2008 and December 2010) and the South West (from roll out of IAPT in the South West in 2008, to April 2011), IAPT services have provided the following:

- 147 of the 151 Primary Care Trusts in England have a service from this programme in at least part of their area and about 60 per cent of the adult population has access. In the South West SHA, all 14 PCTs offer IAPT.
- 3,660 new cognitive behavioural therapy workers have been trained. In the South West there are currently 360 therapists and 159 new therapists being trained.
- 491,000 people started treatment, 282,000 completed it. As for the South West, 161,897 people have been referred for psychological therapies; 92,084 have started psychological therapies and 48,882 have completed the course of therapies.
- 95,000 people moved to recovery and 18,200 came off sick pay or benefits. In the South West, 17,174 have completed therapies and 3002 people were able to come off sick pay or benefits.

## **Guidelines:**

The NICE guideline on the management of bipolar disorders, published in 2006, recommends clear protocols for the delivery and monitoring of psychosocial and psychological interventions of individuals with bipolar disorder in primary as well as secondary care. It recommends the use of cognitive behavioural therapy (CBT) as one of the treatments for those patients with chronic and recurrent depressive symptoms (including after an acute (on chronic) episode). The guideline recommends that CBT is to be given with prophylactic medication. The guideline also recommends CBT for those patients who are pregnant, if pharmacotherapy can be minimized or avoided.

SIGN (Scottish Intercollegiate Guidelines Network, 2005) recommends CBT as one of the psychosocial maintenance treatments for the management of (chronic) bipolar disorder, and the British Association for Psychopharmacology recommends the use of CBT for acute episodes as an adjunct to pharmacotherapy to shorten the episode. These documents report a low level of evidence for CBT for relapse prevention.

The New Horizons cross-government strategy (Department of Health, 2009) places emphasis on developing mental health services that are accessible, integrated and safe. At present, the extent to which IAPT services are, or should be, made accessible to people with bipolar disorder is not clear.

There is no national guidance available to those delivering IAPT services regarding how these services can be delivered to individuals with bipolar disorder in a safe and integrated manner.

## **NHS Priority:**

### **Regional**

#### **SW SHA Priorities framework 2008-11**

Depression in general is reflected in the framework under the aims of

- i) 'staying healthy' - reducing suicide rates
- ii) 'mental health and well-being'
  - a. adults with mild to moderate depression and anxiety to have access to psychological therapies in every PCT,
  - b. for those with serious mental illness who are discharged to primary care to have a named worker in primary care to ensure rapid response and access to support.

Addressing this question would enhance local ability to provide care pathways that accord with best practice, in that the proposed development would facilitate people with bipolar disorder in accessing appropriate care, attaining earlier intervention, receiving skilled assessment and accessing evidence based treatment.

Depression is also included as a focus of action in delivering the QIPP agenda.

## Local

All Peninsula PCTs have mental health high on their lists of priorities. Plymouth and Cornwall PCTs also have reducing suicide as a key priority.

### Existing Research:

#### Published research

The searches we conducted did not identify any evidence regarding the effectiveness of CBT therapies designed for unipolar depression, as are used in IAPT, for the treatment of people with bipolar disorder.

We did however find some information on the effectiveness of CBT specified for bipolar disorder. We are not able to confirm the extent that the CBT regimes implemented as interventions in these studies are similar or not to those currently being provided in the IAPT programme.

A systematic review and meta-analysis by Lynch and colleagues in 2010 pooled the data from four trials and found that, although the results of these trials favour CBT for patients with chronic bipolar disorders on medication, the results were not statistically significant<sup>1</sup>.

The four trials identified in the above systematic review<sup>1</sup>, as well as two other controlled trials of CBT versus treatment as usual or wait-listed controls in bipolar patients, all demonstrated increased functioning, increased adherence to medications, decreased relapses, decreased mood fluctuations, decreased need for medications, and reduced hospitalizations<sup>2,3,4,5,6,7</sup>. These papers however demonstrated some elements of bias (e.g. lack of, or unclear blinding), and as such, the information presented in them need to be interpreted with caution.

There is some evidence from studies with less robust designs that suggest that CBT may help reduce depressive symptoms, improve longer-term outcomes, or improve treatment adherence<sup>8,9,10</sup> in people with bipolar disorder.

Another randomized controlled trial compared pharmacotherapy to pharmacotherapy with a range of adjunct psychotherapies (including CBT) for patients with bipolar disorder. This study found that over one year, treatment with any of the intensive psychotherapies was associated with a higher recovery rate from depression than treatment with pharmacotherapy alone<sup>11</sup>.

#### Ongoing research

We identified four ongoing trials of the effectiveness of CBT in patients with bipolar disorder<sup>12,13,14,15</sup>.

Three of these studies are based in the US and one in the UK. They all include patients with bipolar disorders and investigate the effectiveness of CBT on reducing mania or depressive symptoms. They are reported to be completing at the end of 2011<sup>12,13,15</sup> or have completed data collection in 2011 but have not been published at the present time<sup>14</sup>.

## **Feasibility:**

This question was developed in consultation with senior members of 'MDF: the Bipolar Organisation' (Manic Depression Fellowship). They are a third-sector organisation that represents the interests of people with bipolar disorder. The MDF have expressed considerable enthusiasm for addressing this issue. In addition to consulting upon the proposed work, the MDF have offered to assist with training IAPT workers in how to assess and respond to clients with bipolar disorder (with appropriate remuneration to trainers). It would be helpful to collaborate with MDF on this project.

There is capacity locally to carry out this work. A Senior Lecturer in Clinical Psychology who works within the Mood Disorders Centre (MDC) at the University of Exeter, and specialises in developing psychological therapies for individuals with bipolar disorder, is a part of the question submission team. Within the wider MDC there is a wealth of expertise in the evaluation and improvement of both psychological therapies and health services for individuals with mood disorders.

## **References:**

1. Lynch, D., K. R. Laws and P. J. McKenna (2010). "Cognitive behavioural therapy for major psychiatric disorder: does it really work? A meta-analytical review of well-controlled trials." *Psychol Med* 40(1): 9-24.

**BACKGROUND:** Although cognitive behavioural therapy (CBT) is claimed to be effective in schizophrenia, major depression and bipolar disorder, there have been negative findings in well-conducted studies and meta-analyses have not fully considered the potential influence of blindness or the use of control interventions. **METHOD:** We pooled data from published trials of CBT in schizophrenia, major depression and bipolar disorder that used controls for non-specific effects of intervention. Trials of effectiveness against relapse were also pooled, including those that compared CBT to treatment as usual (TAU). Blinding was examined as a moderating factor. **RESULTS:** CBT was not effective in reducing symptoms in schizophrenia or in preventing relapse. CBT was effective in reducing symptoms in major depression, although the effect size was small, and in reducing relapse. CBT was ineffective in reducing relapse in bipolar disorder. **CONCLUSIONS:** CBT is no better than non-specific control interventions in the treatment of schizophrenia and does not reduce relapse rates. It is effective in major depression but the size of the effect is small in treatment studies. On present evidence CBT is not an effective treatment strategy for prevention of relapse in bipolar disorder.

2. Zaretsky, A., W. Lancee, C. Miller, A. Harris and S. V. Parikh (2008). "Is cognitive-behavioural therapy more effective than psychoeducation in bipolar disorder?" *SO: Canadian journal of psychiatry. Revue canadienne de psychiatrie*(7): 441-448.

**OBJECTIVE:** Psychosocial research in bipolar disorder (BD) has not yet assessed the relative benefits of a short course of psychoeducation (PE), compared with a longer course of cognitive-behavioural therapy (CBT) containing psychoeducational principles. This pilot study evaluated the efficacy and added benefit of adding a course of CBT to a standard course of brief PE, as maintenance therapy for BD.

**METHOD:** Seventy-nine consenting adult men and women with BD on stable medication regimens, who were in full or partial remission from an index episode (BD I = 52; BD II = 27), were randomized to receive either 7 sessions of individual PE, or 7 sessions of PE followed by 13 additional individual sessions of CBT. Weekly mood and medication adherence was rated using the National Institute of Mental Health's Life Chart Method, while psychosocial functioning and mental health use were assessed monthly. **RESULTS:** Forty-six participants completed the entire study. Participants who received CBT in addition to PE experienced 50% fewer days of depressed mood over the course of one year. Participants who received PE alone had more antidepressant increases compared with those who received CBT. There were no group differences in hospitalization rates, medication adherence, psychosocial functioning, or mental health use. **CONCLUSIONS:** Pilot data from this real-world study suggest that even after medication treatment has been optimized, a longer course of adjunctive CBT may offer some additional benefits over a shorter course of PE alone for the maintenance treatment of BD. Larger randomized controlled trials with equal treatment lengths are indicated.

3. Ball, J. R., P. B. Mitchell, J. C. Corry, A. Skillecorn, M. Smith and G. S. Malhi (2006). "A randomized controlled trial of cognitive therapy for bipolar disorder: focus on long-term change." *SO: The Journal of clinical psychiatry*(2): 277-286.

**BACKGROUND:** This study reports the outcome of a randomized controlled trial of cognitive therapy (CT) for bipolar disorder. The treatment protocol differed from other published forms of CT for bipolar disorder through the addition of emotive techniques. **METHOD:** Fifty-two patients with DSM-IV bipolar I or II disorder were randomly allocated to a 6-month trial of either CT or treatment as usual, with both treatment groups also receiving mood stabilizers. Outcome measures included relapse rates, dysfunctional attitudes, psychosocial functioning, hopelessness, self-control, and medication adherence. Patients were assessed during treatment by independent raters blind to the patients' group status. **RESULTS:** At posttreatment, patients allocated to CT had experienced less severe depression scores (Beck Depression Inventory and Montgomery-Asberg Depression Rating Scale) and less dysfunctional attitudes. After controlling for the presence of major depressive episode at baseline, there was a statistical trend toward a greater time to depressive relapse ( $p=.06$ ) for the CT group. At 12-month follow-up, the CT group showed a trend toward lower Young Mania Rating Scale scores and improved behavioral self-control. The Clinical Global Impressions-Improvement scale, comparing the 18 months prior to treatment to the severity of illness status at follow-up, showed a substantial difference between groups in favor of CT. **CONCLUSION:** Our findings corroborate previous bipolar disorder research in demonstrating the value of CT, particularly immediately post-treatment, and indicate some continuation (albeit diminishing) of benefits in the succeeding 12 months. These findings suggest that psychological booster sessions may be crucial for maintaining the beneficial effects of cognitive therapy.

4. Scott, J., E. Paykel, R. Morriss, R. Bentall, P. Kinderman, T. Johnson, R. Abbott and H. Hayhurst (2006). "Cognitive-behavioural therapy for severe and recurrent bipolar disorders: randomised controlled trial." *SO: The British journal of psychiatry : the journal of mental science*: 313-320.

**BACKGROUND:** Efficacy trials suggest that structured psychological therapies may

significantly reduce recurrence rates of major mood episodes in individuals with bipolar disorders. AIMS: To compare the effectiveness of treatment as usual with an additional 22 sessions of cognitive-behavioural therapy (CBT). METHOD: We undertook a multicentre, pragmatic, randomised controlled treatment trial (n=253). Patients were assessed every 8 weeks for 18 months. RESULTS: More than half of the patients had a recurrence by 18 months, with no significant differences between groups (hazard ratio=1.05; 95% CI 0.74-1.50). Post hoc analysis demonstrated a significant interaction (P=0.04) such that adjunctive CBT was significantly more effective than treatment as usual in those with fewer than 12 previous episodes, but less effective in those with more episodes. CONCLUSIONS: People with bipolar disorder and comparatively fewer previous mood episodes may benefit from CBT. However, such cases form the minority of those receiving mental healthcare.

5. Lam, D., E. Watkins, P. Hayward, J. Bright, K. Wright, N. Kerr, G. Parr Davis and P. Sham (2003). "A randomized controlled study of cognitive therapy for relapse prevention for bipolar affective disorder: outcome of the first year." SO: Archives of general psychiatry(2): 145-152.

BACKGROUND: Despite the use of mood stabilizers, a significant proportion of patients with bipolar affective disorder experience frequent relapses. A pilot study of cognitive therapy (CT) specifically designed to prevent relapses for bipolar affective disorder showed encouraging results when used in conjunction with mood stabilizers. This article reports the outcome of a randomized controlled study of CT to help prevent relapses and promote social functioning. METHODS: We randomized 103 patients with bipolar 1 disorder according to the DSM-IV, who experienced frequent relapses despite the prescription of commonly used mood stabilizers, into a CT group or control group. Both the control and CT groups received mood stabilizers and regular psychiatric follow-up. In addition, the CT group received an average of 14 sessions of CT during the first 6 months and 2 booster sessions in the second 6 months. RESULTS: During the 12-month period, the CT group had significantly fewer bipolar episodes, days in a bipolar episode, and number of admissions for this type of episode. The CT group also had significantly higher social functioning. During these 12 months, the CT group showed less mood symptoms on the monthly mood questionnaires. Furthermore, there was significantly less fluctuation in manic symptoms in the CT group. The CT group also coped better with manic prodromes at 12 months. CONCLUSION: Our findings support the conclusion that CT specifically designed for relapse prevention in bipolar affective disorder is a useful tool in conjunction with mood stabilizers.

6. Scott, J., A. Garland and S. Moorhead (2001). "A pilot study of cognitive therapy in bipolar disorders." Psychological Medicine, 2001, , 31: 459-467.

Background. The efficacy and effectiveness of cognitive therapy (CT) is well established for unipolar disorders, but little is known about its utility in bipolar disorders. This study aimed to explore the feasibility and efficacy of using CT as an adjunct to usual psychiatric treatment in this patient population. Method. Subjects referred by general adult psychiatrists were assessed by an independent rater and then randomly allocated to immediate CT (N=21) or 6-month waiting-list control, which was then followed by CT (N=21). Observer and self-ratings of symptoms and functioning were undertaken immediately prior to CT, after a 6-month course of CT and a further 6-months later. Data on relapse and hospitalization rates in the 18

months before and after commencing CT were also collected. Results. At 6-month follow-up, subjects allocated to CT showed statistically significantly greater improvements in symptoms and functioning as measured on the Beck Depression Inventory, the Internal State Scale, and the Global Assessment of Functioning than those in the waiting-list control group. In the 29 patients who eventually received CT, relapse rates in the 18 months after commencing CT showed a 60% reduction in comparison with the 18 months prior to commencing CT. Seventy per cent of subjects who commenced therapy viewed CT as highly acceptable. Conclusion. Although the results of this study are encouraging, the use of CT in subjects with bipolar disorders is more complex than in unipolar disorders and requires a high level of therapist expertise. The therapy may prove to be particularly useful in the treatment of bipolar depression

7. Lam, D. H., J. Bright, S. Jones, P. Hayward, N. Schuck, D. Chisholm and P. Sham (2000). Cognitive therapy for bipolar illness : a pilot study of relapse prevention. *Cognitive Therapy Research*. 24: 503-520.

Background. Although cognitive behavioural therapy (CBT) is claimed to be effective in schizophrenia, major depression and bipolar disorder, there have been negative findings in well-conducted studies and meta-analyses have not fully considered the potential influence of blindness or the use of control interventions. Method. We pooled data from published trials of CBT in schizophrenia, major depression and bipolar disorder that used controls for non-specific effects of intervention. Trials of effectiveness against relapse were also pooled, including those that compared CBT to treatment as usual (TAU). Blinding was examined as a moderating factor. Results. CBT was not effective in reducing symptoms in schizophrenia or in preventing relapse. CBT was effective in reducing symptoms in major depression, although the effect size was small, and in reducing relapse. CBT was ineffective in reducing relapse in bipolar disorder. Conclusions. CBT is no better than non-specific control interventions in the treatment of schizophrenia and does not reduce relapse rates. It is effective in major depression but the size of the effect is small in treatment studies. On present evidence CBT is not an effective treatment strategy for prevention of relapse in bipolar disorder.

8. Fava, G., G. Bartolucci, C. Rafanelli and L. Mangelli (2001). Cognitive-behavioral management of patients with bipolar disorder who relapsed while on lithium prophylaxis. *J Clin Psychiatry*. 62: 556-559.
9. Zaretsky, A., Z. Segal and M. Gemar (1999). Cognitive therapy for bipolar depression: a pilot study. *Can J Psychiatry*. 44: 491-494.
10. Cochran, S. (1984). Preventing medical noncompliance in the outpatient treatment of bipolar affective disorders. *Journal of Consulting and Clinical Psychology*. 52: 873-878.
11. Miklowitz, D. J., M. W. Otto, E. Frank, N. A. Reilly Harrington, S. R. Wisniewski, J. N. Kogan, A. A. Nierenberg, J. R. Calabrese, L. B. Marangell, L. Gyulai, M. Araga, J. M. Gonzalez, E. R. Shirley, M. E. Thase and G. S. Sachs (2007). "Psychosocial treatments for bipolar depression: a 1-year randomized trial from the Systematic Treatment Enhancement Program." *SO: Archives of general*

psychiatry(4): 419-426.

**CONTEXT:** Psychosocial interventions have been shown to enhance pharmacotherapy outcomes in bipolar disorder. **OBJECTIVE:** To examine the benefits of 4 disorder-specific psychotherapies in conjunction with pharmacotherapy on time to recovery and the likelihood of remaining well after an episode of bipolar depression. **DESIGN:** Randomized controlled trial. **SETTING:** Fifteen clinics affiliated with the Systematic Treatment Enhancement Program for Bipolar Disorder. Patients A total of 293 referred outpatients with bipolar I or II disorder and depression treated with protocol pharmacotherapy were randomly assigned to intensive psychotherapy (n = 163) or collaborative care (n = 130), a brief psychoeducational intervention. **INTERVENTIONS:** Intensive psychotherapy was given weekly and biweekly for up to 30 sessions in 9 months according to protocols for family-focused therapy, interpersonal and social rhythm therapy, and cognitive behavior therapy. Collaborative care consisted of 3 sessions in 6 weeks. **MAIN OUTCOME MEASURES:** Outcome assessments were performed by psychiatrists at each pharmacotherapy visit. Primary outcomes included time to recovery and the proportion of patients classified as well during each of 12 study months. **RESULTS:** All analyses were by intention to treat. Rates of attrition did not differ across the intensive psychotherapy (35.6%) and collaborative care (30.8%) conditions. Patients receiving intensive psychotherapy had significantly higher year-end recovery rates (64.4% vs 51.5%) and shorter times to recovery than patients in collaborative care (hazard ratio, 1.47; 95% confidence interval, 1.08-2.00; P = .01). Patients in intensive psychotherapy were 1.58 times (95% confidence interval, 1.17-2.13) more likely to be clinically well during any study month than those in collaborative care (P = .003). No statistically significant differences were observed in the outcomes of the 3 intensive psychotherapies. **CONCLUSIONS:** Intensive psychosocial treatment as an adjunct to pharmacotherapy was more beneficial than brief treatment in enhancing stabilization from bipolar depression. Future studies should compare the cost-effectiveness of models of psychotherapy for bipolar disorder. **TRIAL REGISTRATION:** clinicaltrials.gov Identifier: NCT00012558.

12. Kirk, J. and A. Gumley (2011). Bipolar Intervention Study: Cognitive Interpersonal Therapy (BISCIT). University of Glasgow NCT01315028. from <http://clinicaltrials.gov/ct2/show/NCT01315028?term=bipolar&intr=cognitive+behavioural+therapy&rank=8>.
13. Deckersbach, T. (2010). Mindfulness-Based Cognitive Behavior Therapy for Bipolar Disorder (MBCT). Massachusetts General Hospital, USA. NCT01126827. from <http://www.clinicaltrials.gov/ct2/show/NCT01126827?term=bipolar+and+CBT&rank=4>.
14. Henin, A., D. Hirshfeld-Becker, J. Biederman, E. Mick and S. Safren (2010). Cognitive-Behavior Therapy for Young Adults With Bipolar Disorder. National Institute of Mental Health (NIMH, USA). NCT01176825. from <http://clinicaltrials.gov/ct2/show/NCT01176825?term=bipolar&intr=cognitive+behavioural+therapy&rank=5>.
15. Deckersbach, T. (2009). Effectiveness of Cognitive Behavioral Therapy for Treating Depression in People With Bipolar I Disorder. National Institute of

Mental Health (NIMH, USA). NCT00595387. from <http://clinicaltrials.gov/ct2/show/NCT00595387?term=bipolar&intr=cognitive+behavioural+therapy&rank=1>.