National Institute for Health and Care Excellence

4-year surveillance (2017) – Bipolar disorder (2014) NICE guideline CG185

Appendix B: stakeholder consultation comments table

Consultation dates: 10 to 24 August 2017

Do you agree with the proposal not to update the guideline?

Stakeholder	Overall response	Comments	NICE response
Association for Cognitive Analytic Therapy (ACAT)	No	There is a new published pilot RCT of CAT in Bipolar Disorder that does not appear to have been referenced by NICE. It supports a new research recommendation looking at the clinical and cost effectiveness of CAT in the treatment of adults with bipolar disorder. Evans M et al (2016) Cognitive Analytic Therapy for Bipolar Disorder: A Pilot Randomized Controlled Trial. Clinical Psychology and Psychotherapy. DOI: 10.1002/cpp.2065	Thank you for your comments. The study by Evans et al. (2016) was identified by the 2017 surveillance review and was not included as there is insufficient data in the abstract to draw conclusions from the results. The process to determine whether a study is included in the surveillance review only considers evidence at the abstract level.
Cheshire and Wirral Partnership NHS Foundation Trust	Yes	No comment	Thank you for your response.
British HIV Association (BHIVA)	No	Please see comments below on areas excluded.	Thank you for your comments. Please see below for the NICE response.
Royal College of Nursing (RCN)	Yes	The RCN has no adverse comments	Thank you for your response.
British Association for Psychopharmacology	No	We have a number of concerns regarding the CG 185 Guideline, specifically in regard to psychological therapies for Bipolar disorder. There are conceptual, methodological and factual errors throughout the document.	Thank you for your comments. During the development of the guideline, the committee discussed the evidence base for psychological interventions in relation to bipolar depression. It was acknowledged that there was insufficient evidence to conclude that unipolar depression and bipolar depression were distinct. It was

		Whilst the general guideline acknowledges “bipolar depression”, for some reason Section 1.2.5 states people should be offered “ a psychological intervention that has been developed specifically for bipolar disorder and has a published evidence-based manual describing how it should be delivered **or** a high-intensity psychological intervention (cognitive behavioural therapy, interpersonal therapy or behavioural couples therapy) in line with recommendations 1.5.3.1–1.5.3.5 in the NICE clinical guideline on depression.” Given that bipolar depression is acknowledged as a different entity, it is difficult to understand why the option “or” should be given to therapies have no clear evidence base for improvement of bipolar depression. An example is CBT, where two of the NICE (single trial) meta-analyses show a beneficial effect-for active control, as opposed to CBT. We are unaware why couples therapy should be viewed on a par with other psychological treatments for bipolar depression. There is a factual error regarding the relapse prevention meta-analysis, which has been raised in print by Jauhar et al (1). The meta-analysis conducted includes four trials, showing a benefit for CBT in relapse prevention. In the NICE meta-analysis the largest trial of CBT. In relapse prevention (2) is excluded. It was stated by the NICE committee (3) that this study included patients currently not euthymic at entry to trial. There is a clear factual error in the NICE/NCCMH search strategy here. Another study included in the NICE meta-analysis (4) included explicitly depressed patients (4), another two did not explicitly state whether participants were euthymic at study entry (5,6). Inclusion of the Scott study significantly affects the results of the NICE meta-analysis (1). On reading through the evidence on psychological therapies, the quality of included trials measuring outcome post-treatment is poor-most included trials are rated low or very low quality, though this is not acknowledged within the guideline. Finally, there are methodological concern relating to the conduct of the meta-analyses, and reporting of findings. Multiple analyses took place throughout the NICE meta-analysis-almost 200 comparisons are conducted from 50 studies, a number of which include only one trial. There is no multiple comparison testing. Furthermore, from the composite met-analyses of combined psychotherapies, it is not clear why the guideline reports positive findings as evidence supporting	determined that recommendations could be extrapolated across guidelines. It was also determined of importance that recommendation 1.6.2 is included which advises that psychological therapists working with bipolar depression should have training in, and experience of, working with people with bipolar disorder. Although the evidence base was of poor quality, it was also recognised that relapse prevention and recovery are important, and endeavoured to capture this in the guideline as far as the evidence would allow. To this end, section 1.9 in the recommendations was included to provide a focus in these areas. In regards to methodological or factual errors within the meta-analysis conducted during the development of the guideline, all NICE guidelines undergo a quality assurance process during their development to identify and rectify potential errors. During the 2014 update of NICE guideline CG185, the committee discussed the evidence contained within the meta-analysis and reached a consensus agreement to take into account the totality of evidence when developing the recommendations.

		guidance, whilst ignoring negative results of other composite analyses. **References** 1. Jauhar S, McKenna PJ, Laws KR. NICE guidance on psychological treatments for bipolar disorder: searching for the evidence. Lancet Psychiatry. 2016;3(4):386–388. 2. Scott J, Paykel E, Morriss R, Bentall R, Kinderman P, Johnson T, et al. Cognitive–behavioural therapy for severe and recurrent bipolar disorders. Br J Psychiatry. 2006 Apr 1;188(4):313–20. 3. Kendall T, Morriss R, Mayo-Wilson E, Meyer TD, Jones SH, Oud M, et al. NICE guidance on psychological treatments for bipolar disorder. Lancet Psychiatry. 2016 Apr 1;3(4):317–20. 4. Ball JR, Mitchell PB, Corry JC, Skillecorn A, Smith M, Malhi GS. A randomized controlled trial of cognitive therapy for bipolar disorder: focus on long-term change. J Clin Psychiatry. 2006 Feb;67(2):277–86. 5. Cochran SD. Preventing medical noncompliance in the outpatient treatment of bipolar affective disorders. J Consult Clin Psychol. 1984;52(5):873–8. 6. Perry A, Tarrier N, Morriss R, McCarthy E, Limb K. Randomised controlled trial of efficacy of teaching patients with bipolar disorder to identify early symptoms of relapse and obtain treatment. BMJ. 1999 Jan 16;318(7177):149–53.	
Royal College of Paediatrics and Child Health	Yes	It appears that updating would be best deferred until outcome of several current studies is known.	Thank you for your comments. The ongoing studies will be monitored and considered at the next surveillance review when results publish.

Do you agree with the proposal to remove the research recommendation: RR-01

What is the clinical and cost effectiveness of structured psychological interventions for young people with bipolar depression?

Stakeholder	Overall response	Comments	NICE response

Association for Cognitive Analytic Therapy (ACAT)	Yes	No comment	Thank you for your response.
Cheshire and Wirral Partnership NHS Foundation Trust	Yes	No comment	Thank you for your response.
British HIV Association (BHIVA)	No response	No comment	Thank you for your response.
Royal College of Nursing (RCN)	No	No comment	Thank you for your response.
British Association for Psychopharmacology	Yes	No comment	Thank you for your response.
Royal College of Paediatrics and Child Health	No	Research in this area is ongoing and the studies are listed as being expected to inform the next guideline update. It would therefore seem counter intuitive to remove this recommendation.	Thank you for your comments. No new evidence relevant to the research recommendation was found and no ongoing studies were identified. It was determined that due to a lack of research activity in this area, the research recommendation will be removed.

Do you agree with the proposal to remove the research recommendation: RR-03

What is the clinical and cost effectiveness of fluoxetine combined with olanzapine versus an alternative selective serotonin reuptake inhibitor (SSRI) combined with olanzapine in the treatment of moderate to severe bipolar depression?

Stakeholder	Overall response	Comments	NICE response
Association for Cognitive Analytic Therapy (ACAT)	Yes	No comment	Thank you for your response.
Cheshire and Wirral Partnership NHS Foundation Trust	Yes	No comment	Thank you for your response.

British HIV Association (BHIVA)	No response	No comment	Thank you for your response.
Royal College of Nursing (RCN)	Yes	If this gap has been identified as addressed	Thank you for your comments. No new evidence relevant to the research recommendation was found and no ongoing studies were identified. It was determined that due to a lack of research activity in this area, the research recommendation will be removed.
British Association for Psychopharmacology	Yes	No comment	Thank you for your response.
Royal College of Paediatrics and Child Health	No response	No comment	Thank you for your response.

Do you agree with the proposal to remove the research recommendation: RR-04

What is the clinical and cost effectiveness of a specialised collaborative care service for people admitted to hospital with bipolar disorder compared with usual treatment delivered by generic care services?

Stakeholder	Overall response	Comments	NICE response
Association for Cognitive Analytic Therapy (ACAT)	Yes	No comment	Thank you for your response.
Cheshire and Wirral Partnership NHS Foundation Trust	Yes	No comment	Thank you for your response.
British HIV Association (BHIVA)	No response	No comment	Thank you for your response.
Royal College of Nursing (RCN)	Yes	If this gap has been identified as addressed	Thank you for your comments. No new evidence relevant to the research recommendation was found and no ongoing studies were identified. It was determined that due to a lack of research activity in this area, the research recommendation will be removed.

British Association for Psychopharmacology	No	This seems to us to be an important recommendation to keep in. Since the implication is that this question has been answered, in what sense is this so?	Thank you for your comments. No new evidence relevant to the research recommendation was found and no ongoing studies were identified. It was determined that due to a lack of research activity in this area, the research recommendation will be removed.
Royal College of Paediatrics and Child Health	No response	No comment	Thank you for your response.

Do you agree with the proposal to remove the research recommendation: RR-05

What is the clinical and cost effectiveness of face-to-face cognitive behavioural therapy (CBT) compared with internet-facilitated CBT in the long-term management of bipolar disorder?

Stakeholder	Overall response	Comments	NICE response
Association for Cognitive Analytic Therapy (ACAT)	Yes	No comment	Thank you for your response.
Cheshire and Wirral Partnership NHS Foundation Trust	Yes	No comment	Thank you for your response.
British HIV Association (BHIVA)	No response	No comment	Thank you for your response.
Royal College of Nursing (RCN)	Yes	If this gap has been identified as addressed	Thank you for your comments. No new evidence relevant to the research recommendation was found and no ongoing studies were identified. It was determined that due to a lack of research activity in this area, the research recommendation will be removed.
British Association for Psychopharmacology	Yes	No comment	Thank you for your response.
Royal College of Paediatrics and Child Health	No response	No comment	Thank you for your response.

Do you have any comments on areas excluded from the scope of the guideline?

Stakeholder	Overall response	Comments	NICE response
Association for Cognitive Analytic Therapy (ACAT)	No	No comment	Thank you for your response.
Cheshire and Wirral Partnership NHS Foundation Trust	Yes	Aripiprazole is now generic and becoming more cost effective option. It would worth reconsidering recommending its use in mania as it would expand the choice for patients, and for its metabolic friendly adverse effect profile. Expecting organisation to provide Bipolar Specialist psychological interventions is not quite realistic and very costly. A generic Cognitive Behavioural Therapy would be reasonable and appropriate.	Thank you for your comments. The evidence identified for aripiprazole provided inconclusive results for its effectiveness in an adult population with bipolar disorder. Aripiprazole is recommended for children and young people to treat mania and is included in a NICE technology appraisal (TA292). Recommendations referring to specialist bipolar services include teams/services which currently exist. The importance is that these services have the necessary skills and training to assess and manage people with bipolar disorder – management may include the use of CBT as a treatment option.
British HIV Association (BHIVA)	Yes	Bipolar disorder is associated with periods of disinhibited behaviour so an HIV test should be offered as opt out. Maniform psychosis can be a feature of late HIV and an HIV test should be offered. Mania and psychosis are described in HIV cognitive impairment	Thank you for your comments. Whilst it is recognised that certain symptoms of bipolar disorder may present in individuals with HIV, no new evidence was found suggesting the benefit of routine HIV testing in this population. A consideration is also given to the resource implication of offering routine HIV testing and whether this is justified without current sufficient evidence. Also, please refer to the published NICE guideline on HIV testing.
Royal College of Nursing (RCN)	No	No comment	Thank you for your response.
British Association for Psychopharmacology	See comments	We have a number of concerns regarding the CG 185 Guideline, specifically in regard to psychological therapies for Bipolar disorder. There are conceptual, methodological and factual errors throughout the document. Whilst the general guideline acknowledges “bipolar depression”, for some reason Section 1.2.5 states people should be offered “ a psychological intervention that has been developed specifically for bipolar disorder and has a published evidence-based manual describing how it should be delivered **or** a high-intensity psychological	Thank you for your comments. Please see above for the NICE response to concerns regarding psychological therapies for bipolar disorder. Regarding lithium: During the development of the guideline, the guideline committee considered lithium as the preferred choice of drug as it has a better profile than valproate in the long-term management of bipolar disorder. At the time it was determined that individual medications be used with clinical judgement and in some clinical circumstances other medications might be preferable to lithium. In

		intervention (cognitive behavioural therapy, interpersonal therapy or behavioural couples therapy) in line with recommendations 1.5.3.1–1.5.3.5 in the NICE clinical guideline on depression." Given that bipolar depression is acknowledged as a different entity, it is difficult to understand why the option "or" should be given to therapies have no clear evidence base for improvement of bipolar depression. An example is CBT, where two of the NICE (single trial) meta-analyses show a beneficial effect-for active control, as opposed to CBT. We are unaware why couples therapy should be viewed on a par with other psychological treatments for bipolar depression. There is a factual error regarding the relapse prevention meta-analysis, which has been raised in print by Jauhar et al (1). The meta-analysis conducted includes four trials, showing a benefit for CBT in relapse prevention. In the NICE meta-analysis the largest trial of CBT. In relapse prevention (2) is excluded. It was stated by the NICE committee (3) that this study included patients currently not euthymic at entry to trial. There is a clear factual error in the NICE/NCCMH search strategy here. Another study included in the NICE meta-analysis (4) included explicitly depressed patients (4), another two did not explicitly state whether participants were euthymic at study entry (5,6). Inclusion of the Scott study significantly affects the results of the NICE meta-analysis (1). On reading through the evidence on psychological therapies, the quality of included trials measuring outcome post-treatment is poor-most included trials are rated low or very low quality, though this is not acknowledged within the guideline. Finally, there are methodological concern relating to the conduct of the meta-analyses, and reporting of findings. Multiple analyses took place throughout the NICE meta-analysis-almost 200 comparisons are conducted from 50 studies, a number of which include only one trial. There is no multiple comparison testing. Furthermore, from the composite met-analyses of combined psychotherapies, it is not clear why the guideline reports positive findings as evidence supporting guidance, whilst ignoring negative results of other composite analyses. **References** 1. Jauhar S, McKenna PJ, Laws KR. NICE guidance on psychological treatments for bipolar disorder: searching for the evidence. Lancet Psychiatry. 2016;3(4):386–388.	these circumstances the prescriber would select alternatives over lithium. The guideline committee acknowledged the poor evidence base and used their expert judgement when drafting the recommendations. Although aripiprazole and lamotrigine are now licensed for use in long-term treatment, no conclusive new evidence on the effectiveness of aripiprazole was found in this indication and no evidence was found at all for lamotrigine in the bipolar disorder population. At this time there is insufficient evidence to impact the recommendations.

		2. Scott J, Paykel E, Morriss R, Bentall R, Kinderman P, Johnson T, et al. Cognitive–behavioural therapy for severe and recurrent bipolar disorders. Br J Psychiatry. 2006 Apr 1;188(4):313–20. 3. Kendall T, Morriss R, Mayo-Wilson E, Meyer TD, Jones SH, Oud M, et al. NICE guidance on psychological treatments for bipolar disorder. Lancet Psychiatry. 2016 Apr 1;3(4):317–20. 4. Ball JR, Mitchell PB, Corry JC, Skillecorn A, Smith M, Malhi GS. A randomized controlled trial of cognitive therapy for bipolar disorder: focus on long-term change. J Clin Psychiatry. 2006 Feb;67(2):277–86. 5. Cochran SD. Preventing medical noncompliance in the outpatient treatment of bipolar affective disorders. J Consult Clin Psychol. 1984;52(5):873–8. 6. Perry A, Tarrier N, Morriss R, McCarthy E, Limb K. Randomised controlled trial of efficacy of teaching patients with bipolar disorder to identify early symptoms of relapse and obtain treatment. BMJ. 1999 Jan 16;318(7177):149–53. The NICE Guideline recommends that if Lithium is ineffective as a first line maintenance agent, then valproate should be added. This is over simplistic: • If there is no suggestion that lithium has led to any benefit at all, then wouldn't it make more sense for lithium to be withdrawn, given its potential to cause acute and chronic side effects, and an alternative maintenance agent commenced in its place? • If lithium has been partially effective as a maintenance agent, then it would be reasonable to consider adding another maintenance agent to it. However, there is no RCT evidence to indicate that the combination of lithium and valproate is more effective than lithium alone (see results of BALANCE study). As such why is valproate, as oppose to other drugs known to be effective as monotherapy maintenance agents, singled out to add to lithium? There is no mention of aripiprazole or lamotrigine being used as long-term treatments though each has a license for maintenance treatment.	

Royal College of Paediatrics and Child Health	No	No comment	Thank you for your response.

Do you have any comments on equalities issues?

Stakeholder	Overall response	Comments	NICE response
Association for Cognitive Analytic Therapy (ACAT)	No	No comment	Thank you.
Cheshire and Wirral Partnership NHS Foundation Trust	No	No comment	Thank you.
British HIV Association (BHIVA)	No	No comment	Thank you.
Royal College of Nursing (RCN)	No	No comment	Thank you.
British Association for Psychopharmacology	No	No comment	Thank you.
Royal College of Paediatrics and Child Health	No	No comment	Thank you.