NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Centre for Clinical Practice

Review consultation document

Review of Clinical Guideline (CG78) – Borderline Personality Disorder

1. Background information

Guideline issue date: 2009
2 year review: 2011 (first review)
National Collaborating Centre: Mental Health

2. Consideration of the evidence

Literature search

Through an assessment of abstracts from a high-level randomized control trial (RCT) search, new evidence was identified related to the following clinical areas within the guideline:

- Psychological interventions
- Settings for delivery of treatments
- Pharmacological interventions

Through this stage of the process, a sufficient number of studies relevant to the first two of the clinical areas above were identified from the high level RCT search to allow an assessment for a proposed review decision and are summarized in Table 1 below.

From initial intelligence gathering, qualitative feedback from other NICE departments, the views expressed by the Guideline Development Group, as well as the high-level RCT search, an additional focused literature search was also conducted for the following clinical area:

- Clinical and cost-effectiveness of pharmacological therapies in the management of patients with borderline personality disorders

The results of the focused searches are also summarized in table 2 below. All references identified through the high-level RCT search, initial intelligence gathering and the focused searches can be viewed in Appendix 1.

Table 1

Clinical area 1: Psychological interventions		
Clinical question	**Summary of evidence**	**Relevance to guideline recommendations**
Q: Which psychological therapy is most effective? (CBT, mentalisation, behaviour therapy, psychodynamic, CAT, group therapy, family therapy, schema-focused therapy, transference-focused and DBT, miscellaneous) **Relevant section of**	Through an assessment of the abstracts from the high-level RCT search, eleven studies relevant to the clinical questions covered in this clinical area of the guideline were identified. **Psychological interventions** • One RCT aimed to identify studies providing information on treatment completion in psychotherapy models that have been shown to be effective for BPD.[1] The authors concluded that borderline personality disorder should no longer be associated with high rates of dropout from treatment. However, the substantial variation in completion rates between studies remains unexplained. Research on the psychological processes involved in dropping out of treatment could further improve dropout rates.	No new evidence was identified which would invalidate current guideline recommendation(s).

guideline 5: Psychological And Psychosocial Treatments In The Management Of Borderline Personality Disorder **Recommendations** 5.12.1.1 to 5.12.1.3	• One RCT investigated whether combined treatment with a modified version of interpersonal psychotherapy (IPT) is still superior to antidepressants (ADs) when treating patients with a single diagnosis of BPD.[2] The results showed that combined therapy with adapted IPT was superior to fluoxetine alone in BPD patients, concerning a few core symptoms of the disorder, anxiety, and quality of life. • One RCT aimed to compare dialectical behaviour therapy (DBT) and treatment as usual plus waiting list for DBT (TAU+WL).[3] The authors concluded that DBT produced non-significant reductions in deliberate self-harm (DSH) and hospitalization when compared to the TAU+WL control, due in part to the lower than expected rates of hospitalization in the control condition. Nevertheless, DBT showed significant benefits for the secondary outcomes of improved disability and quality of life scores, a clinically useful result that is also in keeping with the theoretical constructs of the benefits of	

	DBT. • One RCT compared cognitive therapy (CT) with Rogerian supportive therapy (RST) in borderline personality disorder.[4] The results showed that CT retained the patients in therapy longer, showed earlier positive effects on hopelessness and impulsivity, and demonstrated better long-term outcomes on global measures of improvement. • One RCT examined the 6-year outcome of patients with borderline personality disorder who were randomised to 1 year of cognitive-behavioural therapy for personality disorders (CBT-PD) or treatment as usual (TAU).[5] Although the use of CBT-PD did not demonstrate a statistically significant cost-effective advantage, the findings indicate the potential for continued long-term cost-offsets that accrue following the initial provision of 1 year of CBT-PD. However, the quality of life and affective disturbance remained poor. • One RCT aimed to evaluate the success of implementing outpatient	

	schema focused therapy (ST) for borderline patients in regular mental healthcare and to determine the added value of therapist telephone availability outside office hours in case of crisis (TTA).[6] The authors concluded that ST for BPD can be successfully implemented in regular mental healthcare. Treatment results and dropout were comparable to a previous clinical trial. No additional effect of extra crisis support with TTA outside office hours ST was found. • One RCT tested the effectiveness of adding an eight-month, thirty-session schema-focused therapy (SFT) group to treatment-as-usual (TAU) individual psychotherapy for borderline personality disorder (BPD).[7] This study supports group SFT as an effective treatment for BPD that leads to recovery and improved overall functioning. • One RCT sought to evaluate the clinical efficacy of dialectical behaviour therapy compared with general psychiatric management, including a combination of psychodynamically informed therapy and	

	symptom-targeted medication management for borderline personality disorder.[8] These results suggest that individuals with borderline personality disorder benefited equally from dialectical behaviour therapy and a well-specified treatment delivered by psychiatrists with expertise in the treatment of borderline personality disorder • One RCT examined the efficacy of Manual Assisted Cognitive Therapy (MACT) as a stand-alone treatment for Borderline Personality Disorder (BPD) with suicidal ideation, and piloted a Therapeutic Assessment (TA) intervention randomly assigned to MACT or MACT+TA.[9] The authors concluded that although MACT was associated with significant reductions in BPD features and suicidal ideation, less than half of the sample completed the treatment. • One study aimed to investigate the effects of motive-oriented therapeutic relationship (MOTR) in early-phase treatment (up to	

	session 10), with BPD patients on therapeutic alliance, session impact, and outcome.[10] The results suggested a specific effectiveness of MOTR on the interpersonal problem area, on the quality of the therapeutic alliance and the quality of the therapeutic relationship, as rated by the patient. These results may have important clinical implications for the early-phase treatment of patients presenting with BPD. • One review conducted a meta-analysis to examine the efficacy and long-term effectiveness of DBT in patients with BPD.[11] The conclusions were that future research should compare DBT with other active borderline-specific treatments that have also demonstrated their efficacy using several long-term follow-up assessment points. **Summary** For psychological treatment options in the management of patients with BPD, most of the studies and reviews looking at different forms of	

	psychological interventions such as interpersonal psychotherapy (IPT), dialectical behaviour therapy (DBT), cognitive therapy (CT), cognitive behavioural therapy for personality disorders (CBT-PD) schema focussed therapy (ST), manual assisted cognitive therapy (MACT), and motive oriented therapeutic relationship, showed some form of effectiveness in managing symptoms including self harm, suicidal ideation, improved overall functioning, improved quality of life, and reduced anxiety, of patients with BPD. But any form of psychological intervention is allowed to be used provided it suits the patient needs and the patient is happy to comply with it. Also, it should be used for no less than three months. Therefore, no new evidence has been identified that would change the current recommendations.	
Clinical area 2: Settings for delivery of treatments		
Clinical question	**Summary of evidence**	**Relevance to guideline recommendations**

Q: What type of services maximise effectiveness and safety and minimise harm (taking into account long-term outcomes) for the delivery of specific treatments for people with borderline personality disorder? (for example, day hospitals, inpatient, therapeutic communities, use of enhanced care programming, team-based or individual-based care, partial	Through an assessment of the abstracts from the high-level RCT search, one study relevant to the clinical questions covered in this clinical area of the guideline were identified. • One study tested the effectiveness of an 18-month mentalization-based treatment (MBT) approach in an outpatient context against a structured clinical management (SCM) outpatient approach for treatment of borderline personality disorder.[12] Structured treatments improve outcomes for individuals with borderline personality disorder. A focus on specific psychological processes brings additional benefits to structured clinical support. Mentalization-based treatment is relatively undemanding in terms of training so it may be useful for implementation into general mental health services. Further evaluations by independent research groups are now required. **Summary** Regarding the effectiveness of the settings for the management of patients	No new evidence was identified which would invalidate current guideline recommendation(s).

hospitalisation) **Relevant section of guideline** 8. The configuration and organisation of services **Recommendations** 8.4.5	with BPD, a study showed that mentalization based treatment (MBT) in an outpatient context against a structured clinical management (SCM) can be implemented and is undemanding but further evaluations are required. No new evidence has been identified that would change the current recommendations.	

Table 2: Summary of articles from the focused search

Clinical area 1: Pharmacological interventions		
Clinical question	**Summary of evidence**	**Relevance to guideline recommendations**
Q: Which pharmacological therapies maximise benefits while	Through an assessment of the abstracts from the focused search and the high level RCT search 12 studies relevant to the clinical question were identified. One study examined Quetiapine and its potential effect on symptoms and	Potential new evidence was identified which could invalidate current guideline recommendation(s).

minimising harms? **Relevant section of guideline** 6. Pharmacological And Other Physical Treatments In The Management Of Borderline Personality Disorder **Recommendations** 6.12.1.1 to 6.12.1.4	explored a tolerated dosing pattern in patients diagnosed with borderline personality disorder (BPD).[13] Significant reductions in symptoms assessed by objective rating scales were observed in this pilot study of quetiapine administered to subjects with BPD. The dosing strategy in the study was well tolerated. One study investigated duloxetine in the treatment of patients with BPD. Initial results suggest that duloxetine is an effective and well-tolerated treatment for BPD, with positive effects on somatic symptoms.[14] One study designed to evaluate the effect of Olanzapine and Sertraline in patients suffering from borderline personality disorder.[15] As result of this study it appears that Olanzapine and Sertraline are effective in alleviating symptoms of patients with borderline personality disorder. One study evaluated treatment with variably dosed olanzapine in individuals with borderline personality disorder.[16] Individuals treated with olanzapine and placebo showed significant but not statistically different improvements on overall symptoms of borderline personality disorder.	

	One study compared the effectiveness of olanzapine versus haloperidol in BPD. [17] There seem to be no significant difference between olanzapine and haloperidol regarding the management of mental and behavioural symptoms of patients with BPD. One study assessed the longer-term efficacy of lamotrigine in therapy for aggression in women with BPD.[18] Lamotrigine appears to be an effective and relatively safe agent in the longer-term treatment of aggression in women with BPD. Another study evaluated the effectiveness of lamotrigine in reducing affective instability in borderline personality disorder (BPD).[19] Results from the study suggest that lamotrigine is an effective treatment for affective instability and for the general impulsivity characteristic of BPD. One study evaluated the efficacy and tolerability of ziprasidone in the treatment of adult patients with borderline personality disorder.[20] This trial	

	failed to show a significant effect of ziprasidone in patients with borderline personality disorder. A Cochrane review assessing the effects of drug treatment in BPD patients was identified.[21] The available evidence indicates some beneficial effects with second-generation antipsychotics, mood stabilisers, and dietary supplementation by omega-3 fatty acids. However, these are mostly based on single study effect estimates. Antidepressants are not widely supported for BPD treatment, but may be helpful in the presence of comorbid conditions. Total BPD severity was not significantly influenced by any drug. No promising results are available for the core BPD symptoms of chronic feelings of emptiness, identity disturbance and abandonment. Conclusions have to be drawn carefully in the light of several limitations of the RCT evidence that constrain applicability to everyday clinical settings (among others, patients' characteristics and duration of interventions and observation periods). One review of double-blind, controlled studies of psychotropic drugs	

	evaluated the evidence base supporting their use in treatment of borderline personality disorder.[22] A growing body of data suggests that there are psychotropic agents who appear to be well tolerated, and which to varying degrees may be expected to ameliorate the domains of psychopathology associated with borderline personality disorder. One review evaluated current pharmacological treatment algorithms and guidelines for BPD.[23] Drug therapy tailored to well-defined symptom domains can have beneficial effects in BPD. At short term, antipsychotics can have significant effects on cognitive-perceptual symptoms, anger, and mood lability, but the wide and long-term use of antipsychotics in these patients remains controversial. The findings from this study raise questions on current pharmacological algorithms and clinical guidelines. One review evaluated the evidence of effectiveness of pharmacotherapy in treating different facets of the psychopathology of borderline personality disorder.[24] The current evidence from randomised controlled trials suggests that drug treatment, especially with mood stabilisers and second-	

	generation antipsychotics, may be effective for treating a number of core symptoms and associated psychopathology, but the evidence does not currently support effectiveness for overall severity of borderline personality disorder. **Summary** The guideline does not recommend any specific pharmacotherapy for the management of patients with BPD and therefore this could be potential new evidence which might change the current recommendations. The results of the focused search showed some evidence supporting the use of different pharmacological interventions which have beneficial effects in patients with borderline personality disorder.	

A couple of recent ongoing clinical trials (publication dates unknown) were identified focusing on efficacy and safety of olanzapine and quetiapine, use of lamotrigine in patients with affective instability, efficacy of dialectical behavioural and group schema therapy in patients with borderline personality disorder.

No evidence was identified that was relevant to research recommendations in the original guideline.

In conclusion, some new evidence contradicts current guideline recommendations on the pharmacological therapies for patients with borderline personality disorder, but the evidence does not appear robust enough to completely change the current recommendations in the guideline. There are only single trials on pharmacological interventions with very small number of participants, therefore, the results may not be statistically precise and significant.

Guideline Development Group and National Collaborating Centre perspective

A questionnaire was distributed to GDG members and the National Collaborating Centre to consult them on the need for an update of the guideline. One response was received with the respondent highlighting that there might be some potential new evidence on pharmacological therapies for patients with borderline personality disorder.

The respondent felt that there is insufficient variation in current practice supported by adequate evidence at this time to warrant an update of the current guideline.

Implementation and post publication feedback

In total 43 enquiries were received from post-publication feedback, most of which were routine. One theme emerging from post-publication feedback was related to recommendations within the guideline (why does the guideline recommend the use of drugs for BPD, but also recommend the use of drugs in a crisis). This feedback contributed towards the development of the clinical questions as described above.

An analysis by the NICE implementation team indicated the issue of drugs for the treatment of BPD which is currently not recommended in the guideline but a Cochrane review[21] shows some evidence of efficacy for certain drugs.

Some new evidence (Cochrane review and the query raised by a stakeholder) was identified through post publication enquiries or implementation feedback but that it would not indicate a need to update the guideline.

Relationship to other NICE guidance

The following NICE guidance is related to CG78:

Guidance	**Review date**
PH 28- Promoting the quality of life of looked-after children and young people.	October 2013
PH 20- Promoting young people's social and emotional wellbeing in secondary education.	Not known
CG 38- The management of bipolar disorder in adults, children	July 2011

and adolescents, in primary and secondary care. CG 16- Self-harm: The short-term physical and psychological management and secondary prevention of self-harm in primary and secondary care.	February 2012
Related NICE guidance not included in CG78	
None	
Related NICE guidance in progress	
Self-harm: the longer term management of self-harm.	

Anti-discrimination and equalities considerations

No evidence was identified to indicate that the guideline scope does not comply with anti-discrimination and equalities legislation. The original scope is inclusive of both adults and children with a diagnosis of borderline personality disorder. It also included people with a learning disability.

Conclusion

Through the process additional areas were identified which were not covered in the original guideline scope but it was not enough to warrant an update of the guideline. From the evidence and intelligence identified through the process, it suggests that some areas of the guideline may need updating at this stage, particularly in relation to:

- Pharmacological therapies for people with borderline personality disorder. But the evidence is not robust enough to completely change

the current recommendations in the guideline. There are only single trials on pharmacological interventions with a very small number of participants, therefore, the results may not be statistically precise and significant.

The CG78: Borderline personality disorder guideline should not be updated at this time.

3. Review recommendation

The guideline should not be considered for an update at this time.

Centre for Clinical Practice
31st October, 2011

Appendix I

1 . Barnicot K, Katsakou C, Marougka S et al. (2011) Treatment completion in psychotherapy for borderline personality disorder: a systematic review and meta-analysis. Acta Psychiatrica Scandinavica 123:327-338.

2 . Bellino S, Rinaldi C, and Bogetto F. (2010) Adaptation of interpersonal psychotherapy to borderline personality disorder: a comparison of combined therapy and single pharmacotherapy. Canadian Journal of Psychiatry - Revue Canadienne de Psychiatrie 55:74-81.

3 . Carter GL, Willcox CH, Lewin TJ et al. (2010) Hunter DBT project: randomized controlled trial of dialectical behaviour therapy in women with borderline personality disorder. Australian & New Zealand Journal of Psychiatry 44:162-173.

4 . Cottraux J, Note ID, Boutitie F et al. (2009) Cognitive therapy versus Rogerian supportive therapy in borderline personality disorder. Two-year follow-up of a controlled pilot study. Psychotherapy & Psychosomatics 78:307-316.

5 . Davidson KM, Tyrer P, Norrie J et al. (2010) Cognitive therapy v. usual treatment for borderline personality disorder: prospective 6-year follow-up. British Journal of Psychiatry 197:456-462.

6 . Nadort M, Arntz A, Smit JH et al. (2009) Implementation of outpatient schema therapy for borderline personality disorder with versus without crisis support by the therapist outside office hours: A randomized trial. Behaviour Research and Therapy 47:961-973.

7 . Farrell JM, Shaw IA, and Webber MA. (2009) A schema-focused approach to group psychotherapy for outpatients with borderline personality disorder: a randomized controlled trial. Journal of Behavior Therapy & Experimental Psychiatry 40:317-328.

8 . McMain SF, Links PS, Gnam WH et al. (2009) A randomized trial of dialectical behavior therapy versus general psychiatric management for borderline personality disorder.[Erratum appears in Am J Psychiatry. 2010 Oct;167(10):1283]. American Journal of Psychiatry 166:1365-1374.

9 . Morey LC, Lowmaster SE, and Hopwood CJ. (15-8-2010) A pilot study of Manual-Assisted Cognitive Therapy with a Therapeutic Assessment

augmentation for Borderline Personality Disorder. Psychiatry Research 178:531-535.

10 . Kramer U, Berger T, Kolly S et al. (2011) Effects of motive-oriented therapeutic relationship in early-phase treatment of borderline personality disorder: A pilot study of a randomized trial. Journal of Nervous and Mental Disease 199:244-250.

11 . Kliem S, Kroger C, and Kosfelder J. (2010) Dialectical behavior therapy for borderline personality disorder: a meta-analysis using mixed-effects modeling. Journal of Consulting & Clinical Psychology 78:936-951.

12 . Bateman A and Fonagy P. (2009) Randomized controlled trial of outpatient mentalization-based treatment versus structured clinical management for borderline personality disorder. American Journal of Psychiatry 166:1355-1364.

13 . Adityanjee, Romine A, Brown E et al. (2008) Quetiapine in patients with borderline personality disorder: an open-label trial. Annals of Clinical Psychiatry 20:219-226.

14 . Bellino S, Paradiso E, Bozzatello P et al. (2010) Efficacy and tolerability of duloxetine in the treatment of patients with borderline personality disorder: a pilot study. Journal of Psychopharmacology 24:333-339.

15 . Jariani M, Saaki M, Nazari H et al. (2010) The effect of Olanzapine and Sertraline on personality disorder in patients with methadone maintenance therapy. Psychiatria Danubina 22:544-547.

16 . Schulz SC, Zanarini MC, Bateman A et al. (2008) Olanzapine for the treatment of borderline personality disorder: variable dose 12-week randomised double-blind placebo-controlled study. British Journal of Psychiatry 193:485-492.

17 . Shafti SS and Shahveisi B. (2010) Olanzapine versus haloperidol in the management of borderline personality disorder: a randomized double-blind trial. Journal of Clinical Psychopharmacology 30:44-47.

18 . Leiberich P, Nickel MK, Tritt K et al. (2008) Lamotrigine treatment of aggression in female borderline patients, Part II: an 18-month follow-up. Journal of Psychopharmacology 22:805-808.

19 . Reich DB, Zanarini MC, and Bieri KA. (2009) A preliminary study of lamotrigine in the treatment of affective instability in borderline personality disorder. International Clinical Psychopharmacology 24:270-275.

20 . Pascual JC, Soler J, Puigdemont D et al. (2008) Ziprasidone in the treatment of borderline personality disorder: a double-blind, placebo-controlled, randomized study. Journal of Clinical Psychiatry 69:603-608.

21 . Stoffers J, Vollm BA, Rucker G et al. (2010) Pharmacological interventions for borderline personality disorder. [Review] [113 refs][Update of Cochrane Database Syst Rev. 2006;(1):CD005653; PMID: 16437535]. Cochrane Database of Systematic Reviews CD005653-

22 . Abraham PF and Calabrese JR. (2008) Evidenced-based pharmacologic treatment of borderline personality disorder: a shift from SSRIs to anticonvulsants and atypical antipsychotics?. [Review] [37 refs]. Journal of Affective Disorders 111:21-30.

23 . Ingenhoven TJ and Duivenvoorden HJ. (2011) Differential effectiveness of antipsychotics in borderline personality disorder: meta-analyses of placebo-controlled, randomized clinical trials on symptomatic outcome domains. Journal of Clinical Psychopharmacology 31:489-496.

24 . Lieb K, Vollm B, Rucker G et al. (2010) Pharmacotherapy for borderline personality disorder: Cochrane systematic review of randomised trials. [Review] [55 refs]. British Journal of Psychiatry 196:4-12.