Borderline personality disorder: treatment approaches and perspectives

Katharine J Nelson[1], Alexandra Zagoloff[1], Sandra Quinn[1], Heather E Swanson[1], Claire Garber[1] & S Charles Schulz*,[1]

[1]Department of Psychiatry, University of Minnesota, F282/2A West, 2450 Riverside Avenue, Minneapolis, MN 55455, USA

*Author for correspondence:
Fax: +1 612 273 9779
scs@umn.edu

Practice points

- Patients with borderline personality disorder (BPD) are truly suffering and are at high risk of mortality. Suicidal or nonsuicidal self-injury behaviors need to be taken seriously and should not be dismissed as primarily attention seeking.
- BPD carries a generally favorable prognosis for key outcome variables compared with many in the field's previous conceptualization of the disorder.
- Help-seeking patients with BPD should be screened for this disorder and provided with reputable psychoeducation and educational resources regarding the nature and management of their symptoms.
- Comorbid medical and psychiatric conditions should be addressed and treated, while also accounting for the role of the BPD symptoms, which can confer treatment resistance to other disorders.
- Early evidence exists for use of medications in a symptom-targeted manner; however, polypharmacy and benzodiazepines should be avoided.
- Evidence-based psychotherapies exist that have been shown to significantly improve patient outcomes, including reduction in suicide, suicidal ideation and improved affective regulation.
- As with all psychiatric disorders, adopting strategies to cultivate a healthy treatment alliance with patients manifesting interpersonal dysfunction is an important aspect of clinical care.

Borderline personality disorder is a disorder associated with significant morbidity, mortality and imparts a significant societal toll. The field of research into the pathophysiology, conceptualization and treatment approaches for borderline personality disorder is rapidly expanding. Once considered by many to be a diagnosis consisting of fixed and untreatable patient characteristics, our current understanding had lead to a more hopeful prognosis and a set of therapeutic approaches to accelerate patient recovery. These approaches include evidence-based psychotherapy, domain-targeted medication treatment and combined strategies. Despite this growth in the literature and improvement in patient care, significant opportunities exist to further our understanding and implement best practices in the clinical realm, research and physician education.

Keywords: affective dysregulation • borderline personality disorder • nonsuicidal self-injury • suicide • treatment

Over the past three decades, borderline personality disorder (BPD) has emerged as the most widely studied of all the personality disorders, which has lead to significant advances in our understanding of its etiology, pathophysiology and treatment. BPD is characterized by a pattern of unstable relationships, self-image and affect, in addition to significant impulsivity, nonsuicidal self-injury and suicidal behaviors [1]. BPD

Future Medicine part of fsg

is observed across cultures and epidemiologic studies have generally estimated its prevalence in community samples to be approximately 0.7–1%, as noted in a community sample of 2053 individuals in Norway [2]. A more recent examination of personality disorder prevalence was conducted as part of the National Epidemiological Survey on Alcohol and Related Conditions (NESARC), which surveyed over 40,000 people in the USA and using revised, more conservative criteria than the initial analysis, found the community prevalence to be approximately 2.7% [3]. Initial data indicated BPD is present more frequently in women; however, the NESARC data noted equal prevalence in men and women in community samples and identified high rates of comorbidity with mood, anxiety and substance use disorders [4]. Patients with BPD have a 50-fold higher rate of suicide than the general population [5].

Nine criteria for BPD are described in the DSM5, five of which are required to qualify for the diagnosis [1]. Extrapolating from these diagnostic criteria, signs and symptoms of BPD can be categorized into four symptom domains that serve as a framework for the Revised Diagnostic Interview for Borderlines, a research diagnostic tool with utility in clinical settings [6]. Symptoms domains include: affective (extreme moodiness, chronic feelings of emptiness, frequent feelings of anger or frequent angry acts), cognitive (serious identity disturbance, stress-related paranoia or dissociation), behavioral (suicide threats, attempts, or self-injury, other impulsive behaviors) and interpersonal (efforts to avoid abandonment, unstable relationships that alternate between idealization and devaluation) [7].

Though BPD is has classically been considered a chronic, difficult-to-treat condition with poor prognosis, large, multisite prospective trials have produced data that demonstrate a more optimistic picture [8,9]. The CLPS, funded by the National Institute of Mental Health, characterized the 10-year course of BPD as demonstrating high rates of remission and low rates of relapse, even though social functioning continued to be impaired [8]. The MSAD at 16 years of follow-up, high rates of sustained remission (78–99%) and moderate rates of recovery (40–60%) based on continued difficulty with vocational and social functioning [9].

As is the case with the majority of psychiatric conditions, the etiology of BPD tends to be multifactorial and complex, with significant interplay between genetics, temperamental characteristics, abnormalities in brain structure and function, and environmental factors, such as difficult or invalidating relationships with family members and traumatic experiences. High rates of heritability are noted in twin studies of personality disorders [10]; however, in a recent systematic review of the literature, no clear genetic polymorphism has yet been identified [11].

Recent advances in neuroimaging have demonstrated various structural and functional patterns evident in BPD. Some of the findings in structural studies include a decrease in grey matter volume in both the anterior cingulate gyrus [12] and the medial temporal lobe [13] and general volume reductions in the hippocampus and amygdala [14]. Using diffusion tensor imaging techniques, white matter tract integrity is decreased in the orbitofrontal cortex [15]. Taken together, these changes indicate that frontolimbic circuitry is disrupted, which may be a physiologic explanation for the lack of emotional modulation seen in BPD [16].

Functional studies further support this model of frontolimbic disinhibition. On both PET scanning [17] and functional MRI [18] in emotionally provoked BPD patients, metabolic rates in the orbitofrontal cortex and amygdala are increased, while activity in the dorsal prefrontal activity is decreased. Healthy controls show the opposite response in the latter region, allowing for more cognitive control of negative emotional responses [17]. When compared with controls, the orbitofrontal cortex and anterior cingulate gyrus are less active in BPD patients on PET imaging. These areas, which help modulate the expression of emotions, are proposed to be less available to modulate the increased activity of the amygdala [16]. Schulz *et al.* conducted PET scan imaging to describe the relationship between regional brain metabolism and clinical rating assessments of BPD in 14 women and noted a significantly negative correlation in frontal glucose metabolism and validated measures for hostility [19].

Common approaches to diagnosis & treatment

Despite the fact that BPD has classically been considered resistant to treatment, the expanding literature exploring etiologic factors, symptom domains, neurophysiology and generally favorable disease course has allowed for greater examination of the role and outcomes of BPD treatment. This article will provide a comprehensive discussion of pharmacologic and psychotherapeutic treatment approaches; however, general best practices are important to consider in the role of comprehensive care.

Accurate diagnosis and psychoeducation regarding the symptoms and prognosis of BPD are as essential in the treatment of BPD as with any other psychiatric disorder. A treatment alliance and structured clinical care can serve as a foundation for diagnosis, discussion and education. The high placebo response rates

in medication treatment research of participants with BPD points to the importance of identification of the presence of the disorder and structured monitoring. [20]. Zanarini and Frankenburg conducted a trial in which 50 women with BPD were provided with diagnostic disclosure and 30 of these participants were randomized to receive psychoeducation while 20 were assigned to a wait list. Primary outcomes were measured after 12 weeks. Participants who received the psychoeducation demonstrated significantly greater improvements in two core elements of BPD: impulsivity and unstable relationships [21]. Gunderson has developed a comprehensive approach to BPD treatment, good psychiatric management (GPM; formerly general psychiatric management) based on the manualization of the American Psychiatric Association Practice Guideline for the Treatment of Patients with Borderline Personality Disorder [22], in which comprehensive BPD treatment is provided by an expert psychiatrist providing medication management, psychoeducation and psychotherapeutic interactions in the context of regular structured follow-up. GPM has been compared with dialectical behavior therapy (DBT) in one single blind trial of 180 outpatients over 1 year with equivalent improvements on all primary and most secondary outcomes [23].

Pharmacotherapy

Appropriate medication treatment may theoretically accelerate the recovery of deficits noted in neuroimaging studies discussed previously. The latest version of the American Psychiatric Association Practice Guideline for the Treatment of Patients with Borderline Personality Disorder [22] was published in 2001. Therefore, this publication is considered to be in need of updating to take into account the significant clinical trials and treatment insights accumulated over the past decade. In this time, meta-analyses of pharmacotherapy for BPD have been completed by researchers in Germany [24] and The Netherlands [25], and practice guidelines have been produced for the National Health Services by Great Britain [26] and Australia [27]. The outcome of this work has resulted in diverging international viewpoints on the issue of pharmacotherapeutic management in BPD. All will acknowledge the reality that many patients with BPD are on multiple medications and medication management strategies are frequently pursued, even in the absence of a US FDA or other governmental indication for medication treatment of BPD. Additionally, many of psychotherapeutic trials for the treatment of BPD do not exclude patients on medications. It is worth noting, there are no long-term medication treatment studies; most clinical trials are 12–16 weeks in length.

The German and Dutch meta-analyses identified early evidence supporting the use of certain medications or classes of medications in the management of BPD symptoms. The Dutch conducted a meta-analysis by Ingenhoven , which included 21 studies examining the classes of antipsychotics, antidepressants and mood stabilizers, and the effects on the symptoms of cognitive perceptual symptoms, impulsive behavioral control and affective dysregulation (including subdomains of depressed mood, anxiety, anger and mood lability) [25]. Mood stabilizers showed a very large effect on impulsive behavioral control and anger, and a larger effect on global functioning than antipsychotics. Mood stabilizers also resulted in a large reduction in anxiety and moderate improvement in depressed mood. Antipsychotics resulted in a moderate effect on cognitive perceptual symptoms and a moderate to large effect on anger. Antidepressants only resulted in a small effect on anxiety and anger, although did not have a significant effect on any other domains.

The German study consisted of a Cochrane Review by Stoffers *et al.*, which examined 28 studies involving 1742 participants and concluded that evidence for the use of medications for BPD is limited, although findings identified early evidence for the use of second-generation antipsychotics, mood stabilizers and omega-3 fatty acids [24]. The medications included in this review were first-generation antipsychotics (fluphenthixol decanoate, haloperidol and thiothixene), second-generation antipsychotics (aripirazole, olanzapine and ziprasidone), mood stabilizers (carbamazepine, valproate semisodium, lamotrigine and topiramate), antidepressants (amitriptyline, fluoxetine, fluvoxamine, phenelzine sulfate and mianserin) and dietary supplementation (omega-3 fatty acid). Of note, polypharmacy is not supported by the evidence and by consensus should be avoided. The total severity of BPD was not significantly reduced by any particular medication. Overall, antidepressants are not widely supported for BPD treatment, although may be beneficial for the treatment of comorbid depression. For the predominate symptom of cognitive perceptual symptoms, antipsychotics (olanzapine and aripiprazole) were most effective. Mood stabilizers (topiramate, lamotrigine) and the antipsychotic, aripiprazole, were the most effective pharmacologic treatment for impulsive behavioral dyscontrol. The symptom of affective dysregulation was best treated by antidepressants (amitriptyline), mood stabilizers (topiramate, lamotrigine and valproate), antipsychotics (haloperidol, olanzapine and aripiprazole) or omega-3 fatty acids (fish oil). Specifically, amitriptyline, valproate and fish oil target depressed mood, while lamotrigine and haloperidol target anger in these trials. Suicidal behavior and

suicidality were best treated with antipsychotics (fluphenthixol decanoate) or omega-3 fatty acids (fish oil). Interpersonal problems were treated most effectively with antipsychotics (aripiprazole) or mood stabilizers (valproate and topiramate). There are no clear data on pharmacologic treatment decreasing the BPD symptoms of chronic feelings of emptiness, identity disturbance and feelings of abandonment. Adverse events were limited, with the exception of olanzapine, which exhibited a possible increase in self-harming behavior in addition to significant weight gain and sedation. By contrast, a significant decrease in weight was noted in patients treated with topiramate.

The NICE guidelines conducted by the National Collaborating Centre for Mental Health for the national health system of Great Britain did not identify evidence sufficient to justify recommending a medication treatment strategy through their governmental practice guidelines [26]. The NICE guidelines have a series of strategies of managing care in a structured manner utilizing psychotherapeutic and systems-based interventions. These guidelines do mention the short-term use of sedating antihistamines in the case of crisis; however, this specific recommendation was not based on scientific literature. The Australian guidelines were developed utilizing a methodology based on the data produced by the NICE guidelines and generated similar conclusions, although adopts a slightly more open stance on the use of medications [27].

Studies examining the combination of medication and psychotherapy to treat BPD have shown favorable results in regards to utilizing medication in combination DBT. Linehan conducted a study of 24 women with BPD and high levels of irritability and anger who were assigned to 6 months of DBT alone, or DBT and olanzapine. Both groups had significant improvement in irritability, depression, aggression and self-injury. However, irritability and aggression decreased more rapidly for the group treated with DBT and olanzapine [28]. Soler *et al.* conducted a double-blind, placebo-controlled trial including 60 patients with BPD in DBT for 4 months. These patients were randomly assigned to take olanzapine or placebo. Results showed that the combination of DBT and olanzapine improved most symptoms and had a lower drop-out rate [29].

For treatment of BPD, in most trials antipsychotics were dosed at a third to a half of the typical dose used when treating a primary psychotic disorder, while antidepressant dosing was typically higher than doses used to treat major depressive disorder. Dosing of mood stabilizers for the treatment of BPD was similar to dosing used to treat bipolar disorder. Evidence suggests that certain medications should be avoided in BPD, such as benzodiazepines [30], which can inhibit learning and interfere with acquiring new skills during the psychotherapeutic treatment. Of note, medications that have a high risk of toxicity if taken as an overdose, such as tricyclic antidepressants, should be prescribed cautiously due to the high suicidal behavior risk in BPD and not prescribed to actively suicidal patients [31].

A reasonable approach to practice is to first determine treatment for any comorbid psychiatric illness and then to identify the prominent symptom domain a patient with BPD may experience. Research trials often focus on specific symptom domains, such as cognitive–perceptual symptoms, impulsive–behavioral dyscontrol and affective dysregulation. Based on clinical experience, this approach can assist in guiding treatment choices, facilitating psychotherapeutic effect and promote the reduction of polypharmacy [32].

Psychotherapeutic treatment modalities

Four comprehensive psychotherapies exist to address the complexities involved in treating BPD [33]: DBT [34], schema therapy [35], mentalization-based treatment (MBT) [36] and transference-focused therapy (TFP) [37]. Systems training for emotional predictability and problem-solving (STEPPS [38]) is also gathering an evidence base [39].

Dialectical behavior therapy

DBT is an intervention originally designed to treat chronically suicidal, multiproblem patients. The treatment is principle-based with manualized protocols and includes components of individual therapy, skills training groups (with modules encompassing evidence-based approaches to improving mindfulness, emotion regulation, distress tolerance, and interpersonal effectiveness), phone coaching and a consultation team for clinicians [34]. In total, 13 randomized controlled trials have been published demonstrating effectiveness of DBT for the treatment of BPD, the largest body of research supporting any psychotherapy for the treatment of this disorder [40]. Furthermore, data are beginning to support DBT's cost–effectiveness, primarily by reducing mental health hospitalizations [41]. Given DBT's emphasis on skills training and strategies to generalize skill application, the DBT Ways of Coping Checklist [42] was designed to identify whether group members were using skillful or ineffective strategies to solve problems. The measure has since been used to evaluate one's use of skills as an outcome and mediator of treatment [43]. Not only did participants of DBT report using three-times more skills than those in a control condition, but also their use of skills mediated decreases in suicide attempts and depression, and an increase in control over anger. Current research investigates expansions of DBT through mobile phone applications [44] and formally addressing

post-traumatic stress disorder by adding a prolonged exposure protocol [45]. DBT requires a time investment of attendance at a weekly skills group and weekly individual session for 1 year. A long-term follow-up study of 50 consecutive in patients with BPD found a significant number of participants maintained the beneficial effects of the therapy and did not meet criteria for BPD 30 months after hospital discharge [46].

Schema therapy

Young developed the concept of modes to capture the differing coping styles that exist within an individual with BPD and often lead to destructive behavior. The modes represent the patient as child, parent, and healthy adult, and include: abandoned/abused child, angry/impulsive child, detached protector, punitive parent and healthy adult modes. The four purported mechanisms of change include limited reparenting, experiential techniques, education and cognitive restructuring, and behavioral pattern breaking. During the initial phase of treatment, the therapist seeks to provide a supportive environment that compensates for the ways in which the patient's parents failed to meet her needs throughout development. Next, the therapist utilizes imagery work to facilitate discussion and processing of challenging episodes from childhood. The 'empty chair' technique may be employed in the use of dialog to facilitate communication between the fearful and critical facets of the patient. Letter writing, the third experiential technique, allows the patient to write letters (not intended to be sent) to people whose behavior was harmful so that the patient has the opportunity to communicate her feelings and needs. Education is considered therapeutic in that it teaches adaptive needs and emotional experiencing. Cognitive restructuring focuses on the development of moderate interpretations of others' and one's own behavior. In the final phase of treatment, patients learn to apply what they have learned in session to life outside of session through generalization [35].

New research supports the development of group work using schema-focused therapy (SFT). Patients with BPD were randomly assigned to treatment as usual (TAU) or TAU plus SFT. The SFT-TAU group had a higher retention rate, greater decrease in BPD symptoms and symptom severity, improved functioning, and greater change in no longer meeting criteria for BPD [47]. A Dutch study evaluated whether treatment effectiveness was improved by adding therapist telephone availability outside of office hours. While 42% of patients no longer met criteria for BPD after 18 months of treatment, therapist telephone availability did not significantly add to the improvement [48].

Mentalization-based treatment

Mentalizing is defined as the process by which an individual makes sense of herself and others in terms of mental states. According to this theory, this process is especially challenging for individuals with BPD during periods of emotional arousal. Consequently, the goals of treatment include the development of this process and its maintenance when an attachment system is active [49]. Further, the theory suggests that affect dysregulation, impulsivity, and unstable relationships (the core features of BPD) are linked with one another through difficulties with understanding the mental states of self and others [50].

A randomized controlled trial compared mentalization-based treatment by partial hospitalization (MBT) to treatment as usual (TAU) 8 years after patients had entered the study and 5 years after MBT was complete. Five years postdischarge, MBT patients demonstrated significant improvement compared with TAU on suicidality, diagnostic status, service use, medication use, global functioning, and vocational status [51]. Another randomized controlled trial compared MBT with structured clinical management. Both groups demonstrated significant improvement across outcome measures (suicidal and severe self-injurious behaviors, hospitalization, self-reported symptoms, social and interpersonal functioning). Patients in the MBT group showed a steeper improvement in self-report symptoms and crisis situations [52]. MBT has been adapted for use with adolescents who self-harm and an initial randomized controlled trial produced encouraging results [53].

Transference-focused psychotherapy

Mechanisms of change in TFP are considered at the level of the patient and the level of the therapist. The patient is believed to hold polarized representations of the self and others, and change occurs when these representations are integrated. The following interventions from the therapist are presumed to facilitate change: structured treatment approach, use of clarification, confrontation, and 'transference' interpretations of the therapeutic relationship [37].

A European randomized controlled trial compared TFP with treatment by experienced community providers. Patients in TFP were significant less likely to drop out from treatment and to attempt suicide. These patients also demonstrated significantly greater improvement in BPD symptoms, psychosocial functioning, personality organization and inpatient admissions. Patients in both groups made significant improvements in depression and anxiety. Neither group demonstrated significant change in self-harm [54].

STEPPS

STEPPS is a group treatment that follows a manual and takes place over 20 weeks. Sessions address the following information: concept of BPD, reinforcement team (support system), education about schemas in BPD, relaxation breathing and distancing from emotional intensity, the emotional intensity continuum, cognitive distortions and alternative thoughts, distraction and positive affirmations, problem solving, lifestyle behaviors, skills to reduce self-harm, antecedents of unhelpful behavior, and interpersonal boundaries and relationships. A randomized controlled trial compared TAU with TAU plus STEPPS. Although there were no differences for suicide attempts, self-harm and hospitalizations, the STEPPS group demonstrated significantly greater improvements in impulsivity, negative affectivity, mood, global functioning and multiple subscales on the Zanarini Rating Scale for BPD. Most of these gains were maintained at 1-year follow-up [38]. STEPPS has been described as an 'augmentation of or adjunct to' other treatments for BPD and was notable for its inclusion of individuals from the patient's system (significant other, relative) [55].

Physician training considerations

BPD is believed to be present in over 10% of psychiatric inpatients [56] and an even higher proportion of psychiatric outpatients. Due to the significant interpersonal dysfunction and psychiatric morbidity, patients with BPD generally require significant physician, nursing and staff time and resources. The early body of literature in this regard reveals significant opportunities for additional research. However, given the prevalence of BPD and the existence of evidence-based approaches, treatment of BPD should be explicitly addressed in residency training programs. These factors underscore the importance of effective curricula designed to prepare resident psychiatrists with the skills needed to effectively treat this patient population while managing stress associated with the treatment relationship. Despite this importance, a recent survey of Psychiatry Program Directors indicated discouraging results in that only about half of responders had formal BPD courses in their didactic curricula [57]. Although this survey did not have a robust response, the initial results are indicative of a broader issue of curricular deficits.

Since DBT and other treatments have emerged as evidence-based approaches for addressing BPD symptoms, most literature examining training considerations for residency programs focused on the training and application of these modalities. The early research examining this training approach suggests that comprehensive training in DBT specifically during residency may substantially improve the care of patients with BPD and residents' sense of efficacy in their care of patients. Survey data of psychiatry program directors and residents have also revealed a deficit in training residents in DBT and that the training that does exist leaves residents without the skills or confidence they need to really be effective with this modality [58]. Specifically, when a small sample of psychiatrists were surveyed regarding using DBT in years after finishing residency, the data, while only representative of a very small sample size, showed an association supporting higher exposure to DBT training in residency and greater confidence and use of DBT skills after graduation [59].

There are many challenges associated with the realistic implementation of better training in residency for treating BPD. BPD patients are generally complex and challenging patients for experienced providers and even more so for less experienced learners [60]. While training programs are in the process of establishing consensus on how residency training should be improved, there are programs that have made successful efforts at improving the training in treating patients with BPD. The University of Utah (UT, USA), for example, was able to design and implement a residency DBT clinic into their existing curriculum with little disruption and show measurable improvements in resident skills [61]. Columbia University (NY, USA) has been issued a R25 Training Grant by the National Institute of Mental Health to develop and describe a robust DBT training program for their psychiatry residents [62]. New York University School of Medicine (NY, USA) designed an applicable model for implementing TFP in residency training programs for the treatment of personality disorders and provided rationale for its utility in the management of acute care, as well as the outpatient setting [63]. Nelson described an approach to a complex case of BPD on the inpatient setting and the role of the resident's training, including skill and attitude enhancement [64]. These are just a few examples of some of the efforts being made by individual programs. The existing data suggest there are opportunities to better prepare residents to be able to effectively manage and treat this challenges of BPD.

Conclusion & future perspective

Although the increased rate and quality of BPD research has lead to significant progress in our understanding of the disorder, there is still significant opportunity for further elucidation of relevant understanding. The morbidity and mortality associated with this disorder mandates our continued effort to build our knowledge base and development of effective treatment options. Neuroimaging studies have surmised that frontolimbic system dysfunction may play a significant role in BPD, but the molecular and neurochemical basis of this abnormality has not been fully examined. In addi-

tion, many structural and functional patterns evident in BPD have been elucidated, but because of the significant psychopathologic comorbidity present in this population, specificity of these findings remains unclear. Therefore, continued research into neuropathophysiologic differences in patients with BPD as compared with healthy controls or other patients with psychiatric conditions but without BPD will be important in establishing causation. By improving our understanding of these biologic aspects of BPD, perhaps we can utilize the information gained in neuroimaging studies to guide and individualize treatment strategies to meet patients' needs.

In the ongoing effort to better describe factors contributing to the etiology of BPD, future research should attempt to integrate the various biopsychosocial variables into a cohesive model. This would include examining how biologic factors (genetics, brain structure/function and neurotransmitters) lead to and influence the outward manifestations of BPD (affect, behavioral and cognition). In prospective studies, the behavioral aspects tend to respond fairly quickly to treatment, whereas affective and interpersonal symptoms are fairly stable and less responsive to treatment [65]. As a result, observable measures (e.g., aggressive, self-injurious behaviors and suicidal ideation, among others) tend to be the focus of research, although they are likely secondary to deep-seated developmental characteristics. Although personality disorders are characterized as being stable and unchanging, BPD may not be as unalterable as was initially thought, thus the issues below the surface must not be neglected and/or dismissed in future research studies. It is our hope, through multisite, multiarm clinical trials, examining both somatic and psychotherapeutic treatment modalities, these aforementioned areas will continue to be explored, providing much needed knowledge and relief for our patients suffering with BPD.

Financial & competing interests disclosure

SC Schulz has served as a consultant for TEVA, Eli Lilly and Genentech and has received grant/research support from the National Institute of Mental Health, AstraZeneca, Otsuka, Myriad/RBM and FORUM. The authors have no other relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript apart from those disclosed.

No writing assistance was utilized in the production of this manuscript.

References

1 American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition*. American Psychiatric Association, VA, USA (2013).

2 Torgersen S, Kringlen E, Cramer V. The prevalence of personality disorders in a community sample. *Arch. Gen. Psychiatry* 58, 590–596 (2001).

3 Trull TJ, Jahng S, Tomko RL, Wood PK, Sher KJ. Revised NESARC personality disorder diagnoses: gender, prevalence, and comorbidity with substance dependence disorders. *J. Pers. Disord.* 24, 412–426 (2010).

4 Grant BF, Chou SP, Goldstein RB *et al.* Prevalence, correlates, disability, and comorbidity of DSM-IV borderline personality disorder: Results from the Wave 2 National Epidemiologic Survey on Alcohol and Related Conditions. *J. Clin. Psychiatry* 69(4), 533–535 (2008).

5 Skodol A, Gunderson JG, McGlashan T *et al.* Functional impairment in patients with schizotypal, borderline, avoidant, and obsessive-compulsive personality disorders. *Am. J. Psychiatry* 159, 276–283 (2002).

6 Zanarini MC, Gunderson JG, Frankenburg FR, Chauncey DL. The revised diagnostic interview for borderlines: discriminating BPD from other Axis II disorders. *J. Pers. Disord.* 3(1), 10–18 (1989).

7 Zanarini MC. Diagnostic specificity and long-term prospective course of borderline personality disorder. *Psychiatr. Ann.* 42, 53–58 (2012).

8 Gunderson JG, Stout RL, McGlashan TH*et al.* Ten-year course of borderline personality sisorder: psychopathology and function from the collaborative longitudinal personality disorders study. *Arch. Gen. Psychiatry* 68(8), 827–837 (2011).

9 Zanarini MC, Frankenburg FR, Reich DB, Fitzmaurice G. Attainment and stability of sustained symptomatic remission and recovery among patients with borderline personality disorder and Axis II comparison subjects: a 16-year prospective follow-Up Study. *Am. J. Psychiatry* 169, 476–483 (2012).

10 Torgerson S, Lygren S, Oien PA *et al.* A twin study of personality disorders. *Compr. Psychiatry* 41(6), 416–425 (2000).

11 Calati R, Gressier F, Balestri M, Serretti A. Genetic modulation of borderline personality disorder: Systematic review and meta-analysis. *J. Psychiatr. Res.* 47(10), 1275–1287 (2013).

12 Hazlett EA, New AS, Newmark R *et al.* Reduced anterior and posterior cingulate gray matter in borderline personality disordera. *Biol. Psychiatry* 58(8), 614–623 (2005).

13 Soloff P, Nutche J, Goradia D, Diwadkar V. Structural brain abnormalities in borderline personality disorder: a voxel-based morphometry study. *Psychiatry Res.* 164(3), 223–236 (2008).

14 Nunes PM, Wenzel A, Borges KT, Porto CR, Caminha RM, de Oliveira IR. Volumes of the hippocampus and amygdala in patients with borderline personality disorder: a meta-analysis. *J. Pers. Disord.* 23(4), 333–345 (2009).

15 Carrasco JL, Tajima-Pozo K, Díaz-Marsá M *et al.* Microstructural white matter damage at orbitofrontal areas

in borderline personality disorder. *J. Affect. Disord.* 139, 149–153 (2012).

16 New AS, Perez-Rodriguez M, Ripoll LH. Neuroimaging and borderline personality disorder. *Psychiatr. Ann.* 42(2), 65–71 (2012).

17 New AS, Hazlett EA, Newmark RE *et al.* Laboratory induced aggression: a positron emission tomography study of aggressive individuals with borderline personality disorder. *Biol. Psychiatry* 66(12), 1107–1114 (2009).

18 Minzenberg MJ, Fan J, New AS, Tang CY, Siever LJ. Frontolimbic dysfunction in response to facial emotion in borderline personality disorder: an event-related fMRI study. *Psychiatry Res.* 155(3), 231–243 (2007).

19 Schulz SC, Camchong J, Romine A *et al.* An exploratory study of the relationship of symptom domains and diagnostic severity to PET scan imaging in borderline personality disorder. *Psychiatry Res.* 214(2), 161–168 (2013).

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

21 Zanarini MC, Frankenburg FR. A preliminary, randomized trial of psychoeducation for women with borderline personality disorder. *J. Pers. Disord.* 22(3), 284–290 (2008).

22 American Psychiatric Association Practice Guidelines . Practice guidelines for the treatment of patients with borderline personality disorder. American Psychiatric Association. *Am. J. Psychiatry* 158(Suppl. 10), 1–52 (2001).

23 McMain SF, Guimond T, Streiner DL, Cardish RJ, Links PS. Dialectical behavior therapy compared with general psychiatric management for borderline personality disorder: clinical outcomes and functioning over a 2-year follow-up. *Am. J. Psychiatry* 169, 650–661 (2012).

24 Stoffers J, Völlm BA, Rücker G, Timmer A, Huband N, Lieb K. Pharmacological interventions for borderline personality disorder. *Cochrane Database Syst. Rev.* 2010(6), CD005653 (2010).

25 Ingenhoven T. Effectiveness of pharmacotherapy for severe personality disorders: meta-analysis of randomized controlled trials. *J. Clin. Psychiatry* 71(1), 14–25 (2010).

26 National Collaborating Centre for Mental Health. *National Institute for Health and Clinical Excellence (NICE) Borderline Personality Disorder: Treatment and Management. National Clinical Practice Guideline Number 78.* The British Psychological Society and The Royal College of Psychiatrists, Leicester, UK (2009).

27 Australian Government National Health and Medical Research Council. *Clinical Practice Guideline for the Management of Borderline Personality Disorder.* Australian Government National Health and Medical Research Council, Canberra, Australia, 1–166 (2012).

28 Linehan MM, McDavid JD, Brown MZ, Sayrs JH, Gallop RJ. Olanzapine plus dialectical behavior therapy for women with high irritability who meet criteria for borderline personality disorder: a double-blind, placebo-controlled pilot study. *J. Clin. Psychiatry* 69(6), 999–1005 (2008).

29 Soler J, Pascual JC, Campins J *et al.* Doubleblind, placebo-controlled study of dialectical behavior therapy plus olanzapine for borderline personality disorder. *Am. J. Psychiatry* 162(6), 1221–1224 (2005).

30 Cowdry RW, Gardner DL. Pharmacotherapy of borderline personality disorder. Alprazolam, carbamazepine, trifluoperazine, and tranylcypromine. *Arch. Gen. Psychiatry* 45(2), 111–119 (1988).

31 Soloff PH, George A, Nathan RS, Schulz PM, Perel JM. Behavioral dyscontrol in borderline patients treated with amitriptyline. *Psychopharmacol. Bull.* 23(1), 177–181 (1987).

32 Nelson KJ, Schulz SC. Pharmacologic treatment of borderline personality disorder. *Curr. Psychiatry* 10(8), 30–40 (2011).

33 Zanarini MC. Psychotherapy of borderline personality disorder. *Acta Psychiatr. Scand.* 120(5), 373–377 (2009).

34 Linehan MM. Cognitive-Behavioral Treatment of Borderline Personality Disorder. The Guilford Press, NY, USA (1993).

35 Kellogg SH, Young JE. Schema therapy for borderline personality disorder. *J. Clin. Psychol.* 62(4), 445–458 (2006).

36 Fonagy P, Bateman AW. Mechanisms of change in mentalization-based treatment of BPD. *J. Clin. Psychol.* 62(4), 411–430 (2006).

37 Levy KN, Clarkin JF, Yeomans FE, Scott LN, Wasserman RH, Kernberg OF. The mechanisms of change in the treatment of borderline personality disorder with transference focused psychotherapy. *J. Clin. Psychol.* 62(4), 481–501 (2006).

38 Blum N, St John D, Pfohl B *et al.* Systems Training for Emotional Predictability and Problem Solving (STEPPS) for outpatients with borderline personality disorder: a randomized controlled trial and 1-year follow-up. *Am. J. Psychiatry* 165, 468–478 (2008).

39 Stoffers J, Völlm B, Rücker G, Timmer A, Huband N, Lieb K. Psychological therapies for people with borderline personality disorder. *Cochrane Database Syst. Rev.* 8, CD005652 2012.

40 Linehan MM, Dimeff LA, Koerner K, Miga EM. *Research on Dialectical Behavior Therapy: Summary of the Data to Date.* Behavioral Tech, LLC, WA, USA (2013).

41 Krawitz R. Financial cost–effectiveness of dialectical behavior therapy. Miga E, Karlson A, DuBose T (Eds). http://behavioraltech.org/downloads/Financial-Cost-Effectiveness-DBT.pdf

42 Neacsiu AD, Rizvi SL, Vitaliano PP, Lynch TR, Linehan MM. The dialectical behavior therapy ways of coping checklist: development and psychometric properties. *J. Clin. Psychol.* 66(6), 563–582 (2010).

43 Neacsiu AD, Rizvi SL, Linehan MM. Dialectical behavior therapy skills use as a mediator and outcome of treatment for borderline personality disorder. *Behav. Res. Ther.* 48(9), 832–839 (2010).

44 Rizvi SL, Dimeff LA, Skutch J, Carroll D, Linehan MM. A pilot study of the DBT coach: an interactive mobile phone application for individuals with borderline personality disorder and substance use disorder. *Behav. Ther.* 42(4), 589–600 (2011).

45 Harned MS, Korslund KE, Foa EB, Linehan MM. Treating PTSD in suicidal and self-injuring women with borderline personality disorder: development and preliminary evaluation of a Dialectical Behavior Therapy Prolonged Exposure Protocol. *Behav. Res. Ther.* 50(6), 381–386 (2012).

46 Fassbinder E, Rudolf S, Bussiek A *et al.* Effectiveness of dialectical behavior therapy for patients with borderline personality disorder in the long-term course – a 30-month-follow-up after inpatient treatment. *Psychother. Psychosom. Med. Psychol.* 57(3–4),161–169 (2007).

47 Farrell JM, Shaw IA, Webber MA. A schema-focused approach to group psychotherapy for outpatients with borderline personality disorder: a randomized controlled trial. *J. Behav. Ther. Exp. Psychiatry* 40(2), 317–328 (2009).

48 Nadort M, Arntz A, Smit JH *et al.* Implementation of outpatient schema therapy for borderline personality disorder with versus without crisis support by the therapist outside office hours: a randomized trial. *Behav. Res. Ther.* 47(11), 961–973 (2009).

49 Fonagy P, Bateman A. The development of borderline personality disorder – a mentalizing model. *J. Pers. Disord.* 22(1), 4–21 (2008).

50 Fonagy P, Luyten P. A developmental, mentalization-based approach to the understanding and treatment of borderline personality disorder. *Develop. Psychopathol.* 21(4), 1355–1381 (2009).

51 Bateman A, Fonagy P. 8-year follow-up of patients treated for borderline personality disorder: mentalization-based treatment versus treatment as usual. *Am. J. Psychiatry* 165(5), 631–638 (2008).

52 Bateman A, Fonagy P. Randomized controlled trial of outpatient mentalization-based treatment versus structured clinical management for borderline personality disorder. *Am. J. Psychiatry* 166(12), 1355–1364 (2009).

53 Rossouw TI, Fonagy P. Mentalization-based treatment for self-harm in adolescents: a randomized controlled trial. *J. Am. Acad. Child Adolesc. Psychiatry* 51(12), 1304–1313 e1303 (2012).

54 Doering S, Horz S, Rentrop M *et al.* Transference-focused psychotherapy v. treatment by community psychotherapists for borderline personality disorder: randomised controlled trial. *Br. J. Psychiatry* 196(5), 389–395 (2010).

55 Silk KR. Augmenting psychotherapy for borderline personality disorder: the STEPPS program. *Am. J. Psychiatry* 165(4), 413–415 (2008).

56 Widiger T, Weissman MM. Epidemiology of borderline personality disorder. *Hosp. Commun. Psychiatry* 42, 1015–1021 (1991).

57 Sansone RA, Kay J, Anderson JL. Resident didactic education in borderline personality disorder, is it sufficient? *Acad. Psychiatry* 37(4), 287–288 (2013).

58 Sharma B, Dunlop BW, Ninan PT, Bradley R. Use of dialectical behavior therapy in borderline personality disorder: a view from residency. *Acad. Psychiatr.* 31(3), 218–224 (2007).

59 Frederick JT, Comtois KA. Practice of dialectical behavior therapy after psychiatry residency. *Acad. Psychiatr.* 30(1), 63–68 (2006).

60 Occhiogrosso M, Auchincloss EL. The challenge of treating (and supervising) patients with borderline personality disorder in a residents' clinic. *Psychodyn. Psychother. Psychiatry* 40(3), 451–468 (2012).

61 Lajoie T, Sonkiss J, Rich A. Development and clinical outcomes of a dialectical behavior therapy clinic. *Acad. Psychiatry* 35(5), 325–327 (2011).

62 Brodsky BS, Stanley B, Cabaniss DL. Dialectical behavior therapy for psychiatric residency training programs. *Psychiatr. Ann.* 43, 162–168 (2013).

63 Zerbo E, Cohen S, Bielska W, Caligor E. Transference focused psychotherapy in the general psychiatry residency: a useful and applicable model for residents in acute clinical settings. *Psychodyn. Psychiatry* 41(1), 163–181 (2013).

64 Nelson KJ. Managing borderline personality disorder on general psychiatric units. *Psychodyn. Psychiatry* 41, 563–574 (2013).

65 Choi-Kain LW, Zanarini MC, Frankenburg FR *et al.* A longitudinal study of the 10-year course of interpersonal features in borderline personality disorder. *J. Pers. Disord.* 24, 365–376 (2010).