Review

Evaluating treatments of borderline personality disorder

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Practice Points

- Borderline personality disorder (BPD) is a frequently encountered psychiatric illness that requires specialized treatment.
- Proper treatment relies on proper diagnosis, for which there are several specialized instruments but significant changes are expected in the coming years.
- Specialized psychotherapies are the treatment of choice for patients with BPD, although common factors may explain a large proportion of the treatment effects.
- Dialectical behavior therapy is the best studied psychotherapy for BPD, although a number of other therapies have increasing amounts of research to support their efficacy.
- Pharmacotherapy trials for BPD are in their infancy with only one medication receiving a substantial amount of focus. Many of these trials suffer from a variety of significant limitations.
- Medications, if used, should be limited to adjunct treatments for specific symptoms, with patients made fully aware of the risks of side effects and conflicting evidence supporting their use.
- Future options for the treatment of BPD may include a focus on early intervention and integration of psychotherapy.

SUMMARY Borderline personality disorder (BPD) is a complex psychiatric disorder that has a history of being difficult to treat. The past two decades have seen remarkable changes in the field with an increasing number of specialized psychotherapies and medications tested. Many of these studies have limitations that are specific to the treatment of BPD, including complexities regarding diagnosis, comorbidities, choice of outcome measures and choice of comparison treatment. Evaluating these studies, particularly in the context of changing diagnostic systems, is highly important. The future of BPD treatment, which can include earlier diagnosis and intervention, as well as integration of different psychotherapies, rests on a solid understanding of the evidence that exists today.

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Over the past two decades, there has been a proliferation of treatments for borderline personality disorder (BPD). Many of the psychotherapies that have been developed for BPD demonstrate impressive reductions in self-harm, suicide attempts and days hospitalized [1], while many of the pharmacotherapies demonstrate reductions in symptoms such as anger, impulsivity and mood lability [2]. Unfortunately, there are a number of challenges in selecting and accessing the best psychotherapies and the research supporting the use of medications demonstrates significant limitations and conflicting results. Appropriate evaluation of the multitude of treatment options for patients with BPD is necessary, as this disorder is associated with significant distress and dysfunction [3,4].

Epidemiology

Diagnosing BPD is the crucial first step, as it is a serious psychiatric problem that is frequently encountered in all clinical settings. Approximately 6% of patients seen in a family medicine clinic suffer from BPD [5] and they account for up to 10% of psychiatric outpatients [6], and an even higher proportion of psychiatric inpatients [7,8]. The prevalence of BPD in the community is substantially lower at 1–2% [9–11], and although earlier research demonstrated a 2:1 female:male gender ratio [9], more recent studies find no gender differences [10], suggesting that there are a significant number of men with BPD who do not come to clinical attention. The course of patients with BPD is more optimistic than previously believed. Over time, patients with BPD tend to remit from the diagnosis, with 85–93% of patients experiencing remission from the diagnosis for at least a 1- or 2-year period within 10 years of follow-up [4,12]. Relapse rate is relatively low in the two main prospective studies, although psychosocial functioning remains significantly and clinically impaired for many patients, even among those who remitted [12,13]. Suicide rates vary by duration of follow-up and by study, with one study reporting 4% completing suicide after 10 years [4] and another study finding a 10% completed suicide rate by 27 years [14]. Mortality rates due to other causes are also higher than expected [14] and patients who do not remit from BPD have more medical comorbidities and poorer health behaviors [15]. Psychiatric comorbidities, including mood disorders, anxiety disorders, substance use disorders and some other personality disorders, are also very high [16–18] and this plays a significant role in evaluating treatment studies. These findings suggest that, although the more apparent symptoms, such as self-harm and suicidality, might decrease substantially [12,19], there is still progress to be made in devising treatments for patients with BPD.

Diagnosing BPD

The first step in evaluating the treatment of BPD rests on determining how the diagnosis was made. According to Diagnostic and Statistical Manual of Mental Disorders (DSM-IV-TR), the symptoms that patients suffering from BPD experience can be divided into several categories and patients need to meet five out of nine criteria [20]. In brief, patients with BPD experience intense and rapidly fluctuating emotions, termed 'affective instability' [20], which often switch between intense sadness, anger and anxiety with a pattern that is different than in mood disorders [21,22]. Anger and chronic feelings of emptiness, which are related to hopelessness and isolation [23], are the other affective symptoms in BPD and are the slowest symptoms to remit [19]. The affective symptoms contribute to interpersonal problems that lead to chaotic relationships, one of the most sensitive and specific symptoms of BPD [24], a tendency for patients suffering from BPD to view others as all good or all bad [20,25] and fear of abandonment. Patients with BPD often have disturbances in identity and have frequently shifting goals, values and self-image [20]. Impulsivity can manifest as impulsive binge eating, spending, alcohol or drug use, or aggression [26]. Self-harm, such as cutting, is also reported by 84% of patients with BPD at some point in their lives, often as a means of self-soothing or regulating their emotions [27]. Suicidal behaviors, including gestures, threats and attempts, are also a common symptom and major reasons for clinical attention, with 41% of patients who present to the emergency room with a history of multiple suicide attempts meeting the diagnosis of BPD [28]. Finally, nearly half of patients with BPD experience transient psychotic symptoms when highly stressed [29,30].

Diagnosing BPD can be done in a standard clinical interview [31]. According to the DSM-IV-TR, problems must persist for most of a patient's life and typically start in adolescence or early adulthood [20]. The diagnosis can also

be made in those under 18 years of age who have experienced the symptoms consistently for 1 year or longer [20]. In practice, treatment often begins in early adulthood [32], suggesting that the diagnosis is not often made in adolescence and treatment is often unnecessarily delayed. This is likely due to the stigma regarding the diagnosis [33,34]. If clinicians are unsure about the diagnosis, there are semi-structured interviews and self-report measures that can assist in the diagnosis. The Diagnostic Interview for Borderlines – Revised [26] is a semi-structured interview that can be completed within 30 min, is the gold standard and has excellent reliability [35]. A number of self-report measures, such as the McLean Screening Instrument for Borderline Personality Disorder, the Borderline Syndrome Index and the Zanarini Rating Scale for Borderline Personality Disorder (ZAN-BPD), have also been developed to diagnose and assess the severity of BPD [36–39].

■ Diagnostic and Statistical Manual of Mental Disorders, edition 5

The current diagnostic system in psychiatry, the DSM-IV-TR [20], will be revised with a new edition expected for release in 2013. There will be a number of substantial changes in DSM-5 [201], with the current axis II being removed and the personality disorders section receiving a significant restructuring. One of the main goals of the revision is to change the current categorical structure of personality disorders to a hybrid categorical and dimensional model [40], with the idea that a dimensional component better reflects the state of knowledge in personality psychology, as exemplified by the Five Factor Model of personality [41]. Another major goal is to refine the diagnostic categories for personality disorders, as there is a high rate of overlap and the most common personality disorder diagnosis is personality disorder not otherwise specified [42]. The core traits of BPD are well reflected in the new model [201], but the new proposal has generated controversy amongst experts, many of whom believe that the proposed hybrid model will be difficult to use clinically, leading to lower reliability and increasing reluctance to make the diagnosis; both problems that the new system was developed to solve [43,44]. The new system will also create a discontinuity in research for BPD and this is particularly true in the ongoing longitudinal studies or treatment follow-up studies where one consistent diagnostic system has been in use for an extended period of time [45,46].

Treatments for BPD

Treatments of BPD have proliferated over the past 20 years, following the publication of the original paper supporting the use of dialectical behavior therapy (DBT), a specialized psychotherapy that was developed specifically for BPD to target the symptoms of recurrent suicidality and self-harm [47,48]. Treatments can be divided into psychotherapy and pharmacotherapy, as there has been minimal research investigating other treatments, such as electroconvulsive therapy [49]. These two main branches of treatment will be reviewed, along with an overarching therapeutic approach. Key points in evaluating treatments for BPD will be emphasized.

There are several challenges in providing appropriate care for patients with BPD. One of the first challenges can be seen in the diversity in opinion among the different guidelines. The American Psychiatric Association Guidelines for the Treatment of Borderline Personality Disorder [50], which are no longer considered current as they have not been updated in over 5 years, provide complex pharmacotherapeutic algorithms focusing on different symptom clusters of BPD, in addition to psychotherapy. By contrast, the more recent NICE guidelines for BPD state that "drug treatment should not be used specifically for BPD or for the individual symptoms or behavior associated with the disorder" [51]. Finally, the World Federation of Societies of Biological Psychiatry (WFSBP) developed a set of guidelines that specifically cover the pharmacotherapy of BPD. These guidelines suggest that there may be some medications that can help with specific symptoms, but there is no medication that improves BPD psychopathology in general [52]. This diversity of opinions in the guidelines leaves clinicians with more questions than answers when it comes to treating BPD.

■ Psychotherapies for BPD

Dialectical behavior therapy

DBT developed out of cognitive behavior therapy (CBT), but with added components from eastern traditions [48]. The theory behind DBT is that patients develop BPD out of a combination of genetic susceptibility to dysregulation, particularly emotional dysregulation, and an environment, who is invalidating of their experiences. This leads

to a pattern of ineffective interactions between the child, who would react in an intense and often unpredictable manner, and the caregivers that frequently minimize or invalidate the experience of the child, leading to escalation and other dysfunctional coping mechanisms [48]. In practice, DBT is a structured therapy that includes weekly individual therapy sessions and weekly skills training sessions. The focus of the individual sessions is based on the hierarchy of treatment goals in DBT, with life-threatening and self-harm behaviors as the primary focus of treatment. The skills training sessions are organized similar to a classroom setting and involve two therapists teaching skills in four domains: mindfulness (being aware of one's emotions), distress tolerance (tolerating and accepting difficult situations or emotions), emotion regulation (using various therapeutic techniques to modify thoughts and emotions) and interpersonal effectiveness. The techniques used in DBT emphasize the dialectic, or acceptance of seemingly contradictory perspectives, between validation and change.

There is a substantial body of research supporting the use of DBT to treat patients with BPD. The first study demonstrated a number of significant effects, including reductions in self-harm, reduced inpatient treatment and a much higher treatment retention rate [47]. Subsequent studies of DBT have found similar results [53–55], with some studies also demonstrating improvements in other domains, such as social and global functioning [56] or quality of life [54]. DBT was originally designed to last 1 year with a stated aim of reducing suicidality and self-harm. A subsequent treatment phase was proposed to focus on other symptoms [48], but this part of treatment has never been well described or studied. DBT is also the specialized psychotherapy with the most evidence demonstrating effectiveness in patients with BPD comorbid with substance dependence [57]. One recent meta-analysis of DBT demonstrated moderate effect size improvements on suicidal behaviors, self-harm and even global functioning [58].

Several challenges limit wider use of DBT and highlight areas of focus for future studies. Training to become a DBT therapist can take several years. DBT was also designed to be practiced in a team setting, with a strong emphasis placed on weekly team consultation meetings [48]. Taken together, establishing a new DBT team requires several therapists who have dedicated a significant amount of time to receive training that is only available in a few specialized centers. Incorporating components of DBT in nonspecialized clinical practice may be effective, but this has never been demonstrated. At present, there are no studies demonstrating the long-term benefits of DBT compared with treatment as usual. The longest follow-up periods have been 1 year [55,59] and some benefits were maintained, although it is unclear whether these differences continue past 1-year follow-up. This is especially important when one considers that a third of patients with BPD remit from the diagnosis within 2 years, even without any specialized form of treatment [60].

The choice of outcome measures is another limitation of the early DBT trials that should be kept in mind when evaluating other treatment studies for BPD. Many of the early studies focused on frequency of self-harm, suicidal behavior and hospitalizations as the primary outcomes, but it is unclear how other symptoms of BPD may have changed. Some newer studies use continuous measures of BPD severity, such as the ZAN-BPD [39], but there is a paucity of studies that assess global functioning or quality of life. Although hospitalization rates are important for cost–benefit analyses and play a role in quality of life, other outcome measures should be included in future studies of BPD.

Mentalization-based treatment

Where DBT evolved out of CBT roots, mentalization-based treatment (MBT) developed out of psychodynamic theory and practice [61]. According to MBT, BPD arises when the primary caregiver does not appropriately 'mirror' the child's experiences and leaves the child unable to develop a coherent and unified sense of self. This primarily occurs when there are attachment problems in early childhood [62], leading to deficits in the ability to mentalize. Mentalizing is defined as the capacity to appreciate and interpret the mental states, including thoughts, emotions and drives, of oneself and others. The goal of MBT is to help patients to become more skilled at mentalizing.

MBT is conducted in weekly individual and group therapy sessions and treatment typically lasts for 18 months. The research to support MBT is limited to one study in outpatients [63] and one study in patients who attended a psychoanalytically oriented partial hospitalization program that was focused on mentalization

[64]. These studies demonstrate robust treatment effects that lead to reductions in suicidal behaviors, self-harm, hospitalizations and improvements in social and global functioning, and other symptoms [63,64]. Benefits obtained from the partial hospitalization studies were maintained at 18-month [65] and 8-year follow-ups [46].

MBT has become increasingly popular, with a number of books and articles describing applications to other contexts beyond BPD [66,67]. Training is simpler for MBT than some of the other specialized psychotherapies, but still encourages therapists to work as part of a MBT team [68]. This is reflected in one of the main limitations with MBT: both randomized controlled trials (RCTs) were conducted by the developers of the treatment. This problem is common to most of the psychotherapy and pharmacotherapy studies of BPD. Another issue to assess when evaluating these trials is to carefully review what is included in the treatments. The first MBT study [64] included many other components to treatment and, until the publication of their outpatient study [63], it was unclear which component of treatment was effective. Similar care must be taken particularly when evaluating the scant research on inpatient or day program treatments, as they typically include a number of potentially therapeutic components.

Other psychotherapies for BPD

DBT and MBT may be the most popularized psychotherapies for BPD, but there are many other therapies that have RCT evidence of their effectiveness. All of the therapies can be placed on a spectrum with CBT-based treatments at one end and psychodynamic therapies at the other end [25]. Several of the therapies with the most evidence and that characterize the different parts of the spectrum will be briefly evaluated.

Amongst the other CBT-based therapies, the one that has the most research support is systems training for emotional predictability and problem solving (STEPPS). Unlike the other treatments, STEPPS was designed to be an augmentation to existing treatments of any form, including individual psychotherapy, family therapy or pharmacotherapy [69]. STEPPS is conducted in 20 weekly group sessions that are similar to the skills training sessions found in DBT but with less emphasis on the components from eastern traditions. Even in 20 sessions, STEPPS was able to demonstrate significant improvements in a number of measures, including symptoms of BPD and global functioning, but there was no significant change in suicidal behaviors, self-harm or hospitalizations [69]. Similar results were obtained by a second group [70]. These results suggest that shorter treatments may also be effective for BPD.

Schema-focused therapy (SFT) lies at the midpoint between the CBT and psychodynamic ends of the spectrum. According to SFT, patients with BPD have four primary schemas, which are specific patterns of thinking, feeling and acting that can be activated by different situations. The goal of treatment is to change these. Treatment uses four primary techniques to help the patient change their schemas: the 'limited reparenting' relationship involves the development of a secure and appropriate attachment to the therapist that changes dynamically over time and as needed in the therapy; re-evaluation of past experiences by pretending one is interacting with people or situations from their past; psychoeducation and cognitive restructuring; and behavioral pattern breaking [71,72]. SFT was compared with another specialized psychotherapy for BPD, transference-focused psychotherapy (TFP), and both therapies demonstrated significant reductions in BPD symptoms and improvements in functioning after 3 years of treatment, with some measures favoring SFT [72]. The cost–effectiveness of a 3-year treatment is questionable and there are few data to show that such a lengthy treatment is necessary, even though it may be more cost effective than 3 years of TFP [73].

At the psychodynamic end of the spectrum is TFP. This therapy is a twice-weekly individual therapy that emphasizes the relationship between the therapist and the patient. Traditional psychodynamic methods of confrontation and interpretation are used to help patients rebuild a unified sense of themselves and others. TFP was compared with SFT, as previously described [72], and demonstrated significant benefits. TFP was also compared with DBT and supportive therapy in a three-arm trial [74]. Results indicated that all three treatments led to benefits, with some areas of superiority for TFP and some areas of superiority for DBT [74]. Finally, TFP was recently compared with community treatment by experts and TFP again demonstrated superiority [75].

Common factors among psychotherapies

There are at least eight different types of psychotherapy that demonstrate effectiveness for the

treatment of BPD [76]. Most of these therapies have substantially different theoretical models to explain how BPD develops and use diverse therapeutic techniques in session. Despite the differences, there appear to be some common factors to psychotherapy that explain the effectiveness of the comparison psychotherapies and can also explain part of the effect of the specialized psychotherapies. Comparisons between six of the specialized psychotherapies for BPD have elucidated factors specific to these therapies [77]. All therapies establish a clear treatment framework with a clear description of how treatment will proceed. The therapist is almost always very active in the session and shifts focus between many components: attending to the patient's emotions, highlighting the connection between emotional experiences and behaviors, interventions that help the patient understand himself or herself, emphasizing and motivating change, and focusing on the therapeutic relationship [77]. Most of the therapies use multimodal treatments that include group and individual therapy as well as treatment team meetings that provide support for the therapists. Some therapies also have explicit treatment targets, but only some emphasize the importance of attaining and improving functioning in life outside of treatment [77]. Most therapies emphasize the patient's experiences in the present and spend less time focusing on early childhood events, even though these early events may have played a role in the development of the patient's symptoms.

The importance of these common factors may explain why certain comparisons produce less robust effects. When a specialized form of psychotherapy for adolescents with BPD known as cognitive analytic therapy was compared with a manualized good clinical care, there were no differences between treatments [78]. When DBT was compared with a highly structured therapy called general psychiatric management, which attempted to build on common therapeutic factors, there were no significant differences found between DBT and general psychiatric managemen [79]. As previously mentioned, when several of the specialized therapies were compared with each other, differences remained on select measures, but all treatment groups showed marked improvements [72,74]. This has led to some researchers calling for integration of psychotherapies that use the best components from these different therapies [80]. These results suggest that, when evaluating psychotherapy trials, the choice of comparator is highly important. Comparator treatments that build on the common factors of BPD psychotherapy are more likely to be as effective as the psychotherapy under study.

■ Pharmacotherapy for BPD

Antidepressants

There have been relatively few RCTs of antidepressants in BPD and many of the studies that have been conducted suffer from notable methodological limitations. One of the first issues is the question of what the medication is treating. Given the extremely high degree of comorbid depression in patients with BPD [17], it is possible that the antidepressants may actually be treating symptoms of a major depressive disorder (MDD), even though treatments of MDD in patients with BPD are generally less likely to be effective [81]. However, if one excludes patients with MDD from studies, then the samples would not reflect the patients typically seen in clinical practice and may represent a less impaired subgroup. Other frequently encountered exclusion criteria are a history of self-harm or suicidality. As these are both frequent symptoms of BPD [20,27], exclusion of patients with these symptoms severely limits the generalizability of findings.

Of the RCTs that have been done, there is mixed support for the use of selective serotonin reuptake inhibitors. One study demonstrated a reduction in the symptom of rapid mood shifts after 6 weeks of fluvoxamine but no change in impulsivity or aggression [82]. There have been three studies of fluoxetine. Fluoxetine demonstrated a reduction in one of two measures of aggression in a study of mixed personality disorder patients who have a history of aggression [83] and this effect may be partially explained by polymorphisms of the serotonin transporter gene [84]. The second study of fluoxetine demonstrated a reduction in anger [85]. However, the addition of fluoxetine to DBT did not lead to improvements in aggression or any other measures [86]. Among the older antidepressants, the results are similarly mixed or even less impressive [87–90], and these medications pose a significantly higher risk in overdose [91].

Mood stabilizers

Mood stabilizers have been increasingly studied in the treatment of BPD with some positive results, although several factors need to be assessed when

reviewing these studies. One of the primary clinical concerns is the safety of any medication in overdose and this is particularly salient when treating a disorder in which overdoses are common. Mood stabilizers, particularly when compared with selective serotonin reuptake inhibitors, may be toxic in overdose [91] and this may limit their use, although if they have demonstrated effectiveness, patients should also not be deprived of a potentially helpful medication. It remains unclear how helpful mood stabilizers truly are because the studies that have been conducted suffer from very small sample sizes and there is minimal replication of findings. Duration of treatment is also a concern in most pharmacotherapy studies, with treatment lasting 8–12 weeks and few trials continuing to open-label follow-ups. Most patients with BPD receive medications for years [32] and it is unclear whether the effectiveness of these medications remains after 8–12 weeks.

Of the mood stabilizers that have been studied, lamotrigine, topiramate and divalproex have received the most attention. In two small studies, lamotrigine has demonstrated some reductions in affective lability, impulsivity and anger with one study continuing to find benefit at an 18-month follow-up [92–94]. Topiramate is associated with reductions in anger after 8–10 weeks with gains also maintained at the 18-month follow-up [95–99]. Finally, divalproex has conflicting studies, with one demonstrating no changes in anger or depression [100], but a larger study by the same team demonstrating reduction in aggression with divalproex [101].

Antipsychotics

Many antipsychotics have been studied in BPD over the years and these studies highlight two other important points when evaluating treatments for BPD. Historically, completion rates in most studies of BPD have been very low and this is one of the reasons why the high retention rates found in the initial trial of DBT were so impressive [47]. A recent meta-analysis of psychotherapy trials found a treatment completion rate of 75%, although there was substantial variation between studies [102]. No such meta-analysis has been conducted for pharmacotherapy trials, but completion rates vary dramatically, with one large study reporting 65% completion [103], and the smaller studies ranging from 91% completion [104] to 48% completion [105]. Studies of other medications had even lower completion rates [100,106].

Olanzapine has been the most studied medication for BPD. Early and smaller studies indicated improvements in all domains compared with placebo [107], aggression and some affective symptoms when compared with fluoxetine [108], and similar results when combined with DBT [109,110]. More recent studies with over 150 patients in each arm found minimal or no end point differences between olanzapine and placebo after 12 weeks of treatment except that the patients on olanzapine had significantly greater weight gain and other side effects, but patients on olanzapine did improve more quickly [103,111]. Of the other atypical antipsychotics, aripiprazole has demonstrated benefit in several domains [104,112] but ziprasidone demonstrated no difference from placebo [105]. For the typical antipsychotics, haloperidol has received mixed support, with one study finding reductions in several measures [88] and a second study finding no difference from placebo on a number of measures after 5 weeks [113] but worsening symptoms at 16 weeks [90]. Most of these studies demonstrated greater side effects for those taking antipsychotics, which is an important consideration, since specialized psychotherapies are the treatment of choice.

General treatment principles for patients with BPD

Specialized psychotherapy should be the primary form of treatment for patients with BPD. As the number of therapies increases and includes shorter-term treatments, accessibility should improve. In the absence of a specialized psychotherapy, any form of therapy that emphasizes the common treatment factors [77] is likely to be somewhat helpful. The benefits of using a medication must be balanced with the side-effect risks, with no studies looking at the long-term benefits of treatment. Recent meta-analyses have supported the use of mood stabilizers or atypical antipsychotics for treatment of specific symptoms of BPD [2,114–117]. None suggest that medication is a treatment for BPD on its own. Unfortunately, these meta-analyses suffer from the same limitations as the individual medication studies and two further limitations. Since there are so few studies, medications are often combined by class and very few studies are excluded for methodological reasons. This makes interpretation of these meta-analyses difficult. Until further studies are done, medications as the primary form of treatment should be avoided due to side effects and

play, at most, a secondary role in the treatment of specific symptoms of BPD. Some medications, such as benzodiazepines, may even worsen BPD symptoms and should be avoided whenever possible [87]. Combined psychological and pharmacological treatment by specialized teams is generally preferred in a complex disorder such as BPD.

Future perspective

Treatment of BPD has changed dramatically over the past two decades. Despite significant improvements in psychotherapy and promising pharmacotherapeutic options, more questions remain.

Similar to the change that is happening in the field of schizophrenia, BPD researchers are increasingly focusing on early detection and intervention. At present, psychotherapy studies for adolescents with BPD are limited to one study of cognitive analytic therapy, a combination of CBT and psychoanalytic principles, which demonstrated no difference compared with manualized good clinical care, although both groups demonstrated significant improvements [78]. Other models of care for adolescents with BPD have been developed [118,119], including a variation of DBT for adolescents that has not yet been tested [120,121]. Recent research has highlighted similarities between BPD in adolescents and adults [122,123], leading the way for earlier diagnosis and intervention. Hopefully, engaging in treatment at this critical developmental period would improve long-term symptomatic and functional outcomes, as recent research has demonstrated that higher levels of education are associated with better outcomes [122].

The longitudinal course of BPD is increasingly well characterized [4,12,14], but with an aging population, there is remarkably little literature on the course, symptoms and treatment of BPD in the geriatric population. As most patients with BPD resolve before reaching the geriatric age group [4,14], there may be less need to focus on this population, but it is possible that this population presents differently and should be treated differently. Finally, since recent epidemiological surveys have found similar rates of BPD for men and women [10], it remains unclear why so few men enter treatment and this population should also receive more clinical attention as they have so far been excluded from many psychotherapy and pharmacotherapy trials.

Diagnosing all personality disorders, including BPD, will be in a state of flux over the coming years with the advent of DSM-5 and International Classification of Disease, Eleventh Revision (ICD-11) [124,201]. Several other models are competing for attention [41,125,126] and it remains unclear how clinicians and researchers will adapt to the new diagnostic system and integrate it with previous research. As there are no definitive biochemical, neuroanatomical or neuropsychological markers specific enough to help diagnose BPD, identification continues to rely on clinical assessment. This highlights the usefulness of other standardized instruments to assess BPD, such as the Diagnostic Interview for Borderlines – Revised [26,35], which have been used for many years. Research to clarify some of the less specific symptoms of BPD, such as feelings of emptiness and identity disturbance, may also lead to better diagnosis in the future.

Another promising area of research is psychotherapy integration. The numerous specialized psychotherapies for BPD demonstrate a 'dodo bird' effect where almost all therapies are effective and essentially equivalent. Attempts to deconstruct the different therapies to identify key components have been limited [55,127,128], although identification of common factors and using this knowledge to develop integrated models of therapy may lead to promising results in the future [77,80,129]. An integrated therapy may have the advantages of being more effective, maximizing the cost–benefit, potentially consolidating and facilitating training, and leading to improved access. Comorbidities in patients with BPD are also very common, particularly alcohol and substance abuse [16,17], and few studies attempt to develop integrated treatments. DBT [57,130] has some evidence in substance-abusing populations and another therapy called dynamic deconstructive psychotherapy has some evidence in alcohol-abusing patients with BPD [131]. An integrated treatment should provide a model, not just for the treatment of BPD, but also for the most important comorbidities. Long-term psychosocial functioning is generally impaired in patients with BPD [13] and adding in evidence-based vocational or social rehabilitation may be another option to explore. Integrated therapy may be the important next step in the treatment of patients with BPD, although further research is needed to identify the key components of the existing treatments. Once these dismantling studies have been conducted and the 'active ingredients' have been identified, an integrated treatment can be developed.

However, it is also possible that this may lead to further proliferation of approaches, each with less evidence than before and lacking the potentially important structure provided by the current specialized psychotherapies. If an integrated therapy is developed, it will need to be subjected to the same study as all the current treatments require, but there is potential for improved treatment for patients with BPD.

Further research on pharmacotherapy for BPD is also essential. Other than for olanzapine, most medications have only had one or two small studies, often with notable methodological limitations. In general, many of the pharmacotherapy trials are limited by small sample sizes and, when larger samples are studied, the effects seen in smaller studies diminish or disappear altogether [103,107,111]. In contrast to psychotherapy trials that include patients with multiple comorbidities and suicidal behaviors, pharmacotherapy trials generally have strict exclusion criteria, which lead to samples that are very different from what is seen in practice. Many pharmacotherapy trials also measure outcomes as changes in depressive, anxious or general psychiatric symptoms. Using a standardized instrument to measure symptom severity in BPD, such as the ZAN-BPD [39], can help measure change in BPD symptoms and focusing on global functioning or quality of life may be even more important. Pharmacotherapy studies are between 8 and 12 weeks duration, in contrast to psychotherapy trials that generally extend for longer periods of time, often with follow-up after 1 year, and this follow-up period is necessary to help identify medications that work over longer periods of time. Finally, few medications have been studied by different groups and without pharmaceutical funding support; replication of findings is essential and this is an equally important issue for specialized psychotherapies for BPD. Future pharmacotherapy studies should have larger samples, less stringent exclusion criteria, more useful outcome measures, longer durations of treatment and follow-up, and be replicated by different groups in order to be more relevant to everyday clinical practice. Several medications may show promise as adjuncts for symptomatic improvements, but higher quality trials are needed.

Conclusion

BPD is a serious mental illness that has been the subject of increasing research. New treatments have been developed and continue to be studied. For a variety of reasons, many of the studies that have been done have suffered from several methodological limitations, including small sample sizes, overly stringent exclusion criteria, poor choice of outcome measures, low completion rates, a lack of replication and others. Specialized psychotherapy is the treatment of choice, with a more limited role for medications. As research on the treatment of BPD continues, it becomes increasingly important to highlight some of the unique factors that go into designing and evaluating research on BPD. The outlook for patients with BPD is remarkably better now than it was 20 years ago and hopefully the next 20 years will bring even more advances.

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- ▪ of interest
- ▪▪ of considerable interest

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